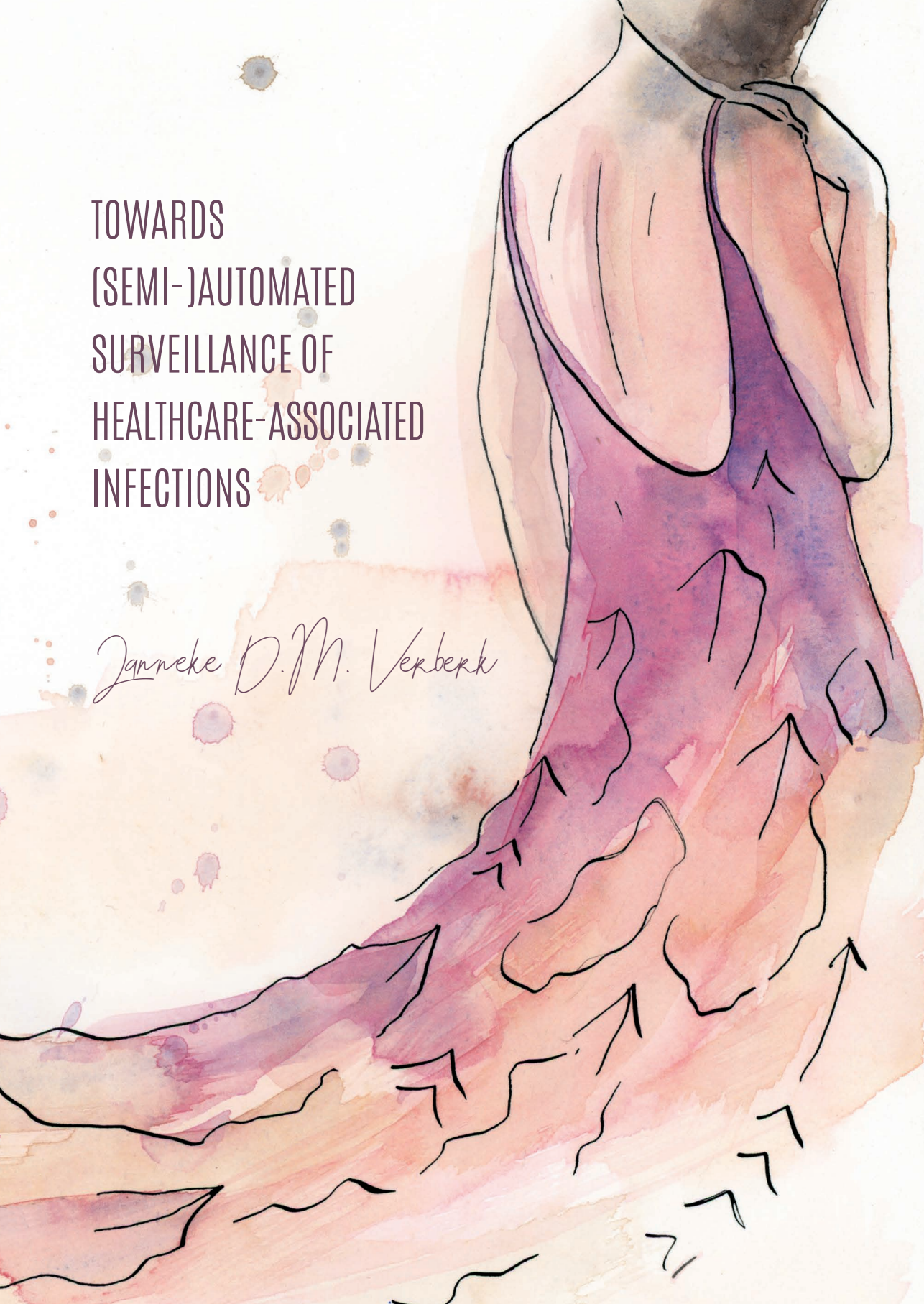
TOWARDS (SEMI-)AUTOMATED SURVEILLANCE OF HEALTHCARE-ASSOCIATED INFECTIONS

Janneke D.M. Verberk



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Towards (semi-)automated surveillance of healthcare-associated infections

Op weg naar (semi-)geautomatiseerde surveillance van zorginfecties
(met een samenvatting in het Nederlands)

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Janneke D.M. Verberk

INTRODUCTION

Healthcare-associated infections

Healthcare-associated infections (HAIs) are infections that patients can acquire during their stay in a healthcare facility, such as hospitals or nursing homes, and which were not present or incubating at the time of admission. HAIs can develop at each body site or organ system, but are often associated with devices used in care, such as catheter-related bloodstream infections (CRBSIs), catheter-related urinary tract infections, ventilator-associated pneumonia, or related to operative procedures such as surgical site infections (SSIs).[1]

The burden of HAIs differs throughout the world: the prevalence is higher in low- to middle income countries compared to high-income countries.[2] As reported by the European Centre for Disease Prevention and Control (ECDC), on a daily basis 3.5% – 10.5% patients acquire a HAI in Europe, resulting in approximately 4 million patients with a HAI and 37,000 deaths each year.[3] Thereby, higher rates are reported for intensive care units and high risk populations.[4-6] In the Unites States (US), each year around 4.5% (1.7 million) patients are affected resulting in an economic burden of 6.5 billion US dollar.[7,8] In the Netherlands, in 2020 around 7.1% of the admitted patients developed a HAI with SSI, lower respiratory tract infections and bloodstream infections most prevalent.[9] Although sometimes HAIs can be treated easily, in the majority of patients HAIs lead to prolonged hospital stays, increased use of antimicrobial agents, increased morbidity, excess deaths and high burden and costs for health systems, patients and their family.[1,2,10-14] Especially if the HAI is caused by an antimicrobial-resistant microorganism, treatment can be difficult or even impossible with detrimental consequences for the patient.[15]

Surveillance of healthcare-associated infections

Several studies, in particular the ground-breaking US SENIC project (Study on the Efficacy of Nosocomial Infection Control) published in 1985, demonstrated that surveillance plays an important role in HAI prevention and control.[16-19] The Centers for Disease Control and Prevention of the US defines surveillance as 'the ongoing, systematic collection, analysis, and interpretation of health-related data essential to planning, implementation, and evaluation of public health practice'.[20] By performing surveillance, the data collected are reported back to clinicians and stakeholders and will provide insight in trends. Actions and interventions can be undertaken in response to increased infection rates in order to improve patient safety.[21]

Although monitoring infections may seem like an easy task, in practice it is complex because the surveillance requires standardised case definitions, alignments in diagnostic methods,

clear inclusion rules for the population under surveillance (the denominator), and expertise within the hospital to conduct the surveillance and to interpret the surveillance results. In addition to these factors, correction for case-mix is required for meaningful interpretation of results within and between centres. Several surveillance networks have been established to provide guidelines and surveillance protocols to obtain reliable and comparable results. For example, in the Netherlands the nosocomial surveillance network PREZIES was established in 1996, Germany started the KISS network in 1997 followed by the French RAISIN in 1998; all coordinated by national public health institutes.[22-25] Most national networks also participate in the European Network HAI-Net, which is coordinated by the ECDC.[26,27]

As HAIs are considered preventable, national and local healthcare inspectorates, hospital boards or insurance companies use HAI rates obtained by surveillance for benchmarking, public reporting, and to evaluate quality.[28,29] In a number of countries the growing demand for transparency and accountability by media, accreditation organisations and legislative bodies has resulted in mandatory participation in surveillance networks and public disclosure of HAI rates.[29] In countries such as the US, the surveillance results are used in pay-for-performance programmes with financial penalties based on HAI occurence.[21,28,30,31]

In most hospitals, surveillance is performed manually by an infection control practitioner (ICP) according to the national surveillance protocol and guidelines. Each (electronic) record of each individual patient is retrospectively screened for inclusion rules, and whether the case definition applies. Although this traditional way of performing surveillance is seen as the reference standard, it is considered labour-intensive, prone to subjectivity, and poor interrater reliability has been reported.[32-37] Furthermore, it seems that ICPs with increasing experience enhances case finding, and that within the first years of surveillance activity sensitivity may be impaired.[38] Therefore, the traditional surveillance is often seen as 'the-more-you-look-the-more-you-find' principle and the reliability and comparability of surveillance data are therefore disputed.[34,39,40]

Automation is considered as the possible solution to overcome the drawbacks of the traditional way of performing surveillance as it will decrease variability and subjectivity across institutions and reduces workload.[41] The move towards automation is supported by the availability and developments of electronic medical record systems, which evolved in the 1980's from paper files to electronic medical records in which patient encounters and follow-up notes were recorded. The current state of electronic health records (EHR) differs from the standard electronic medical record from the 1980's as it contains a broader view of the patient (e.g. including clinical data, administrative data and diagnostic test results), integrates data from ancillary systems, and therefore provides multiple opportunities for sharing, linking,

online access and research.[42-45] The improvements in information technology infrastructures and the increased use of HAI metrics as a quality indicator have led to an increased demand for more standardisation by automated surveillance systems to – partially or completely – replace human work.

Automated surveillance

Over the past years, several automated surveillance (AS) systems have been developed targeting different types of HAIs. Surveillance of HAIs can be automated to varying degrees, but in general there are two methods: semi-automated and fully automated surveillance (**Figure 1.1**). In semi-automated surveillance, an algorithm classifies patients in low- or high probability for a certain HAI. The high-probability records need manual assessment to confirm or reject the HAI, the

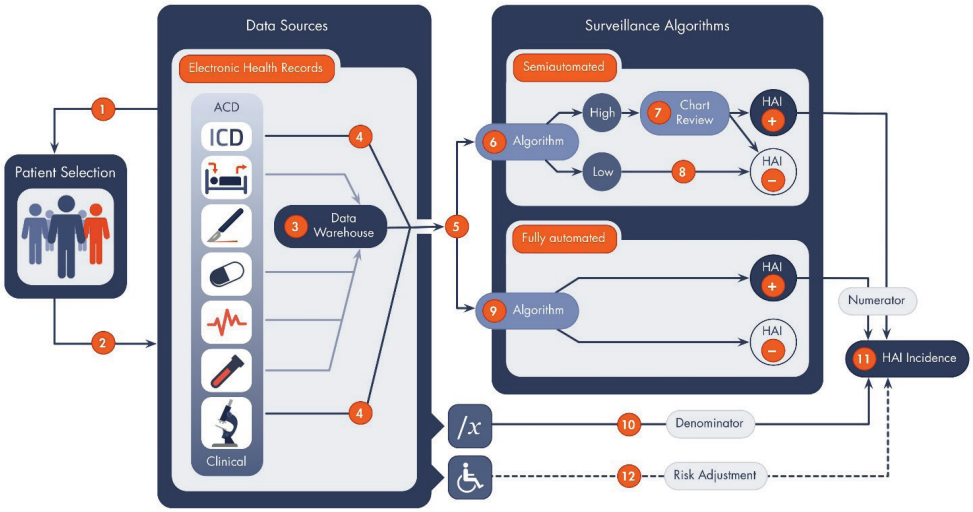

Figure 1.1. Overview of semi-automated and fully automated surveillance of healthcare-associated infections. Patients are included in surveillance based on administrative records (e.g. admission records or procedure codes) (1). For these patients, the required administrative and/or clinical data are extracted from EHRs (2). Some data may be obtained through data warehouses (3), whereas other data may need to be extracted directly from unlinked EHRs (4). Some data sources require cleaning or pre-processing before they can be incorporated in an algorithm (5). In the case of semi-automated surveillance, the algorithm classifies patients as having a low or high HAI probability (6). Medical charts of high-probability patients are manually evaluated by an infection control practitioner to assess HAI status (7), whereas low-probability patients are assumed not to have developed an HAI (8). In the case of fully automated surveillance, the algorithm classifies patients according to their HAI presence or absence without manual confirmation (9). Finally, denominator data (number or time at risk) are obtained (10), either manually or electronically, and combined with the numerator (HAI cases) to determine the HAI incidence (11). For unbiased interpretation of the incidence, determination of risk adjustment variables (e.g. surgical wound class, American Society of Anaesthesiologists score, prior surgery) is indispensable, and should ideally be collected electronically as well (12).
Abbreviations: EHRs = electronic health records; HAI = healthcare-associated infection.
Figure and legend from Sips et al. 2017.[49]

low-probability records are assumed free of HAI. By applying this method there is still a manual confirmatory step, however, this allows for nuanced clinical interpretation of the patient's condition and thus acceptance in the field.[21,46,47] In fully automated surveillance, the algorithm classifies patients in having an HAI or not without any human interference. This is even more standardised and time saving compared to semi-automated surveillance, however requires highly standardised, complete data sources and adapted, objectified case definitions.[21,48-50] Subsequently, the construct that is targeted by the AS may differ from the conventional case definition and may therefore not be favoured by clinicians.[46,51] Results of both AS methods are promising, not only in terms of time saving, but also because of high sensitivity (70% to 100%).[52,53] Studies reported even superiority of AS compared to manual surveillance as more HAIs were detected by the algorithms.[54-58]

In both semi- and fully automated surveillance, input source data is required. Algorithms may combine multiple routine care data to optimise case finding, such as administrative data, demographics, clinical chemistry, microbiology-, pharmacy-, or radiology information, or narrative clinical information.[49,52] Data types are either in structured format (e.g. admission dates, medications or microbiology results) or unstructured free-text narratives (e.g. clinical progress notes, radiology reports or discharge summaries).[43,59,60] Most of these sources are stored in the EHR or brought together and linked with information from other medical information systems within a so called digital data warehouse or clinical data repository. Some studies used administrative codes only, such as International Classification of Diseases (ICD)-10, however this was considered inaccurate.[61-64] Generally, algorithms deploying multiple different data sources lead to better case finding.[54,65,66]

The selection and use of data sources or indicators for algorithm development is first dependent on data availability, and subsequently on expert (clinical) knowledge, statistical methods, machine learning, artificial intelligence or fuzzy logic techniques.[67-75] In case of unstructured data, techniques such as text mining or natural language processing are required.[59,76,77] The majority of algorithms are classification algorithms to determine the HAI state, or rule-based algorithms that represent infection criteria from the case definition.[78-85] The complexity between methods varies, but in general, the more understandable for clinicians and IPC staff the better acceptance and chances for implementation in the field.[48]

Despite the developments in EHRs and international publications of several (successful) surveillance algorithms, surveillance is still performed manually in many settings and algorithms are rarely used in daily practice. This is mainly because the majority of AS systems that have been described are developed in a research setting, applied to one dataset to perform the investigation, and limited to a single – often academic – centre.[86] Crucial information needed for implementation is often not reported, such as selection of the study population (denominator)

or maintenance activities of the system. Two systematic reviews by Cato et al.[86] and Streefkerk et al.[53] report the lack of validation of data completeness, validation of the denominator, or having a separate cohort to validate the algorithm performance, reducing the reliability and reproducibility of these AS methods. Moreover, a review of de Bruin et al.[54] reported that only 8 (25%) AS systems included in their review were used in clinical routine. Hence, knowledge about generalisability and feasibility of AS methods for large-scale implementation is lacking and there is minimal experience in how to use and organise AS in daily routines.

THESIS AIM AND OUTLINE

The aim of this thesis is to evaluate current traditional surveillance methods and to explore the feasibility and generalisability of AS methods in different hospitals.

In the first part of this thesis, the value and usefulness of surveillance data is demonstrated by two studies: **Chapter 2** presents the effect of antibiotic-impregnated external ventricular drains as opposed to plain silicone drains on the occurrence of ventriculostomy-related infections, and in **Chapter 3** the change in HAI rates in Dutch hospitals during the SARS-CoV-2 pandemic is investigated.

In the second part of this thesis the current traditional surveillance activities in the Netherlands are evaluated. In **Chapter 4** we explored experiences of ICPs and medical professionals regarding the CRBSI surveillance and CRBSI definition, and their suggestions for improvements. Subsequently, in **Chapter 5** the quality of the traditional SSI surveillance (the reference standard) in colorectal surgery patients is reported in terms of reliability and validity. Because the development, validation and implementation of AS systems takes time, efforts are made in **Chapter 6** to investigate whether small changes can be taken in short time to reduce the workload in the current traditional surveillance: we investigated the importance of three risk factors for SSI, to advice whether they should be preserved in the surveillance protocol.

The last part of this thesis focuses on the generalisability and feasibility of (semi-)automated surveillance. In **Chapter 7** the current methods and state of AS in Europe are described, together with key aspects of implementation and three examples of successful AS systems. In **Chapter 8** & **Chapter 9,** algorithms for semi-automated surveillance of SSI after respectively orthopaedic and colorectal surgeries are validated in multiple centres to investigate their potential for large-scale implementation. In **Chapter 10** we explored whether the performance of the algorithm as described in Chapter 9 could be improved by incorporating unstructured (free-text) clinical notes.

The last chapter of this thesis, **Chapter 11**, provides general discussion on (automated) surveillance of HAI, including future considerations.

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PART I

Examples of using surveillance data in practice

2

Preventing ventriculostomy-related infections with antibiotic-impregnated drains in hospitals – A two centre Dutch study

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ABSTRACT

This observational cohort study assessed the effect of the introduction of antibiotic-impregnated external ventricular drains (AI-EVDs) as opposed to plain silicone EVDs on the occurrence of ventriculostomy-related infections (VRIs) in two Dutch hospitals, without other changes to their clinical practice. VRI was defined by Centers for Disease Control and Prevention (CDC) criteria and a culture-based definition. A propensity score-adjusted competing risks survival analysis showed that introduction of AI-EVDs did not significantly decrease the risk of VRI in routine care nor affect its bacterial aetiology, also after adjustment for confounding and competing events.

INTRODUCTION

External ventricular drains (EVDs) are frequently used in neurosurgical patients to monitor intracranial pressure and drain cerebrospinal fluid (CSF).[1] Although placement of a catheter is a successful strategy to manage secondary hydrocephalus, the development of meningitis or ventriculitis is not uncommon, with incidences up to 22% being reported.[2] These ventriculostomy-related infections (VRIs) are often caused by coagulase-negative *Staphylococci* (CoNS), *Staphylococcus aureus* or Gram-positive cocci such as *Enterococcus faecalis*.[2-4] Antibiotic-impregnated EVDs (AI-EVDs) have been developed to prevent VRIs; they consist of a silicone matrix impregnated with antimicrobials to prevent drain colonisation by Gram-positive bacteria.

Several trials have been conducted to date, but these have not unequivocally demonstrated a consistent benefit of AI-EVDs in routine care settings. This study aimed to compare the occurrence and bacterial aetiology of VRIs in neurosurgical patients treated with antibiotic-impregnated EVDs versus plain EVDs in Dutch hospitals.

METHODS

Study design and participants

This study is a post-hoc analysis of a previous investigation on surveillance methods for VRI.[4] Patients from two Dutch hospitals receiving an EVD were included from January 2012 to December 2013 in hospital A, and from April 2012 to April 2013 in hospital B. All adult patients (≥ 18 years) who received an EVD were eligible for inclusion. Exclusion criteria were death, discharge or transfer to another hospital within 24 hours of drain placement, first drain placed elsewhere or pre-existing meningitis.

We compared the incidence of VRI in patients receiving an antibiotic-impregnated EVD, impregnated with 0.15% clindamycin and 0.054% rifampin (Bactiseal, Codman, Johnson & Johnson, Raynham, MA, USA) to those receiving a standard silicone drain. Hospital A converted to AI-EVDs in October 2012. In hospital B, patients admitted between April and September 2012 received either a standard silicone drain or AI-EVD, as decided by the treating physician, and starting September 1st 2012 almost all patients received AI-EVDs. All EVDs were placed under perioperative antibiotic prophylaxis and drain management practices did not change during the study. For each patient, demographic characteristics, clinical, therapeutic and microbiological information was collected from the patients' medical record. Approval and a waiver of informed consent were obtained from the Institutional Review Board of the University Medical Centre Utrecht.

Outcomes

The primary endpoint of this study was the occurrence of VRIs. This was defined according to modified criteria from the Centers for Disease Control and Prevention (CDC) for healthcare-associated meningitis as described previously.[4] In addition, a culture-based definition was applied, defining infection as the occurrence of a single positive CSF culture irrespective of the microorganism isolated. For both definitions, infection must have developed when the drain was *in situ* or within seven days after drain removal.[4] Moreover, the distribution of causative microorganisms was assessed along with their antimicrobial resistance profiles.

Statistical analyses

To evaluate the effect of AI-EVDs on the occurrence of infection, a propensity score-adjusted competing risks analysis was performed considering mortality as the competing event. The latter accounts for possible bias introduced by non-informative censoring. We used propensity scores (PS) to adjust for confounding factors. PS were estimated by regressing treatment status (AI-EVD versus plain EVD) on age, sex, American Society of Anesthesiologists (ASA) classification, Acute Physiology and Chronic Health Evaluation (APACHE) score, indication for drain placement, prior neurosurgery in the last 30 days and emergency of drain placement; all were selected based on literature and clinical judgment.[5] To assess PS balance, patients' characteristics were compared across PS tertiles. All analyses were conducted at the patient level.

Proportional hazard assumptions were checked by examining Schoenfeld residuals and cumulative incidence plots. To account for missing data, multiple imputation (five sets) was applied with pooling using Rubin's rule.[6] Analyses were performed using SPSS 20.0 for Windows (SPSS Inc. Chicago IL) and R version 2.15.0 (cmprsk and function CumIncidence, http://www.r-project.org). A probability value of $p \leq 0.05$ was considered statistically significant.

RESULTS

During the study period, 215 patients received one or more EVDs of whom 181 patients receiving 248 drains satisfied the inclusion criteria: 65 (35.9%) received a plain EVD and 116 (64.1%) an AI-EVD. The most common indications for drain placement were hydrocephalus after intracerebral haemorrhage, CSF leakage, tumour, trauma, or as per-operative prophylaxis (**Table 2.1**). The majority received a single EVD during their admission (82.9%), when excluding drains placed after the development of VRIs.

Table 2.1. Overview of patient characteristics and outcomes.

Characteristics (n (%)) unless specified)	Plain EVD (n = 65)	AI-EVD (n = 116)
Age (mean (SD))	55.9 (16.3)	62.5 (11.7)
Male gender	27 (41.5)	46 (39.7)
APACHE IV score (median (IQR))[a]	75.5 (51 – 88)	70.5 (48 – 94)
ASA classification[b]		
I	5 (7.7)	14 (12.1)
II	9 (13.8)	24 (20.7)
III	11 (16.9)	26 (22.4)
IV	6 (9.2)	17 (14.7)
V	4 (6.2)	2 (1.7)
Indication for first drain		
Hydrocephalus after intracerebral haemorrhage	56 (86.2)	85 (73.3)
CSF leakage	-	1 (0.9)
Tumour or per-operative	5 (7.7)	18 (15.5)
Trauma	1 (1.5)	2 (1.7)
Other	3 (4.6)	10 (8.6)
Drain placed on day of hospital admission	41 (63.1)	68 (58.6)
Admitted to ICU first day of drainage	48 (73.8)	88 (75.9)
Emergency placement of first drain	49 (75.4)	98 (84.5)
Duration of surgery first drain in minutes (median (IQR))	31 (21 – 114)	33 (20 – 61)
Prior neurosurgery in last 30 days	10 (15.4)	22 (19)
Number of drains placed [c]		
1	54 (83.1)	96 (82.8)
2	10 (15.4)	16 (13.8)
≥ 3	1 (1.5)	4 (3.4)
Outcomes		
Infection by CDC definition	10 (15.4)	17 (14.7)
Infection by CB definition	9 (13.8)	18 (15.5)
Censored as death under CDC definition	17 (26.2)	42 (36.2)
Censored as death under CB definition	17 (26.2)	39 (33.6)
Total drain duration (days, median, IQR)	8 (5 – 13.5)	9 (5 – 14)

[a] Missing (n (%)): AI-EVD 16 (13.8), plain EVD 9 (13.8).
[b] Missing (n (%)): AI-EVD 33 (28.4), plain EVD 30 (46.2).
[c] Number of drains placed prior to development of VRI.
Abbreviations: AI-EVD = antibiotic-impregnated external ventricular drain; n = number; SD = standard deviation; CSF = cerebrospinal fluid; APACHE = Acute Physiology and Chronic Health Evaluation; IQR = interquartile range; ASA = American Society of Anesthesiologists; ICU = intensive care unit; CDC = Centers for Disease Control and Prevention; CB = culture-based.

In patients receiving an AI-EVD, 17 patients developed a VRI (14.7%), compared to 10 (15.4%) receiving a plain EVD (p = 0.89). For the culture-based definition this was 18 (15.5%) and 9 (13.8%) respectively (p = 0.76). Cumulative incidence curves are shown in **Figure 2.1**. In competing risks analysis the adjusted subdistribution hazard ratio was 0.91 (95% confidence interval (CI) 0.18 to 1.52) for patients with an AI-EVD compared to patients with a plain EVD. Based on the culture-based definition this subdistribution hazard ratio was 1.04. (95%

CI 0.48 to 2.25). Sensitivity analysis stratified by hospital revealed that AI-EVDs had opposite effect in the individual centres, despite almost equal infection rates in the plain EVD groups of both hospitals (**Supplemental Table S2.1**).

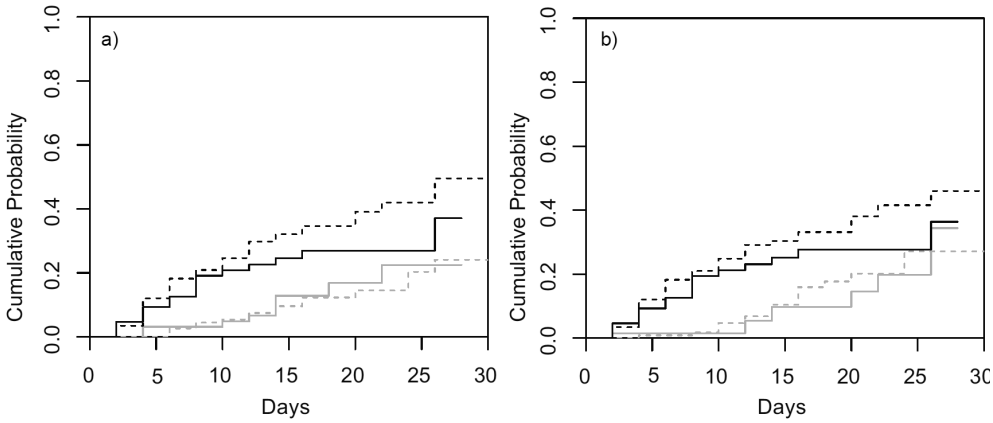

Figure 2.1. Cumulative incidence plots representing the risk on ventriculostomy-related infections (VRIs) and death over time. (A) Cumulative incidence curves for infection or death according to the definition of the Centers for Disease Control and Prevention. Solid grey line, plain EVD (VRI); broken grey line, AI-EVD (VRI); solid black line, plain EVD (deceased); broken black line, AI-EVD (deceased). (B) Incidence curves for the culture-based (CB) definition. Solid grey line, plain EVD (CB); broken grey line, AI-EVD (CB); solid black line, plain EVD (deceased); broken black line, AI-EVD (deceased).

Under the CDC definition, most cases were caused by CoNS (47.1% in AI-EVD; 40.0% plain EVD group), and in approximately one third of cases no microorganism was identified (35.3% and 30.0% respectively). In AI-EVD patients, the remaining VRIs were attributed to *Enterococcus faecalis* (n = 1), *Streptococcus sanguis* (n = 1) or *Serratia marcescens* (n = 1), while in plain EVD patients *Enterococcus faecium* (n = 1), *Staphylococcus aureus* (n = 1), or *Pseudomonas aeruginosa* (n = 1) were the other causative pathogens. Resistance to rifampicin and clindamycin was found in six cases (35.3%) in the AI-EVD group and one case in the plain EVD group (10.0%). The distribution of microorganisms and resistance profiles was almost similar under the culture-based definition (**Supplemental Table S2.2**, **Supplemental Figure S2.1**). Resistance to rifampin/clindamycin was more common in hospital B.

DISCUSSION AND CONCLUSION

Antibiotic-impregnated EVDs are increasingly being adopted as prevention against VRIs, although their efficacy in routine clinical care has not been fully demonstrated. This study could not demonstrate a statistically significant benefit of AI-EVDs versus plain EVDs on the incidence of infection, both under the VRI definition and when considering all positive CSF

cultures. In addition, there was no change in the distribution of causative microorganisms and the majority of infections was caused by CoNS; bacteria that are targeted by the antibiotics incorporated in AI-EVDs. Although resistance occurred in some CoNS, some VRI cases were caused by microorganisms with proven susceptibility to the antimicrobials used. Therefore, considering the high costs of AI-EVDs, the potential emergence of antibiotic-resistant strains and given their uncertain incremental benefit, we recommend careful evaluation of the large-scale adoption of AI-EVD use in Dutch hospitals.

Introduction of AI-EVDs had opposite effects in the individual hospitals despite comparable rates of VRI in the plain EVD groups. This may in part be explained by differences between hospitals regarding drain handling protocols. Hospital B had a daily CSF sampling protocol as opposed to sampling on clinical indication only in hospital A, hence increasing the risk of pathogens being introduced by frequent drain manipulation and the likelihood of identifying contaminant microorganisms in CSF. Although this sampling frequency did not change during the study period, the potential protective effect of AI-EVDs may have been obviated by the frequency of manipulation. The opposite effects of AI-EVDs may indicate that hospital-related factors or drain maintenance procedures contribute more to the risk of infection than the type of drain as such. Second, after introduction of AI-EVDs microorganisms resistant to rifampin/clindamycin became more common in hospital B than in hospital A, despite low baseline resistance levels in both hospitals. This increased resistance level may explain the failure of AI-EVDs in hospital B.

Our findings regarding AI-EVD efficacy mirror contradicting results from randomised controlled trials.[3,7,8] In addition, the generalisability of prior trials was somewhat limited as patients received both prophylactic and maintenance antibiotics (the duration of which was often unspecified) and patients with multiple subsequent catheters were not included, while this is a frequent situation in critically ill neurosurgical patients.[3,7,9] Moreover, in one trial the diagnosis was based on culture results only.[3] In the current study there were discrepancies in infections identified when only considering positive CSF cultures or also taking clinical signs into account. Approximately 30% of patients had a culture-negative VRI, indicating the importance of including clinical symptoms as endpoints instead of relying on a positive CSF culture alone. Conversely, a culture-based definition hampers distinguishing contaminants from true infection.

This study differs from previous studies in assessing specifically the impact of AI-EVDs on clinically relevant infections and culture-based infections in a routine care setting. The transition to AI-EVDs was not part of any other intervention or prevention programme. This is the first study performing time-to-event survival analysis, whilst accounting for the

occurrence of competing events. The main limitation of the present study was its observational nature, and although we have used propensity scores to address confounding, some residual confounding may remain. In addition, the modest sample size may have limited the likelihood of finding statistically significant results. The differences in drain handling practices between both hospitals complicate interpretation, but also illustrate the potential value of AI-EVDs in the context of other preventive measures.

In conclusion, in this study the introduction of AI-EVDs in routine clinical practice did not decrease the risk of VRI and did not change the bacterial aetiology, as compared to standard EVDs.

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CONFLICT OF INTEREST STATEMENT

Janneke Verberk, Jan Willem Berkelbach van der Sprenkel, Mark Arts, Paul Dennesen, Marc Bonten and Maaike van Mourik declare that they have no conflict of interests.

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SUPPLEMENTARY MATERIAL

Supplemental Table S2.1. Subdistribution hazard ratios stratified by hospital.

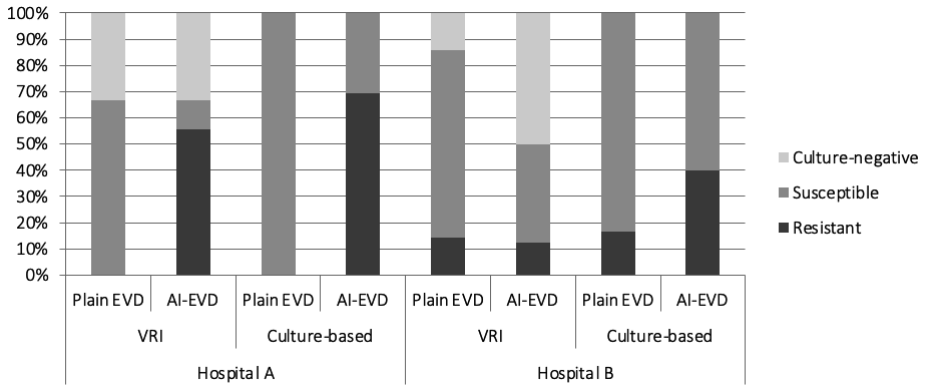
SHR (95% CI)	Hospital A	Hospital B
VRI definition		
Crude	0.61 (0.22 – 1.64)	1.15 (0.33 – 3.98)
Adjusted	0.53 (0.18 – 1.52)	1.56 (0.38 – 6.50)
Culture-based definition		
Crude	0.46 (0.14 – 1.49)	1.99 (0.58 – 6.80)
Adjusted	0.32 (0.09 – 1.16)	2.37 (0.62 – 8.99)

Abbreviations: SHR = subdistribution hazard ratio; 95% CI = 95% confidence interval; VRI = ventriculostomy-related infection.

Supplemental Table S2.2. Resistance percentages stratified by hospital.

	Resistance in plain EVD group (%)	Resistance in AI-EVD group (%)
VRI definition		
Hospital A	14.3	12.5
Hospital B	0	55.6
Culture-based definition		
Hospital A	16.7	40.0
Hospital B	0	38.5

Resistance was defined as resistance to both antimicrobials (if tested), or if one was not tested, proven resistance to the other antimicrobial.
Abbreviations: VRI = ventriculostomy-related infection; EVD = external ventricular drain.



Supplemental Figure S2.1. Percentage resistance of causative organisms under both definitions stratified by hospital.
Resistance was defined as resistance to both antimicrobials (if tested), or if one was not tested, proven resistance to the other antimicrobial.
Abbreviations: AI-EVD = antibiotic-impregnated external ventricular drain; EVD = external ventricular drain; VRI = ventriculostomy-related infection definition; culture-based = culture-based definition.

Healthcare-associated infections in Dutch hospitals during the COVID-19 pandemic

3

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ABSTRACT

Introduction: During the COVID-19 pandemic hospitals reorganised their resources and delivery of care, which may have affected the number of healthcare-associated infections (HAIs). We aimed to quantify changes in trends in the number of HAIs in Dutch hospitals during the COVID-19 pandemic.

Methods: National surveillance data from 2016 – 2020 on the incidence of surgical site infections (SSIs) and catheter-related bloodstream infections (CRBSIs), and prevalence of HAIs measured by point prevalence surveys (PPS) were used to compare rates between the pre-pandemic (2016 – February 2020) and pandemic (March 2020 – December 2020) period.

Results: No differences in SSI rates were observed during the pandemic, except for a decrease after colorectal surgeries (6.3%; 95% CI 6.0 – 6.6%) pre-pandemic versus 4.4% (95% CI 3.9 – 5.0%) pandemic). The observed CRBSI incidence in the pandemic period (4.0/1,000 CVC days; 95% CI 3.2 – 4.9) was significantly higher than predicted based on pre-pandemic trends (1.4/1,000; 95% CI 1.0 – 2.1), and was increased in both COVID-19 patients and non-COVID-19 patients at the intensive care unit (ICU). The total HAI prevalence among hospitalised patients was higher during the pandemic period (7.4%) compared to pre-pandemic period (6.4%), mainly because of an increase in ventilator-associated pneumonia (VAP), gastro-intestinal infections (GIs) and central nervous system (CNS) infections.

Conclusion: Rates of CRBSIs, VAPs, GIs and CNS infections among hospitalised patients increased during the first year of the pandemic. Higher CRBSI rates were observed in both COVID-19 and non-COVID-19 ICU population. The full scope and influencing factors of the pandemic on HAIs needs to be studied in further detail.

INTRODUCTION

When the World Health Organisation on March 11, 2020 officially declared the coronavirus disease 2019 (COVID-19) a global pandemic,[1] COVID-19 hospitalisations in the Netherlands were already increasing rapidly. The high influx of patients impacted the critical care capacity, work processes, and availability and use of protective equipment in hospitals.[2-5] To handle the pressure and high demand of care during this crisis, hospitals reorganised their resources and delivery of care.[6] For example, elective surgeries were postponed or cancelled, intensive care unit (ICU) bed capacity was scaled up, the ratio of healthcare workers allocated to patients was reduced, external staff was hired, and changes to daily care routines, such as the frequency of patient washing, was reduced.[7-9]

During this pandemic situation, attention to infection prevention and control (IPC) measures may have been deprived given the high work pressure, or redirected towards the prevention of SARS-CoV-2 transmission.[10] In addition, patients hospitalised with COVID-19 are known for having comorbidities, long hospital stays and complex care with multiple invasive devices, putting them at higher risk for healthcare-associated infections (HAIs).[11] Hence, an increase of HAIs could be expected and is also reported by previous studies.[12,13] On the other hand, hospitals applied strict, aggressive IPC measures to prevent within-hospital transmission of SARS-CoV-2. As a result, a positive (indirect) effect on HAI occurrence can be expected as well and has been reported by others.[14-16]

Given these contrasting findings, there is need for adequate HAI reporting not limited to COVID-19 cohorts only, with sufficient historical data to allow pre-pandemic comparisons. The aim of this study was to quantify trends in the number of HAIs in Dutch hospitals during the COVID-19 pandemic, using national surveillance data that continued collection during the pandemic. Second, HAI types were compared between COVID-19 patients versus non-COVID-19 patients.

METHODS

Study design and data sources

In this retrospective cohort study, data were derived from the Dutch national nosocomial surveillance network (PREZIES). In short, acute care hospitals voluntarily participate in one or more of the three surveillance modules targeting different HAIs: 1) surgical site infection (SSI) incidence surveillance on targeted procedures (see **Supplemental Table S3.1** for an overview of the procedures); 2) hospital-wide catheter-related bloodstream infection (CRBSI)

incidence surveillance in patients with a central venous catheter (CVC) in place for ≥ 48 hours; and 3) bi-annually point prevalence surveys (PPS) performed in March and October in which the prevalence of all type of HAIs are measured in all admitted patients (excluding patients admitted to psychiatry and day-care units). For each module, infection control practitioners in each hospital manually review medical records retrospectively according to the national surveillance protocols and annotate which patients meet infection case definitions. The surveillance protocols and case definitions are based on the (European) Centres for Disease Control and Prevention and are described elsewhere.[17-19] Only in the CRBSI and PPS modules information was collected about whether the patient was admitted to the hospital due to COVID-19 (positive test at admission). Hospitals that reported their surveillance data yearly to PREZIES over the years 2016 – 2020 were included in this study and used to evaluate the infection rates during the pre-pandemic and pandemic period.

Definition pre-pandemic and pandemic period

Based on COVID-19 hospitalisation rates in the Netherlands, the SSI and CRBSI data were divided in pre-pandemic (January 2016 to February 2020) and pandemic (from 1st of March 2020 to December 2020). The PPS surveys of 2016 – 2019 were defined as pre-pandemic and the surveys of March and October 2020 were defined as the pandemic period.

Statistical analyses

Per module, patient-, CVC-, or surgery-related characteristics were reported and compared between the pre-pandemic and pandemic period, using a chi-square test for categorical variables and Mann-Whitney U test for continuous variables. Thereafter, we quantified the number of HAIs during the pandemic. For the SSI and CRBSI incidence, we estimated the expected infection rates for the pandemic period based on pre-pandemic data and compared this with the actual observed rates in the pandemic period. To estimate the expected incidence rate for SSI, the National Nosocomial Infections Surveillance System (NNIS) risk index in pre-pandemic data was used to predict the risk of SSI for each NNIS category for the pandemic period (**Supplemental Figure S3.1**). The NNIS risk index, ranging from 0 to 3, is composed of 1 point for each of the following criteria: wound class classified as contaminated or infected; American Society of Anesthesiologists (ASA) score of 3, 4, or 5; and an operation duration above the 75th percentile.[20] The predicted infection rate was compared with te observed infection rate using a chi-square test. In addition, two sensitivity analyses for SSI were performed. First, the same analyses were repeated for deep SSI only, with the rationale that superficial SSIs may have been missed during follow-up in the pandemic period: patients

avoided contact with healthcare providers afraid of becoming infected with SARS-CoV-2, patients did not want to be a burden on the system, and follow-up appointments were replaced by remote care because of stay-at-home orders.[9] Second, trends in SSI incidence rates were checked per surgical specialty. In case an increasing or decreasing trend was detected pre-pandemic, the expected SSI rate was recalculated based on 2019 data only.

To estimate the expected CRBSI incidence per 1,000 CVC days in the pandemic period, the mean pre-pandemic incidence per 1,000 CVC days for each of the three application-based categories (total parenteral nutrition (TPN); dialysis; and the remaining other applications) was multiplied with the pandemic number of CVCs in each category (**Supplemental Figure S3.1**). The predicted and observed incidence rates were compared using a mid-p exact test.

For PPS data, the difference in observed HAI rates between the pre-pandemic and pandemic period was tested using chi-square 2-tailed test with Yates' correction.

Last, differences in patient characteristics, medical device use, and HAIs were investigated in COVID-19 patients versus non-COVID-19 patients based on CRBSI and PPS data, by using a chi-square test or Mann-Whitney test. A p-value of < 0.05 was considered statistically significant and analyses were performed using SAS version 9.4 software (SAS Institute, Cary, NC).

RESULTS

Table 3.1 shows the number of hospitals participating in the three different modules, per year. The number of hospitals reporting PPS data during the pandemic year 2020 was less than half compared with previous years. Subsequent analyses were performed for the SSI, CRBSI and PPS module, using data from 51, 11 and 10 hospitals respectively that reported their yearly surveillance data in 2016 – 2020 to PREZIES (**Table 3.1**). In these hospitals, the absolute annual number of surgeries (for SSI) and admissions (for PPS) was lower in 2020 compared to previous years, while there was a slight increase in the number of inserted CVCs (CRBSI module).

Table 3.1. Overview of hospitals included in this study.

	Number of hospitals reporting data to PREZIES	Number of hospitals included in this study reporting data each year in 2016 – 2020 (general/ teaching/academic)	Number of surgeries, CVCs and patients included, respectively
SSI module		**51 (33/16/2)**	
2016	84	NA	48,760
2017	81	NA	50,487
2018	75	NA	51,816
2019	68	NA	56,286
2020	66	NA	45,656
CRBSI module		**11 (8/3/0)**	
2016	31	NA	2,454
2017	28	NA	2,030
2018	26	NA	1,735
2019	21	NA	2,019
2020	18	NA	2,286
PPS module		**10 (6/1/3)**	
2016	40	NA	4,036
2017	37	NA	3,956
2018	27	NA	3,841
2019	30	NA	4,273
2020	11	NA	3,124

Abbreviations: SSI = surgical site infection; NA = not applicable; CRBSI = catheter-related bloodstream infection; PPS = point prevalence survey, CVCs = central venous catheters.

Healthcare-associated infections during the first pandemic year

Surgical site infections

Within the SSI module, 217,212 surgeries were included in the pre-pandemic period versus 35,793 surgeries during the pandemic. Compared to the pre-pandemic period, patients operated during the pandemic period were more often of the male gender, had slightly higher ASA- and NNIS scores and had shorter hospital stays (**Table 3.2**). The observed SSI incidence for all type of surgeries combined in the pandemic period was significantly lower than predicted (1.8% versus 2.1%, respectively) (**Figure 3.1** and **Table 3.3**). When stratified by surgery type, only the SSI incidence after colon surgery was significantly lower during the pandemic ($p < 0.01$; **Table 3**). During 2016 – 2019, already a decreasing trend in SSI incidence after colorectal surgeries was observed (7.2%; 7.2%; 6.3%; 5.0%, respectively), while the proportion of closed procedures increased ($p < 0.01$; **Supplemental Figure S3.2**). When calculating the expected SSI incidence after colorectal surgery based on 2019 data only,

the SSI rate in de pandemic was as predicted (predicted SSI rate = 5.1%; 95% CI 4.5 – 5.8; observed SSI rate = 4.4%; 95% CI 3.9 – 5.0; p = 0.1). Sensitivity analysis comparing observed and expected incidence of deep SSI only showed similar results (**Supplemental Table S3.2**).

Table 3.2. Patient-, surgery-, and central venous catheter characteristics.

	Pre-pandemic (n (%))	Pandemic (n (%))	p-value
SSI module	217,212 surgeries	35,793 surgeries	
Age in years (median (IQR))	67.7 (57.5 – 74.7)	67.3 (56.4 – 74.5)	<0.01
Sex (male (n (%)))	67.137 (31.6)	11.193 (34.0)	<0.01
Body mass index (median (IQR))	27.3 (24.4 – 30.8)	27.2 (24.3 – 30.7)	<0.01
Length of stay in days (median (IQR))	2 (0 – 274)	1 (0 – 95)	<0.01
Duration of surgery in minutes (median (IQR))	62 (47 – 80)	59 (44 – 76)	<0.01
ASA classification (n (%))			<0.01
1	38,062 (17.5)	5,083 (14.2)	
2	130,422 (60.0)	21,954 (61.3)	
3	38,025 (17.5)	7,223 (20.2)	
4	1,138 (0.5)	217 (0.6)	
5	58 (0.0)	4 (0.0)	
Unknown/NA	9,507 (4.4)	1,312 (3.6)	
NNIS index (n (%))			<0.01
0	139,092 (64.0)	21,199 (59.2)	
1	59,217 (27.3)	11,009 (30.8)	
2	8,891 (4.1)	2,186 (6.1)	
3	248 (0.1)	66 (0.2)	
Unknown/NA	9,764 (4.5)	1,333 (3.7)	
Type of surgery (n (%))			<0.01
Cardiothoracic surgery	5,596 (2.6)	948 (2.6)	
Mamma surgery	24,556 (11.3)	4,080 (11.4)	
Colon surgery	26,832 (12.4)	4,770 (13.3)	
Orthopaedic surgery	140,821 (64.8)	22,353 (62.5)	
Obstetrics	15,465 (7.1)	2,896 (8.1)	
Neurosurgery	3,942 (1.8)	746 (2.1)	
CRBSI module	8,595 patients (10,546 CVCs)	1,929 patients (2,614 CVCs)	
Age in years (median (IQR))	69.5 (60.3 – 76.5)	68.6 (59.1 – 74.5)	<0.01
Sex (male (n (%)))	5,044 (58.7)	1,259 (65.3)	<0.01
Number of CVCs per patient (median (IQR))	1.2 (1 – 1)	1.3 (1 – 1)	<0.01
CVC days (median (IQR))	5 (3 – 8)	6 (4 – 9)	<0.01
ICU (n (%))			<0.01
Yes	6,574 (76.5)	1,591 (82.5)	
No	2,021 (23.5)	338 (17.5)	
CVC use (n (%))*			
Total parenteral nutrition	1,889 (17.9)	428 (16.4)	0.06
Antibiotics	5,037 (47.8)	1,624 (62.1)	<0.01
Dialysis	1,191 (11.3)	312 (11.9)	0.36
Hemodynamic monitoring	5,466 (51.8)	1,500 (57.4)	<0.01
Other	1,861 (17.6)	304 (11.6)	<0.01

Table 3.2. (Continued)

	Pre-pandemic (n (%))	Pandemic (n (%))	p-value
PPS module	16,106 patients	3,124 patients	
Age group (n (%))			<0.01
< 1 year	1,191 (7.3)	272 (8.7)	
1-19 year	804 (5.0)	163 (5.2)	
20-29 year	708 (4.4)	126 (4.0)	
30-39 year	1,032 (6.4)	194 (6.2)	
40-49 year	1,080 (6.7)	211 (6.8)	
50-59 year	1,951 (12.1)	405 (13.0)	
60-69 year	2,972 (18.5)	556 (18.1)	
70-79 year	3,430 (21.3)	705 (22.6)	
80-89 year	2,412 (15.0)	406 (13.0)	
≥ 90 year	526 (3.3)	76 (2.4)	
Sex (male (n (%)))	8,060 (50.0)	1,625 (52.0)	0.04
Specialism (n (%))			<0.01
Cardiology	1,654 (10.3)	304 (9.7)	
Surgery	2,284 (14.2)	434 (13.9)	
Internal medicine	1,908 (11.8)	332 (10.6)	
Paediatrics	1,140 (7.1)	216 (6.9)	
Respiratory medicine	1,285 (8.0)	235 (7.6)	
Other	7,835 (48.6)	1,603 (51.3)	
McCabe (n (%))			<0.01
Non-fatal (> 5 year)	11,615 (72.1)	2,141 (68.5)	
Ultimately fatal (1-5 year)	1,394 (8.7)	311 (10.0)	
Rapidly fatal (< 1 year)	308 (1.9)	69 (2.2)	
Unknown	2,789 (17.3)	603 (19.3)	
ICU (n (%))			<0.01
Yes	1,170 (7.3)	281 (9.0)	
No	14,936 (92.7)	2,843 (91.0)	
Medical devices (n (%))**			
Urethral catheter	3,374 (20.9)	711 (22.8)	0.02
Peripheral catheter	9,011 (56.0)	1,767 (56.6)	0.5
Mechanical ventilation	482 (3.0)	128 (4.2)	<0.01
Central venous catheter	1,572 (9.8)	458 (14.7)	<0.01
Antibiotics (n (%))			<0.01
Yes	6,065 (37.7)	1,330 (42.6)	
No	10,041 (62.3)	1,794 (57.4)	

* Patients can have a CVC for multiple applications. Percentages are calculated as the proportion of CVCs for a specific use out of all CVCs.
** Patients can have multiple devices at the same time. Percentages are calculated as the proportion of patients with a specific device out of the total number of patients.
Abbreviations: n = number; SSI = surgical site infection; IQR = interquartile range; NA = not applicable; NNIS = National Nosocomial Infections Surveillance System; CRBSI = catheter-related bloodstream infection; CVC = central venous catheter; ICU = intensive care unit; PPS = point prevalence survey.

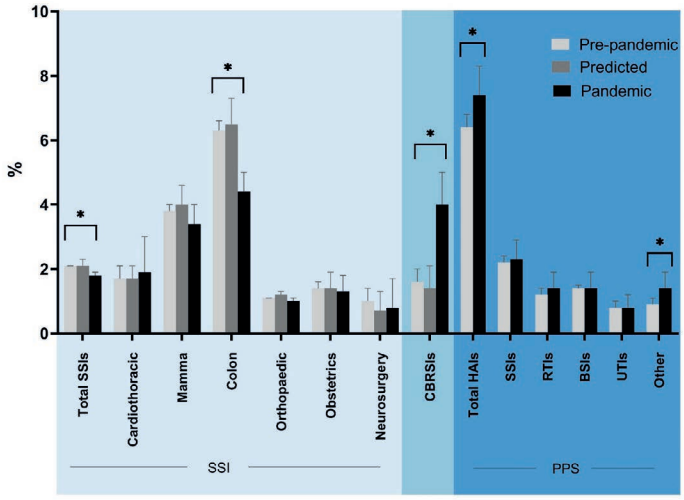

Figure 3.1. Infection rates pre-pandemic, and predicted and observed infection rates during the pandemic period.
Abbreviations: SSIs = surgical site infections; CRBSIs = catheter-related bloodstream infections; HAIs = healthcare-associated infections; PPS = point prevalence survey; RTIs = respiratory tract infections; BSIs = bloodstream infections; UTIs = urinary tract infections.

Table 3.3. Infection rates pre-pandemic, predicted infection rates during pandemic, and observed infection rates during the pandemic.

	Pre-pandemic (% (95% CI))	**Predicted** (% (95% CI))	**Pandemic** (% (95% CI))
SSI incidence			
Total	**2.1 (2.0 – 2.1)**	**2.1 (2.0 – 2.3)**	**1.8 (1.6 – 1.9)***
Cardiothoracic surgery	1.7 (1.4 – 2.1)	1.7 (1.4 – 2.1)	1.9 (1.2 – 3.0)
Mamma surgery	3.8 (3.6 – 4.0)	4.0 (3.4 – 4.6)	3.4 (2.9 – 4.0)
Colon surgery	**6.3 (6.0 – 6.6)**	**6.5 (5.9 – 7.3)**	**4.4 (3.9 – 5.0)***
Orthopaedic surgery	1.1 (1.0 – 1.1)	1.2 (1.0 – 1.3)	1.0 (0.9 – 1.1)
Obstetrics	1.4 (1.2 – 1.6)	1.4 (1.0 – 1.9)	1.3 (1.0 – 1.8)
Neurosurgery	1.0 (0.7 – 1.4)	0.7 (0.4 – 1.3)	0.8 (0.4 – 1.7)
CRBSI incidence			
	1.6 (1.3 – 2.0)	**1.4 (1.0 – 2.1)**	**4.0 (3.2 – 5.0)***
HAI prevalence			
Total	**6.4 (6.0 – 6.8)**	NA	**7.4 (6.5 – 8.3)***
SSIs	2.2 (1.9 – 2.4)	NA	2.3 (1.9 – 2.9)
RTIs	1.2 (1.1 – 1.4)	NA	1.4 (1.1 – 1.9)
BSIs (primary & secondary)	1.3 (1.1 – 1.5)	NA	1.4 (1.1 – 1.9)
UTIs	0.8 (0.7 – 1.0)	NA	0.8 (0.5 – 1.2)
Other	**0.9 (0.8 – 1.1)**	NA	**1.4 (1.1 – 1.9)***

* Statistically significant different from predicted rates.
Abbreviations: 95% CI = 95% confidence interval; SSI = surgical site infection; CRBSI = catheter-related bloodstream infection; HAI = healthcare-associated infection; RTIs = respiratory tract infections; BSIs = bloodstream infections; UTIs = urinary tract infections; NA = not applicable.

Catheter-related bloodstream infections

During the pandemic period, patients with a CVC were slightly younger, more often of the male gender and more often admitted to the ICU compared to the pre-pandemic period. During the pandemic period, the number of inserted CVCs per patient was slightly higher and the CVC duration was longer. CVCs were more frequently used for antibiotics and hemodynamic monitoring and less often for TPN (**Table 3.2**). The observed CRBSI incidence of 4.0/1,000 CVC days (95% CI 3.2 – 4.9/1,000) in the pandemic period was significantly higher than the predicted rate of 1.4/1,000 CVC days (95% CI 1.0 – 2.1/1,000; $p < 0.01$) (**Figure 3.1**).

Point prevalence survey results

In the PPS, during the pandemic period, a higher proportion of hospitalised patients was male, patients had slightly higher McCabe scores and more ICU admissions were observed (**Table 3.2**). The proportion of patients having a medical device increased during the pandemic period, in particular the use of CVCs. The proportion of patients with antibiotic treatment at the time of the survey was slightly higher during the pandemic (42.6%) versus pre-pandemic (37.7%; $p < 0.01$). The total HAI prevalence was higher during the pandemic period compared to pre-pandemic period, mainly because of an increase in gastro-intestinal infections and infections of the central nervous system (**Table 3.3** and **Supplemental Table S3.3**). The proportion of patients with lower respiratory tract infections (LRTIs) in the pandemic period was similar compared to pre-pandemic, however, a larger proportion was associated with mechanical ventilation (ventilator-associated pneumonia (VAP); 22.5% pandemic versus 13.5% pre-pandemic; **Supplemental Table S3.3**).

Healthcare-associated infections within COVID-19 patients

A total of 9 out of 11 hospitals participating in the CRBSI module reported whether the patient was admitted to the hospital due to COVID-19. These COVID-19 patients were more often male, were slightly younger in age, and had significant longer ICU length of stay compared to non-COVID-19 patients with a CVC during the pandemic period. In addition, COVID-19 patients had more CVCs inserted and with a longer duration (**Supplemental Table S3.4**). The CVC was more often used for antibiotics and less for TPN compared to non-COVID-19 patients. The CRBSI incidence was 8.1/1,000 CVC days (95% CI 5.9 – 10.8) in COVID-19 patients compared to 3.4/1,000 (95% CI 2.2 – 5.0) in patients without COVID-19 ($p < 0.01$). When stratifying the COVID-19 patients to ICU and non-ICU, CRBSI rates were 7.8/1,000 CVC days (95% CI 5.6 – 10.7) and 11.1 (95% CI 5.0 – 24.7) respectively. When stratifying the non-COVID-19 patients to ICU and non-ICU, CRBSI rates were 4.8/1,000 CVC days (95% CI 3.0 – 7.6) and 1.7 (95% CI 0.7 – 4.0) respectively. The CRBSI incidence for non-COVID-19

patients in the ICU was significantly higher compared to pre-pandemic years (0.7/1,000; 95% CI 0.5 – 1.1) as well.

Within the PPS module, COVID-19 status was only registered during the survey in October 2020: 50 (6.6%) patients were SARS-CoV-2 positive during admission and were compared with 713 (93.4%) non-COVID-19 patients. COVID-19 patients were more often admitted to the ICU and had more often medical devices. A significantly higher HAI prevalence was observed in this patient group as compared to non-COVID-19 patients (12% versus 0.4% respectively; $p < 0.01$), with bloodstream infections (BSI) as the most predominant manifestation (**Supplemental Table S3.5**).

DISCUSSION

During the first pandemic year CRBSIs, VAPs, gastro-intestinal- and central nervous system infections occurred more frequently among hospitalised patients, while SSIs and catheter-associated urinary tract infection (CAUTI) rates remained stable. HAIs occurred more often in COVID-19 patients, however, in non-COVID-19 patients admitted to the ICU an increase of CRBSI was observed during the pandemic as well.

Regarding SSI, less surgeries were performed in 2020 and the patients that have been operated had slightly higher ASA and NNIS scores compared to previous years, possibly explained by prioritising urgent procedures during the pandemic period. Although this patient population may be more likely to develop SSIs, no increase in incidence was observed. Remarkable is the relative high number of laparoscopic colon surgeries during the pandemic, which may be induced by policies to relieve ICU capacity and the shift to minimally invasive surgery to protect operating room personnel from SARS-CoV-2 aerosol transmission.[21] Future data will show whether open surgery had been replaced during the pandemic by closed surgery, or whether the open surgeries were postponed.

The findings of this study are in line with previous research: several studies reported increases during the pandemic in among others CRBSIs, BSIs, and VAPs.[12,13,22-25] The PPS data showed that the prevalence of LRTIs did not change, however the proportion of LRTIs associated with ventilation increased, likely due to the increased use of mechanical ventilation.[26] Importantly, the work pressure, burden and influx of COVID-19 patients was not constant throughout 2020: COVID-19 surges varied during the year, by region and by hospital.[27] Especially for the PPS, the timing of the surveys (March and October) may not have paralleled the COVID-19 surges and circumstances and therefore may have underestimated potential effects: we did not find any increase in CRBSIs or CAUTIs in the PPS data while this was reported by others.[23,24]

Within the CRBSI module, the number of CRBSI events was too low to perform sub-analyses to evaluate stronger effects on incidence rates during COVID-19 surges.

Most studies published so far are of variable quality as they are limited to retrospective cohort studies. Moreover, they focus solely on COVID-19 patients, and lack standardised case definitions without differentiating between settings or specialties.[28] The current surveillance-based study has a retrospective design as well, however, by using standardised case definitions and large sample sizes from a fixed number of hospitals for several years, the results of our study may be more robust. Still, with our study design, we cannot fully explain (causal) reasons for the change in HAIs observed during the pandemic. Several hypotheses are possible, probably all contributing to some degree. In part, the increase in HAIs can be explained by the fact that hospitalisations were dominated by COVID-19 patients who may have been more vulnerable for HAIs and other co-infections due to immune dysregulation.[29-32] In Germany, there was no ICU overcrowding due to COVID-19 patients because of their high ICU bed capacity as compared with the Netherlands, and no increase in device-associated infections was observed in this country.[33] In addition, COVID-19 patients in general are more exposed to known risk factors for HAIs such as longer durations of mechanical ventilation, higher number of CVCs inserted, corticosteroid treatment, prone positioning, and longer lengths of stay.[24] Although not observed within this study, the composition of characteristics of remaining non-COVID-19 hospitalised patients is likely to be different than pre-pandemic, due to numerous elective procedures that were cancelled and postponed. Unfortunately, within the surveillance modules we only have limited patient- and clinical information, restricting the adjustment for case-mix. Although we used data of a fixed set of hospitals and used the NNIS score and CVC applications to calculate the expected infection rates, we may not have completely addressed the shift in characteristics of the patient population during the pandemic. The increased CRBSI incidence in non-COVID-19 ICU patients may indicate that both a change in patient mix or the reorganisation of care, such as changed IPC practices, modified use of personal protective equipment, and additional (unskilled ICU) temporary staff, may have contributed to the increased infection risk.[5,16,34,35] To fully explain HAI dynamics in pandemic circumstances indicators describing the local healthcare context at institutional level are needed, such as patient characteristics, disruption of IPC practices, prescribing- and (microbiological) order practices, and antimicrobial resistance patterns.[36]

Summarised, we observed an increase in rates of CRBSI, VAP, gastro-intestinal- and central nervous system infections among hospitalised patients during the first pandemic year. Furthermore, CRBSI incidence was also increased in the non-COVID-19 ICU population during the pandemic. The full scope and driving factors of this change in HAIs need to be

studied in more detail to be able to anticipate – from an infection prevention perspective – more adequately on future epidemics of COVID-19 or other severe acute respiratory infections.

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SUPPLEMENTARY MATERIAL

A

$$\textbf{\textit{Expected infection percentage}} = \frac{((\boldsymbol{A} * \boldsymbol{Na}) + (\boldsymbol{B} * \boldsymbol{Nb}) + (\boldsymbol{C} * \boldsymbol{Nc}) + (\boldsymbol{D} * \boldsymbol{Nd}) + (\boldsymbol{E} * \boldsymbol{Ne}))}{(\boldsymbol{Na} + \boldsymbol{Nb} + \boldsymbol{Nc} + \boldsymbol{Nd} + \boldsymbol{Ne})}$$

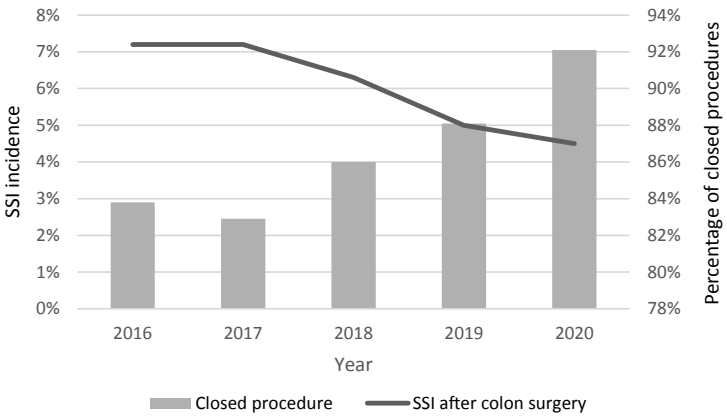
> A = National infection rate in 2016 – Feb2020 in NNIS category 0
> B = National infection rate in 2016 – Feb2020 in NNIS category 1
> C = National infection rate in 2016 – Feb2020 in NNIS category 2
> D = National infection rate in 2016 – Feb2020 in NNIS category 3
> E = National infection rate in 2016 – Feb2020 in NNIS category 'unknown'
> Na = number of surgeries with NNIS category 0 in pandemic period
> Nb = number of surgeries with NNIS category 1 in pandemic period
> Nc = number of surgeries with NNIS category 2 in pandemic period
> Nd = number of surgeries with NNIS category 3 in pandemic period
> Ne = number of surgeries with NNIS category 'unknown' in pandemic period

B

$$\textbf{\textit{Expected infection percentage}} = \frac{((\boldsymbol{A} * \boldsymbol{Na}) + (\boldsymbol{B} * \boldsymbol{Nb}) + (\boldsymbol{C} * \boldsymbol{Nc}))}{(\boldsymbol{Na} + \boldsymbol{Nb} + \boldsymbol{Nc})}$$

> A = National infection rate in 2016 – Feb2020 in group of CVC for total parenteral nutrition (TPN) use
> B = National infection rate in 2016 – Feb2020 in group of CVC for dialysis use
> C = National infection rate in 2016 – Feb2020 of remaining categories (no TPN or dialysis)
> Na = number of CVCs for TPN use in pandemic period
> Nb = number of CVCs for dialysis in pandemic period
> Nc = number of CVCs of remaining categories (no TPN or dialysis) in pandemic period

Supplemental Figure S3.1. Calculations expected surgical site infection rate (A) and catheter-related bloodstream infections per 1,000 catheter days (B).
Abbreviations: NNIS = National Nosocomial Infections Surveillance System risk index; CVC = central venous catheter; TPN = total parenteral nutrition.



Supplemental Figure S3.2. Trends in total surgical site infection (SSI) rate after colorectal surgery and open versus closed procedures.

Supplemental Table S3.1. Procedures under surveillance for surgical site infections.

Type of surgery	Procedure
Cardiothoracic surgery	Coronary artery bypass, Aortic valve surgery, Implantable cardioverter defibrillator or pacemaker implantation
Mamma surgery	Mastectomy, Breast lumpectomy
Colon surgery	Colorectal resections, Cholecystectomy
Orthopaedic surgery	Arthroplasty of hip, Arthroplasty of knee
Obstetrics	Caesarean section
Neurosurgery	Laminectomy Exploration or decompression of spinal cord through excision or incision into vertebral structures

Supplemental Table S3.2. Infection rates pre-pandemic, expected infection rates during pandemic, and observed infection rates during the pandemic for deep surgical site infections only.

	Pre-pandemic (% (95% CI))	**Predicted** (% (95% CI))	**Pandemic** (% (95% CI))
Deep SSI incidence			
Overall	1.0 (1.0 – 1.1)	1.0 (0.9 – 1.1)	0.9 (0.8 – 1.0)
Cardiothoracic surgery	0.9 (0.7 – 1.2)	0.9 (0.7 – 1.2)	1.1 (0.6 – 1.9)
Mamma surgery	0.4 (0.4 – 0.5)	0.5 (0.3 – 0.8)	0.9 (0.6 – 1.2)
Colon surgery	**2.7 (2.5 – 2.9)**	**2.9 (2.4 – 3.4)**	**1.8 (1.5 – 2.3)***
Orthopaedic surgery	0.9 (0.8 – 0.9)	1.0 (0.8 – 1.1)	0.8 (0.7 – 0.9)
Obstetrics	0.2 (0.2 – 0.3)	0.2 (0.1 – 0.5)	0.2 (0.1 – 0.4)
Neurosurgery	0.1 (0.0 – 0.3)	0.1 (0.0 – 0.4)	0.1 (0.0 – 0.8)

Abbreviations: 95% CI = 95% confidence interval; SSI = surgical site infection.

Supplemental Table S3.3. Distribution of healthcare-associated infections in pre-pandemic and pandemic PPS cohort.

(n (%))	**Pre-pandemic** n = 16,106	**Pandemic** n = 3,124
HAI (total)	1,028 (6.4)	230 (7.4)
SSIs	347 (33.8)	73 (31.7)
RTIs *Of which lower RTIs* *Associated with mechanical ventilation (VAP)*	202 (19.7) *177 (87.6)* *24 (13.5)*	45 (19.6) *40 (88.9)* *9 (22.5)*
BSIs *Of which catheter-related*	205 (20.0) *44 (4.3)*	45 (19.6) *6 (2.6)*
UTIs *Of which catheter-related*	134 (13.0) *81 (7.9)*	25 (10.9) *19 (8.2)*
GTIs	37 (3.6)	16 (7.0)
Skin infections	35 (3.4)	7 (3.0)
Mouth infections	16 (1.6)	5 (2.2)
Central nervous system infections	13 (1.3)	7 (3.0)
Cardiovascular infections	12 (1.2)	3 (1.3)

Supplemental Table S3.3. (Continued)

(n (%))	**Pre-pandemic** n = 16,106	**Pandemic** n = 3,124
Bone infections	11 (1.1)	0 (0.0)
Other systemic infections	8 (0.8)	0 (0.0)
Reproductive tract infections	5 (0.5)	2 (0.9)
Eye infections	2 (0.2)	2 (0.9)
Ear infections	1 (0.1)	0 (0.0)

Percentages are presented as % out of total HAIs.
Abbreviations: n = number; PPS = point prevalence survey; HAI = healthcare-associated infection; SSIs = surgical site infections; RTIs = respiratory tract infections; VAP = ventilator-associated pneumonia; BSIs = bloodstream infections; UTIs = urinary tract infections; GTIs = gastro-intestinal infections.

Supplemental Table S3.4. Differences in COVID-19 patients versus non-COVID patients admitted to the hospital, March 2020 – December 2020*.

	COVID-19 patient (n (%))	**Non-COVID-19 patient (n (%))**	**p-value**
CRBSI module	n = 367	n = 708	
Age in years (median (IQR))	66.2 (57.0 – 71.8)	69.3 (58.3 – 75.1)	<0.01
Sex (male (n (%)))	288 (78.5)	435 (61.4)	<0.01
Number of CVCs per patient (median (IQR))	1.8 (1 – 2)	1.3 (1 – 1)	<0.01
CVC days (median (IQR))	7 (5 – 10)	6 (4 – 9)	<0.01
ICU (n (%))			<0.01
Yes	350 (95.4)	518 (73.2)	
No	17 (4.6)	190 (26.8)	
Length of ICU stay in days (median (IQR))	18 (8 – 33)	4 (2 – 11)	<0.01
CVC use (n (%))§			
Total parenteral nutrition	37 (5.6)	200 (21.9)	<0.01
Antibiotics	454 (69.3)	523 (57.2)	<0.01
Dialysis	92 (14.0)	130 (14.2)	0.94
Hemodynamic monitoring	319 (48.7)	441 (48.2)	0.88
Other	98 (15.0)	144 (15.8)	0.72
CRBSI per 1,000 CVC days (95% CI)	8.1 (5.9 – 10.8)	3.4 (2.2 – 5.0)	<0.01
PPS module	n = 50	n = 713	
Age in years (n (%))			<0.01
< 1 year	0 (0.0)	46 (6.5)	
1-19 year	0 (0.0)	19 (2.7)	
20-29 year	0 (0.0)	17 (2.4)	
30-39 year	1 (2.0)	32 (4.5)	
40-49 year	7 (14.0)	27 (3.8)	
50-59 year	9 (18.0)	72 (10.1)	
60-69 year	8 (16.0)	120 (16.8)	
70-79 year	15 (30.0)	208 (29.2)	
80-89 year	7 (14.0)	151 (21.2)	
≥90 year	3 (6.0)	21 (3.0)	
Sex (male (n (%)))	32 (64.0)	355 (49.8)	0.05

Supplemental Table S3.4. (Continued)

	COVID-19 patient (n (%))	Non-COVID-19 patient (n (%))	p-value
Specialism (n (%))			<0.01
Cardiology	1 (2.0)	81 (11.4)	
Surgery	1 (2.0)	125 (17.5)	
Internal medicine	8 (16.0)	110 (15.4)	
Paediatrics	0 (0.0)	52 (7.3)	
Respiratory medicine	25 (50.0)	53 (7.4)	
Other	15 (30.0)	292 (41.0)	
McCabe (n (%))			0.93
Non-fatal (> 5 year)	44 (88.0)	620 (87.0)	
Ultimately fatal (1-5 year)	5 (10.0)	74 (10.4)	
Rapidly fatal (< 1 year)	1 (2.0)	13 (1.8)	
Unknown	0 (0.0)	6 (0.8)	
ICU (n (%))			<0.01
Yes	13 (26.0)	31 (4.4)	
No	37 (74.0)	682 (95.6)	
Medical devices (n (%))‡			
Urethral catheter	10 (20.0)	147 (20.6)	0.36
Peripheral catheter	39 (78.0)	456 (64.0)	0.04
Mechanical ventilation	5 (10.0)	8 (1.2)	<0.01
Central venous catheter	5 (10.0)	47 (6.6)	0.35
Antibiotics (n (%))			<0.01
Yes	32 (64.0)	266 (37.3)	
No	18 (36.0)	447 (62.7)	
HAIs (% (95% CI))	12 (5.6 – 23.8)	0.4 (0.1 – 1.2)	<0.01

* For PPS, COVID-19 status was only measured in the survey of October 2020. For CRBSI, COVID-19 status was reported by 9 out of 11 hospitals for the majority (56.2%) of the patients: 19.2% were COVID-19 patients, 37.0% non-COVID-19 and for the remaining 43.8% within the CRBSI module, COVID-19 status was unknown.
§ Patients can have a CVC for multiple applications. Percentages are calculated as the proportion of CVCs for a specific use out of all CVCs.
‡ Patients can have multiple devices at the same time. Percentages are calculated as the proportion of patients with a specific device out of the total number of patients.
Abbreviations: n = number; IQR = interquartile range; CRBSI = catheter-related bloodstream infection; CVC = central venous catheter; ICU = intensive care unit; PPS = point prevalence survey.

Supplemental Table S3.5. Distribution of HAI in COVID-19 patients versus non-COVID patients admitted to the hospital, October 2020 – December 2020.

(n (%))	**COVID-19 patient** n = 50	**Non-COVID-19 patient** n = 713
HAIs (total)	6	3
SSIs	0 (0.0)	1(33.3)
VAPs	1 (16.7)	1 (33.3)
BSIs	4 (66.6)	0 (0.0)
UTIs	1 (16.7)	1 (33.3)

Percentages are presented as proportion of total HAIs.
Abbreviations: HAIs = healthcare-associated infections; SSIs = surgical site infections; VAP = ventilator associated pneumonia; BSIs = bloodstream infections; UTIs = urinary tract infections.

PART II

Evaluation of current surveillance activities

4

Do we need to change catheter-related bloodstream infection surveillance in the Netherlands? – A qualitative study among infection prevention professionals

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ABSTRACT

Objectives: Catheter-related bloodstream infections (CRBSI) are a common healthcare-associated infection and therefore targeted by surveillance programmes in many countries. Concerns, however, have been voiced regarding the reliability and construct validity of CRBSI surveillance and the connection with the current diagnostic procedures. The aim of this study was to explore the experiences of infection control practitioners (ICPs) and medical professionals with the current CRBSI surveillance in the Netherlands and their suggestions for improvement.

Design: Qualitative study using focus group discussions (FGDs) with ICPs and medical professionals separately, followed by semi-structured interviews to investigate whether the points raised in the FGDs were recognised and confirmed by the interviewees. Analyses were performed using thematic analyses.

Setting: Basic, teaching and academic hospitals in the Netherlands.

Participants: 24 ICPs and 9 medical professionals.

Results: Main themes derived from experiences with current surveillance were 1) ICPs' doubt regarding the yield of surveillance given the low incidence of CRBSI, the high workload and IT problems; 2) the experienced lack of leadership and responsibility for recording information needed for surveillance; and 3) difficulties with applying and interpreting the CRBSI definition. Suggestions were made to simplify the surveillance protocol, expand the follow-up and surveillance to homecare settings, simplify the definition and customise it for specific patient groups. Participants reported hoping for and counting on automatisation solutions to support future surveillance.

Conclusions: This study reveals several problems with the feasibility and acceptance of the current CRBSI surveillance and proposes several suggestions for improvement. This provides valuable input for future surveillance activities, thereby taking into account automation possibilities.

INTRODUCTION

Catheter-related bloodstream infections (CRBSIs) are common healthcare-associated infections (HAIs). These infections are associated with prolonged hospital stay, increased risk of mortality, and high costs,[1-6] and therefore, one of the major infections targeted by surveillance programmes.[7,8] Despite the substantial decline in CRBSI incidence achieved by implementation of preventive efforts,[9-15] surveillance is still considered essential for identification of infections and for monitoring preventive interventions.

Many (national) surveillance programmes measure CRBSI rates systemically, however all with slightly different definitions for CRBSI (**Box 4.1**).[16-18] The infection criteria used in the Dutch national CRBSI surveillance, coordinated by the surveillance network for HAIs called PREZIES (Dutch acronym for 'PREventie van ZIEkenhuisinfecties door Surveillance'), come closest to those defined by the European Centre for Disease Prevention and Control (ECDC), although the PREZIES definition always requires a positive blood culture obtained via venepuncture to meet criteria for a laboratory-confirmed CRBSI (**Supplemental File S4.1**).[18] **Box 4.2** summarises the Dutch CRBSI surveillance.

Box 4.1. Definitions of central line-associated bloodstream infection and catheter-related bloodstream infection.

The National Healthcare Safety Network of the Centers for Disease Control and Prevention (CDC) provides the central line-associated bloodstream infection (CLABSI) defined as a primary laboratory-confirmed bloodstream infection (BSI) where an eligible line is present.[17]

The European surveillance network healthcare-associated infections (HAI-NET), coordinated by the ECDC, applies a more strict definition relying on a laboratory-confirmed BSI in combination with either a catheter tip culture with the same microorganism or in combination with a positive culture with the same microorganism from pus from insertion site. Additionally, the catheter-related bloodstream infection (CRBSI) can be scored by a quantitative blood culture ratio > 5 of central venous catheter (CVC) blood and peripheral blood, or by differential period of two hours or more of positivity of blood cultures from peripheral blood and CVC blood (CRI-3-CVC).[16] This CRBSI definition is a higher standard of proof of infection compared to the CDC's CLABSI definition.

For the Dutch surveillance, there are five definitions to score a CRBSI, all including clinical signs (fever, chills or hypotension) and absence of other focus of infection. The laboratory-confirmed CRBSI, which comes closest to the ECDC definition, requires also a combination of a positive tip culture along with a peripherally taken positive blood culture with the same microorganism. Next to this laboratory-confirmed definition, there are four other categories to define a CRBSI, trying to cover variations in local practices in the absence of culture results. An overview of the Dutch definitions is given in S**upplemental File S4.1.**

Box 4.2. The Dutch national surveillance strategy for catheter-related bloodstream infections (CRBSIs).

In 2000, the Dutch National Surveillance Network PREventie van ZIEkenhuisinfecties door Surveillance (PREZIES) introduced a national CRBSI surveillance protocol which defines CRBSI and include instructions for the data collection procedure, aiming to align surveillance in hospitals. By executing the surveillance according to this protocol, hospitals can compare their results with aggregated national data, thereby helping starting interventions and improving patient care.

Hospitals include all central venous catheters and peripherally inserted catheters that are in situ for 48 hours in patients ≥ 18 years. Tunnelled catheters are excluded from surveillance. Follow-up ends at day 28, by catheter removal, mortality or by discharge at home or to another hospital. Hospitals are free to organise how they record the data, for example, manually entering data in digital files, or registering data into build-in surveillance packages within their electronic health record. After data collection is completed, hospitals can send their surveillance data to PREZIES by entering the data in an online registration system manually or uploading the data into this system directly according to standardised format. Hospitals can also send their data in a standardised data format to PREZIES.

Participation in all PREZIES surveillance programmes is voluntary, without any consequences related to performance, and hospitals pay a small fee to join the network. With a personal login they have access to an online reporting tool in which they can view their own data and their performance in relation to others (anonymously). Additionally, each year, PREZIES publishes an open, online report providing a summary of the national numbers and trends generated by the surveillance data.

Within the Dutch surveillance network, yearly training meetings are organised for healthcare staff performing surveillance. During these meetings, concerns have been voiced regarding the reliability and construct validity of the CRBSI definition and the connection with the current diagnostic procedures.[19-21] The possible misalignment between the CRBSI definition and diagnostic practices was confirmed by a Dutch study performed on an intensive care unit (ICU) in an academic hospital: they showed that only 2% of patients with a blood culture obtained for clinical reasons (i.e. patients suspected of an infection) had appropriate microbiological diagnostics performed that would allow them to meet the surveillance requirements for a laboratory-confirmed CRBSI. This was mainly due to the lack of blood cultures obtained by venepuncture.[22] Although never formally investigated, these experienced incompatibilities may be one of the reasons for the decreasing number of hospitals participating in the voluntary Dutch national surveillance over the past years.[23] A 2016 surveillance protocol amendment mandating hospital-wide surveillance instead of ICU-only may also have contributed to the decline in participating centers.

These concerns with current CRBSI surveillance and the increasing availability of structured data stored in electronic health records (EHRs) creates a necessity to evaluate whether surveillance can be organised differently, preferably by incorporating automated options. Almost all studies evaluate surveillance programmes by investigating the effectiveness of a programme to reduce HAI.[24-27] We feel that a more fundamental approach is needed to evaluate surveillance programmes and the quality of data it generates. For this purpose, we

collected views and opinions of healthcare professionals involved in the surveillance that may help in designing future (automated) CRBSI surveillance. The aim of this study was 1) to explore the experiences of infection control practitioners (ICP) and medical professionals with the current CRBSI surveillance in the Netherlands; and 2) to collect their suggestions for an optimised CRBSI surveillance.

MATERIALS AND METHODS

From April to July 2019, face-to-face focus group discussions (FGDs) and semi-structured interviews were conducted in order to gain understanding of professionals' experiences with the current CRBSI surveillance in the Netherlands and their suggestions for improvements. The supportive, non-judgemental setting offered by FGD enhances the likelihood of collecting diverse and spontaneous opinions, ideas and feelings.[28] Semi-structured interviews were used to validate the information collected in the FGDs.

Participants

In most hospitals, ICPs keep record of HAIs, including CRBSIs. When the hospital takes part in the national surveillance they perform the data collection according to the PREZIES protocol and annotate records according to the surveillance definition. As they are experienced with executing the surveillance, their opinion, experiences and views are important to investigate. ICPs from hospitals who indicated their intention to send in CRBSI surveillance data to PREZIES in 2017 or 2018 (n = 45) were invited to participate in an FGD by email via the PREZIES-network. FGDs were planned with all interested ICPs such that participants in each session represented different types of hospitals (academic, teaching and general hospitals) and concurrently allowed the largest number of ICPs to attend. ICPs who could not attend an FGD were asked to participate in an interview. Apart from ICPs, we included medical professionals in this study as they are often responsible for the surveillance of CRBSI, and its prevention in their patients. For the FGD with medical professionals, selection was performed using specific-criterion sampling: medical professionals were recruited by the research team via their professional network and chosen based on specific characteristics (medical specialty, gender, working in academic, teaching or general hospital, years of experience and experience in the field of infectious disease surveillance).[29] Travel costs of all participants were reimbursed.

Focus group discussions

We organised two types of focus groups, involving ICPs and medical professionals separately. For the ICPs, consecutive FGDs were planned until no new themes were elicited, assessed by

analysis alongside the FGDs.[30] Thereafter, the FGD with medical professionals was planned. Each FGD was facilitated by the same moderator (JV) and observed by the same researcher (TvdK). We presented ourselves as researchers involved in the national CRBSI surveillance, and aimed to build rapport with the participants in order to encourage them to speak freely and to raise issues of importance to them. During each FGD a topic guide was used (**Supplemental File S4.2**), however, participants were also allowed to go beyond the themes. The ICP FGDs were divided in two parts: first, the experiences with and opinions on the current CRBSI surveillance were discussed. Second, we asked for solutions for the problems that were raised in the first part of the FGD and for suggestions for a renewed surveillance regarding what to measure, how and in what patient groups. During the FGD with medical professionals more fundamental discussions were held about the entity of the infection, patient groups, benchmarking possibilities and suggestions for future surveillance activities (**Supplemental File S4.2**). Each FGD was held in Dutch, lasted approximately two hours and was audio recorded. Field notes were made during each FGD and incorporated in the analysis.

Semi-structured interviews

The same topic list was used as for the ICPs' FGD, complemented with issues that emerged as important from the FGDs. During the interviews, the interviewer investigated whether the points raised in the FGDs were recognised and confirmed by the interviewees.

Data analysis

The FGDs and interviews were audio recorded and transcribed verbatim. The transcripts were used for thematic analysis performed by two researchers independently (JV and TvdK) using NVivo version 10 (QSR International, Melbourne, Australia). The first transcript of the first focus group was read closely and analysed by both researchers independently. The text units were inductively coded into categories and grouped in specific themes and subthemes, according to thematic analysis described by Braun and Clarke.[31,32]. We looked for themes which covered different socioecological aspects and the context (social, organisational and political factors). Both researchers discussed the data and correct interpretation, and an initial thematic map was developed. Transcripts from following FGDs were analysed and discrepancies were discussed. New themes were added to the map and if needed some previous transcripts were recoded. Themes were sorted and categorised in overarching themes resulting in a final thematic map. If controversy remained, another research team member (MvM) was consulted to aid decision making. The results of the ICP group were compared with the medical professionals' group to grasp diverse aspects of the participants' experiences and views. Besides, it was checked whether the themes derived from the FGDs were also covered in the interview transcripts. Findings are

supported by a selection of quotes, translated to English for the purpose of this manuscript. As a quality check, these quotes were reverse-translated by another research team member (SdG) to check their accuracy. The Consolidated criteria for Reporting Qualitative research guidelines were used for reporting the methods, analysis and results.[33]

Patient and public involvement

Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

RESULTS

Response and participants

Fourty-five hospitals had signed up in 2017 or 2018 to send in CRBSI surveillance data to PREZIES; of those, 23 hospitals (51.1%) had (at least) one ICP that wanted to participate in this study. Eventually, 20 ICPs (from 19 hospitals) participated in an FGD. In total three FGDs were held with 6 – 7 participants each. After the FGDs, two interviews were conducted with four persons from two additional hospitals (duration 46.55 minutes and 43.15 minutes, respectively) for the purpose of validating findings. This resulted in 24 participating ICPs (21 hospitals; response 46.6%), representing approximately 25% of all Dutch hospitals. For the medical professionals, one FGD was held with nine medical professionals (doctors, nurse, researcher) from seven specialties and from four different centres. The characteristics of the professionals that participated in an FGD or interview are presented in **Table 4.1**. All medical professionals were aware of the existence of the national CRBSI surveillance and six were actively involved in the CRBSI surveillance of their hospital.

Table 4.1. Characteristics of professionals participating in this study.

Characteristics	**Infection control practitioners (n = 24)**
Gender; female /male	23/1
Years of experience; mean (range)	12.1 (2.5 – 29)
Type of hospital*; general/teaching/academic (% of total Dutch hospitals in each category)	8/10/3 (17.8/38.5/37.5)
	Medical professionals (n = 9)
Gender; female /male	5/4
Years of experience; mean, range	10.1 (1 – 20)
Working areas	Intensive care (n = 2)/Haematology (n = 1)/Nephrology (n = 1)/Paediatric infectious diseases (n = 1)/ Surgery (n = 1)/Nursing and vascular access specialist (n = 1)/ Medical microbiology (n = 1)/Research(n = 1)

* Corrected for hospital level as for one hospital two infection control practitioners participated in focus group discussions and interviews were held with two infection control practitioners per hospital.
Abbreviations: n = number.

Experiences with the current CRBSI surveillance

Thematic analysis identified three main themes with nine subthemes from the experiences of the participants with the current CRBSI surveillance (**Table 4.2**).

Table 4.2. Overview of themes and subthemes.

Current surveillance	
Main theme	**Subtheme**
1. Balancing costs and benefits	CRBSI surveillance is valuable to monitor quality of care
	Low incidence
	IT problems
	Performing surveillance is too labour-intensive
2. Lack of leadership and responsibility	
3. Problems with the CRBSI definition	Criteria do not cover all CRBSIs
	Criteria not applicable to all patient groups
	Criteria not in line with diagnostic practice
	Large variability in interpretation
	Difficulties in causally relating symptoms to central line
Ideas and suggestions for improvement	
Main theme	**Subtheme**
A. Simplified surveillance	Simpler inclusion criteria and endpoints
	Longer follow-up
B. Extension surveillance to homecare setting	
C. Modification of the definition	Definition customised for specific patient groups
	No CBRSI subcategories
D. More automated solutions	
E. Alternative surveillance options	Surveillance of tip colonisation
	Shorten the period of executing surveillance
	Surveillance of other catheter types

Abbreviations: CRBSI = catheter-related bloodstream infection; IT = information technology.

Theme 1: Balancing the costs and benefits of performing surveillance

One main theme – with four subthemes – that arose from the data was the balance between the effort that was put into surveillance activities compared to the benefits.

CRBSI surveillance is valuable to monitor quality of care

The main reason for all participants to perform surveillance was to generate insights in their CRBSI incidence. According to ICPs, the surveillance results led to opportunities for quality improvement, raised awareness for infection prevention (e.g. in management layers) and

initiated conversations about current practices for example, one ICP gave the example that a peak in the CRBSI surveillance data initiated an assessment about the method of catheter insertion and method of care and how they could be improved.

> *'For us it is mainly a quality indicator, we just want to keep numbers as low as possible and the only way to find that out is to register infections.'* (FGD-MP05)

Low incidence

Some ICPs were doubtful whether it is worthwhile continuing the CRBSI surveillance, given their stable low incidence over the years and the many hours they spend on executing surveillance.

Information technology problems

Most hospitals use a module or package in their EHR to collect and record surveillance data: the stage of development and functionalities vary by hospitals. However, there is a broad variety in information technology (IT) problems infection prevention departments face and the IT support they receive: there are experiences with uncooperative EHR-developers and technical problems of systems, problems with extracting the data from the system, and the feeling that it is very difficult to get things done in this field.

> *'I find that in practice, it is very difficult to get the automation department to do things anyway. I think that's the experience in all hospitals.'* (FGD-ICP017)

ICPs feel they often have to arrange and co-develop EHR improvements, however, according to them it is not their responsibility or skill.

> *'Look, of course we want to know the numbers, but as long as the automation department is holding us back…WE are not going to do this as an infection prevention department. That is not possible, we don't want to, and we don't have the time to do it!'* (FGD-ICP03)

Last, for many health professionals it is unclear what the automatisation possibilities are. They admit that they don't have the knowledge or interest; nevertheless, they do have high expectations of it.

Performing surveillance is too labour-intensive

Performing surveillance is too labour- and time-intensive according to all participants. One ICP called it demotivating. Additionally, the high work pressure people already experience in general and the recent extension to CRBSI hospital-wide surveillance were mentioned.

Executing and coordinating surveillance takes too much time at the expense of other infection prevention tasks. For this reason, many hospitals have data managers, students or administrative support helping with performing the surveillance.

> *'But yes, it is very a time investment and, so to say, the input does not completely weigh up to the benefit.'* (FGD-ICP09)
>
> *'Because people are overloaded, they have so much to do already!'* (FGD-ICP06)

The main reason for the high workload is missing data in the EHR. In most hospitals, healthcare professionals register information in the EHR that ICPs use for the surveillance: after catheter insertion the catheter is registered into the system, nurses add (daily) information about the use of and possible complications associated with the catheter, and record catheter removal. In some hospitals the information entered in the system is automatically extracted and ICPs complement some data fields required for surveillance. In other cases ICPs fill in surveillance data based on free-text notes. ICPs unanimously agreed that information, such as the origin of blood samples, is often missing or not filled in properly. In particular the removal date of the catheter is often lacking, thereby complicating the calculation of line days needed for the denominator of reporting the incidence. Looking up the removal date in free-text clinical notes is experienced as burdensome.

> *'If they don't enter the removal date [of the catheter] you are searching for hours to find it.'* (FGD-ICP02)

This incorrect and missing data lead to incorrect surveillance results. ICPs repeatedly reported that they are aware of incomplete or incorrect surveillance data, however they feel they cannot help it.

> *'We run into a lot of issues and actually, every now and then it seems we generate numbers that are based on shots in the dark….'* (FGD-ICP04)

Theme 2: Lack of leadership and responsibility: ICPs filling the gap

The ICPs as well as the medical professionals agreed that the responsibility for the treatment of the patient and the handling of the catheter lies with the treating physician, and both the medical specialists and nurses are responsible for the care. However, as described above, the information needed to perform CRBSI surveillance is often not fully available from the EHRs. According to the ICPs this is because the people responsible for the patient lack involvement with and interest for surveillance and, hence, responsibility for registering information. Although responsibilities and actions are often described in protocols and documents, ICPs emphasise that practice is not always in accordance with hospital-wide agreements.

> *'In principle, everything you have to do is described, but then... you still can do something different.'* (FGD-ICP17)
>
> *I can't get them to do it! Manually entering data in the system when ordering a blood-or tip culture. They just don't do it.'* (FGD-ICP02)

Most ICPs stated that in the abovementioned situations they take the responsibility to complete the surveillance records by looking up or asking for data, but they feel that it is not their responsibility to do so: they should have a coordinating role and are responsible for the CRBSI reports. Medical professionals agreed and confirmed that information is lacking in the EHR, however they did not provide any suggestions to improve this or who's responsibility it is.

Theme 3: Problems with the CRBSI definition

Criteria do not cover all CRBSIs

ICPs and medical professionals reported several problems regarding the definition that is used in surveillance. First, they emphasised that there are some cases that cannot be scored as a CRBSI according to surveillance criteria, but that are seen as CRBSI according to ICPs or medical doctors. Therefore, they feel that the surveillance does not catch all CRBSIs.

> '*There are CRBSIs that fall outside the criteria of PREZIES. And those, yes those, are the ones you are interested in.*' (FGD-ICP07)

Criteria are not applicable to all patient groups

In the current surveillance, the same definitions are used for all patient groups with a central venous catheter (CVC) or peripherally inserted central catheter (PICC). According to both ICPs and medical professionals, these definitions are not applicable to all patient groups, in particular haematology patients as their clinical symptoms caused by neutropenia are indistinguishable from infection symptoms.

Criteria are not in line with diagnostic practice

Clinical practice is often not in line with the strict criteria to define CRBSIs, making them difficult to score: for example, the blood and tip cultures are not taken within 24 hours of each other, blood samples are obtained via the CVC instead of through a venepuncture, or antibiotics are started before cultures are obtained.

> '*Every now and then you just know for sure that it is one [a CRBSI], but then, for example, the blood culture was taken two hours too late to meet the definition. Very frustrating.*' (Int-ICP22)

Medical doctors confirmed and emphasised that the current surveillance protocol is not in line with their clinical practice.

Large variability in interpretation

Some ICPs experience a large variability in interpretation of the definition and they therefore question the potential for benchmarking.

Difficulties in causally relating symptoms to central line

Last, all participants concluded that patients with a CVC or PICC suspected for infection are complex, and the causes of certain clinical symptoms are not always clear. Causally relating the symptoms to the CVC is therefore difficult. They stated that a CRBSI is sometimes used as a 'residual diagnosis', if no other focus or explanation can be found.

Suggestions for improvement

Five main themes for improvement were addressed: A) a simplified surveillance; B) extending the surveillance to homecare settings; C) modification of the definition; D) more automated surveillance; and E) suggestions for alternative surveillance options (**Table 4.2**). Below a short description is given per theme.

Theme A: Wish for a simplified surveillance

The wish for a more simplified surveillance methodology recurred throughout the dataset. The current surveillance is experienced as too complicated regarding the inclusion criteria for catheters, the information nurses have to enter into EHR systems and the exact endpoints of the surveillance. ICPs brought forward the possibility of registering the incidence only, without collecting additional information for the purpose of case-mix correction, thereby accepting the possible bias. The medical professionals disagreed: they felt case-mix correction is essential to have reliable benchmarking. Both groups agreed that the follow-up was considered too short and should be longer than 28 days.

Theme B: Extending surveillance to homecare setting

Many participants also agreed on the need to extend the current surveillance protocol to patients in homecare settings. Both ICPs and medical professionals argued that they are still responsible for the patient when discharged with a CVC or PICC in situ. Given the increasing trend of shared healthcare and short hospital stays it is valuable to prolong the follow-up for patients who are discharged with a PICC and regularly return to the hospital for check-up visits.

'[….] while more and more patients are treated outside the hospital, and these are completely excluded form surveillance. And in my opinion, that's a shortcoming if you see that length of hospitals stays are becoming shorter and patients are treated under responsibility of the hospital, and we don't pay attention to that.' (FGD-MP07)

Theme C: Modification of the definition

The definition used in surveillance was a recurrent theme in all FGDs and interviews. The wish for an adaptation of this definition was even communicated as a compelling advice rather than a suggestion. Especially the medical professionals advised to adopt a more tailored surveillance definition for specific target groups as the current definitions are not applicable to groups such as haematology patients or children (though the latter is currently not included in national surveillance). ICPs agreed on this and also suggested to create one single definition per patient group instead of the current four categories to score a CRBSI (see **Box 4.1**).

Theme D: More automated solutions

According to all participants much more could be developed, improved and achieved by local automation processes. Their expectations of IT possibilities are high and seen as the solution for workload reduction as it can help with easily recording data, and for the problems they face regarding definition subjectivity through the use of advanced algorithms. Second, ICPs would appreciate if changes to the national surveillance protocol are aligned between the national surveillance organisation PREZIES and EHR-software companies. ICPs often have to arrange changes in EHR systems while they feel it is not their responsibility and they are not comfortable with it.

'Yes and maybe it is very idealistic, but it would be very appreciated if…when for example PREZIES is going to change something in the CRBSI surveillance that there is contact with the most common EHR suppliers, and that PREZIES is not saying to hospitals every time: "it is your problem to fix it in your EHR. Go and find out yourself how you will implement it."' (FGD-ICP02)

Theme E: Suggestions for alternative surveillance options

It was argued that catheter tip colonisation combined with information about the causative microorganism would give more steering information as it is a harbinger of infection and occurs more frequent than the strict definition requiring a positive blood and tip culture. Other suggestion was to reduce the current registration period, for example a registration of 3 months per year, in order to reduce the workload.

> *'We just take one month and then we add additional information to see what is happening over there. You then measure a sort of prevalence. Because now you….you… you are looking for all those catheters the entire year…well you become completely crazy!'* (Int-ICP24)

ICPs indicated they would like to have the possibility to (temporary) monitor other types of catheters, e.g. arterial lines, or specific patient groups or wards. This was contradicted by the medical professionals who argued to stick to CVCs and PICCs for national surveillance for benchmarking purposes, however, to include tunnelled central lines.

None of the participants was interested in shifting the focus of national surveillance from CRBSI to other endpoints such as hospital-acquired bloodstream infections (BSIs) or to measure other quality indicators instead of CRBSI, such as ventilator-associated pneumonia (VAP) for benchmarking purposes.

DISCUSSION

This study revealed multiple problematic factors that ICPs experience in performing the current CRBSI surveillance. Surveillance is experienced as too labour-intensive and complicated with respect to applying the definition, the lack of responsibility in recording data and IT-related problems. To optimise national surveillance, professionals agreed to adapt the surveillance definition to specific patient groups and extending the duration of follow-up and the surveillance to home care. It became clear that all professionals look forward to automation options to facilitate data collection and improve standardisation of surveillance. There were different opinions about the types of catheters to include in surveillance: medical professionals suggested to continue CVC and PICC surveillance, however including tunnelled catheters, while ICPs were more in favour of more choice in selecting the type of catheter under surveillance and were less interested in benchmarking.

A comparable study was performed in Sweden by Ridelberg et al.[34]: by interviewing 22 ICPs they evaluated obstacles concerning the surveillance process of their biannual point prevalence surveys, focusing on the challenges in using HAI results. Although this study evaluated a different type of surveillance, similar obstacles were reported such as limited involvement of clinical staff and nurses and shortage of personnel resources and technical problems. The high workload and labour-intensiveness is mentioned by several other surveys and quantitative studies and is therefore a recurrent theme in performing surveillance.[35-37] Almost all studies evaluating surveillance programmes focus mainly on the effectiveness to reduce HAI.[24-27] We feel that a more fundamental approach is needed to evaluate surveillance

programmes and the quality of data it generates. In our opinion, evaluating surveillance should also include a discussion about the effort taken to collect these data, what we actually measure and how. Collecting meanings and views about current surveillance activities in a systematic way is valuable as it enables the discovery of barriers that should be tackled to make surveillance more relevant, effective, feasible and reliable. The value of using CRBSI for benchmarking has been questioned due to high variability in CRBSI rates caused by differences in diagnostic practices, subjective interpretation, and CRBSI rates close to zero limiting meaningful comparisons.[21,26,38-42] Hence, effort is put into development of alternative definitions of CRBSI in different patient groups[43-45] or for alternative quality outcome measures for benchmarking such as hospital-onset bacteraemia.[46,47]

The development of automated surveillance methods is another strategy to improve the quality of CRBSI surveillance, which limits subjectivity and reduces the time investment. Several research groups developed automated algorithms to detect bloodstream infections in patients with a catheter.[48-51] Despite good performances, all used the CDC definition for automation (central line-associated BSI). To the best of our knowledge, no examples are available for automation using the CRBSI definition, which is a higher standard of proof that the infection is related to the CVC. Additionally, automation does not change the social practices and obstacles of the data collection as described by Dixon-Woods et al.[42] This study, therefore, first identified views and opinions about the current surveillance to guide further development of CRBSI surveillance and automation solutions in the future. Designing IT solutions without identifying underlying problems and views may fail to be helpful and to be accepted in the field. The in-depth information generated in this study is also meant as a preparation for a planned future quantitative study on (semi-)automatisation of CRBSI surveillance.

Strengths and limitations

We collected opinions from professionals from different types of hospitals with a broad range of years of working experience. We included ICPs as the surveillance coordinators using the data, but also medical professionals: the latter have a different view on benchmarking and national surveillance purposes compared to the ICPs. Unfortunately, only one nurse, specialised in vascular access devices, could attend the FGD.

Views from general hospitals may be slightly under-represented in this study, as only about 18% of all Dutch general hospitals participated in our FGDs. These hospitals may experience less difficulties in organising and conducting surveillance, however as brought forward during the FGDs, this is because data collection is performed mainly manually. During the FGDs it became clear that ICPs from small hospitals share the desire to have more IT

solutions, but lack knowledge and expertise in this field. Second, it is possible that hospitals that do not encounter problems are less interested to participate in these FGDs. However, the unexpected high response rate (51.1%) – representing a quarter of all Dutch hospitals – could be considered indicative of the problems in current surveillance activities. Alternatively, non-response may be related to the current shortage of ICP personnel in Dutch hospitals; therefore, not having time to travel and participate in the FGDs. It would be interesting to hear from ICPs of hospitals that do not participate in national surveillance about their reasons for non-participation. However, because we were interested in the experiences with performing the current surveillance we only recruited ICPs via the PREZIES network. Last, this study is performed in a Dutch setting and evaluated the Dutch national CRBSI surveillance. Nevertheless, findings may be recognised by other countries, who may experience similar problems and are also looking for surveillance alternatives.

CONCLUSION

This study describes shortcomings in the current Dutch CRBSI surveillance. According to the participants of this study, the surveillance is considered too labour-intensive, restricted by IT-related problems, and some perceived that the benefits of surveillance do not outweigh the time-investment required from the ICPs, given the low CRBSI incidence. Moreover, the CRBSI-definition is not aligned with daily diagnostic practice and there is a lack of responsibility in recording data required for surveillance. Suggested improvements include: a modification of the definition customised to specific patient groups, automatisation options to improve data collection, standardisation and to reduce workload, and to include catheters in homecare situations and extend the follow-up period. These results provide valuable input for making decisions for future surveillance activities, taking into account automation possibilities.

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AUTHOR CONTRIBUTIONS

JV was responsible for the study conception, design, data collection, analyses and interpretation, as well as for drafting the manuscript, revision and final approval. TvdK was involved in the

data collection and the data analysis. MvM and LD supervised the study. TvdK, SdG, LD, MvM and MB made critical revisions to the paper. All authors approved the final manuscript.

COMPETING INTERESTS

None declared

FUNDING STATEMENT

None declared

DATA AVAILABILITY STATEMENT

No additional data are available.

ETHICS APPROVAL

This study was reviewed by the Medical Institutional Review Board of the University Medical Center Utrecht and was considered not to fall under the Medical Research Involving Human Subjects Act (ref. no. 19/161). Written informed consent was obtained from all participants of this study.

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SUPPLEMENTARY MATERIAL

Supplemental File S4.1. Case definition of central venous catheter-related bloodstream infection (CRBSI) in the PREZIES surveillance.

CRBSI: microbiologically-confirmed CVC-related bloodstream infection

Clinical symptoms [fever (>38°), shivers, hypotension (systolic pressure <100 mmHg)]
And
peripheral venous blood culture is positive
And
positive (semi)quantitative culture of the Central Venous Catheter (CVC)- tip [>15 colony-forming units (cfu)] with identical microorganism
or
quantitative blood culture ratio CVC blood sample/peripheral blood sample > 5;
or
differential delay of positivity of blood cultures: CVC blood sample culture positive two hours or more before peripheral blood culture (blood samples drawn simultaneously); or
positive culture with identical microorganism from pus from CVC insertion site
And
absence of other infection with identical microorganism.

CRBSI, category 1

Clinical symptoms [fever (>38°), shivers, hypotension (systolic pressure <100 mmHg)]
And
positive qualitative culture of the CVC tip
And
peripheral venous blood culture positive with identical microorganism
And
absence of other infection with identical microorganism.

CRBSI, category 2

Clinical symptoms [fever (>38°), shivers, hypotension (systolic pressure <100 mmHg)]
And
positive (semi)quantitative culture of the CVC tip (>15 cfu)
And
no peripheral venous blood sample obtained, however arterial blood culture positive with identical microorganism
And
absence of other infection with identical microorganism.

CRBSI, category 3

Clinical symptoms [fever (>38°), shivers, hypotension (systolic pressure <100 mmHg)]
And
peripheral venous blood culture is positive or no blood cultures taken
And
positive qualitative or quantitative culture of the CVC tip with identical microorganism or no culture of the CVC tip taken
And
fever disappears within 24h after CVC removal
And
absence of other infection with identical microorganism.

CRBSI, category 4

Clinical symptoms [fever (>38°), shivers, hypotension (systolic pressure <100 mmHg)]
And
positive peripheral venous blood culture
And
CVC remains in situ
And
fever disappears within 48 h after start of antibiotic treatment.
And
absence of other infection with identical microorganism.

Notes:

- Catheter-related: the CVC was in situ < 48 hours before the onset of the BSI
- In Dutch clinical practice, CRBSI is usually investigated by culturing both peripheral blood and the CVC tip. If less optimal (laboratory) methods are used, the diagnostic CRBSI categories 1 – 4 are available (hierarchical structure).
- The CRBSI categories specify the laboratory method of culturing the CVC (semi-qualitative of quantitative) and the body site from which the blood culture is drawn (peripheral venous or arterial).
- The CVC and blood samples are preferentially drawn simultaneously or within 24 hours.

Supplemental File S4.2. Topic guide focus group discussions 1) ICPs and 2) medical professionals.

DEMOGRAPHIC DETAILS QUESTIONNAIRE - ICPs

1. Your profession:_____
2. Number of years working experience in this profession:_____
3. Name(s) of your institution(s):_____
4. Did your hospital perform surveillance and send in data to PREZIES last year (2018)?
   ☐ Yes → What modules? _____
   ☐ No
5. Have you performed CRBSI surveillance in the past, according to PREZIES guidelines?
   ☐ Yes → Which time period? _____
   ☐ No
6. Did your hospital adapt the national PREZIES guidelines, or make adaptations in executing the surveillance?
   ☐ Yes → give a short description: _____
   ☐ No

DEMOGRAPHIC DETAILS QUESTIONNAIRE – MEDICAL PROFESSIONALS

1. Your profession: _____
2. Number of years working experience in this profession: _____
3. Name(s) of your institution(s): _____
4. Were you aware of the existence of national CRBSI surveillance?
   ☐ Yes
   ☐ No
5. Are you, apart from this FGD, actively involved in CRBSI surveillance in your hospital?
   ☐ Yes, Please explain: _____
   ☐ No

FOCUS GROUP DISCUSSION: TOPIC GUIDE ICPs

Prior to FGD		
Introduction of researchers	Short introduction of ourselves and roles	
Introduction to study and study aim	Introduce study aim Explain structure of FGD • Experiences with current CRBSI surveillance (Part I) • Solutions and suggestions for problems that arose in part I (Part II) Identify whether there are any questions at this moment	
Confidentially	Please sign informed consents Announcement privacy: anything that has been said within the session will be treated confidentially, just be yourself and speak honestly. Announcement of recording device: responses will be stored in anonymous format. Please fill in questionnaire demographics	
Introduction round participants	Each participant introduces themselves (employer, years of working experience, experience with the Dutch surveillance, motivation to join this FGD).	
FGD Part I: experiences with current CRBSI surveillance		
Question/aim	**Description**	**Probes**
Identify positive and negative points of CRBSI surveillance	Participants write down all positive and negative aspects on post-its, which are then discussed within the whole group	Did someone else also write this down? What do you mean with it? Can you explain to what situations it applies? What do others think about this point? Does anyone have a point related to this? Why did you write this/not wrote this down?
Identify most important positive points	Participants discuss the positive points and rank them from most valuable and positive to less important	Why is this positive point the most valuable one? From which point does the hospital benefit most?
Identify most important negative points	Participants discuss the negative points and rank them from most problematic to less important	Why is this negative point most problematic?
In-depth discussion	The five most important points are discussed in more detail	

Focus group discussion: topic guide ICPs. (Continued)

	Break	
FGD Part II: solutions, suggestions, wishes and ideas		
Identify solutions for the negative points raised in Part I	Participants write down one solution for each problem that has been raised in Part I, which are then discussed within the group.	How could you make better use of point X? Can you add something? Do you have an example that is in use in your own hospital? Do you know examples we can learn from? Why would this be a solution?
Inventory of other ideas and wishes	Within the group other ideas, wishes, or new surveillance proposals – apart from the problems – are discussed and added to the list of solutions.	Do you have an out-of-the-box idea? Why would you want this? What is the motivation? How would you do that? In which patient groups?
Scoring of best suggestions given in Part II	Participants can award five stars to the solution/wish/suggestion they prefer. Stars can be divided if more than 1 suggestion is preferred.	What is according to you the best solution/adaptation? And why? Why did you give all your stars to this suggestion?
Closure		
Closure and notifications	Summarise and conclude FGD Thank you to participants Instructions to reimburse travel costs	

FOCUS GROUP DISCUSSION: TOPIC GUIDE MEDICAL PROFESSIONALS

Prior to FGD	
Introduction of researchers	Short introduction of ourselves and roles
Introduction to study and study aim	Introduce study aim Explain structure of FGD Identify whether there are any questions at this moment
Confidentially	Please sign informed consents Announcement privacy: anything that has been said within the session will be treated confidentially, just be yourself and speak honestly. Announcement of recording device: responses will be stored in anonymous format. Please fill in questionnaire demographics
Introduction round participants	Each participant introduces themselves (profession, employer, years of working experience, affinity with/role in surveillance, motivation to join this FGD).

Focus group discussion: topic guide medical professionals. (Continued)

FGD MEDICAL PROFESSIONALS		
Question/aim	**Description**	**Probes**
Identify positive and negative points of CRBSI surveillance	Moderator gives a presentation about current surveillance and the positive and negative points that has been raised during the ICP FGDs. Participants discuss these findings and add their points.	Do you have something to add to this list? What is your opinion/experience with current practices? If you hear these problems, what do you think? Do you agree with these points?
Inventory of entity of infection and benchmarking possibilities	Participants discuss what they want to measure for surveillance: catheter-related or catheter-associated bloodstream infections? Which outcomes are best for benchmarking?	What is the difference? What outcome is good to compare between hospitals?
Identify types of catheters for surveillance	Participants write down all types of catheters that are present within their medical profession/ward and choose which they would include for national surveillance and benchmarking.	Which catheters are used in your specialty? Why do you think these are (not) suitable for national surveillance? Why did you choose these catheters?
	Break	
Identify patient groups	Participants sum all patient groups with catheters in situ and discuss them.	How do these groups differ from each other? Can you compare these groups?
Inventory of suggestions for renewed surveillance	Catheter types and patient groups are summarised and discussed to identify catheters and groups that are suitable for national surveillance and benchmarking.	How can we improve current surveillance? Do you have any new ideas? How would you design the surveillance, which strategy would you use?
Closure		
Closure and notifications	Summarise and conclude FGD Thank you to participants Instructions to reimburse travel costs	

Reliability and validity of multicentre surveillance of surgical site infections after colorectal surgery

5

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ABSTRACT

Background: Surveillance is the cornerstone of surgical site infection prevention programmes. The validity of the data collection and awareness of vulnerability to inter-rater variation is crucial for correct interpretation and use of surveillance data. The aim of this study was to investigate the reliability and validity of surgical site infection (SSI) surveillance after colorectal surgery in the Netherlands.

Methods: In this multicentre prospective observational study, seven Dutch hospitals performed SSI surveillance after colorectal surgeries performed in 2018 and/or 2019. When executing the surveillance, a local case assessment was performed to calculate the overall percentage agreement between raters within hospitals. Additionally, two case-vignette assessments were performed to estimate intra-rater and inter-rater reliability by calculating a weighted Cohen's Kappa and Fleiss' Kappa coefficient. To estimate the validity, answers of the two case-vignettes questionnaires were compared with the answers of an external medical panel.

Results: 1,111 colorectal surgeries were included in this study with an overall SSI incidence of 8.8% (n = 98). From the local case assessment it was estimated that the overall percent agreement between raters within a hospital was good (mean 95%; range 90 – 100%). The Cohen's Kappa estimated for the intra-rater reliability of case-vignette review varied from 0.73 to 1.00, indicating substantial to perfect agreement. The inter-rater reliability within hospitals showed more variation, with Kappa estimates ranging between 0.61 and 0.94. In total, 87.9% of the answers given by the raters were in accordance with the medical panel.

Conclusions: This study showed that raters were consistent in their SSI-ascertainment (good reliability), but improvements can be made regarding the accuracy (moderate validity). Accuracy of surveillance may be improved by providing regular training, adapting definitions to reduce subjectivity, and by supporting surveillance through automation.

INTRODUCTION

Surgical site infections (SSIs) are one of the most common healthcare-associated infections (HAIs),[1] and are associated with substantial morbidity and mortality, increased length of hospital stay and costs.[2-6] The highest SSI incidences are reported after colorectal surgeries, possibly due to the risk of (intra-operative) bacterial contamination and post-operative complications.[7-9] Worldwide, incidence rates range from 5% to 30% and are affected by several risk factors, including the type of surgery, age, sex, underlying health status, diabetes mellitus, blood transfusion, ostomy creation, prophylactic antibiotic use[10-12] and by the definition used to identify SSIs.[4,13]

Surveillance is an important component of prevention initiatives and most surveillance programmes include colorectal surgeries.[14] Large variabilities in SSI rates between centres remain, even after correction for factors that increase the risk of SSIs. Previous studies reported significant variability in surveillance methodology and in inter-rater agreement, introducing uncertainty regarding whether observed differences in colorectal SSI rates reflect real differences in hospital performance.[15-21]

For the purpose of comparing SSI rates between hospitals, accurate adherence to standardised surveillance protocols is required. Furthermore, case definitions should be unambiguous to avoid subjective interpretation. To reduce subjectivity the Dutch national surveillance network (PREZIES) has modified the case definition on two criteria as compared to the definitions set out by the (European) Center of Disease Control and Prevention ((E)CDC).[22-25] First, the diagnosis of an SSI made by a surgeon or attending physician only is not incorporated in the Dutch definitions. Second, in case of anastomotic leakage or bowel perforation, a deep or organ-space SSI can only be scored by purulent drainage from the deep incision, or when there is an abscess or other evidence of infection involving the deep soft tissues found on direct examination. A positive culture obtained from the (deep) tissue is not applicable in case of anastomotic leakage. Moreover, to increase standardisation, the Dutch surveillance only includes primary resections of the large bowel and rectum, in contrast to the (E)CDC, who also allows biopsy procedures, incisions, colostomies or secondary resections.

Awareness of the correctness of applying the definition and vulnerability to inter-rater variation is crucial for correct interpretation and use of surveillance data. The aim of this study was to investigate the reliability and validity of SSI surveillance after colorectal surgery using the Dutch (PREZIES) SSI definitions and protocol. Secondary aims were to report the accuracy of determining anastomotic leakage and to provide insights in the SSI incidence and epidemiology in the Netherlands.

METHODS

Study design

In this multicentre prospective observational study, seven Dutch hospitals (academic (tertiary referral university hospital) n = 2; teaching n = 3; general n = 2) collected surveillance data for occurrence of SSI after colorectal surgeries performed in 2018 and/or 2019, according to the Dutch PREZIES surveillance protocol.[23,25,26] Three hospitals had no prior experience in performing SSI surveillance after colorectal surgeries and four hospitals already performed this surveillance for more than five years as part of their quality programme. Participation in SSI surveillance after colorectal surgery is voluntary, hence not all hospitals include this in their surveillance programme. When executing the surveillance, additionally intra- and inter-rater reliability and validity were determined by two case-vignette assessments and a local case assessment. Reliability refers to the consistency and reproducibility of SSI-ascertainment and was determined by three agreement measures: 1) the intra-rater reliability, reflecting the agreement within one single rater over time; 2) the inter-rater reliability, which is the agreement between two raters within one hospital; and 3) the overall inter-rater reliability between all 14 raters of seven hospitals.[27,28] Validity refers to how accurately the surveillance definition is applied and was determined by the correctness of ascertainment compared to a medical panel as described in detail below. The Medical Ethical Committee of the University Medical Centre Utrecht approved this study and waived the requirement of informed consent (reference number 19-493/C). All data were processed in accordance with the General Data Protection Regulation. Hospitals were randomly assigned the letters A – G for reporting of the results.

SSI surveillance after colorectal surgery

All hospitals included all primary colorectal resections of the large bowel and rectum performed in 2018 and/or 2019 in patients above the age of 1 year. Per hospital two raters, mostly ICPs, manually reviewed the electronic medical records for all included procedures retrospectively and classified procedures into three categories: (1) no SSI; (2) superficial SSI or (3) deep SSI or organ-space SSI within a follow-up period of 30 days post-surgery. SSIs were registered in their own hospital's surveillance registration system. All identified SSIs and questionable cases were validated and discussed with each facility's medical microbiologist or surgeon after completing the assessments which are described below.

Case-vignette assessment

Case-vignettes were used to assess the validity, intra-rater and inter-rater reliability. Four medical doctors developed standardised case-vignettes in Dutch language, based on 20 patients selected from a previous study.[29] Each vignette described demographics, the medical history, type of surgical procedure and the post-operative course. An external medical panel of seven experts in the field of colorectal surgeries and surveillance classified the case-vignettes as a superficial SSI, deep SSI, or no SSI according to the Dutch SSI definition, and indicated presence or absence of anastomotic leakage. Their conclusion was considered the reference standard. Each rater who performed surveillance completed the case-vignettes individually through an online questionnaire. Three months later, the same vignettes were judged once more by the same raters, but presented in a different random order.

Local case assessment

The reliability of surveillance data also depends on the ability to find the information necessary for case-ascertainment in the medical records. As this is not measured by the case-vignettes, we additionally performed a local case assessment: within each hospital, 25 consecutive colorectal surgeries included in surveillance were scored independently by the two raters, on separate digital personal forms. After sending the completed forms to the research team, raters discussed the results and entered the final decision into their hospital's surveillance registration system.

Training

Before starting the surveillance activities, a training session was organised to ensure the quality of the data collection and to practice SSI case-ascertainment. Thereby, before starting the reliability assessments, each ICP had to complete at least 20 inclusions for surveillance to assure familiarity with the surveillance procedure. In case of any questions, the research team was available to provide assistance.

Statistical analyses

Descriptive statistics were generated to describe the surveillance period, number of inclusions and epidemiology. The number of SSIs per hospital were reported and displayed in funnel plots. The primary outcomes of this study were the reliability and validity of the surveillance. From the case-vignette assessments, the intra-rater and inter-rater reliability were analysed by calculating a weighted Cohen's Kappa coefficient (κ). The scale used to interpret the κ estimates was as follows: ≤ 0, no agreement; 0.01 – 0.20, slight agreement; 0.21 – 0.40, fair agreement; 0.41 – 0.60, moderate agreement; 0.61 – 0.80, substantial agreement; 0.81 – 1.00,

almost perfect agreement.[27] For the inter-rater reliability within a hospital, we used the second questionnaire round of the case-vignettes, to account for a possible learning curve over time. The overall inter-rater reliability among all 14 raters was estimated using a weighted Fleiss' Kappa. For all Kappa's, 95% confidence intervals were estimated using bootstrapping methods (1,000 repetitions). Inter-rater reliability was also measured from the local case assessment, from which the overall percentage agreement was calculated per hospital. Validity was determined by comparing the answers of the two case-vignettes questionnaires with the answers of the medical panel. The same comparison was performed to investigate the accuracy related to the determination of anastomotic leakage. Analyses were performed with R version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria)[30] with the use of packages *irr*[31] for inter-rater reliability and the *boot*[32] package for bootstrapping.

RESULTS

Epidemiology

1,111 colorectal surgeries were included in the surveillance, in majority right-sided hemicolectomies (n = 445; 40.1%). The overall incidence of SSI was 8.8% (n = 98); 46.9% developed superficial SSI (n = 46) versus 53.1% deep SSI (n = 52). In 23 deep SSIs (44.2%) there was anastomotic leakage. **Table 5.1** provides an overview of the cumulative incidence of SSIs per hospital and **Figure 5.1** displays the incidence of SSIs taking into account the number of surgical procedures. SSIs were observed more frequently in open surgeries than laparoscopic procedures, with the highest SSI incidence in open sigmoid colectomies (19.4%), followed by open left hemicolectomies, open right hemicolectomies and open low anterior resections (17.5%; 11.0% and 9.6% respectively). Other risk factors are shown in **Table 5.2**.

Table 5.1. Overview of colorectal surgeries and number of SSIs per participating hospital.

	Type of hospital	Surveillance period	Number of colorectal surgeries (n)	Superficial SSI (n (%))	Deep SSI (n (%))	Total SSIs (n (%))
Hospital A	General	2019	221	1 (0.5)	9 (4.1)	10 (4.5)
Hospital B	Teaching	2019	205	10 (4.9)	7 (3.4)	17 (8.3)
Hospital C	General	2019	148	4 (2.7)	3 (2.0)	7 (4.7)
Hospital D	Academic	2018 – 2019	84	4 (4.8)	8 (9.5)	12 (14.3)
Hospital E*	Teaching	2019[a]	144	3 (2.1)	9 (6.3)	12 (8.3)
Hospital F*	Teaching	2019[a]	142	12 (8.5)	11 (7.7)	23 (16.2)
Hospital G*	Academic	2018 – 2019[a]	167	12 (7.2)	5 (3.0)	17 (10.2)
Total			1,111	46 (4.1)	52 (4.7)	98 (8.8)

* Hospitals that started surveillance for the purpose of this study.
[a] January – June 2019.
Abbreviations: n = number; SSI = surgical site infection.

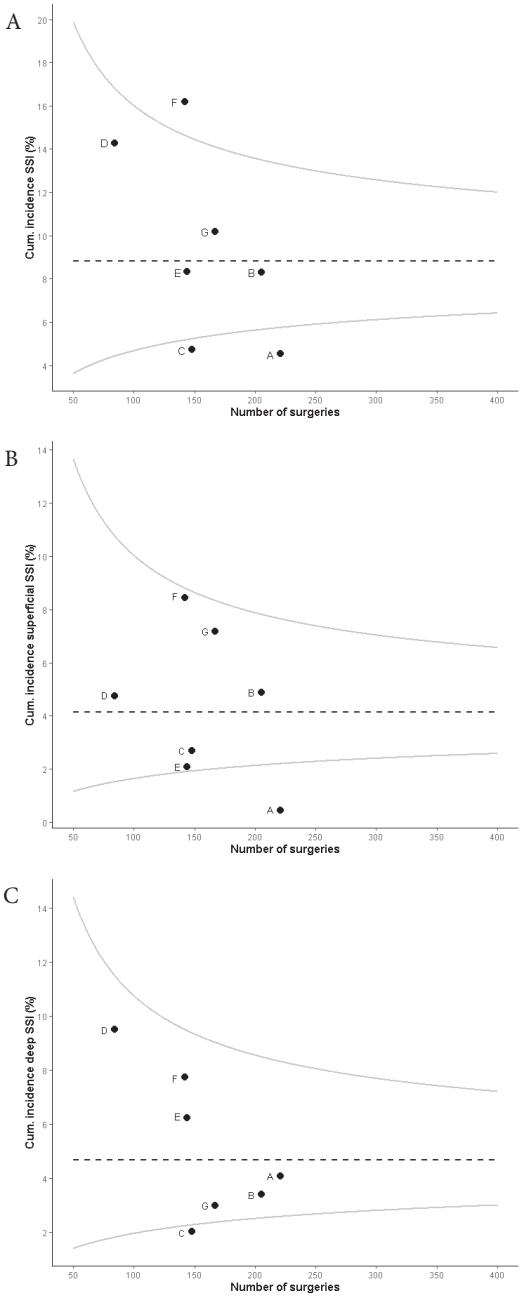

Figure 5.1. Overview of surgical site infection (SSI) incidence per hospital accounting for the number of surgical procedures. The black dotted line shows the mean incidence rate, the grey curved lines are the corresponding 95% confidence interval. (A) Overview of all SSIs per hospital; (B) Overview of superficial SSIs per hospital; (C) Overview of deep SSIs per hospital.

Table 5.2. Baseline characteristics and risk factors of patients who underwent a primary colorectal surgery.

	No SSI (n = 1,013)	Superficial SSI (n = 46)	Deep SSI (n = 52)
Sex (n (%))			
Male	506 (50.0)	29 (63.0)	31 (59.6)
Female	507 (50.0)	17 (37.0)	21 (40.4)
Age in years (mean (SD))	65.7 (13.7)	61.8 (15.0)	63.2 (15.4)
Pre-operative risk factors			
BMI (mean (SD))	26.1 (4.6)	27.0 (4.8)	27.6 (7.0)
Missing (n (%))	29 (2.9)	2 (4.3)	2 (3.8)
ASA grade (n (%))			
Grade I	94 (9.3)	5 (10.9)	3 (5.8)
Grade II	542 (53.5)	20 (43.5)	24 (46.2)
Grade III	289 (28.5)	12 (26.1)	17 (32.7)
Grade IV	43 (4.2)	5 (10.9)	2 (3.8)
Grade V	7 (0.7)	-	-
Missing (n (%))	38 (3.8)	4 (8.6)	6 (11.5)
Procedure-related risk factors			
Type of surgery (n (%))			
Right hemicolectomy, closed procedure	285 (28.1)	9 (19.6)	6 (11.5)
Right hemicolectomy, open procedure	129 (12.7)	6 (13.0)	10 (19.3)
Left hemicolectomy, closed procedure	72 (7.1)	1 (2.2)	5 (9.6)
Left hemicolectomy, open procedure	33 (3.3)	3 (6.5)	4 (7.7)
Sigmoid colectomy closed procedure	171 (16.9)	2 (4.3)	5 (9.6)
Sigmoid colectomy open procedure	108 (10.7)	17 (37.0)	9 (17.3)
Low anterior colectomy, closed procedure	168 (16.6)	4 (8.7)	12 (23.1)
Low anterior colectomy, open procedure	47 (4.6)	4 (8.7)	1 (1.9)
Surgical approach (n (%))			
Closed	696 (68.7)	16 (34.8)	28 (53.8)
Open	317 (31.3)	30 (65.2)	24 (46.2)
Duration of surgery in minutes (median (IQR)) [a]	132 (68)	143 (64)	137 (56)
Missing (n (%))	11 (1.1)	-	-
Emergency (n (%)) [b]			
Yes	124 (18.8)	13 (48.1)	12 (40.0)
No	528 (80.1)	14 (51.9)	18 (60.0)
Missing (n (%))	7 (1.1)	-	-
Wound class (n (%)) [c]			
Clean-Contaminated (class 2)	724 (81.0)	20 (58.8)	26 (63.4)
Contaminated (class 3)	104 (11.6)	2 (5.9)	7 (17.1)
Dirty-infected (class 4)	65 (7.3)	11 (32.4)	8 (19.5)
Missing (n (%))	1 (0.1)	1 (2.9)	-
Malignancy (n (%))			
Yes	695 (68.6)	24 (52.2)	33 (63.5)
No	243 (24.0)	20 (43.5)	16 (30.8)
Missing (n (%))	75 (7.4)	2 (4.3)	3 (5.8)
Stoma (n (%))			
Yes	233 (23.0)	28 (60.9)	22 (42.3)
No	780 (77.0)	18 (39.1)	30 (57.7)

Table 5.2. (Continued)

	No SSI (n = 1,013)	Superficial SSI (n = 46)	Deep SSI (n = 52)
Post-operative risk factors			
30-day mortality (n (%)) [d]			
Yes	28 (3.8)	1 (3.2)	4 (10.5)
No	703 (96.2)	30 (96.8)	34 (89.5)
ICU admission (n (%)) [e]			
Yes	162 (24.6)	11 (40.7)	16 (53.3)
No	497 (75.4)	16 (59.3)	14 (46.7)
Microbiology			
Microorganism (n (%))			
No microorganism identified or no culture taken	NA	28 (60.9)	15 (28.8)
Positive culture [f]	NA	18 (39.1)	37 (71.2)
Escherichia coli		6 (25.0)	20 (31.3)
Enterococcus faecalis		2 (8.3)	7 (10.9)
Enterococcus faecium		3 (12.5)	6 (9.3)
Pseudomonas aeruginosa		5 (20.8)	6 (9.3)
Klebsiella pneumonia		1 (4.2)	4 (6.3)
Staphylococcus aureus		2 (8.3)	0 (0.0)
Other		5 (20.9)	21 (32.9)

[a] Not available for hospital F.
[b] Not available for hospital D, E and G, so percentage was calculated without these hospitals.
[c] Not available for hospital F, so percentage was calculated without this hospital.
[d] Not available for hospital E and G, so percentage was calculated excluding these hospitals.
[e] Not available for hospital D, E and G, so percentage was calculated excluding these hospitals.
[f] Percentage was calculated relative to the total number of cultured microorganisms.
Abbreviations: SSI = surgical site infection; n = number; SD = standard deviation; BMI = body mass index; ASA = American Society of Anesthesiologists; IQR = Interquartile range; ICU = Intensive Care Unit; NA = not applicable.

Reliability and validity

All 14 raters completed the two rounds of online questionnaire with case-vignettes. Of those, two had less than one year of experience with HAI surveillance, six had 2 – 5 years of experience, five persons 6 – 15 years and one more than 25 years. The estimated Cohen's Kappa for agreement within a rater (intra-rater reliability) calculated from the case-vignette assessment varied from 0.73 to 1.00, indicating substantial to perfect agreement (**Table 5.3**). The inter-rater reliability within hospitals showed more variation, with lowest estimates reported for hospital A ($\kappa = 0.61$; 95% CI 0.23 – 0.83) and the highest in hospital C ($\kappa = 0.94$; 95% CI 0.75 – 1.00). The overall inter-rater agreement of all 14 raters in the second round case-vignettes was 0.72 (95% CI 0.59 – 0.83). From the local case assessment it was estimated that the overall percent agreement between raters within a hospital was almost perfect (mean = 95%; range 90% – 100%). Regarding the accuracy of determining SSIs correctly, 87.9% (range 70% – 95%) of the answers given by the raters were in accordance with the medical panel:

three raters had similar SSI rates compared to the medical panel, five raters underestimated the number of SSIs, four had higher SSI rates because of incorrect ascertainment and there were two raters who had overestimated SSI in the first round, and an underestimation in the second round. Presence of anastomotic leakage was accurately scored in the vignettes where it was present, however misclassified in cases where anastomotic leakage was absent (**Table 5.3**).

DISCUSSION

In this study we observed good reliability of SSI surveillance after colorectal surgeries in seven Dutch hospitals. Based on the case-vignette assessment, the intra-rater reliability was estimated substantial to perfect (κ = 0.71 – 1.00) and the inter-rater agreement within hospitals was substantial, but varied between hospitals (κ = 0.61 – 0.94). The local case assessment showed 95% agreement within hospitals. Despite the fact that individual raters were consistent in their scoring, validity was moderate: in 12.1% (range 5% – 30%) the case-ascertainment was not correct as compared to the conclusions of the medical panel. The SSI rate determined by surveillance would therefore be under- or overestimated.

To the best of our knowledge, there is only one other study assessing the inter-rater reliability explicitly for SSI after colorectal surgeries. Hedrick et al.[18] concluded from their results that SSIs could not reliable be assigned and reproduced: they demonstrated large variation in SSI incidence between raters with only modest inter-rater reliability (i.e. κ = 0.64). They therefore opt for alternative definitions such as the ASEPSIS score.[33] In the present study similar estimates for inter-reliability were found in 2 out of 7 hospitals (κ = 0.61 in hospital A and κ = 0.65 in hospital E), for the other five hospital we found estimates above 0.69. The higher reliability estimates found in the present study may be explained by several factors. First, the definitions and method used in the Netherlands aim to be more objective: a previous study has shown that surgeon's diagnosis – not included the Dutch definition – lead to biased results.[34,35] Another factor that may influence reliability is the years of surveillance experience of the raters and their ability to find information in the electronic health records needed for case-ascertainment.[36] From **Table 5.3** it seems that more experienced raters produce more consistent results. However, the design of this study did not allow to investigate this type of causal relationships.

The reliability estimates of this study show that SSIs after colorectal surgery are an appropriate measure to use for surveillance: the same result can be consistently achieved, making them

Table 5.3. Intra-rater-, inter-rater reliability and accuracy measured by two questionnaire rounds of 20 case vignettes each.

		Years of working experience in infectious disease surveillance	Intra-rater reliability (κ (95% CI))#	Inter-rater reliability per hospital (κ (95% CI))#	Accuracy (%, First round/ Second round)	Accuracy in determination of presence of anastomotic leakage, n=4. (%, First round/ Second round)	Accuracy in determination of absence of anastomotic leakage, n=16. (%, First round/ Second round)
Hospital A	Rater 1	4 – 5	0.78 (0.46 – 1.00)	0.61 (0.23 – 0.83)	95/85	75/100	93/87
Hospital A	Rater 2	2 – 3	0.95 (0.74 – 1.00)		85/80	100/75	93/93
Hospital B	Rater 1	11 – 15	0.83 (0.49 – 0.99)	0.72 (0.42 – 1.00)	80/85	75/100	93/93
Hospital B	Rater 2	6 – 10	0.73 (0.44 – 1.00)		95/90	100/100	93/93
Hospital C	Rater 1	11 – 15	1.00 (1.00 – 1.00)	0.94 (0.75 – 1.00)	90/90	75/75	93/93
Hospital C	Rater 2	11 – 15	0.94 (0.76 – 1.00)		90/95	75/75	93/93
Hospital D	Rater 1	0 – 1	0.75 (0.47 – 1.00)	0.69 (0.36 – 0.92)	90/85	100/100	93/87
Hospital D	Rater 2	4 – 5	0.89 (0.72 – 1.00)		90/95	100/100	93/87
Hospital E*	Rater 1	2 – 3	0.89 (0.59 – 1.00)	0.65 (0.38 – 0.92)	80/80	100/100	93/93
Hospital E*	Rater 2	4 – 5	0.73 (0.46 – 1.00)		85/70	100/100	93/81
Hospital F*	Rater 1	2 – 3	0.79 (0.57 – 1.00)	0.69 (0.34 – 0.92)	90/90	100/100	87/81
Hospital F*	Rater 2	11 – 15	0.89 (0.59 – 1.00)		90/90	100/100	87/87
Hospital G*	Rater 1	0 – 1	0.79 (0.55 – 1.00)	0.84 (0.61 – 1.00)	90/90	100/100	87/93
Hospital G*	Rater 2	> 25	0.94 (0.75 – 1.00)		95/90	100/100	93/93

* Hospitals that started surveillance for the purpose of this study.
# Inter-rater reliability was calculated from the second round questionnaire case vignettes.
Abbreviations: κ = Cohen's Kappa coefficient; 95% CI = 95% confidence interval; n = number.

reproducible and suitable for monitoring trends and detecting changes in SSI rates within a hospital. However, at this moment, using SSI incidence as a quality measure for benchmarking may be hampered because of three reasons. First, we found that on average 12.1% of patients in the case-vignettes were misclassified: one rater misclassified 6 out of 20 vignettes while another had only one misclassification. This will lead to unreliable comparisons of SSI rates, although in practice difficult cases may be discussed in a team hence improving accuracy. As superficial SSIs rely on more subjective criteria, focusing on deep SSI may improve accuracy and comparability. Additionally, we observed that anastomotic leakage was too often assigned while it was actually absent. This may lead to an underestimation as these cases cannot be scored by a positive culture anymore according to the Dutch definition (as explained in the introduction). Second, Kao et al.[16] and Lawson et al.[15] investigated whether SSI surveillance after colorectal surgeries has good ability to differentiate high and low quality performance (i.e. the statistical reliability of SSIs). They both concluded that the measure can only be used as hospital quality measure when an adequate number of cases have been reported, which can be challenging for some hospitals as shown in **Table 5.1**. Third, another challenge in using SSI rates for interhospital comparisons is the lack of a sufficient method for risk adjustment. To obtain valid SSI comparisons, you have to correct for differences in the surveillance population and their risk factors. However, to date no method has been proven generalisable and appropriate.[12,37] The points raised above show that the overall SSI incidence of 8.8% in this study is difficult to compare to others. Overall, the SSI incidence was lower compared to other studies, but in line with numbers previously reported to the Dutch national surveillance network.[13,38,39]

When SSIs after colorectal surgery are used for monitoring and perhaps benchmarking, continuous training of raters is required to assure correct use and alignment of surveillance definitions and methodology. Reliability and validity of surveillance may be improved by automatisation methods as they can help to support case finding.[40-42] Furthermore, hospitals should perform a certain number of colorectal surgeries to generate representative estimates of performance. If there is no appropriate case-mix correction, comparisons should be made with caution, preferably between similar types of hospitals with comparable patient groups.

Strengths and limitations

This study was performed within multiple Dutch centres, including different types of hospitals. The 14 raters in this study were well-trained according to standardised methods to minimalise differences possibly caused by years of surveillance experiences between hospitals. Unfortunately, this design was not suitable for explaining which factors enhance SSI-ascertainment or will improve reliability and validity estimates. Second, we aimed to produce

Cohen's Kappa coefficients from the local case assessment as well, however it appeared that there was too little variation in outcomes and number of cases hindering this calculation.

Conclusion

Awareness of the validity of surveillance and vulnerability to inter-rater variation is crucial for correct interpretation and use of surveillance data. This study showed that raters were consistent in their SSI-ascertainment, but improvements can be made regarding the accuracy. Hence, SSI surveillance results for colorectal surgery are reproducible and thus suitable for monitoring trends, but not necessarily correct and therefore less adequate for benchmarking. Based on prior literature, accuracy of surveillance may be improved by providing regular training, adapting definitions to reduce subjectivity, and by supporting case finding by automation.

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ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The Medical Ethical Committee of the University Medical Centre Utrecht approved this study and waived the requirement of informed consent (reference number 19-493/C).

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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AUTHORS' CONTRIBUTIONS

JV conceptualised and designed the study, was responsible for the data management, analyses and interpretation and wrote the first draft of the manuscript. SvR and MvM participated in conceptualisation, study designing and manuscript drafting. DH, HW, AV, CM, ER, EH, SV and MB reviewed the manuscript for intellectual content and scientific integrity. All authors read and approved the final manuscript.

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6

Contribution of prior, multiple- and repetitive surgeries to the risk of surgical site infections in the Netherlands

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ABSTRACT

Objective: Surveillance is an important strategy to reduce the incidence of surgical site infections (SSIs). We investigated whether prior, multiple-, or repetitive surgeries are risk factors for SSI, and whether they should be preserved in the protocol of the Dutch national SSI surveillance network.

Methods: Dutch national SSI surveillance data 2012 – 2015 were selected, including 34 commonly performed procedures from 8 major surgical specialties. Definitions of SSIs followed international standardised criteria. We used multivariable multilevel logistic regression techniques to evaluate whether prior, multiple-, or repetitive procedure(s) are risk factors for SSIs. We considered surgeries clustered within partnerships of medical specialists and within hospitals (random effects) and different baseline risks between surgical specialties (fixed effects). Several patient and surgical characteristics were considered possible confounders and were included where necessary. We performed analyses for superficial and deep SSIs combined as well as separately.

Results: In total, 115,943 surgeries were reported by 85 hospitals; among them, 2,960 (2.6%) resulted in SSIs (49.3% deep SSIs). The odds ratio (OR) for having prior surgery was 0.94 (95% confidence interval (CI) 0.74 – 1.20); the OR for repetitive surgery was 2.39 (95% CI 2.06 – 2.77); and the OR for multiple surgeries was 1.27 (95% CI 1.07 – 1.51). The latter effect mainly caused by prolonged duration of surgery.

Conclusions: Multiple- and repetitive surgeries significantly increased the risk of an SSI, whereas prior surgery did not. Therefore, prior surgery is not an essential data item to include in the national SSI surveillance network. The increased risk of SSIs for multiple surgeries was mainly caused by prolonged duration of surgery, therefore, it may be sufficient to report only duration of surgery to the surveillance network, instead of both (the variables duration of surgery and multiple surgeries).

INTRODUCTION

Surgical site infections (SSIs) are among the most common healthcare-associated infections (HAIs), and they occur in approximately 3% of all surgical patients.[1,2] The highest incidence of SSI has been described in colorectal surgery, with incidence rates as high as 30%.[3-7] The cumulative incidence of SSI varies by the type of surgical procedure, by hospital, and by the quality of data collection; it also depends on the criteria used to define the infection.[8,9] SSIs are a major concern, because they lead to increased morbidity and mortality, longer hospital stays, and higher costs.[10,11] In addition, the emergence of antibiotic-resistant strains, the increased use of nonhuman implants in surgical procedures and an ageing patient population with high morbidity are making infection prevention practices more complicated.[12-14]

Surgical site infection surveillance is an essential step in identifying local problems and priorities and in evaluating the effectiveness of infection prevention activities.[15] Research has shown that SSI surveillance results in enhanced infection prevention control actions and interventions leading to a significant reduction of SSIs.[16,17] In the Netherlands, the Dutch surveillance network for healthcare-associated infections PREZIES (Dutch acronym for 'PREventie van ZIEkenhuisinfecties door Surveillance') monitors the cumulative SSI incidence and SSI risk factors.[18]

Within the PREZIES network, patient-related, procedure-related, and post-operative risk factors are collected for a set of index-surgeries to interpret national trends and comparisons between hospitals (**Table 6.1**).[12] Some risk factors, however, are presumed rather than established risk factors. For instance, the variables 'prior surgery', 'multiple surgical procedures' and 'repetitive surgeries' are included in the surveillance network, but their direct association with the occurrence of SSIs has not yet been adequately studied (**Table 6.1**).

Table 6.1. Definitions as used in the PREZIES protocol of the Dutch SSI surveillance (2014, version 1.0).[18]

Index-surgery
The first (or primary) surgery to an organ or body structure (i.e. bone, joint, vessel) ever. Restricted to a list of 34 surgical procedures, see **Supplemental Table S6.1**. Previous minimally invasive procedures to the same organ or body structure as the index-surgery (such as keyhole surgeries, biopsies or inserting stents) are allowed (see definition Prior surgery). If a patient has two different surgical procedures performed at the same time, only one surgical procedure is included in the surveillance. The surgeon decides which procedure serves as index-surgery.
Prior surgery
Small minimally invasive procedures to the *same organ or body structure* (i.e. bone, joint, vessel) as the index-surgery, performed during the year prior to the index-surgery. For instance keyhole surgeries, biopsies or inserting stents.

Table 6.1. (Continued)

Examples: meniscectomy prior to total knee replacement, insertion of a pacemaker prior to Coronary Artery Bypass Grafting.
Additional for abdominal procedures: Any small or large surgical procedure performed during the year prior to the index-surgery, not to exactly the same organ or body structure (i.e. joint, vessel) as the index surgery, but still in the *abdominal region. Example: a Caesarean Section 6 months prior to a colectomy is reported as a prior surgery.*
Multiple surgery(ies) Additional surgical procedures performed during the index-operation, performed in the *same surgical area* as the index-surgery (through the same incision). *Example: tubal ligation performed during Caesarean Section.*
Repetitive surgery A surgical procedure, for any reason other than SSI, within the follow-up period of the index-surgery, performed in the *same surgical area* as where the index-surgery has been performed (through or just next to the old incision). *Examples: dislocation following total hip replacement, anastomotic leakage following colectomy.*

Because the workload related to data collection for surveillance is burdensome, it is essential to incorporate only important risk factors that are easy to measure. Doing so would not only result in a reduced workload for hospital personnel but also would improve the willingness of healthcare facilities to participate in the surveillance network. In this study, we investigated whether prior, multiple-, and repetitive surgeries are relevant risk factors for SSIs, and we sought to determine whether data pertaining to these factors should continue to be collected in the Dutch national surveillance network.

MATERIALS AND METHODS

Participants and data collection

For this observational cohort study, we used PREZIES SSI surveillance data from January 2012 to January 2015. Details of the surveillance have been described previously.[19,20] In short, the PREZIES surveillance database contains prospectively collected data of 34 commonly performed surgical procedures (i.e., so-called index-surgeries, **Supplemental Table S6.1**) of 8 major surgical specialties: cardiovascular, breast, gastro-intestinal, vascular, orthopaedic surgeries, gynaecology, neurosurgery, and cosmetic surgeries.[18,19] For each surgical procedure under surveillance, data concerning the patient, surgery, and infection were collected in a prospective manner according to the surveillance protocol by trained infection prevention professionals and medical microbiologists.[17,18] Retrospective on-site validation was performed by the PREZIES team.[18] Hospitals can report the causative microorganism; however, this is not mandatory because the diagnosis of SSI can be based on clinical symptoms alone (**Table**

6.2). Participation in the surveillance network is voluntary for all healthcare facilities in the Netherlands, including university hospitals, general hospitals, and private medical centres (hereafter, cumulatively referred to as hospitals). In addition, hospitals are free to choose when and how long they participate in the surveillance network and which surgical procedures they report.

Table 6.2. Definitions used to diagnose surgical site infections in the Dutch SSI surveillance. Reprinted from the PREZIES protocol (2014, version 1.0).[18]

Superficial incisional SSI
Infection occurs within 30 days after surgery, and infection involves only skin or subcutaneous tissue of the incision, and at least one of the following: 1. Purulent drainage from the superficial incision 2. At least one of the following signs or symptoms: pain or tenderness, localised swelling, erythema, or heat, AND Microorganisms isolated from an aseptically obtained culture from the superficial incision 3. At least one of the following signs or symptoms: pain or tenderness, localised swelling, erythema, or heat, AND Superficial incision is deliberately opened by the surgeon (not applicable if culture-negative incision)
Deep incisional SSI
Infection occurs within 30 days after surgery if no implant is left in place, or within 1 year if an implant is in place and the infection is related to the surgery. Infection involves deep soft tissues (e.g., fascial and muscle layers) of the incision and at least one of the following: 1. Purulent drainage from the deep incision, excluding organ/space[#] 2. An abscess or other evidence of infection involving the deep soft tissues is found on direct examination, during repetitive operation, or by histopathologic or radiological examination[*] 3. At least one of the following signs or symptoms: pain or tenderness, localised swelling, erythema, heat, or fever (> 38°C), AND A deep incision that spontaneously dehisces or is deliberately opened by a surgeon (a culture-negative finding does not meet this criterion)[$]
Organ/space SSI*
Infection occurs within 30 days after surgery if no implant is left in place or within 1 year if an implant is in place. Infection involves any part of the anatomy (e.g., organs or organ spaces), which was opened or manipulated during an operation and at least one of the following: 1. Purulent drainage from a drain that is placed through the stab wound into the organ/ space 2. An abscess or other evidence of infection involving organ/space, which is found on direct examination, during repetitive surgery, or by histopathologic or radiological examination 3. Microorganisms isolated from an aseptically obtained culture from the organ/space[$]

[#] Report infection that involves both superficial and deep incision sites as a deep incisional SSI.
[*] Report an organ/space SSI that drains through the incision as a deep incisional SSI.
[$] Not applicable for colectomy followed by anastomotic leakage or perforation.

Due to the increase in outpatient care, same-day surgery, and shorter hospitalisations, many SSIs develop post discharge.[20-23] To detect post-discharge SSIs, two standardised methods of post-discharge surveillance were chosen by PREZIES and were mandatory.[20,22,24] For all surgeries included in surveillance, a follow-up period of 30 days was required. This follow-up period was extended to 1 year for deep SSIs if a nonhuman implant was used. The surveillance ended (1) if the follow-up period was completed; (2) if a deep SSI was diagnosed; or (3) the patient died.

Definitions and outcome

In total, 34 types of index-surgeries can be included for surveillance. The definition of an index-surgery is given in **Table 6.1**.[18] Operation types with at least 100 completed records were included.

The risk factors under investigation in this study were 'prior surgery', 'multiple surgical procedures' and 'repetitive surgery'. Detailed definitions for these variables are summarised in **Table 6.1**.[18] In short, prior surgery is a surgery performed within 1 year prior to the index surgery. Multiple surgical procedures refer to an additional surgical procedure performed during the index surgery. In case of multiple index surgeries, the designation of the primary index surgery is left to the discretion of the surgeon. Repetitive surgeries are defined as a reoperation for any reason other than an SSI.

The primary end point of this study was the cumulative incidence of SSI as defined by criteria from the (European) Centers for Disease Control and Prevention ((E)CDC), translated and modified by PREZIES (**Table 6.2**).[18,25-27] Organ-space and deep SSIs are grouped under the umbrella term 'deep SSI' because, in practice, it is difficult to distinguish deep SSIs from organ-space SSIs.[18,28] In this study, 3 outcomes were considered. The first outcome was the cumulative incidence of SSIs (total), which indicates the development of an SSI regardless of the type of infection (deep or superficial). In addition, as secondary outcomes, we used the incidences of superficial SSIs and deep SSIs, respectively, to determine whether risk factors are different for these types of infection.[8,29,30]

Statistical analyses

Results are reported as medians and means for continuous variables and as frequencies and proportions for categorical variables. Box-and-whisker-plots were generated to describe the distribution of SSIs for the 8 selected specialties.

We used multivariable multilevel logistic models to estimate the odds of an SSI due to prior, multiple-, or repetitive surgeries. We considered possible clustering of the data by adding random effects of the combination of surgical specialty and hospital, thereby creating partnerships of surgical specialties within hospitals. Surgical specialty was added as fixed effect to the model to correct for the baseline differences in SSI risk per type of surgical specialty. Possible confounders were selected based on literature and clinical judgment and were tested using a stepwise forward selection method. If a covariate changed the odds ratio (OR) by 10% or more, this variable was considered a confounder and was included in the final model. For all three potential risk factors, the following possible confounders were considered: age, gender, body mass index (BMI), normal body temperature during the surgery (normothermia), wound class, American Society of Anesthesiologists (ASA) class, malignancy and the use of an implant in surgery. In addition, for the analyses focusing on prior surgery and repetitive surgery, the possible confounder duration of surgery was also investigated. In addition, for repetitive surgery, the variables prior surgery and multiple surgeries were considered additional potential confounders: for multiple surgeries, the possible influence of prior surgery and repetitive surgeries was examined. For multiple surgeries, the influence of the duration of surgery was additionally analysed because, with more operational procedures in one session, the operation time is likely to be longer. Therefore, we investigated the extent to which the relationships among these factors could influence the results. Odds ratios and 95% confidence intervals (95% CI) were calculated for the three outcomes: total SSI, superficial SSI and deep SSI.

For the sensitivity analysis, the analyses for superficial and deep SSIs were repeated after excluding breast surgeries. Because it is notoriously difficult to distinguish superficial SSIs from deep SSIs in breast surgeries without implants, the results of analysing deep and superficial SSIs separately may not be reliable for this specialty. Therefore, we repeated the separate analyses for deep and superficial infections excluding all breast surgeries.

Descriptive analyses were performed using SPSS version 22.0 software (SPSS, Chicago, IL). The multivariable multilevel models were analysed using SAS version 9.3 software (SAS Institute, Cary, NC). A $p \leq 0.05$ was considered statistically significant.

RESULTS

In total, 115,944 surgeries were reported between January 2012 and January 2015 in the PREZIES database. Only surgical procedures reported more than 100 times were included for analysis, resulting in the inclusion of 115,943 surgeries of 7 specialties reported by 85 hospitals. Among the included surgeries, 2,960 (2.6%) SSIs were diagnosed: 1,502 of these

(50.7%) were superficial and 1,458 (49.3%) were deep SSIs. In 1,170 deep SSIs (80.2%) and 906 superficial SSIs (60.3%), a causative organism was reported.

Table 6.3 shows the baseline characteristics for the included surgeries, stratified by the three investigated risk factors. Box-and-whisker-plots (**Figure 6.1**) illustrate SSI incidences for each surgical specialty. The highest SSI incidences were found in gastrointestinal surgery, followed by vascular and breast surgery. For vascular operational procedures, two hospitals had exceptionally high infection rates (24.5% and 25.0%), but had reported only 49 and 20 surgeries respectively (data not shown).

Data regarding prior surgery were available for 108,618 patients. Of 3,511 patients with a prior surgery 87 (2.5%) developed an SSI compared to 2,757 of 105,107 patients without prior surgeries (2.6%). Prior surgery was more often performed on women, due to the high number of caesarean sections and hysterectomies. We found no significant association between prior surgery and the development of SSIs (either deep, superficial or both combined (i.e. total SSI)), and no confounders were detected (**Table 6.4**).

Having had multiple surgeries during the index-surgery was positively associated with prior surgery, repetitive surgery, suspicion of malignancy, and an increased mean duration of surgery. Of 3,542 patients with multiple surgeries, 178 (5.0%) developed an SSI, compared to 2,782 of 112,401 (2.5%) in the group without multiple surgeries. An increased OR of developing an SSI was found for patients having multiple surgeries, which was significant for deep SSIs and all SSIs combined (OR = 1.48; 95% CI 1.17 – 1.88; OR = 1.27; 95% CI 1.07 –1.50, respectively) but was not statistically significant for superficial SSIs (OR = 1.14; 95% CI 0.90 – 1.43). When excluding breast surgeries from the analyses, effects for deep and superficial SSIs became more similar; however, only the result for deep SSIs was statistically significant. After adjusting for duration of surgery in the models, no effect of multiple surgeries on deep SSIs, superficial SSIs, or both was found (OR range = 0.94 – 1.15, data not shown).

Of 115,943 patients, 3,013 underwent a repetitive surgery. In these patients, 236 (8.5%) developed an SSI compared to 2,724 of 112,930 patients (2.4%) in the group without repetitive surgery. For patients who developed an SSI, the median time to repetitive surgery was 6 days versus 13 days for people without an SSI ($p \leq 0.001$). Most repetitive surgeries were reported for breast surgeries. Odds ratios for the relationship between repetitive surgeries and all SSI types (total), superficial SSIS, or deep SSIs were all significantly increased (OR range = 1.73 – 3.44) (**Table 6.4**). After excluding breast surgeries from the analyses, the effects were even stronger. Body mass index was found to confound the relationship between repetitive surgery and superficial SSIs.

Table 6.3. Baseline characteristics of patients, specified for each of the three risk factors under investigation.

	Prior surgery n = 108,618*		Multiple surgeries n = 115,943		Repetitive surgeries n = 115,943	
	Yes	No	Yes	No	Yes	No
Patient characteristics (n (%))	**n = 3,511 (3.2)**	**n = 105,107 (96.8)**	**n = 3,542 (3.1)**	**n = 112,401 (96.9)**	**n = 3,013 (2.6)**	**n = 112,930 (97.4)**
Age (median (range))	61(12 – 95)	65 (2 – 103)	63 (2 – 98)	65 (3 – 103)	66 (15 – 96)	65 (2 – 103)
Male gender	662 (18.9)	31,367 (29.8)	989 (27.9)	32,650 (29.1)	977 (32.4)	32,662 (28.9)
BMI (mean (SD))	27.7 (± 5.4)	27.7 (± 5.1)	27.0 (± 5.2)	27.8 (± 5.2)	26.6 (± 5.1)	27.8 (± 5.2)
ASA classification	3,421 (97.4)	95,807 (91.2)	3,147 (88.8)	103,194 (91.8)	2,587 (85.9)	103,754 (91.9)
Low (I and II)	3,063 (89.5)	82,340 (85.9)	2,658 (84.5)	89,032 (86.3)	2,070 (80.0)	89,620 (86.4)
High (III, IV and V)	358 (10.5)	13,467 (14.1)	489 (15.5)	14,162 (13.7)	517 (20.0)	14,134 (13.6)
Wound class	3,402 (96.9)	97,470 (92.7)	3,160 (89.2)	104,895 (93.3)	2,616 (86.8)	105,439 (93.4)
1	2,766 (81.3)	74,823 (76.8)	1,928 (61.0)	81,241 (77.4)	1,909 (73.0)	81,260 (77.1)
2	562 (16.5)	20,006 (20.5)	1,052 (33.3)	20,993 (20.0)	567 (21.7)	21,478 (20.4)
3	48 (1.4)	1,848 (1.9)	111 (3.5)	1,882 (1.8)	76 (2.9)	1,917 (1.8)
4	26 (0.8)	793 (0.8)	69 (2.2)	779 (0.7)	64 (2.4)	784 (0.7)
Malignancy	3,478 (99.1)	104,208 (99.1)	3,467 (97.9)	111,333 (99.0)	2,979 (98.9)	111,821 (99.0)
Yes	1,618 (46.5)	14,922 (14.3)	1,726 (49.8)	15,586 (14.0)	1,417 (47.6)	15,895 (14.2)
No	1,860 (53.5)	89,286 (85.7)	1,741 (50.2)	95,747 (86.0)	1,562 (52.4)	95,926 (85.8)
Prior surgery			3,378 (95.4)	105,240 (93.6)	2,889 (95.9)	105,729 (93.6)
Yes	NA	NA	566 (16.8)	2,945 (2.8)	228 (7.9)	3,283 (3.1)
No			2,812 (83.2)	102,295 (97.2)	2,661 (92.1)	102,446 (96.9)
Multiple surgeries	3,511 (100)	105,107 (100)			3,013 (100)	11,2930 (100)
Yes	566 (16.1)	2,812 (2.7)	NA	NA	294 (9.8)	3,248 (2.9)
No	2,945 (83.9)	102,295 (97.3)			2,719 (90.2)	109,682 (97.1)
Repetitive surgeries	3511 (100)	105107 (100)	3542 (100)	112401 (100)		
Yes	228 (6.5)	2661 (2.5)	294 (8.3)	2719 (2.4)	NA	NA
No	3283 (93.5)	102446 (97.5)	3248 (91.7)	109682 (97.6)		

Table 6.3. (Continued)

	Prior surgery n = 108,618*		Multiple surgeries n = 115,943		Repetitive surgeries n = 115,943	
	Yes	**No**	**Yes**	**No**	**Yes**	**No**
Surgery-related characteristics (n (%))						
Specialty	3,511 (100)	105,107 (100)	3,542 (100)	112,401 (100)	3,013 (100)	112,930 (100)
Cardiovascular surgery	47 (1.3)	6,485 (6.2)	336 (9.5)	6,201 (5.5)	345 (11.4)	6,192 (5.5)
Breast surgery	1,501 (42.8)	9,845 (9.4)	1,164 (32.9)	10,830 (9.6)	1,062 (35.3)	10,932 (9.7)
Gastro-intestinal surgery	394 (11.2)	19,141 (18.2)	982 (27.7)	19,567 (17.4)	694 (23.0)	19,855 (17.6)
Vascular surgery	47 (1.3)	1,793 (1.7)	188 (5.3)	1,757 (1.6)	110 (3.6)	1,835 (1.6)
Orthopaedic surgery	1,142 (32.5)	50,383 (47.9)	402 (11.3)	54,452 (48.4)	701 (23.3)	54,153 (47.9)
Gynaecological surgery	370 (10.5)	15,861 (15.1)	437 (12.3)	17,907 (15.9)	86 (2.9)	18,258 (16.2)
Neurosurgery	10 (0.3)	1,599 (1.5)	33 (0.9)	1,687 (1.5)	15 (0.5)	1,705 (1.5)
Duration of index-surgery in minutes (mean (SD))	77.6 (± 52.2)	76.1 (± 42.6)	115.4 (± 79.5)	75 (± 40.4)	99.0 (± 60.8)	77.5 (± 42.3)
Implant	3,511 (100)	105,107 (100)	3,542 (100)	112,401 (100)	3,013 (100)	112,930 (100)
Yes	1,313 (37.4)	57,901 (55.1)	1,114 (31.5)	61,518 (54.7)	1,295 (43.0)	61,337 (54.3)
No	2,198 (62.6)	47,206 (44.9)	2,428 (68.5)	50,883 (45.3)	1,718 (57.0)	51,593 (45.7)
Normothermia	3,511 (100)	105,107 (100)	3,542 (100)	112,401 (100)	30,135 (100)	112,930 (100)
Yes	2,165 (61.7)	58,113 (55.3)	2,167 (61.2)	62,184 (55.3)	1,676 (55.6)	62,639 (55.5)
No	183 (5.2)	8,782 (8.4)	216 (6.1)	9,936 (8.8)	180 (6.0)	9,972 (8.8)
Not measured	1,163 (33.1)	38,212 (36.3)	1,159 (32.7)	40,317 (35.9)	1,157 (38.4)	40,319 (35.7)

*Missing: n = 7,325 (6.3%) for prior surgery, due to transfers between hospitals and incomplete patient records.
Abbreviations: n = number; BMI = body mass index; SD = standard deviation; ASA = American Society of Anesthesiologists; NA = not applicable.

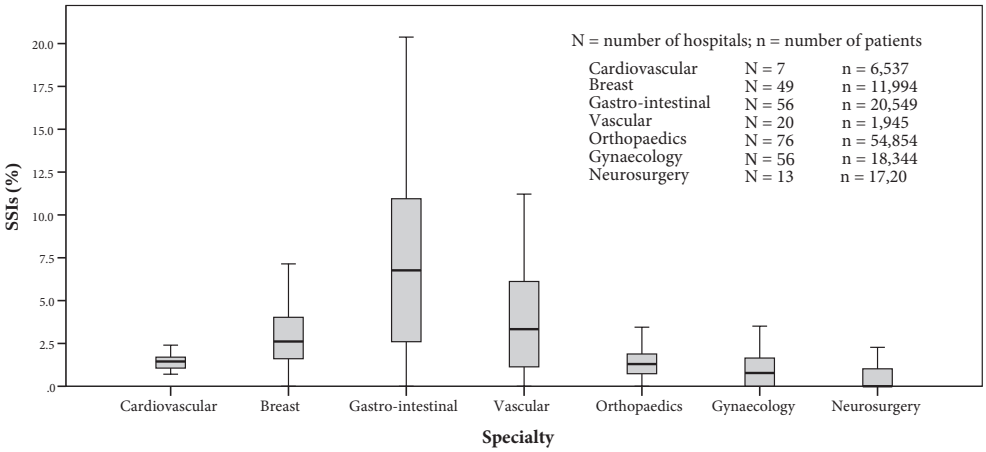

Figure 6.1. Distribution of surgical site infection (SSI) incidence in hospitals per surgical specialty.

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Table 6.4. Results of multivariable multilevel analyses for prior, multiple- and repetitive surgery(ies) on the outcomes of SSI (total, superficial and deep).

	Prior surgery			
(n (%))	**Yes n = 3,511**	**No n = 105,107**	**OR (95% CI) all surgeries**	**OR (95% CI) without breast surgeries**
SSI (Total)	87 (2.4)	2,757 (2.6)	0.94 (0.74 – 1.20)	1.03 (0.79 – 1.36)
Superficial SSI	47 (1.3)	1,397 (1.3)	0.79 (0.56 – 1.10)	0.84 (0.55 – 1.28)
Deep SSI	40 (1.1)	1,360 (1.3)	1.12 (0.81 – 1.57)	1.25 (0.88 – 1.76)
	Multiple surgeries			
	Yes n = 3,542	**No n = 112,401**		
Total SSI	178 (5.0)	2,782 (2.5)	**1.27 (1.07 – 1.50)**	**1.31 (1.08 – 1.58)**
Superficial SSI	92 (2.6)	1,410 (1.3)	1.14 (0.90 – 1.43)	1.28 (0.94 – 1.65)
Deep SSI	86 (2.4)	1,372 (1.2)	**1.48 (1.17 – 1.88)**	**1.37 (1.06 – 1.78)**
	Repetitive surgery			
	Yes n = 3,013	**No n = 112,930**		
Total SSI	236 (7.8)	2,724 (2.4)	**2.31 (1.99 – 2.68)**	**2.99 (2.52 – 3.51)**
Superficial SSI	91 (3.0)	1,411 (1.2)	**1.62 (1.27 – 2.06)***	**2.14 (1.63 – 2.82)****
Deep SSI	145 (4.8)	1,313 (1.2)	**3.44 (2.85 – 4.14)**	**3.95 (3.26 – 4.79)**

* Adjusted for BMI. Non-adjusted OR = 1.57 (95% CI 1.25 – 1.97).
** Adjusted for BMI. Non-adjusted OR = 1.99 (95% CI 1.54 – 2.56).
Abbreviations: n = number; OR = odds ratio; 95% CI = 95% confidence interval; SSI = surgical site infection.

DISCUSSION

The analyses show that multiple- and repetitive surgeries significantly increased the odds of SSIs: ORs were 1.27 and 2.31 for developing deep and superficial SSIs combined respectively, and the OR was even larger for deep SSIs. Having had a prior surgery did not, however, significantly increase the odds of SSIs, so we concluded that prior surgery is not a risk factor for the development of an SSI. Because retrieving information about prior surgery(ies) per patient is time-consuming and laborious, we consider it no longer worthwhile to report this variable in our surveillance system.

Patients with multiple procedures during the index surgery had increased odds of developing SSIs. When analysing this association for superficial and deep SSIs separately, we observed a significantly increased and slightly larger risk for deep SSI compared to superficial SSI. When excluding breast surgeries from the analyses, effects found for deep and superficial SSIs became more similar; however, only the risk for deep SSI was statistically significant increased. A possible explanation could be that, with more procedures performed through the same incision during one surgery, more deep tissue is handled and damaged, resulting in a greater risk for deep SSI.[31] Another possibility is that the longer duration of the surgery rather than the secondary procedure itself (compared to patients with a single operation, i.e., only the index surgery) is responsible for the higher odds. A longer duration of surgery has been associated with an increased risk of SSI,[5,7,30,32-35] and with more operational procedures in one session, time between incision and closure is likely to be longer. When we included duration or surgery in the model of multiple surgeries and superficial infections, no effect of multiple surgeries was found. Based on these findings, we concluded that multiple surgeries are an indirect risk factor for developing SSI, and therefore, the related data are useful data to report to the surveillance network. However, when duration of surgery is also reported to the surveillance network, it is worthwhile to consider discontinuing the reporting of multiple surgeries, especially because the duration of surgery is easier to interpret and to report. Additional research with more detailed information about multiple surgeries will be valuable to validate our findings.

Repetitive surgery is reported for SSI surveillance if a patient is reoperated on for any reason other than infection. This study showed that repetitive surgery is a risk factor for SSIs, and this might be explained by the fact that in repetitive surgeries the incision (or the area around the incision) is reopened, resulting in more scar tissue and new opportunities for skin flora to invade the wound. Furthermore, we found that a higher BMI distorts the relation between repetitive surgeries and superficial SSIs.

Strengths and limitations

To the best of our knowledge, this study is the first multicentre study investigating the effect of prior, multiple-, and repetitive surgeries on SSIs, including several surgical specialties. A major strength of this study is that the Dutch surveillance network consists of many general hospitals, as well as university hospitals and private medical centres, providing a good reflection of care institutions in the Netherlands. In addition, mandatory standardised post-discharge surveillance methods were used in all of these hospitals. Thanks to the large study population, sound statistical methodology and the use of standardised definitions for SSIs, we believe that reliable and robust results were achieved.

This study has several limitations. First, despite the broad range of patient- and procedure-related data collected for surveillance, additional factors may contribute to SSI incidence that are not reported for surveillance, such as surgeon expertise and organisational and environmental factors. However, these factors are hospital specific and difficult to measure, and little is known about the actual adherence of individual surgeons to guidelines and work agreements. Secondly, surveillance data rely on the ability of surveillance personnel to find and report data consistently and correctly.[14] For example, we have become aware that, for breast surgeries without implants, it is very difficult to distinguish deep SSIs from superficial SSIs, and assigning SSIs for this type of surgery to either deep of superficial is, in fact, unreliable. Therefore, currently, the PREZIES network has stopped distinguishing deep from superficial SSIs for this type of surgery. For the interpretation for deep and superficial SSI, therefore, the analyses excluding breast surgeries are preferable. Third, some heterogeneous surgical procedure types are included in surgical specialties; the risk for may not be increased for all index surgeries within a specialty. Finally, we are aware that some variables might be interpreted differently by hospital personnel. Although large abnormalities can be identified through validation of the data, some small errors will always remain. Nevertheless, we assume that a few misinterpretations of the protocol in such a large national surveillance network will not significantly modify the associations we found.

Future recommendations

Future studies should be conducted to determine the risk differences in developing SSIs considering timing and the type of reoperation. We could not determine whether all types of reoperations and the timing of them are equally important because data regarding the type and reason to perform a repetitive surgery were not available for all specialties. Further investigation is needed to determine whether reporting repetitive surgeries for surveillance purposes can be simplified, or whether reporting is needed for only a selection of surgical

procedures. If such a customised surveillance is possible, SSI surveillance will be more efficient.

In conclusion, we aimed to optimise the current SSI surveillance system in the Netherlands by investigating whether prior, multiple-, and repetitive surgery(-ies) are true risk factors for SSI. Multiple- and repetitive surgeries significantly increased the overall odds of an SSI, whereas a prior surgery did not. Because retrieving information about prior surgeries is time-consuming and laborious, we consider it no longer worthwhile to report this data to the surveillance network, and therefore, we have excluded this variable from the Dutch SSI surveillance protocol. Additionally, we found that reporting multiple surgeries is not required for surveillance if duration of surgery has already been reported. Other national SSI surveillance protocols could also consider removing prior surgery as well as multiple surgeries when duration of surgery is included in the surveillance data.

ACKNOWLEDGEMENTS

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None reported.

POTENTIAL CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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SUPPLEMENTARY MATERIAL

Supplemental Table S6.1. Overview of the 34 operation types included in the Dutch surveillance protocol and their infection rates.

Specialism	Code in PREZIES	Description	Number of surgeries (n (%))	SSI (n (%))
Cardiovascular surgery n = 6,537	BYPASS	Coronary Artery Bypass Grafting (CABG)	4017 (61.5)	63 (1.6)
	KLEPOP	Aortic valve replacement, open procedure	1487 (22.7)	10 (0.7)
	KLEPGS	Aortic valve replacement, endoscopic procedure	167 (2.6)	0 (0.0)
	BYPKLP	Combined CABG and aortic valve replacement	866 (13.2)	15 (1.7)
	PACICD	Pacemaker/Implantable cardioverter defibrillator surgery	0 (0)	-
Breast surgery N=11,994	MAMABL	Mastectomy	5109 (42.6)	204 (4.0)
	MAMLUM	Lumpectomy	6885 (57.4)	132 (1.9)
Gastro-intestinal surgery n = 20,549	COREOP	Right hemicolectomy, open procedure	2026 (9.9)	281 (13.8)
	COREGS	Right hemicolectomy, laparoscopic procedure	1563 (7.6)	154 (9.8)
	COLIOP	Left hemicolectomy, open procedure	585 (2.9)	95 (16.2)
	COLIGS	Left hemicolectomy, laparoscopic procedure	480 (2.3)	54 (11.2)
	SIGMOP	Sigmoidectomy, open procedure	992 (4.8)	198 (20.0)
	SIGMGS	Sigmoidectomy, laparoscopic procedure	1175 (5.7)	102 (8.7)
	LOWAOP	Low anterior resection, open procedure	584 (2.8)	96 (16.4)
	LOWAGS	Low anterior resection, laparoscopic procedure	817 (4.0)	97 (11.9)
	CHOLOP	Cholecystectomy, open procedure	334 (1.6)	29 (8.7)
	CHOLGS	Cholecystectomy, laparoscopic procedure	9990 (48.6)	215 (2.2)
	APPEOP	Appendectomy, open procedure	818 (4.0)	25 (3.1)
	APPEGS	Appendectomy, laparoscopic procedure	1185 (5.8)	24 (2.1)
Vascular surgery n =1,945	RCAOOP	Aortoiliac bypass, open procedure	440 (22.6)	13 (3.0)
	RCAOEN	Aortoiliac bypass, laparoscopic procedure	317 (16.3)	3 (0.9)
	BLVBUI	Reconstruction of other abdominal blood vessels	409 (21.0)	4 (1.0)
	FEMBYP	Femoropopliteal or femoro-crural bypass, open procedure	463 (23.8)	63 (13.6)
	DESFEM	Desobstruction common femoral artery, open procedure	316 (16.2)	11 (3.5%)

Supplemental Table S6.1. (Continued)

Specialism	Code in PREZIES	Description	Number of surgeries (n (%))	SSI (n (%))
Orthopaedic surgery n = 54,854	HEUPPR	Total hip replacement	27645 (50.4)	434 (1.6)
	KOPHAL	Partial hip replacement	3964 (7.2)	153 (3.7)
	KNIEPR	Total knee replacement	23245 (42.4)	259 (1.1)
Gynaecological surgery n = 18,344	ABDUTE	Abdominal hysterectomy	1860 (10.1)	26 (1.4)
	VAGUTE	Vaginal hysterectomy	1098 (6.0)	12 (1.1)
	PROLUT	Vaginal hysterectomy with prolapse repair	553 (3.0)	2 (0.4)
	SECTIO	Caesarean section	14833 (80.8)	173 (1.2)
Neurosurgery n = 1,720	LAMINE	Laminectomy	1720 (100.0)	12 (0.7)
Cosmetic surgery n = 1	BORSTZ	Breast augmentation without lifting	1 (100.0)	0 (0.0)
	BORSTM	Breast augmentation with lifting	0 (0.0)	-

PART III

Towards (semi-)automated surveillance of healthcare-associated infections

7

Automated surveillance systems for healthcare-associated infections: results from a European survey and experiences from real-life utilisation

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ABSTRACT

Background: As most automated surveillance (AS) methods to detect healthcare-associated infections (HAIs) have been developed and implemented in research settings, information about the feasibility of large-scale implementation is scarce.

Aim: To describe key aspects of the design of AS systems and implementation in European institutions and hospitals.

Methods: An online survey was distributed via email in February/March 2019 among 1) PRAISE (Providing a Roadmap for Automated Infection Surveillance in Europe) network members; 2) corresponding authors of peer-reviewed European publications on existing AS systems; and 3) the mailing list of national infection prevention and control focal points of the European Centre for Disease Prevention and Control. Three AS systems from the survey were selected, based on quintessential features, for in-depth review focusing on implementation in practice.

Findings: Through the survey and the review of three selected AS systems, notable differences regarding the methods, algorithms, data sources and targeted HAIs were identified. The majority of AS systems used a classification algorithm for semi-automated surveillance and targeted HAIs were mostly surgical site infections, urinary tract infections, sepsis or other bloodstream infections. AS systems yielded a reduction of workload for hospital staff. Principal barriers of implementation were strict data security regulations as well as creating and maintaining an information technology infrastructure.

Conclusion: AS in Europe is characterised by heterogeneity in methods and surveillance targets. To allow for comparisons and encourage homogenisation, future publications on AS systems should provide detailed information on source data, methods and the state of implementation.

INTRODUCTION

Healthcare-associated infections (HAIs) are a worldwide concern due to their implications on morbidity, mortality and costs.[1-3] In Europe, annually, around 3.2 million people are affected by HAIs.[4] Surveillance of HAIs is listed as a core component of effective infection prevention and control (IPC) programmes by the World Health Organisation,[5] and has been demonstrated to effectively reduce HAI occurrence.[6-9] Despite the adoption of electronic health records (EHRs), the majority of surveillance activities still rely on manual patient chart review by infection control staff, a process that is often paper-based and resource-intensive.[10, 11] This conventional surveillance is prone to human error as well as low inter-rater reliability.[12-14] The opportunities arising from improved information technology (IT) infrastructures in many hospitals have incentivised the development of automated surveillance (AS) systems to overcome the limitations of traditional manual surveillance.[15, 16]

Surveillance of HAIs can be automated to various degrees, but generally two methods can be distinguished: semi-automated surveillance and fully automated surveillance.[15, 17] In semi-automated surveillance, an algorithm classifies patients in a high-or low probability for certain HAIs. Whereas 'high-probability' patients require a manual confirmation to classify them as having a HAI or not, low-probability patients are assumed to not have HAIs and no manual assessment is performed. The algorithms used in semi-automated surveillance can be classification algorithms or decision trees, comprising of a set of indicators derived from structured data from hospital information systems.[18-21] The selection of indicators incorporated in the algorithms is based on previous experience and clinical knowledge, statistical methods or machine learning techniques.[18, 19, 22-24] For fully automated surveillance, algorithms perform HAI ascertainment without human interference. Algorithms for fully automated surveillance have been developed using (clinical) indicators by various techniques such as statistical models or machine learning, or by using data that represent infection criteria (rule-based algorithms).[25-33] For incorporating unstructured data in the algorithm, text-mining techniques can be used.[27, 34-36] Overall, most published AS methods reduce the workload and some showed even higher sensitivity compared to manual surveillance.[20, 37-39]

Though many AS methods and algorithms show promising results, the majority has been developed and implemented in (single-centre) research settings and information about the feasibility of large-scale implementation is scarce. Research showed that only 25% of the systems are actually used in clinical routine.[39-41] The PRAISE network (Providing a Roadmap for Automated Infection Surveillance in Europe) was established to support the transition to large-scale implementation. This network involved 30 experts from 10 countries, representing different types of institutions, such as hospitals and public health institutes. The PRAISE

network recently developed a roadmap to bring AS from the research setting to large-scale implementation.[17] As part of this project, the network investigated and evaluated AS systems that are currently implemented and in use by means of a survey.

The aim of this study was to describe key aspects of AS systems and implementation thereof in European institutions and hospitals based on survey results. Furthermore, we selected AS systems that were included in the survey and for further elaboration on their distinctive features and real-life implementation challenges.

METHODS

The PRAISE network developed a survey with the main aim to map the current state of AS systems for HAIs in Europe, including existing systems as well as pre-implementation research, and to illustrate key aspects of AS systems (including types of HAIs under surveillance, degree of automation, underlying algorithms), and identify barriers and limitations. Furthermore, the survey aimed to describe extraction and utilisation of raw data (e.g. migration of patient-related data into a data warehouse), and learn about implementation, maintenance and evaluation of AS systems. As a secondary objective, the survey aimed to identify existing AS systems to be selected for a more in-depth investigation through follow-up interviews and complementary literature searches.

In February and March 2019, the survey was distributed among network members via e-mail (purposive sampling). Invitations were also sent to corresponding authors of peer-reviewed publications on AS in Europe published between 2010 and 2019. To achieve maximum dissemination, survey invitees were encouraged to share the survey link with other suitable persons (snowball sampling). Furthermore, the questionnaire was distributed via the mailing list of national IPC focal points of the European Centre for Disease Prevention and Control (ECDC). The survey language was English and contained both multiple choice and free text questions. Data were entered online and data entry was possible from February, 13rd 2019 until July, 22nd 2019. A reminder was sent to all invitees in May 2019. The survey comprised of a maximum of 29 questions that explored different aspects of AS (**Supplemental File S7.1**). Nineteen questions were directly targeted to learn about specifications of existing AS systems, additional questions collected context information.

Only responses from European institutions who fully completed the survey were included. Where more than one response per institution was received ('duplicates'), responses were merged. Free text answers were grouped into thematic groups at the discretion of the study team in order to increase the intelligibility of the content. From the responses received, three AS

systems were selected by the authors, based on quintessential characteristics, to be described in greater detail and to further illustrate the possibilities and variability of AS systems.

RESULTS

A total of 25 responses were transmitted to the PRAISE network. Three responses were excluded due to incompleteness (n = 1) and country of origin outside of Europe (n = 2). In three cases, two responses were attributable to the same institution and therefore merged, leaving 19 responses for further analysis. The data were from 11 countries (The Netherlands (n = 5); France (n = 4); Sweden (n = 2); Austria, Belgium, Denmark, Finland, Germany, Norway, Switzerland, Wales (all n = 1)). Eight responses pertained to a surveillance network, and 11 pertained to a hospital (tertiary care university centres (n = 9); non-university teaching hospitals (n=2)).

Twelve (63%) survey participants reported that AS was in use at their hospital or surveillance network at the time of the survey (surveillance network (n = 5); hospital (n = 7: six university hospital, one non-university hospital)). Seven (37%) participants stated that AS had been considered but was not implemented at the time of the survey (surveillance network (n = 3); hospital (n = 4: three university hospital, one non-university hospital)). Reasons for non-implementation reported by surveillance networks were a lack of data harmonization and willingness of the participating hospitals. Hospitals reported the lack of digitalization of patient data and insufficient IT infrastructure along with low prioritization by hospital management and data security concerns.

Automated surveillance systems

Existing AS systems mostly targeted surgical site infections (SSIs), urinary tract infections (UTIs), central line-associated or -related bloodstream infections, and sepsis or other bloodstream infections (**Figure 7.1**). Whereas four (surveillance network (n = 2); hospital (n = 2)) institutions reported employing a fully automated surveillance method, seven (surveillance network (n = 3); hospital (n = 4)) reported conducting semi-automated surveillance. Information on this aspect was not provided by one institution. Classification models (n = 8) were the most prevalent algorithm type. A machine learning system or regression model was reported by one participant each. Two participants were unable to provide specifics on underlying algorithms. Specifics on the source data included in the AS system are illustrated in **Figure 7.2**. Five AS systems (all from hospitals) reported migration of most or all data sources into a clinical data warehouse, and seven AS systems (surveillance network (n = 5); hospital (n = 2)) relied on collecting data from multiple separate data sources.

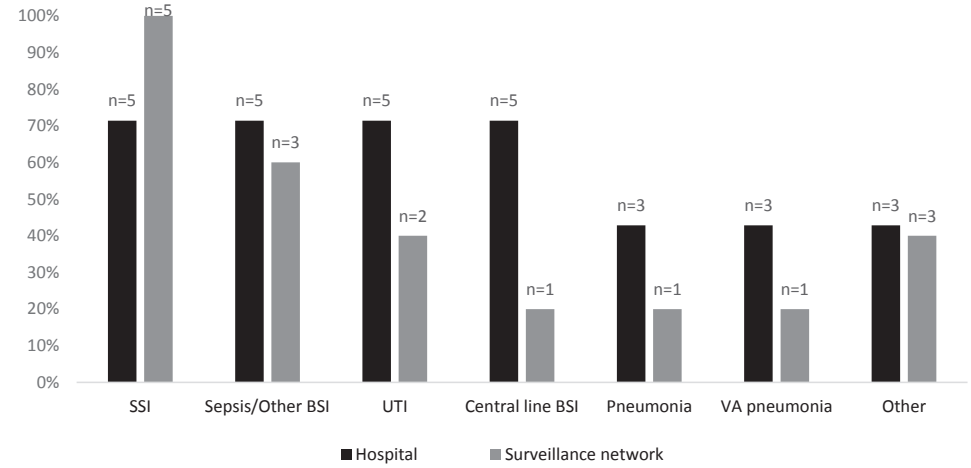

Figure 7.1. Healthcare-associated infections under surveillance in existing automated surveillance systems at the surveillance network (grey bars, n = 5) and hospital level (black bars, n = 7).
Abbreviations: BSI = bloodstream infection; SSI = surgical site infection; UTI = urinary tract infection; VA = ventilator-associated.

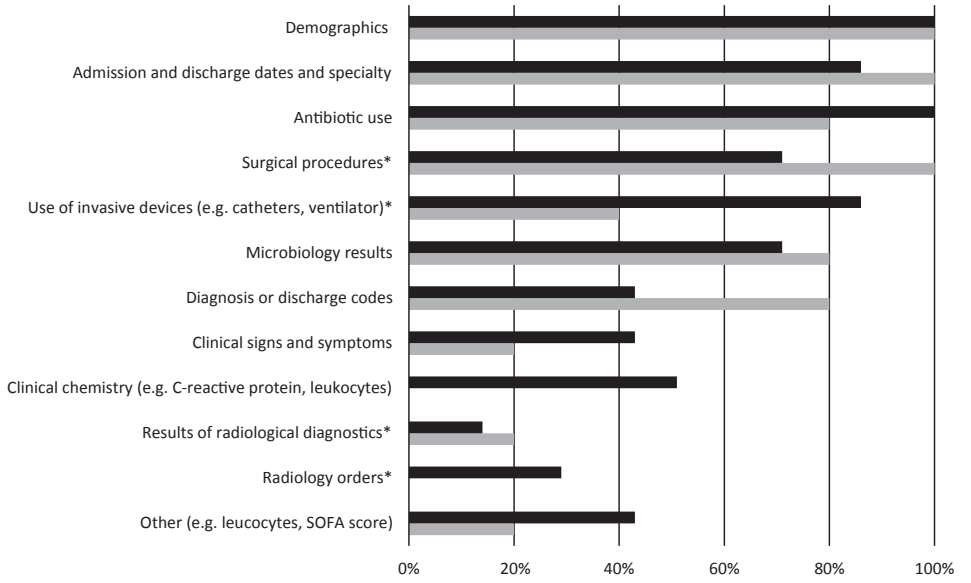

Figure 7.2. Source data types included in existing automated surveillance systems at the surveillance network (grey bars, n = 5) and hospital (black bars, n = 7) level.
* Note that relevance of these data sources depend on the targeted infection (e.g. use of invasive devices is not applicable to surgical site infection surveillance).
Abbreviations: SOFA = Sequential Organ Failure Assessment.

Experience of implementing AS

Table 7.1 summarises experienced advantages of the AS system, key determinants of successful implementation and barriers, as well as potential improvements. Most noticeably, time efficiency and reduction of workload for hospital staff were cited as the most important advantages of AS. Conversely, creation and maintenance of sophisticated IT infrastructures as well as strict data security regulations were reported as the most significant barriers for successful AS implementation.

Table 7.1. Reported experiences of users of semi- and or fully automated surveillance systems at the surveillance network (n = 5) and hospital (n = 7) level.

Topic	Surveillance network	Hospital
Key advantages of automated surveillance systems over manual surveillance systems	• Time efficiency/Reduction of workload • Re-allocation of saved IPC resources • Greater uniformity and validity of data across different hospitals • High acceptance by staff in participating hospitals	• Time efficiency/Reduction of workload • Re-allocation of saved IPC resources • Better involvement of non-IPC staff • Inclusion of larger amounts of data (e.g. more procedures, more types of HAIs) to generate a more comprehensive overview • Higher structural uniformity of collected data • Real-time data view
Key determinants of successful implementation of automated surveillance systems	• Legal regulations (mandatory participation) • Flexibility for participating hospitals with regard to software selection • Clearly defined responsibilities • Frequent exchange with regional/hospital partners • Availability of high quality data	• Support from hospital management • Functioning cooperation with an IT department • Existence of a data warehouse • Exclusion of unnecessary details • Involvement of frontline healthcare workers into the daily workflow
Barriers of successful implementation of automated surveillance systems	• Strict data protection regulations • Heterogeneity of data sources and data quality • Lack of adequate IT infrastructures	• Strict data protection regulations • Difficult accessibility and low quality of data sources • Lack of quality control of source data • Lack of prioritization within hospital
Possible further improvements of implemented automated surveillance systems	• Further integration of data sources • More freedom concerning data protection regulations (e.g. access to non-anonymised data)	• Harmonization with existing (international) HAI definitions • More comprehensive data reporting • Flexibility concerning included data (e.g. in case of outbreaks) • Reduction of manual work processes

Abbreviations: IPC = infection prevention and control; IT = information technology; HAI = healthcare-associated infection.

In-depth view of three existing AS systems

There is a large variety in the methods, algorithms, data sources and targeted HAIs used for AS, complicating head-to-head comparisons. Additionally, information publicly available regarding surveillance systems is not exhaustive, and usually has a technical focus, whereas the process of actual implementation, architecture, maintenance and workflow are generally not systematically published.[42] For these reasons, three successfully implemented AS systems are described in greater detail, focusing on the aspects that are not described in scientific reports.[18, 20, 29, 30, 42, 43] A concise overview of these systems is provided in **Table 7.2**.

Table 7.2. System features and lessons learned from automated surveillance systems HAIBA, semi-automated SSI surveillance (UMCU), and HAI-proactive.

	HAI-proactive	UMCU	HAIBA
Country	Sweden	the Netherlands	Denmark
Year of implementation	Currently being implemented	2015	2015
Administration level	Regional	Local (institutional)	National
Type of system	Fully automated rule-based algorithm	Semi-automated classification tree	Fully automated rule-based algorithm
HAI targets	Hospital-onset sepsis, UTI	Deep-Incisional SSI (after THA, TKA, cardiac, spinal, IO surgeries)	HOB, UTI, CDI, Deep-Incisional SSI (after THA and TKA)
Data sources	Structured/unstructured EHR data	Structured EHR data	Structured data from national registries
Data type included	Microbiology, Antibiotics, Clinical	Administrative, Microbiology, Antibiotics	Administrative, Microbiology
Sensitivity	> 85% compared to manual surveillance	> 95% compared to manual surveillance	36% compared to PPS
Reporting	Manual to healthcare providers	Online dashboard within institution	Automated output reports
Lessons Learned	• Unstructured free text data is useful for finding symptoms • Legislation and data protection regulation can be very time consuming elements in the development and implementation of systems	• Distinction primary and non-primary procedures not always feasible • Collection of risk factor data is limited to those variables documented systematically in the EHR	• Develop a system in close collaboration with the end users. This ensures algorithms and outputs are meaningful and increases trust in the system • Changes in the data sources can have a major impact

Abbreviations: UTI = urinary tract infection; SSI = surgical site infection; EHR = electronic health record; THA = total hip arthroplasty; TKA = total knee arthroplasty; IO = intra-ocular; HOB = hospital-onset bloodstream infection; CDI = *Clostridioides difficile* infection; PPS = point prevalence survey.

Danish Hospital-Associated Infections Database (HAIBA)

Increased attention to HAIs and the increasing threat of antimicrobial resistance has led to the vision of establishing the Healthcare-Associated Infections Database (HAIBA) in Denmark. HAIBA was developed on request of the Danish Ministry of Health by the Statens Serum Institute in collaboration with the Danish Regions, departments of clinical microbiology, infection control units and clinical societies. The first edition of HAIBA was launched in March 2015, and soon became the main tool for monitoring of HAIs in Denmark, replacing the prevalence surveys.[44-46] HAIBA's data are publicly available on www.esundhed.dk, and sent to regional servers, where they are integrated on hospital-intranet pages and in hospital management systems.

Data, algorithms and method of validation

All patients that have been in contact with the Danish healthcare system, both in outpatient and inpatient settings, are included in the HAIBA surveillance system. HAIBA generates incidence data by fully automated surveillance for the following: hospital-onset bacteraemia (i.e. positive blood cultures more than 48 hours after admission), UTIs, *Clostridioides difficile* infections and deep SSIs after total hip and knee replacement.[29, 43, 44] The algorithms are rule-based and use data from existing data sources: 1) the Danish Microbiology Database, a real-time database including all microbiological testing; 2) the National Patient Registry, containing administrative data on admissions and ambulatory contacts with the secondary and tertiary healthcare system, diagnosis codes (Danish adaptation of the ICD-10 classification), and operation codes (Nordic Classification of Surgical Procedures); and 3) the civil registration registry. Data from these registries are linked by a personal health identification number, and are updated, extracted and evaluated by algorithms every night; as a result of the COVID-19 pandemic and competing server capacity, the update frequency has been reduced to weekly. The algorithms were validated by comparing with results from prevalence surveys and manual evaluation of medical records for discrepant cases.

The Danish Health Data Authority maintains the servers. The surveillance system is maintained at Statens Serum Institute, encompassing IT infrastructure (i.e. servers, connections with data sources), applications (i.e. visualization software), adjustment of data model and algorithms to new features in data sources (i.e. new variables, changes in data models, new classification systems such as ICD-10).

Next steps

A change in the Danish law is expected to facilitate data sharing between regions on the level of individual patients. This will further increase the possibilities for applying surveillance data for specific IPC use cases.

Semi-automated SSI surveillance

From 2010 onwards, the University Medical Centre Utrecht (UMCU) has been developing AS of HAIs using internal funds. After an implementation period of two years to prepare the infrastructure, a semi-automated surveillance system was launched in 2015 for surveillance of SSI after orthopaedic and cardiac surgery.

Data, algorithms and method of validation

Patients are automatically included in the surveillance, based on procedure codes for targeted surgical procedures. After a 120-day follow-up period, algorithms are applied to identify patients with a high probability of having developed an SSI in the 90 days following surgery. Manual chart review verifying an SSI is performed for these patients only. Surveillance results are documented in the EHR, and used for feedback to clinicians, both in yearly reports and via an interactive online dashboard.

The source data required for inclusion of patients in the surveillance, application of the algorithm, and some risk factors are extracted from a clinical data warehouse that is maintained by the hospital's IT department. Classification algorithms are applied to administrative data (information about admissions and discharges), antibiotic prescriptions, surgical procedures and results of microbiological testing. Algorithms are run bi-monthly by a local data manager. Maintenance is performed yearly by the infection control department and includes updates of procedure codes, validation of the algorithm and evaluation of IT infrastructure.

Next steps

Development of new algorithms and HAI outcomes is ongoing, in close collaboration with clinical departments. Experiences are being transferred to the national surveillance network 'PREZIES' that is currently preparing a strategy to implement the semi-automated algorithm for SSIs after orthopaedic surgery nationally.[20]

HAI-Proactive

The national innovation project 'HAI-proactive', supported by the Swedish Innovation Agency (VINNOVA), aims to develop fully automated surveillance tools for HAIs. The project, headed

by Karolinska University Hospital (KUH) and Region Stockholm, is organised in three phases: 1) collaboration building between healthcare providers, academic institutions, and industry (2015); 2) prototype development (2016 – 2018); and 3) implementation (2018 – 2021).

Data, algorithms and method of validation

To date, two rule-based algorithms for healthcare-associated sepsis and UTIs have been developed locally, using data of a testbed that consists of EHR data from KUH from 2008 – 2014.[30, 31] Both algorithms include all patients aged > 18 years that have been admitted to the hospital for > 24 hours. The sepsis algorithm was developed using retrospective data to identify patients fulfilling the Sepsis-3 clinical criteria, based on structured data from antibiotics, microbiological test results and sequential organ failure (SOFA) scores.[30] The algorithm accounts for baseline values and dynamic changes in the SOFA score. The algorithm for UTIs is designed to perform surveillance of microbiologically confirmed UTIs according to ECDC definitions.[31] It is a rule-based algorithm that utilises microbiological culture results and information on symptoms both from structured and unstructured (text) data from EHRs. Performance of algorithms is assessed in validation sets of care episodes that have been annotated by infectious disease physicians.

Next steps

Currently, the project works towards implementation of the surveillance algorithms within a centrally organised data warehouse that receives comprehensive EHR data from multiple hospitals in Region Stockholm and Region Västerbotten, Sweden. Data is planned to be extracted daily by the IT department, to which algorithms are applied to continuously monitor patients for sepsis or UTI cases. Aggregated results will be reported back to local care providers for epidemiological surveillance. Future targets are to develop algorithms for other HAIs and to utilise data for HAI risk prediction as well as increasing the amount of incorporated primary healthcare data.

DISCUSSION

The current landscape of AS of HAIs in Europe is promising in terms of innovation and research, but at the same time heterogeneous with regards to methods, algorithms, data sources and targeted HAIs. Overall, AS systems based on classification algorithms for semi-automated surveillance were found to be most prevalent. Workload reduction and time efficiency were identified as primary benefits of AS over the conventional approach. Moreover, we described three examples of successfully operating systems in more detail. Sharing more

detailed information on the development and implementation can support others who intent to start, implement or use AS surveillance.

Although it is encouraging that some AS systems are operational and in use, AS in Europe is to a certain extent still in its infancy, because many institutions face multiple barriers impeding successful implementation. Main barriers perceived and reported by institutions already using AS systems and those that do not include a lack of harmonised IT infrastructure and strict data protection regulations. This finding underscores the need for standardisation and interoperability of medical data across different institutions to support the reuse of EHR data for the development of more efficient and less resource intensive surveillance methods. Furthermore, while data security and privacy regulations are a cornerstone in the practice of medicine, our findings illustrate the need to clarify or even adapt certain regulations that could potentially discourage important developments benefiting patient safety as well as the need to broadly implement technical solutions that facilitate use of personal (health) data under the current regulations.

Heterogeneity in AS systems is in itself not a limiting factor, however, it hampers comparisons. There are several systematic reviews trying to compare systems, however, they all concluded that certain performance characteristics were missing and methodological differences impede head-to-head comparisons.[39-41, 47, 48] For institutions interested in establishing AS, it is difficult to choose an approach that suits their needs. To facilitate more widespread development of AS and the ability to compare surveillance systems, essential specifications in future publications on surveillance systems should be described (**Box 7.1**). First, it would be helpful if all systems clearly explain what population they include in their surveillance, and the data sources and data cleaning steps utilised for population selection and algorithm application. Second, it is important that both the algorithm and the definitions of targeted HAIs are described in detail, as in some AS systems existing HAI definitions are adapted.[17] Third, performance characteristics should be reported, such as sensitivity, specificity, positive predictive value, negative predictive value, time savings or reduction in the number of charts to review. Fourth, it should be clearly described how the system was validated (i.e. against which reference standard, in what time period and in how many patients), so others can assess their validation method. Last, authors should be explicit about the phase the proposed AS method is in at the time of writing (development phase, implementation phase, or in actual use in the clinic or surveillance network). To encourage implementation, it will be helpful if logistics and organisational matters are systematically reported in scientific publications or reports, such as maintenance needs, specifics on algorithm application (e.g. frequency), and barriers and facilitators of implementation (**Box 7.1**).

Box 7.1. Items for reporting automated surveillance systems in (scientific) publications.

- Describe data sources needed for patient selection and algorithms
- Describe inclusion criteria of the patient population under surveillance and clarify how they are selected (manual, partially or fully automated including details)
- Describe what healthcare-associated infection definitions are targeted by the algorithm, and how they are adapted for automating purposes
- Describe the algorithm and algorithm performance (in terms of sensitivity, specificity, positive predictive value, negative predictive value, time savings and/or reduction in records to review)
- Describe the method of validation (reference standard used, sample size)
- Clarify the phase of the automated surveillance system (development phase, implementation phase or in actual use)
- If implemented, describe the workflow and maintenance of the surveillance system
- If implemented, describe barriers/facilitators of implementation

The main limitation of the current study is that no systematic review of AS systems was performed, and therefore we do not know whether all AS systems that have been developed and implemented in Europe are included in the survey responses. However, as the actual state of implementation often remains unclear in research papers targeted by systematic reviews, we have chosen to broaden our scope by opting for a survey, using snowball sampling. We have also actively invited researchers of published papers to complete the survey.

In conclusion, creating and maintaining IT infrastructures and data security restrictions represent the most relevant challenges and barriers for AS implementation. Existing AS systems in Europe encompass a variety of data sources, algorithms and HAI targets, thereby reducing comparability across systems. In order to facilitate comparisons and stimulate exchange of experiences and surveillance methodology, it should be encouraged to describe AS systems with a standardised minimum set of information.

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DECLARATIONS

Declarations of interest: none.

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SUPPLEMENTARY MATERIAL

Supplemental File S7.1. Survey.

Automated surveillance survey

Introduction

DATA Shortname / Alias: **hosp_network**

1. Do you work in a hospital and/or for a surveillance network?

- ○ I work in a hospital
- ○ I work for a surveillance network
- ○ I work both in a hospital and for a surveillance network

DATA Shortname / Alias: **hosp_network_name** Variable name: **hosp_network_name**

2. Please indicate the name of your hospital/surveillance network

DATA Shortname / Alias: **currently_in_use**

3. What is your experience with automated surveillance of healthcare-associated infections?

- ○ Automated surveillance is currently in use (in any form) in my hospital or surveillance network
- ○ Automated surveillance was used or considered , but at this moment not implemented

DATA Shortname / Alias: **barriers** Variable name: **barriers**

4. If you have considered automated surveillance but not implemented, what barriers did you encounter and/or what prohibits you from using automated surveillance?

Automated surveillance system

DATA Shortname / Alias: **target_HAI**

5. What healthcare-associated infections are targeted by the automated surveillance system?

- ☐ Surgical site infection
- ☐ Central line-associated or catheter-related bloodstream infection
- ☐ Sepsis or other bloodstream infection
- ☐ Urinary tract infection (incl. catheter-associated)
- ☐ Pneumonia
- ☐ Ventilator-associated pneumonia
- ☐ Other - Write In
- ☐ Other - Write In

DATA Shortname / Alias: **semi_fully** Variable name: **semi_fully**

6. Is the system semi- or fully automated?
In other words, is there manual assessment of pre-selected patient charts (semi-automated), or does the system determine HAI status without the need for manual chart review (fully automated)?

- ○ Semi-automated
- ○ Fully-automated
- ○ Unsure

7. Which type of algorithm is applied in your surveillance system?

- ○ Classification model
- ○ Regression model
- ○ Machine learning
- ○ Other - Write In
- ○ I don't know

Automated system characteristics

DATA Shortname / Alias: **data sources**

8. What types of data are included by the automated surveillance system?
If systems for different HAI include different types of data, please indicate the total of all data sources used.

- ☐ Demographic information (age, gender, identifyer)
- ☐ Diagnosis or discharge codes
- ☐ Admission and discharge dates, specialty
- ☐ Surgical procedures
- ☐ Use of devices (e.g. catheters, ventilator)
- ☐ Microbiological culture results
- ☐ Antibiotic use
- ☐ Orders for radiological diagnostics/procedures
- ☐ Results of radiological diagnostics (report)
- ☐ Clinical Chemistry (e.g. C-reactive protein, leukocytes)
- ☐ Clinical signs and symptoms
- ☐ Other - Write In
- ☐ Other - Write In

9. If you can, please provide details on how the algorithm identifies patients with a HAI cq. patients requiring manual chart review.
If there are (scientific) publications regarding the algorithm, please list them here.

DATA Shortname / Alias: **data_casemix** Variable name: **data_casemix**

10. Can you automatically extract data necessary to perform case-mix adjustment (wound class, ASA classification, BMI, duration of surgery, etc)? And if so, what data?

DATA Shortname / Alias: **DWH** Variable name: **DWH**

11. Are data available in a clinical data warehouse?

- ○ Yes, all data sources
- ○ Yes, most data sources
- ○ No, we extract data from independent sources

DATA Shortname / Alias: **in_exclusion** Variable name: **in_exclusion**

12. Please describe briefly how patients are included or excluded for surveillance.
Patients selected automatically? Automated application of exclusion criteria, for example non-primary procedures, pre-existing infections?

DATA Shortname / Alias: **data_extraction** Variable name: **data_extraction**

13. Please describe briefly the process of data extraction.
Who is involved (role/position); extraction performed manually or by script; frequency of procedures

DATA Shortname / Alias: **data_analysis** Variable name: **data_analysis**

14. Please describe briefly the process of data analyses
Who is involved (role/position); performed manually or by script; frequency of procedures; continuous or in batches.

DATA Shortname / Alias: **validation_perfromed** Variable name: **validation_perfored**

15. Please describe briefly how the system is maintained.
Who is responsible, what validation checks are incorporated in the maintenance of the system and how frequently is this performed (completeness of population selection; changes in the fields or codes in the EHR; changes in clinical practice; validation of algorithm results...)?

Automated system evaluation

DATA Shortname / Alias: **Validation**

16. How was validation of the algorithm performance performed and what was the performance of this system (compared to traditional surveillance), if known

DATA Shortname / Alias: **feedback** Variable name: **feedback**

17. Are the surveillance results from the automated system used for direct feedback to individual wards/doctors and how are the surveillance data accepted by clinical parties?

DATA Shortname / Alias: **advantages** Variable name: **advantages**

18. In your opinion, what are key advantages of the system over manual surveillance or other automated surveillance systems?

Automated surveillance evaluation (2)

DATA Shortname / Alias: **det_succes** Variable name: **det_succes**

19. In your opinion, what were key determinants in making implementation of the system a success?

DATA Shortname / Alias: **IT-barriers** Variable name: **ITbarriers**

20. What barriers regarding IT, data management or related to data/privacy protection did you encounter when developing or maintaining the system?

DATA Shortname / Alias: **improve** Variable name: **improve**

21. What would you improve in your system if you could?

Additional information

DATA Shortname / Alias: **country** Variable name: **country**

22. What is your country?

DATA Shortname / Alias: **Hospital_type** Variable name: **Hospital_type**

23. How would you best classify your hospital?

- University, tertiary care hospital
- Non-university teaching hospital
- Non-teaching secondary care hospital
- Non-teaching general hospital
- Other - Write In (Required)

DATA Shortname / Alias: **hosp_size** Variable name: **hosp_size**

24. What is the size of your hospital?

Number of beds (if known)

Yearly number of admissions (if known)

DATA Shortname / Alias: **respondent_name** Variable name: **respondent_name**

25. What is your name?

26. We aim to reach as many institutions as possible employing automated surveillance. If you know of other institutions employing automated surveillance, we would be greatful if you can list them below.

DATA Shortname / Alias: **contact** Variable name: **contact**

27. May we contact you with additonal questions if necessary?

- ○ Yes
- ○ No

DATA Shortname / Alias: **email** Variable name: **email**

28. Please provide your email address.

29. Do you have any other comments?

8

Validation of an algorithm for semi-automated surveillance to detect deep surgical site infections after primary total hip or knee arthroplasty – A multicentre study

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ABSTRACT

Objective: Surveillance of healthcare-associated infections is often performed by manual chart review. Semi-automated surveillance may substantially reduce workload and subjective data interpretation. We assessed the validity of a previously published algorithm for semi-automated surveillance of deep surgical site infections (SSIs) after total hip (THA) or total knee arthroplasty (TKA) in Dutch hospitals. In addition, we explored the ability of a hospital to automatically select the patients under surveillance.

Design: Multicentre retrospective cohort study.

Methods: Hospitals identified patients who underwent THA or TKA either by procedure codes or by conventional surveillance. For these patients, routine care data regarding microbiology results, antibiotics, (re)admissions and surgeries within 120 days following THA or TKA were extracted from electronic health records. Patient selection was compared with conventional surveillance and patients were retrospectively classified as low- or high probability of having developed deep SSI by the algorithm. Sensitivity, positive predicted value (PPV), and workload reduction were calculated as compared to conventional surveillance.

Results: Of 9,554 extracted THA and TKA surgeries, 1,175 (12.3%) were revisions and 8,378 primary surgeries remained for algorithm validation (95 deep SSIs; 1.1%). Sensitivity ranged from 93.6% to 100% and PPV ranged from 55.8% to 72.2%. Workload was reduced by ≥ 98%. Also, two SSIs (2.1%) missed by the algorithm were explained by flaws in data selection.

Conclusions: This algorithm reliably detects patients with a high probability of having developed deep SSI after THA or TKA in Dutch hospitals. Our results provide essential information for successful implementation of semi-automated surveillance for deep SSIs after THA or TKA.

INTRODUCTION

Healthcare-associated infections (HAIs) are infections acquired as the result of medical care.[1] The most common HAIs are surgical site infections (SSIs), accounting for > 20% of all HAIs.[2] SSI incidence depends on the type of surgery: in the Netherlands, 1.5% of primary total hip arthroplasties (THAs) and 0.9% of primary total knee arthroplasties (TKAs) are complicated by SSIs, most of which are deep (1.3% and 0.6% respectively).[3,4] This finding is in line with numbers reported in Europe and the United States.[5-7] Deep SSIs after THA or TKA are associated with substantial morbidity, longer postoperative hospital stays, and incremental costs.[3,8,9] Given the aging population, volumes of THA and TKA and numbers of associated SSIs are expected to increase further.[7,10,11]

Accurate identification of SSIs through surveillance is essential for targeted implementation and monitoring of interventions to reduce the number of SSIs.[12,13] In addition, surveillance data may be used for public reporting and payment mandates.[14] In most hospitals, surveillance is performed by manual chart review: an infection control practitioner (ICP) reviews electronic health records (EHRs) to determine whether the definition for an SSI is met. This method is costly, time-consuming and labor intensive. Moreover, it is prone to subjectivity, suboptimal interrater reliability, and the 'more-you-look-more-you-find' principle.[15-19]

The widespread adoption of EHRs facilitates (semi-)automated surveillance using routine care data, thereby reducing workload and improving reliability. SSI surveillance after THA or TKA is particularly suitable for automation because these are high-volume procedures with a low incidence of SSI; hence, the potential gains in efficiency are considerable. In addition, treatment of (possible) SSIs is highly uniform across hospitals, which facilitates algorithmic detection.

As a first step towards semi-automated surveillance of deep SSIs after TKA or THA, a tertiary-care centre developed a classification algorithm relying on microbiology results, reinterventions, antibiotic prescriptions, and admission data (**Table 8.1**).[20] This algorithm retrospectively discriminates between patients who have a low or high probability of having developed a deep SSI, and only patients with a high probability undergo manual chart review. Patients classified as low probability are assumed to be free of deep SSI. In a single-hospital setting, this algorithm identified all deep SSIs after THA or TKA (sensitivity of 100%) and resulted in a reduction of 97.3% charts to review.[20]

Table 8.1. Algorithm specifications.

Category	**Criteria for fulfilment:** ≥ 3 out of these four criteria must be fulfilled to be considered high probability for having deep SSI
Microbiology	≥ 1 positive microbiological culture(s) or ≥ 5 cultures obtained from ≥ 1 potentially relevant body site(s), i.e. wound cultures, pus, joint aspirations, prosthetic material, tissue, blood cultures or unspecified material.
Antibiotics	≥ 14 days of antibiotic exposure, where an 'exposure day' is defined as a day with ≥ 1 prescription for an antibiotic (ATC code of J01).
(Re)admissions	Length of hospital stay of the index admission (i.e., admission during which the index procedure took place) of ≥ 14 days or ≥ 1 readmission(s) for a relevant specialty such as orthopaedics, trauma or surgery.
Reintervention	Any orthopaedic surgical procedure performed by the department of orthopaedics, without further restrictions.

Note: ≥ 3 of these 4 criteria must be fulfilled to be considered high probability for having deep surgical site infection.[20] All criteria should be fulfilled within 120 days after the index surgery.

A prerequisite for large-scale implementation of this algorithm is validation in other centres that may differ in EHR systems, patient populations, diagnostic procedures, or clinical practice. Therefore, the main aim of this study was to validate the performance of this algorithm, defined in terms of sensitivity, positive predictive value (PPV), and workload reduction, for semi-automated surveillance to detect deep SSIs after THA or TKA in general hospitals in the Netherlands. A secondary aim was to explore methods for selection of the surveillance population (denominator data).

METHODS

Study design

This multicentre retrospective cohort study compares the results of a surveillance algorithm to the results of conventional manual surveillance of deep SSIs following THA and TKA. Manual SSI surveillance, considered the reference standard, was executed according to national definitions and guidelines set out by PREZIES; the Dutch surveillance network for healthcare-associated infections.[21,22] SSI surveillance includes all patients aged ≥ 1 year who underwent a primary THA or TKA (so called index surgery); revision procedures were excluded. SSIs were defined using criteria from the (European) Centres for Disease Control and Prevention, translated and adapted for use in the PREZIES surveillance: organ-space SSIs are reported as deep SSIs.[21,22] The mandatory follow-up for THA and TKA SSI surveillance is 90 days after the index surgery.

This study was reviewed by the Medical Institutional Review Board of the University Medical Centre Utrecht and was considered not to fall under the Medical Research Involving Human Subjects Act. Hence the requirement of an informed consent was waived (reference number

17-888/C). From all participating hospitals, approval to participate was obtained from the local boards of directors.

Hospitals

We selected 10 hospitals (~14% of all Dutch hospitals) based on their interest in automated surveillance and expected surgical volume and invited them to participate in the study. Hospitals had to meet the following inclusion criteria: 1) recent participation in PREZIES SSI surveillance for THA and TKA according to PREZIES guidelines; 2) availability of at least two years of THA and TKA surveillance data after 2012 and data on at least 1,000 surgeries; 3) ability to select the surveillance population (the patients who underwent the index surgery) in electronic hospital systems; and 4) ability to extract the required routine care data of these patients from the EHR in a structured format to apply the algorithm.

Data collection from electronic health records and algorithm application

Hospitals were requested to automatically select patients who underwent the index surgeries (denominator data), and to extract the following data for these patients from their EHR: microbiology results, antibiotic prescriptions, (re)admissions and discharge dates, and subsequent orthopedic surgical procedures. All extracted data were limited to 120 days following the index surgery to enable the algorithm to capture SSIs that developed at the end of the 90-day follow-up period. Data extractions were performed between November 18, 2018 and August 16, 2019. **Supplemental Table S8.1** provides detailed data specifications.

Analyses

After extraction and cleaning of data, records of patients in the extractions were matched to patients in the reference standard (PREZIES database). If available, matching was performed using a pseudonymised surveillance identification number. Else, matching was performed for the following patient characteristics: date of birth, sex, date of index surgery, date of admission, and type of procedure. For each hospital, the method of automated selection of index surgeries was described as well as the completeness of the surveillance population (denominator) compared to the reference population reported manually to PREZIES. Subsequently, the algorithm was applied, and patients who underwent THA or TKA surgeries were classified as high- or low probability of having had a deep SSI (**Supplemental Table S8.2)**. Patients were classified as high probability for deep SSI according to the algorithm if they met ≥ 3 of the four criteria (**Table 8.1**).

For each hospital, the allocation of patients with low or high probability by the algorithm was compared to the outcome (deep SSI) as reported in the reference standard. Subsequently, sensitivity, PPV and workload reduction (defined as difference between the total number of surgeries in surveillance and the proportion of surgeries requiring manual review after algorithm application) were calculated with corresponding confidence intervals.[23] For semi-automated surveillance, we considered sensitivity to be the most important characteristic because any false-positive cases are corrected during subsequent chart review, whereas false-negative cases may remain unnoticed. Analyses were performed using SAS version 9.4 software (SAS Institute, Cary, NC).

Discrepancy analyses and validation of the reference standard

Exploratory discrepancy analyses were performed to evaluate and understand possible underlying causes of misclassification by the algorithm. In addition, for each hospital, an on-site visit took place to validate the conventional surveillance (i.e. reference standard PREZIES). This validation was executed by two experienced surveillance advisors of PREZIES, and they were blinded for the outcomes both of the reference standard and the algorithm. For the validation of the conventional surveillance, a maximum of 28 records were selected containing all presumed false positives and false negatives, complemented with a random sample of true positives and true negatives. At least 50% of the reported superficial SSIs in the true-negative group were included in the validation sample. The maximum number was selected for logistic reasons and the time capacity of the validation team.

RESULTS

Overall, four hospitals met the inclusion criteria and were willing to participate in this study: the Beatrix Hospital in Gorinchem, Haaglanden Medical Centre in The Hague (3 locations), Meander Medical Centre in Amersfoort, and Sint Antonius Hospital in Nieuwegein and Utrecht (3 locations). Hospitals were randomly assigned the letters A, B, C, and D. The remaining hospitals were not able to participate for the following reasons: inability to extract historical data due to a transition of EHR (n = 1); inability to extract microbiology results or antibiotic use from historical data in a structured format (n = 3); no approval of the hospital's board to share pseudonymised patient data (n = 1) or no capacity of human resources (ICPs, information technology personnel, and data managers) (n = 1).

Completeness of surveillance population

The four participating hospitals extracted 9,554 THA and TKA procedures performed between 2012 and 2018 along with data required for application of the algorithm

(**Supplemental Table S8.1**). Hospital B used inclusion in conventional surveillance as a selection criterion for the selection of index surgeries and extraction of the data required for the algorithm. These extracted records could be matched using a pseudonymised surveillance identification number, which was also available in the reference standard. By definition, this procedure resulted in a perfect match; hence, no inferences could be made regarding the completeness of the surveillance population when using automated selections, for example, using administrative procedure codes. Hospitals A, C and D selected their surveillance population automatically using administrative THA and TKA procedure codes. For hospital A and D, these records were matched by patient characteristics to the reference standard and, for hospital C, by a pseudonymised surveillance identification number. Matching with the PREZIES database revealed a mismatch for 1,128 records that could not be linked to the reference standard. Manual review of a random sample of these records showed these were mainly revision procedures that were excluded from conventional surveillance. Vice versa, 103 records were in the reference standard, but could not be linked to the extractions. Explanations for this mismatch per hospital are described in **Table 8.2**.

Table 8.2. Overview of data extractions and selection of surveillance population.

	Hospital A	Hospital B	Hospital C	Hospital D
Time period extractions (years)	2012 – 2015	2015 – 2016	2017 – 2018	2012 – 2017[a]
Total number of THA/TKA in extractions (count)	2,604	1,601	1,037	4,311
Matched to PREZIES (count)	2,395	1,601	1,029	3,353
Match made based on	Patient characteristics	Surveillance identification number	Surveillance identification number	Patient characteristics
Records in extractions that could not be linked to reference standard (count (%))[b]	209 (8.0)	NA[c]	8 (0.8)	958 (22.2)
Records in reference standard that could not be linked to extractions (count (%))	48 (2.0)[d]	NA[c]	6 (0.6)[e]	49 (1.5)[f]

[a] Until September 1, 2017.
[b] Manual review of a random sample of these records showed these were mainly revision procedures.
[c] Exploration of automating selecting surveillance population not applicable as hospital collected data for the extractions based on the selection of the conventional surveillance.
[d] Reason for mismatch: typo's and mistakes in the manual data collection.
[e] Reason for mismatch: all emergency cases for which data was incomplete. Automated extractions therefore not possible.
[f] Reason for mismatch: a clear cause was not found, although it is suspected data was lost due to the merger of hospitals and their electronic health records during the study period.
Abbreviations: THA = total hip arthroplasty; TKA = total knee arthroplasty; NA = not applicable.

Algorithm performance

In total, 8,378 primary arthroplasty procedures (4,432 THAs and 3,946 TKAs) in 7,659 patients and 95 SSIs (1.1%) were uniquely matched with the reference standard and were available for analysis of algorithm performance (**Table 8.2**). The algorithm sensitivity ranged from 93.6% to 100.0% and PPV ranged from 55.8% to 72.2% across hospitals (**Table 8.3**). In all hospitals, a workload reduction of ≥ 98.0% was achieved. In hospitals B and D, one and two deep SSIs were missed by the algorithm, respectively. Discrepancy analyses revealed that one case was reclassified into 'no deep SSI', and, hence, was correctly indicated by the algorithm. Of the two truly missed cases, one case was missed by incomplete microbiology data and the other was missed because of unavailability of data regarding the treating specialty of the readmissions, thereby using ward level for the selection of readmissions. Results and details of false-negative and false-positive cases are provided in **Table 8.4**. On-site validation visits found six additional deep SSIs, which were missed in the conventional surveillance but were correctly classified as potential SSIs by the algorithm. Other findings of the on-site validation of the reference standard, but not essential for the assessment of the algorithm, were reclassifications of superficial SSIs to no SSI (n = 6), missed superficial SSIs (n = 2) and errors in the determination of the infection date (n = 4).

DISCUSSION

This study successfully validated a previously developed algorithm for the surveillance of deep SSIs after THA or TKA in four hospitals. The algorithm had a sensitivity ranging from 93.6% to 100.0% and achieved a workload reduction of 98.0% or more, which is in line with the original study and another international study.[20,24] In total, only two SSIs were missed by the algorithm; both were the result of limitations of the use of historical data and can be resolved with the current EHR. Validation of the reference standard revealed six additional deep SSIs that were initially missed by conventional surveillance but classified as high probability of SSI by the algorithm; thus, the accuracy of the surveillance improved. For automated selection of the surveillance population (i.e., denominator data), hospitals should be able to distinguish primary THAs and TKAs from revisions. Our results provide essential information for successful implementation of semi-automated surveillance for deep SSIs after THA or TKA in Dutch hospitals in the future.

The results of this study reveal some preconditions that require attention when further implementing this algorithm for semi-automated surveillance. First, dialogue between information technology personnel, data management, ICPs and microbiologists is essential

Table 8.3. Overview algorithm performance per hospital.

	Number of matched THA/ TKA surgeries (Number of Patients)	Number of deep SSIs according to reference standard (%)	True positives	False positives	False negatives	True negatives	Sensitivity (% (95% CI))	PPV (%(95% CI))	Workload reduction (%)[a]
Hospital A	2,395 (2,196)	**26** (1.1)	26	10	**0**	2,359	100.0 (86.8 – 100.0)	72.2 (54.8 – 85.8)	98.5
Hospital B	1,601 (1,493)	**23** (1.4)	22	10	**1**	1,568	95.7 (78.0 – 99.9)	68.8 (40.0 – 83.3)	98.0
Hospital C	1,029 (962)	**15** (1.5)	15	11	**0**	1,003	100.0 (78.2 – 100.0)	57.7 (36.9 – 76.7)	98.5
Hospital D	3,353 (3,008)	**31** (0.9)	29	23	**2**	3,299	93.6 (78.6 – 99.2)	55.8 (41.3 – 69.5)	98.4

[a] Workload reduction is defined as the proportion of medical records needing manual chart review.
Abbreviations: THA = total hip arthroplasty; TKA = total knee arthroplasty; SSI = surgical site infection; PPV = positive predicted value.

Table 8.4. Overview of discrepancy analysis.

	Hospital A	Hospital B	Hospital C	Hospital D
Number of false negatives (missed deep SSI)	**0**	**1**	**0**	**2**
Reasons				
Reclassification of reference data (true negative)				1
Incorrect selection of readmission[a]		1		
Microbiological cultures performed in external laboratory[b]				1
Number of false positives	**10**	**10**	**11**	**23**
Reasons				
Reclassification of reference data (true positive)	3			3
Incorrect inclusion in surveillance (revision procedure)			1	2
Superficial SSI	1		3	4
Other complications	6	10	6	13
Unknown			1	1

[a] This hospital used data extractions from a previous electronic health record system, where no information was stored regarding the specialty of the readmission. Selection of readmission was therefore made on ward level, instead of treating specialty. Because this patient was readmitted to another ward because of overcapacity of the orthopedic ward, it was missed by the algorithm.
[b] Microbiological cultures of this patient were performed in external laboratory and culture results were therefore not available in the in-house laboratory information system from which the data were extracted to apply the algorithm.
Abbreviations: SSI = surgical site infection.

to identify the correct sources of data for applying the algorithm. In two of four hospitals, interim results revealed that data extractions were incomplete due to unawareness in hospitals of the existence of registration codes. This finding demonstrates the importance of validating the completeness and accuracy of data sources required for the implementation of semi-automated surveillance.[14,25] Second, successful validation of this algorithm does not guarantee that widespread implementation can be taken for granted. It appeared that none of the four hospitals could perfectly select the surveillance population using structured routine care data such as procedure codes (mismatch ranged from 0.8% – 22.2%). Procedure codes are not developed for the purpose of surveillance but for medico-administrative purposes, and they may contain some misclassification in distinguishing between primary procedures and procedures that should be excluded according to conventional surveillance (e.g. revision procedures).[25] For implementation, improvement of patient selection is considered to increase comparability. Mismatches between the data extractions and reference standard (97 records from the reference standard were not found in the hospitals' extractions) were partly the result of typing errors in the manual surveillance, hence, underscoring the vulnerability of traditional manual surveillance.

Although superficial SSIs are included within the conventional method of surveillance, this algorithm was developed to detect deep SSI only. During initial algorithm development superficial SSIs were not taken into account for the following reasons: First, the costs and impact on patient and patient-related outcomes are more detrimental after deep SSIs. In addition, only 20% of all reported SSIs in THAs and TKAs concern superficial SSIs.[4] Third, superficial SSIs are mostly scored by clinical symptoms that are often stored in unstructured data fields (clinical notes) with a wide variety in expressions.[26] These data are complex to use in automatisation processes and will complicate widespread implementation.[27] Fourth, the determination of superficial SSIs requires a subjective interpretation of the definition, making them a difficult surveillance target both for manual and automated surveillance.

Previous studies investigating the use of algorithms in SSI surveillance after orthopaedic surgeries achieved a low(er) sensitivity, applied rather complex algorithms, or used administrative coding data such as ICD-10 codes for infection.[28-30] Although the use of ICD-10 codes for infection is an easy and straightforward method in some settings, relying solely on administrative data is considered inaccurate.[25,31-33] In addition, coding practices differ by country and results cannot be extrapolated. Thirukumaran et al.[27] investigated the use of natural language processing in detecting SSIs. Sensitivity and PPV were extremely high in the centre under study; however, the performance in other centres was not investigated, and the proposed method is rather complex to implement on large scale compared to our method. In contrast, Cho et al.[34] showed a more pragmatic approach in which one algorithm was used to detect SSIs in 38 different procedures, including THAs and TKAs. Although the sensitivity for detecting deep SSIs was 100%, a high number of false positives occurred because of the broad algorithm, resulting in a nonoptimal workload reduction.

Strengths and limitations

The strengths of this study are the multicentre aspect and the use of an algorithm that is relatively simple to apply. All participating hospitals had previously performed conventional surveillance according to a standardised protocol and SSI definitions, enabling optimal comparison and generalisability to the Dutch situation. The algorithm could be successfully applied despite potential differences in clinical and diagnostic practice, as well as the use of different EHRs. Whereas previous studies used complex algorithms and were mostly performed in single tertiary-care centres, this study achieved a near-perfect sensitivity and high workload reduction in small(er) general hospitals, using an algorithm that is likely feasible to implement in these hospitals.

This study has several limitations. First, post-discharge surveillance was limited to patient encounters in the initial hospital. The algorithm will not detect patients who are treated or readmitted in other hospitals, however, this is also the case in conventional surveillance. In the Netherlands, most patients return to the operating hospital in cases with complications such as deep SSIs, especially if they occur within the 90-day follow-up period. Secondly, in this study, we made use of historical data retrieved from the local EHR. Because of shifts in hospital information systems and merger of hospitals, historical data were not accessible for some hospitals, limiting their participation in this retrospective study. Therefore, we have no insight into the feasibility of future large-scale implementation in these hospitals. Lastly, in this study, one hospital used the conventional surveillance to identify the surveillance population and to perform electronic data extractions. Therefore, for this hospital, we were unable to adequately evaluate the quality and completeness of the selected surveillance population if they had been using an automated selection procedure.

In conclusion, a previously developed algorithm for semi-automated surveillance of deep SSI after THA and TKA was successfully validated in this multicentre study; a near-perfect sensitivity was reached, with a ≥ 98% workload reduction. In addition, semi-automated surveillance not only proved to be an efficient method of executing surveillance but also had the potential to capture more true deep SSIs compared to conventional (manual) surveillance approaches. For successful implementation, hospitals should be able to identify the surveillance population using electronically accessible data sources. This study is the first step to broader implementation of semi-automated surveillance in the digital infrastructure of hospitals.

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CONFLICT OF INTEREST

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SUPPLEMENTARY MATERIAL

Supplemental Table S8.1. Specifications of data extractions from the electronic health records needed for algorithm application.

Data variable	Data type	Period
PREZIESnumber or anonymous (surveillance) study number [1]	Numeric/text	NA
Demographics		
Age (in years) or date of birth [1]	Numeric/date	NA
Sex [1]	Numeric	NA
Index surgery		
Date of index surgery [1]	Date	NA
Description procedure; PREZIES code/procedure code (i.e. ICD-9/10/CTG) [1]	Text	NA
Admission of index surgery		
Admission date [1]	Date	NA
Discharge date [1]	Date	NA
Readmission(s)		
Admission date [0..*]	Date	Date of index surgery + 120 days
Discharge date [0..*]	Date	Date of index surgery + 120 days
Treating specialty [0..*]	Text/category	Date of index surgery + 120 days
Reoperation		
Date of reoperation [0..*]	Date	Date of index surgery + 120 days
Procedure code (i.e. ICD-9/10/CTG) [0..*]	Text	Date of index surgery + 120 days
Description of procedure [0..*]	Text	Date of index surgery + 120 days
Treating specialty [0..*]	Text/category	Date of index surgery + 120 days
Microbiology cultures		
Date of culture [0..*]	Date	Date of index surgery + 120 days
Sample number of culture [0..*]	Numeric/text	Date of index surgery + 120 days
Cultured material (i.e. wound, blood) [0..*]	Text/category	Date of index surgery + 120 days
Cultured material open text [0..*]	Text	Date of index surgery + 120 days
Result (species) [0..*]	Text	Date of index surgery + 120 days
Assessment positive/negative [0..*]	Text/category	Date of index surgery + 120 days
Antibiotic use[#]		
Code (ATC in categories J01) OR description [0..*]	Numeric/Text	Date of index surgery + 120 days
Start date [0..*]	Date	Date of index surgery + 120 days
Stop date [0..*]	Date	Date of index surgery + 120 days

[1] = Single record; [0..*] = can appear several times.
[#] Regardless of mode of administration. Including outpatient prescriptions.

General rules for applying the algorithm (data cleaning)

- Patients can be included several times in the data as they can have TKA/THA at different sites, and can have multiple re-admissions, antibiotics or microbiology results.
- If start- and stop date of antibiotic prescriptions or admission/discharge dates are swapped: the number of days is converted from minus to plus.
- If a second or subsequent index surgery takes place within the follow-up period of a previous index surgery, the follow-up period of the first surgery is censored on the date of surgery of the next one (i.e. if a THA takes place within the follow-up period of a previous TKA, the follow-up date of TKA will be the date of surgery of the THA). In this way, a subsequent index surgery does not count as a reoperation of the first index surgery.
- If a person has two index surgeries on the same day, the follow-up period is for both surgeries 90 days, unless another index surgery takes place in this follow-up period (see rule above).
- Microbiology results obtained from 1 culture count as 1 result.
- In case of various assessments (positive/negative) obtained from 1 culture it is counted as positive.
- If an algorithm element cannot be computed due to incomplete data, the index surgery is flagged positive on that algorithm element.

Supplemental Table S8.2. Algorithm specifications.

Elements algorithm	Criteria (high probability if >= 3 criteria are met)[a]:	Specification:
Microbiology	>= 1 positive culture OR >= 5 cultures obtained	>= 1 positive microbiological culture or >= 5 cultures obtained from potentially relevant body site(s), such as wound cultures, pus, joint aspirations, prosthetic material, tissue, blood cultures, unspecified material. All cultures are taken into account from day 1* until end follow-up.
Antibiotics	>/= 14 days of antibiotic exposure post-operative	All antibiotic orders (ATC J01) prescribed from day 2* until end of follow-up, including outpatient prescriptions but excluding ICU prescriptions. All antibiotic episodes are summed up; however overlapping episodes count as 1 day (e.g. two antibiotic prescriptions, one for 4 days and one for 8 days of which 3 days overlap result in a total of 9 days of antibiotic exposure).
(Re) Admissions	Length of stay of initial surgery >= 14 days OR >= 1 re-admission	Length of hospital stay of the index admission (i.e., admission during which the TKA/THA took place) of >= 14 days ((discharge date – date of index surgery) +1) or >= 1 readmission(s) for the relevant specialty (i.e. orthopedics, trauma or surgery), after the index surgery but within follow up
Reoperation	>= 1 reoperation by orthopedics	Surgeries performed by the department of orthopedics, after the index surgery and within the follow-up period. No further restrictions.

* Date of initial, index surgery = day 0.
[a] All criteria should be fulfilled within 120 days after the index surgery.

9

Semi-automated surveillance of deep surgical site infections after colorectal surgeries – A multicentre external validation of two surveillance algorithms

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ABSTRACT

Objective: Automated surveillance methods increasingly replace or support conventional (manual) surveillance; the latter is labour-intensive and vulnerable to subjective interpretation. We sought to validate two previously developed semi-automated surveillance algorithms to identify deep surgical site infections (SSIs) in patients undergoing colorectal surgeries in Dutch hospitals.

Design: Multicentre retrospective cohort study.

Methods: From four hospitals, we selected colorectal surgery patients between 2018 and 2019 based on procedure codes, and we extracted routine care data from electronic health records. Per hospital, a classification model and regression model were applied independently to classify patients into low- or high probability of having developed deep SSI. High-probability patients need manual SSI confirmation; low-probability records are classified as no deep SSI. Sensitivity, positive predictive value (PPV), and workload reduction were calculated compared to conventional surveillance.

Results: In total, 672 colorectal surgery patients were included, of whom 28 (4.1%) developed deep SSI. Both surveillance models achieved good performance. After adaptation to clinical practice, the classification model had 100% sensitivity and PPV ranged from 11.1% to 45.8% between hospitals. The regression model had 100% sensitivity and 9.0% – 14.9% PPV. With both models, < 25% of records needed review to confirm SSI. The regression model requires more complex data management skills, partly due to incomplete data.

Conclusions: In this independent external validation, both surveillance models performed well. The classification model is preferred above the regression model because of source-data availability and less complex data-management requirements. The next step is implementation in infection prevention practices and workflow processes.

INTRODUCTION

Surgical site infections (SSIs) are amongst the most common healthcare-associated infections (HAIs) and result in increased costs, morbidity, post-operative length of stay, and mortality[1-4] Reported SSI rates after colorectal surgery range from 5% to 30%, making them high-incidence procedures.[5-8] Colorectal surgeries are therefore incorporated in most SSI surveillance programmes.

In most hospitals, surveillance is performed manually. However, this is experienced as labour-intensive, and possibly inaccurate and is prone to subjectivity and low interrater agreement, thus limiting comparisons between hospitals.[9-11] The increasing availability of data stored in the electronic health records (EHRs) offers opportunities for (partially) automating SSI surveillance, thereby reducing the workload and supporting standardisation of the surveillance process. To date, several studies have published (semi-)automated methods to automate SSI surveillance after colorectal surgery. Unfortunately, most of these are not feasible for Dutch hospitals 1) because they include elements that are not representative of the Dutch clinical setting and practice; 2) because they have insufficient algorithm performance; 3) because processing time is delayed; or 4) because they are too complex for application in real life.[12-18]

Two published semi-automated surveillance algorithms targeting deep SSI after colorectal surgery may be feasible for the Dutch setting: a classification algorithm[19] and a multivariable regression model.[20] The classification algorithm was pre-emptively designed based on clinical and surveillance practices from a French, a Spanish and a Dutch hospital. The sensitivity was 93.3% – 100% compared to manual surveillance, and the algorithm yielded a workload reduction of 73% – 82%. The regression model was developed using data from a Dutch teaching hospital; we used it to predict the probability of deep SSI for each individual patient. This 5-predictor model had a sensitivity of 98.5% and a workload reduction of 63.3%.[20]

External validation or actual implementation studies of new methods for automated surveillance (AS) are scarce.[21,22] As reported by two systematic reviews, only 23% of the included studies used a separate validation cohort [23] and only 25% of AS were used in clinical routine.[24] Hence, knowledge about generalisability of AS models is limited, and information about the path toward actual implementation is needed.[22,25,26]

In this study, we present an independent and external validation of the previously developed classification and regression model in new cohorts of patients that underwent colorectal surgeries in different types of Dutch hospitals.[21] We investigated the feasibility of data

requirements for both algorithms. If feasible and externally valid, these models can be implemented in SSI surveillance practices and workflow processes.

METHODS

Study design

In this retrospective cohort study, four Dutch hospitals (academic (n = 1); teaching (n = 2); general (n = 1)), each with different, or different versions of, EHR systems, extracted the data needed for algorithm application. To obtain insights in hospitals' clinical practice and patient care, a questionnaire adapted from a previous study[19] was filled in by the hospital staff at the start of the study (**Supplemental File S9.1**). Feasibility of the data collection (a precondition for implementation) was evaluated by assessing the completeness of the surveillance population (denominator) and the ability of the hospitals to automatically collect case-mix variables from their EHR. Thereafter, we applied the two surveillance algorithms to the extracted data. Model results were compared with conventional (i.e. manually annotated) surveillance.[11] Approval for this study was obtained from the institutional review board at University Medical Centre Utrecht (reference no. 20-503/C) and from the local boards of directors of each participating site. Informed consent was waived given the observational and retrospective nature of this study.

Surveillance population and data collection

The hospitals identified patients aged > 1 year undergoing primary colorectal resections in 2018 and/or 2019 based on procedure codes in EHR data. Hospitals could use other data sources to establish inclusion rules to construct the surveillance population and to distinguish secondary procedures or re-surgeries. For the patients included in the surveillance population, structured data were extracted from the EHR including demographics, microbiological culture results, admissions (i.e. prolonged length of stay or readmission), resurgeries, radiology orders, antibiotic prescriptions, and variables for case-mix correction (see **Supplemental Table S9.1**).

Outcome

The outcome of interest was a deep SSI (deep incisional or organ-space) within 30 days after surgery according to the Dutch surveillance protocol.[27] In short, patients having purulent drainage from the deep incision or from a drain that is placed through the wound, or having an abscess, a positive culture from the organ/space, or signs and symptoms of infection

in combination with wound dehiscence and a positive culture of deep soft tissue, or other evidence of infection by direct examination were considered deep SSIs. The criterion of a positive culture is not applicable in case of anastomotic leakage or perforation following the surgery. In each hospital, infection control practitioners (ICPs) manually screened patients to identify deep SSI. This manual surveillance was considered the reference standard. All ICPs performing manual chart review received training to ensure the quality of data collection and case ascertainment.[11] Moreover, all hospitals participated in an on-site visit to validate the conventional surveillance. Details about this on-site validation visit are described below.

Feasibility of data collection

To evaluate the feasibility of the data collection, we evaluated the completeness of the surveillance population (denominator data) by comparing the patients selected by procedure codes with patients included in the reference standard. Additionally, we compared agreement between the case-mix variables (i.e. risk factors: age, sex, ASA classification, wound class, stoma creation, malignancy and anastomotic leakage) that were extracted from the EHR with the case-mix variables that were collected during conventional surveillance.

Algorithm validation

Model validation of the classification model

The classification algorithm was based on the development study, using 5 elements: antibiotics, radiology orders, (re)admissions (i.e. prolonged length of stay, readmissions or death), resurgeries and microbiological cultures (**Figure 9.1-A** and **Supplemental Table S9.2**). All extracted data were limited to 45 days following the colorectal surgery to enable the algorithm to capture deep SSIs that developed at the end of the 30-day follow-up period. In accordance with the development study,[19] patients were classified into low probability of having had a deep SSI (≤ 1 element excluding microbiology, or 2 – 3 elements and no microbiology) and high probability of having had a deep SSI (4 elements excluding microbiology, or 2 – 3 elements and microbiology). High-probability patients required manual SSI confirmation, and low-probability patients were assumed free of deep SSI. If discrepancies were found between the clinical practice reported in the questionnaire and the algorithm, we evaluated whether an adaptation of the classification algorithm could have improved performance. When an algorithm element could not be computed due to incomplete data (e.g. discharge date is missing so length of stay cannot be computed) the patient scored positive on that element.

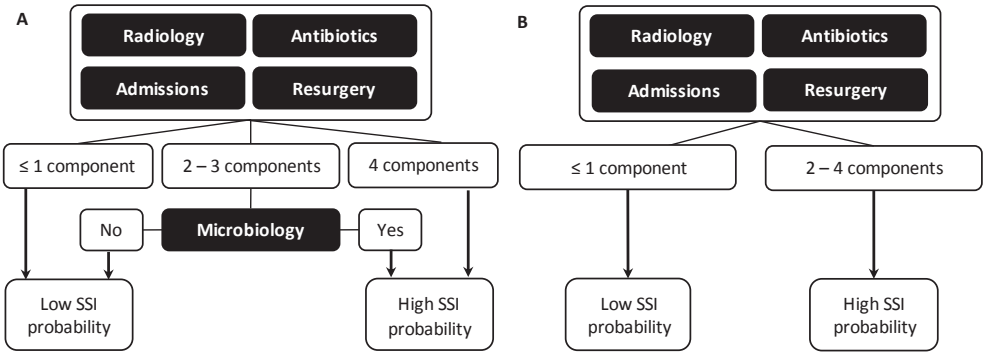

Figure 9.1. Classification model.
(A) Previously developed classification algorithm to classify patients with high or low probability of having had a deep surgical site infection after colorectal surgery. Figure originally published in van Rooden et al. and used with permission.
(B) Modified classification algorithm.
Explanation algorithm elements, for details please see **Supplemental Table S9.2**.
Radiology: ordering CT scan; Antibiotics: ≥ 3 consecutive days of antibiotics post-operative; Admissions: length of stay ≥ 14 days or ≥ 1 readmission or death; Resurgery: ≥ 1 reoperation; Microbiology: ≥ 1 culture.
Abbreviations: SSI = surgical site infection.

Model validation of the regression model

The regression model utilises wound class, hospital readmission, resurgery, postoperative length of stay and death to calculate the probability of deep SSI. Coefficients estimated in the development setting[20] were multiplied with the predictor values of this validation cohort to estimate SSI probability (**Figure 9.2** and **Supplemental Table S9.3**). In accordance with the cutoff point in the development study, patients were classified into low probability of deep SSI (≤ 0.015) and high probability of deep SSI (> 0.015). High-probability patients required manual SSI confirmation, whereas low-probability patients were assumed free of deep SSI. In case a predictor could not be automatically extracted by the hospital or had missing values, the predictor collected by the manual surveillance was used to be able to evaluate algorithm performance.

$$P(DSSI) = \frac{1}{1 + e^{-LP}}$$

LP= -5.234 + 0.890 * contaminated wound (class 3) + 3.037 * re-surgery + 1.489 * readmission + 0.085 * number of postoperative days admitted to the hospital + 1.127 * mortality

Figure 9.2. Previously derived prediction rule for deep surgical site infection (DSSI) after colorectal surgery. For each individual patient, the regression model returns a predicted probability of SSI which can be used to classify patients.
Abbreviations: P(DSSI) = probability of deep surgical site infection; LP = linear predictor.

On-site visit

All hospitals participated in an on-site visit to validate the conventional surveillance . This was executed by two experienced surveillance advisors of the Dutch national HAI surveillance network who were blinded for the outcomes of both the reference standard and the algorithms. For each hospital, a sample of 20 patients was taken from the data according to the hierarchical rules (**Figure 9.3**). All false-negative results were included, to confirm their deep SSI status. Additionally, records from every other group (false-positive, true-positive, and true-negative results) were included until 20 were gathered. The group size of 20 patients was based on the time capacity of the validation team.

Hierarchic rules to select a sample from results classification model (maximum n=20):

1. All false negatives (missed SSI)
2. All superficial SSIs within the false positives
3. Maximum of 5 randomly selected false positives
4. Random 20% true positives
5. All superficial SSIs detected in the true negative group
6. Adding random true negatives till the number of 20 is reached

Figure 9.3. Hierarchic rules for sample selection for on-site validation of reference standard.

Statistical analyses

After data linkage, descriptive statistics were generated. To evaluate data feasibility, missing data patterns were described, and no techniques such as multiple imputation were performed to complete the data. Both models were applied to the data extractions, and results were compared with the reference standard. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and workload reduction were calculated overall and were stratified per hospital. Workload reduction was defined as the proportion of colorectal surgeries no longer requiring manual review after algorithm application. A discrepancy analysis was performed in case of any false-negative results (i.e. missed deep SSI); the algorithm elements were checked in the original data . Data cleaning and statistical analyses for the classification model were carried out in SAS version 9.4 software (SAS Institute, Cary, NC). For the regression model, we used R version 3.6.1 software (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Feasibility of data collection

Completeness of the surveillance population

The exact surveillance population could not be reconstructed, because there were no separate procedure codes or potential inclusion rules to reliably distinguish secondary procedures or resurgeries from primary procedures (range 8.7% – 22.0%, **Table 9.1**). Vice versa, 0 – 25% of patients in the reference standard were not identified when using inclusion rules based on procedure codes (details in **Table 9.1**). Thus, 672 colorectal surgery patients were included in this study, and 28 had deep SSIs (4.1%).

Table 9.1. Overview of data collection and selection of surveillance population.

	Hospital A	Hospital B	Hospital C	Hospital D
Time period extractions (years)	2019	2018 – 2019*	2019	2019*
Total number of colorectal surgeries in reference standard (count)	205	167	221	142
Total number of colorectal surgeries extracted automatically (count)	228	159	236	148
Number of matched records (count)	205	124	212	131
Total number of deep SSI in matched records (count (%))	7 (3.4)	3 (2.4)	7 (3.3)	11 (8.3)
Records in extractions that could not be linked to reference standard (count (%))#	23 (10.1)	35 (22.0)	24 (10.2)	17 (11.4)
Records in reference standard that could not be linked to extractions (count (%))§	0 (0.0)	43 (25.7)	9 (4.1)	11 (7.7)

* until July 1st, 2019.
# Explanation of mismatch: manual review of a random sample of these records showed these were mainly revision/secondary procedures, and for hospital C surgeries performed at another hospital location that are excluded from manual surveillance.
§ Explanation of mismatch:
Hospital B: incorrect inclusions in reference standard as they did not meet inclusion criteria (no primary procedure).
Hospital C: These surgeries were registered as executed by internal medicine department, while for the extractions only resections performed by surgery department were selected.
Hospital D: According to the national surveillance protocol the resection with the highest risk is to be registered in case of more resections during the same surgery. Hospital included the wrong procedure in these cases.
Abbreviations: SSI = surgical site infection.

Completeness data collection

Electronic collection of the minimum required dataset from the EHR was feasible for all variables except wound class. Hospital A used text mining to establish the wound class. For hospitals B and C, wound class as collected during manual surveillance (reference standard) was used. For hospital D, wound class information was not available in source data.

Figure 9.4 shows the percentage of agreement between the case-mix variables extracted from the EHR and those collected manually. Disagreement was mostly related to incomplete data, either variables were not registered in the original source or were not available from source data at all.

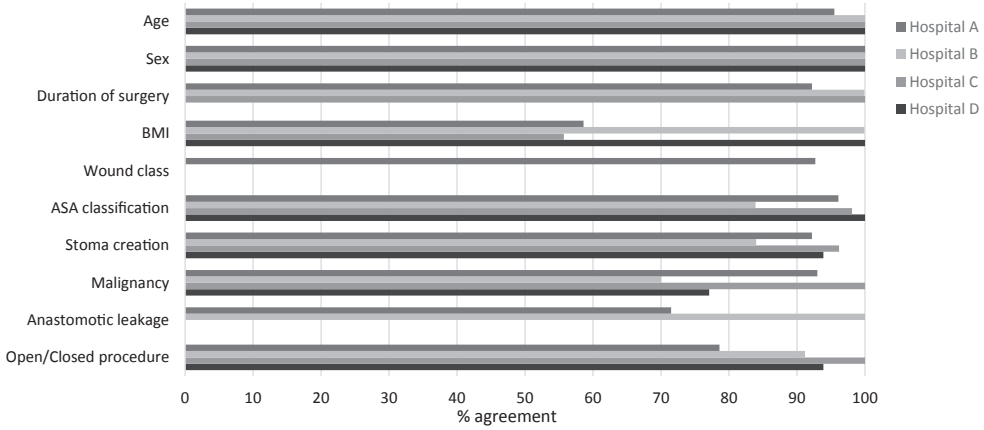

Figure 9.4. Percentage agreement of risk factors extracted automatically compared to manual annotation.
Abbreviations: BMI = body mass index; ASA = American Society of Anesthesiologists.

Algorithm validation

The original classification model had an overall sensitivity of 85.7% (95% CI 67.3 – 96.0%), ranging from 72.7% to 100% between hospitals, a specificity of 92.1% (95% CI 89.7 – 94.0%), PPV of 32.0% (95% CI 21.7 – 43.8%) and an NPV of 99.3% (95% CI 98.3 – 99.8%). For the performance per hospital see **Table 9.2**. Only 8% – 13% of the records required manual review after algorithm application. In hospitals C and D, respectively, one and three deep SSIs were missed by the algorithm (**Table 9.3)**. In contrast to hospitals A and B, both hospitals had reported in the questionnaires that microbiological cultures were not consistently taken in case of suspected infection, and this was reflected in the percentage of patients meeting the microbiology element. Therefore, we adapted the algorithm and classified patients with one element (i.e. radiology order, antibiotics, readmission, or resurgery) as low probability (**Figure 9.1-B**). This model resulted in higher sensitivity (overall sensitivity = 100%; 95% CI 87.7% – 100.0%) but at the cost of lower PPV and less workload reduction (**Table 9.2**).

The regression model could only be validated for hospitals A – C because wound class was not available for hospital D. Similar to the development study, patients with infected wounds (wound class 4) were excluded, leaving respectively 187, 116, and 207 records from hospitals

Table 9.2. Algorithm performance (% (95% confidence interval), unless specified other).

	Sensitivity	Specificity	Positive predictive value	Negative predictive value	% red.
Classification model					
Hospital A	100 (59.0 – 100.0)	90.4 (85.4 – 94.1)	26.9 (11.6 – 47.8)	100 (97.9 – 100.0)	87.4
Hospital B	100 (29.2 – 100.0)	89.3 (82.3 – 100.0)	18.8 (4.0 – 45.6)	100 (96.6 – 100.0)	87.2
Hospital C	85.7 (42.1 – 99.6)	92.2 (87.6 – 95.5)	27.3 (10.7 – 50.2)	99.5 (97.1 – 99.9)	89.7
Hospital D	72.7 (39.0 – 93.9)	97.5 (92.9 – 99.5)	72.7 (39.0 – 93.9)	97.5 (92.9 – 99.5)	91.6
Regression model					
Hospital A	100 (39.8 – 100.0)	78.1 (71.4 – 83.9)	9.0 (2.5 – 21.8)	100 (97.5 – 100.0)	76.5
Hospital B	100 (29.2 – 100.0)	78.9 (70.1 – 85.9)	11.1 (2.3 – 29.2)	100 (95.9 – 100.0)	76.8
Hospital C	100 (59.0 – 100.0)	80.0 (73.8 – 85.3)	14.9 (6.2 – 28.3)	100 (97.7 – 100.0)	77.3
Hospital D	NA	NA	NA	NA	NA
Modified classification model					
Hospital A	100 (59.0 – 100.0)	77.8 (71.3 – 83.4)	13.7 (5.7 – 26.3)	100 (97.6 – 100.0)	75.2
Hospital B	100 (29.2 – 100.0)	80.1 (71.9 – 86.9)	11.1 (2.3 – 29.2)	100 (96.3 – 100.0)	78.3
Hospital C	100 (59.0 – 100.0)	77.6 (71.2 – 83.1)	13.2 (5.4 – 25.3)	100 (97.7 – 100.0)	75.0
Hospital D	100 (71.5 – 100.0)	89.2 (82.2 – 94.1)	45.8 (25.6 – 67.2)	100 (96.6 – 100.0)	81.7

Abbreviations: NA = not applicable; % red. = percentage of workload reduction in number of medical records to review.

Table 9.3. Discrepancy analyses and explanation for deep SSIs not detected by original classification algorithm (false negatives).

False negatives	Number of algorithm elements[#]	Missing elements	Explanation
Patient 1 – Hospital C	3	Microbiology* Resurgery	Treatment differed from regular treatment strategies as no reoperation was performed. Thereby, the deep SSI was scored manually based on one short clinical note stating that pus from the drain was observed.
Patient 1 – Hospital D	2	Microbiology* Resurgery Antibiotics	No reoperation was performed. The antibiotic treatment was not identified by the algorithm as these were home-administered antibiotics which were not included in the data selection.
Patient 2 – Hospital D	3	Microbiology* Readmission	Reoperation took place 3 days after surgery, during the hospitalisation of the index surgery: no readmission needed.
Patient 3 – Hospital D	3	Microbiology* Resurgery	Patient had an endo-sponge placement; however, this reintervention is not registered as resurgery and performed as outpatient treatment by an internist, gastro-enterologist or endoscopist from the gastrointestinal and liver diseases specialty while for the data extractions only resurgeries performed by same specialty as index surgery were selected.

[#] Algorithm elements are radiology orders, antibiotics, (re)admissions, resurgeries and microbiology. Patients needed 4 elements excluding microbiology, or 2 – 3 elements and microbiology to be classified as high probability by the algorithm. See also **Figure 9.1** and **Supplemental Table S9.2**.
* Both hospitals had reported in the questionnaires that cultures were not consistently taken in case of suspected infection.

A – C for analyses, including 4, 3 and 7 deep SSIs. For this model, overall sensitivity was 100% (95% CI 76.8% – 100%); the specificity was 76.9% (95% CI 73.0% – 80.5%); the PPV was 11.9% (95% CI 6.6% – 19.1%) and the NPV was 100% (95% CI 99.0 – 100%). With this algorithm only 22.7% – 23.5% records required manual review. The results per hospital are shown in **Table 9.2**. Due to the small sample size and low number of deep SSIs, discrimination and calibration were not evaluated.

No discrepancies were found during the on-site validation visit in hospital D. In the other three hospitals, on-site validation revealed five additional deep SSIs: two were overlooked in the conventional surveillance and three were initially classified as superficial SSI. All additional deep SSIs were classified correctly as high probability by both the (modified) classification model and the regression model. Other findings of the on-site validation of the reference standard, though not essential for the assessment of the algorithms, were reclassifications of superficial SSIs to no SSI (n = 1), missed superficial SSIs (n = 2), and incorrect inclusions (n = 8).

DISCUSSION

This study demonstrated the external validity, both temporal and geographical, of two surveillance algorithms that identify patients with a high probability of deep SSI after colorectal surgery. Both had a high detection rate for deep SSI and can be used for semi-automated surveillance and, thus, to further improve efficiency and quality of SSI surveillance.

Both the classification model, especially when adapted to local practices, as well as the regression model, performed very well. To select a model for use within an organisation, we considered other aspects of implementation. First, in case of incomplete data, the original development study of the regression model used multiple imputation techniques. For the classification model, the patient scored positive on the algorithm element that could not be computed due to incomplete data. This was a more convenient method for which no complex data management techniques were required. Second, according to the original study, patients with a dirty-infected wound (i.e. wound class 4) were excluded from the cohort of the regression model. However, according to the national surveillance protocol, these cases should have been included in the surveillance. In addition, in two hospitals, wound class was not available in a structured format for automated extraction hindering algorithm application. Third, the classification model was easily be adapted to local practices. For the regression model, a sufficient sample size was required for redevelopment or recalibration in case of low predictive accuracy. This aspect may be challenging for hospitals performing few colorectal resections. Therefore, the (modified) classification model is more feasible and sustainable for real-life implementation within hospitals, improving standardisation and benchmarking. We know from a previous study that the classification model has also been successful in other European countries and in low-risk surgeries such as hip- and knee arthroplasties.[19,28]

For both algorithms, however, several hurdles remain for implementation. The exact surveillance population could not be automatically selected by procedure codes, but a change in the current inclusion criteria or target population could be considered. In this study, 10% – 22% of surgeries detected by procedure codes did not concern a resection, were not the main indication for surgery (but performed concomitant to other intra-abdominal surgeries), or were not the first colon resection for that patient. Also, the variables necessary for case-mix-adjustment are sometimes difficult to extract automatically. Although the search for a proper case-mix correction is ongoing,[14,29-32] automated extraction of a minimal set of risk factors is necessary to interpret the surveillance results and to maintain the workload reduction delivered by (semi-)automated surveillance.

Two findings in this study emphasize that close monitoring, validation of algorithm components, and future maintenance are important to maintaining alignment with clinical practice and guarantee high-quality surveillance. First, as appeared from the questionnaire, two hospitals did not consistently obtain microbiological cultures in case of suspected deep SSI. We advise researchers to first verify whether algorithms align with clinical practice and consider adapting algorithms to differences subsequently.[23,33-35] Secondly, new treatment techniques should also be evaluated regularly and algorithms adapted accordingly. Endo-sponge therapy is increasingly used after anastomotic leakage, however, this intervention is often not registered or is regarded as resurgery but as outpatient treatment performed by a different specialty than the initial colorectal surgery. Each hospital should therefore periodically evaluate care practices and algorithm elements to select the appropriate resurgeries or to include recently introduced interventions, such as endo-sponge therapy, within the resurgery element in the surveillance algorithm.

Strengths and limitations

This study had several strengths. We performed an independent external validation in independent patient data from different types of hospitals, as well as a temporal validation. Apart from algorithm performance, automated selection of patients and case-mix variables were investigated as well, which are prerequisites for actual implementation.

This study also had several limitations. First, both algorithms targeted deep SSIs only, but in colorectal surgeries 20% – 50% of SSIs are superficial.[6,36] Debate continues regarding the inclusion of superficial SSI in surveillance programmes given their subjective criteria and limited clinical implications.[28,37,38] Second, we aimed to validate all published AS systems that appeared applicable to Dutch practice, however, AS systems may have been developed by commercial companies that were not published in scientific literature and were therefore not included. Third, the small sample size and low number of deep SSIs resulted in large confidence intervals for the individual hospitals and impeded the evaluation of discrimination and calibration.[39,40] Although a larger validation cohort is preferred, the numbers used in this study reflect the reality of surveillance practices. Although underpowered, the overall sensitivity and hospitals' individual point estimates were satisfying, and this study provided valuable insights into implementation. Fourth, for both manual- and semi-automated surveillance, post-discharge surveillance was limited to the initial hospital. In the Dutch setting, patients return to the operating hospital in case of complications, so this will likely not lead to underestimation of SSI rates. SSI benchmarking or widespread implementation of

this semi-automated algorithm may be hampered for countries without this follow-up. Last, as actual widespread implementation of AS is still limited,[24-26] this study provides insights into validity and data requirements needed for implementation of semi-automated SSI surveillance after colorectal surgery. However, this study did not include a full feasibility study including economic, legal, and operational assessments. We emphasize that successful implementation also depends on organisational support, information technology knowledge, staff acceptance, change management, and possibilities for integration in workflows.

Conclusion

In this independent external validation both approaches to semi-automated surveillance of deep SSI after colorectal surgery performed well. However, the classification model was proven preferable to the regression model because of source data availability and less complex data-management requirements. Our results have revealed several hurdles when automating surveillance. The targeted surveillance population could not be automatically selected by procedure codes, and not all risk factors were complete or available for case-mix correction. The next step is implementation in infection prevention practices and workflow processes to automatically identify patients at increased risk of deep SSI.

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AUTHOR CONTRIBUTIONS

JV conceptualised and designed the study, was responsible for data management, analyses and interpretation and wrote the first draft of the manuscript. TvdK participated in the analyses and data interpretation. MvM was responsible for the conceptualisation, study designing and data interpretation. NO and MN collected the data. TvdK, DH, NO, MN, SdG, MB and MvM reviewed the manuscript for intellectual content and scientific integrity. All authors have read and approved the final manuscript.

CONFLICT OF INTERESTS

The authors declare that they have no competing interests.

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SUPPLEMENTARY MATERIAL

Supplemental File S9.1. Questionnaire classification model (to be filled in by each hospital).

A . Automated selection of the patients in the study population

1. What data sources are used to select patients that should be in the surveillance?
   Examples are operating records, nursing notes, administrative data or special modules of the electronic health record.

2. Can you provide details?
   incl. specific codes used, in- and exclusion criteria, persons performing the selection etc…

3. Are you able to distinguish primary operations from reoperations or non-primary operations? And if so, how do you make this distinction?
   e.g. specific codes used, criteria, persons performing the selection…

4. Are you able to distinguish resections (removing a part of the large bowel) from other surgeries of the colon (like colostomies)?

5. What challenges do you encounter by selecting primary resections?
   Have you validated your selection? Do you miss certain patients or wrongfully include a fraction of your patients?

B. Clinical practice in all patients suspected for a surgical site infection

Please describe below how patients suspected of SSI are usually diagnosed/treated in your centre

Microbiology

1. Are cultures (almost) always obtained when a patient –after colorectal surgery- is suspected of SSI?
2. What sites/materials are cultured?
3. How often are cultures obtained under antibiotics?

Antibiotics

4. What is the empiric treatment regimen when an SSI is suspected (agent + duration)?
5. If an infection if proven, how long is the patient typically treated with the antibiotics?

Readmissions

6. By what specialty are patients re-admitted because of a suspected SSI? What are the codings for the wards or specialties?

Reoperations

7. Are patients re-operated when an SSI is suspected?
8. What procedure is typically performed (description or operating codes)?
9. By what specialty are reoperations performed? What are the codings for the wards?

Radiology

10. Will there be a radiology order for patients suspected for SSI? If yes: which? (description/codes)?
11. If there is anastomotic leakage, what will be (in most times) the treatment?

C. Information about risk factors

Please indicate in the table below in what way variables can be extracted.

	No	**Yes, Extracted from another source then the built-in SSI surveillance module, namely….**	**Yes, however this information is filled in manually by performing manual surveillance and is extracted from the built-in SSI surveillance module**
Age			
Sex			
BMI			
Duration of surgery			
Wound class			
ASA classification			
Colostomy			
Surgery because of malignancy			
Anastomotic leakage			

Background information of the surveillance algorithms

Supplemental Table S9.1. Minimum required dataset to apply classification model and/or regression model.

Theme	Variable[1]	Format
Identifier	Identification number	numeric/text
Demographics	Age	numeric/text
	Sex	numeric/text
Index surgery (Colorectal surgery)	Date of surgery	date
	Description surgery (e.g. ICD-9/10 /CTG)	text
	Treating specialty	text
	Surgical technique	text
	Date of admission	date
	Date of discharge	date
	Treating specialty	text
	Wound class[#]	numeric/text
Readmission(s)*	Date of admission	date
	Date of discharge	date
	Treating specialty	text
Resurgery*	Date of reoperation	date
	Procedure code (e.g. ICD-9/10/CTG)	text
	Description surgery	text
	Treating specialty	text
Microbiology*[§]	Date of culture taken	date
	Sample number	numeric/text
	Sample material (e.g. blood, tissue)	text
	Sample material additional text	text
	Result	text
	Conclusion/quantity	text
Antibiotics*	Code (ATC in categories J01)/description	text
	Start date	date
	Stop date	date
Radiology*[§]	Date of radiology order	date
	Procedure	numeric/text
	Description	text
	Treating specialty	text
Mortality	30-day mortality	date

[1] All data until 45 days post-surgery for the classification model, 30 days post-surgery for the regression model.
* Data may contain more than 1 record per patient.
[#] Only required for the regression model.
[§] Only required for the classification model.

Supplemental Table S9.2. Algorithm specifications classification model.

Elements algorithm	Criteria[a]	Specification
(Re)Admissions	Length of stay of index admission ≥ 14 days OR ≥ 1 re-admission OR Death	Length of hospital stay of the index admission (i.e., admission during which the colorectal surgery took place) of ≥ 14 days ((discharge date – date of index surgery) +1) OR ≥ 1 readmission(s) for the relevant specialty (i.e. specialty surgery or gastrointestinal oncology surgery), after the index surgery but within FU time OR Mortality within FU time
Resurgery	≥1 reoperation by original surgery specialty	Surgeries performed by the department of surgery or gastrointestinal oncology surgery, after the index surgery and within FU time. No further restrictions.
Antibiotics	≥3 consecutive days of antibiotics (ATC J01) post-operative, starting from day 2	All antibiotic orders (ATC J01) prescribed from day 2* until end of FU, including outpatient prescriptions but excluding ICU prescriptions. Overlapping episodes count as 1 day (e.g. two antibiotic prescriptions, one for 4 days and one for 2 days of which 1 days overlap result in a total of 5 consecutive days of antibiotic exposure).
Radiology	Ordering CT scan	CT scan order within FU time
Microbiology[$]	≥1 culture taken from relevant body sites	≥ 1 culture obtained from potentially relevant body site(s), such as wound cultures, purulent, fluid, drain, tissue, unspecified material. All cultures are taken into account from day 1* until end FU.

* Date of initial, index surgery = day 0.
[a] All criteria should be fulfilled within 45 days after the index surgery (FU time=45 days).
[$] Microbiology element only applied if 2 or 3 criteria from above are met.
Abbreviations: FU = follow-up.

General rules for applying the classification model (data cleaning)

- A patient can only be included in the surveillance once, as only primary resections are included in the surveillance. Secondary colorectal resections are excluded from the surveillance population.
- If a patient has more index colorectal resection procedures during the same surgery, the resection with the highest risk is included in the surveillance. The highest risk is defined as the procedure in which the lowest part of the colon is removed.
- Patients can be included several times in the admission, antibiotic or microbiology data as they can have can have multiple readmissions, antibiotics or microbiology results.
- If start- and stop date of antibiotic prescriptions or admission/discharge dates are swapped: the number of days is converted from minus to plus.
- Microbiology results obtained from 1 culture count as 1 result.
- If an algorithm element cannot be computed due to incomplete data, the index surgery is flagged positive on that algorithm element.

Supplemental Table S9.3. Algorithm specifications prediction model.

Elements algorithm	Criteria[a]	Coefficient
Post-operative length of stay	Length of stay of initial surgery in days	0.085
Resurgery	≥ 1 reoperation by original surgery specialty	3.037
Readmission	≥ 1 readmission(s) for the relevant specialty (i.e. specialty surgery or gastrointestinal oncology surgery), after the index surgery but within FU time	1.489
Wound class	Wound class 2 or wound class 3	0.890
Death	Mortality within FU time	1.127

[a] All criteria should be fulfilled within 30 days after the index surgery (FU time=30 days). Date of initial, index surgery = day 0. Intercept=-5.234.
Abbreviations: FU = follow-up.

10

The augmented value of using clinical notes in semi-automated surveillance of deep surgical site infections after colorectal surgery

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Manuscript in preparation

ABSTRACT

Background: In patients who underwent colorectal surgery, a semi-automated surveillance algorithm based on structured data achieves high sensitivity in detecting deep surgical site infections (SSIs), however, generates a significant number of false positives. The inclusion of unstructured, clinical narratives to the algorithm may decrease the number of patients requiring manual chart review.

Aim: To investigate the performance of a semi-automated surveillance algorithm augmented with an NLP component to improve positive predictive value (PPV) and thus workload reduction (WR).

Methods: Retrospective, observational cohort study in patients who underwent colorectal surgery from January 1, 2015 through September 30, 2020. The previously developed semi-automated surveillance algorithm was validated. Subsequently, natural language processing (NLP) was used to detect keyword counts in clinical notes. Several NLP-algorithms were developed with different count input types and classifiers, and added as component to the original semi-automated algorithm. Traditional manual surveillance was compared with the NLP-augmented surveillance algorithms and sensitivity, specificity, PPV and WR were calculated.

Findings: The original (structured data) algorithm had 97.6% sensitivity (95% confidence interval (95% CI) 87.1 – 100%) and 57.3% WR. From the NLP-augmented models, the decision tree models with discretised counts or binary counts had the best performance (sensitivity = 95.1%; 95% CI 83.5 – 99.4%; WR = 60.9%) and improved PPV by only 2.6% compared to the original algorithm.

Conclusion: The original semi-automated algorithm achieved near-perfect sensitivity and substantial WR. The addition of an NLP component to this algorithm had modest effect on WR (decrease of 1.4 – 12.5%), at the cost of sensitivity. For future implementation it will be a trade-off between optimal case finding techniques versus practical considerations such as acceptability and availability of resources.

INTRODUCTION

Approximately 5% to 30% of colorectal surgery patients develop a surgical site infection (SSI). SSIs result in morbidity, mortality, longer hospital stays and extra costs.[1-3] Monitoring SSIs is an essential policy strategy and has been proven effective in reducing these infections.[4,5] Several (local and national) surveillance programmes target SSI after colorectal surgery; patient records are retrospectively reviewed and manually annotated by infection control practitioners (ICPs) according to surveillance case definitions for SSI.[6-8] This traditional way of performing surveillance is labour-intensive, prone to subjective interpretation, and poor interrater agreement has been reported.[9-11] In the past years, automated surveillance methods that re-use data stored in electronic health records (EHRs) are increasingly developed to reduce workload, and to objectify and align surveillance methods. They are considered an attractive alternative to manual surveillance.[12]

For most automated surveillance algorithms targeting SSI after colorectal surgery, no satisfying results have been reported so far: the methods described are not applicable to different settings, are very complex, have insufficient performance, and are mostly limited to the use of structured data as these are relatively easy to obtain and to process.[13-17] There has been one semi-automated algorithm described and validated in multiple (Dutch) hospitals with promising results.[18] With the use of structured data from radiology orders, admission- and discharge dates, antibiotic prescriptions, and reoperations, the algorithm classifies patients into high- or low probability of having had a deep SSI according to pre-specified rules (**Supplemental Table S10.1**). Only the high-probability records need manual confirmation.[19] Despite high to perfect sensitivity, the workload reduction achieved was not optimal given the large number of false positives.

As the diagnosis of an SSI is mainly dependent on physical examinations and observations that are described in clinical notes, the inclusion of unstructured, free-text information to this algorithm may improve the method by reducing the number of false positives. Natural language processing (NLP) is a technique that processes, learns and understands human language content, and can be used in analysing these unstructured data.[20] Experiences with NLP-supported surveillance algorithms are limited: there are some studies, however, with varying and often inconclusive results.[21-24] Also, the combination of using both structured and unstructured data for surveillance algorithms has not been extensively researched so far, but it is known that in general, the use of more heterogeneous data types result in better performance and case finding.[25,26] The aim of this study was to investigate the performance of the original semi-automated surveillance algorithm augmented with an NLP component to improve positive predictive value (PPV) and to reduce the workload.

METHODS

Study design, setting and study population

This is a retrospective, observational cohort study including patients undergoing colorectal surgery (i.e. primary or secondary colorectal resections, incisions or anastomosis) performed at the Karolinska University Hospital (KUH) Sweden, between January 2015 and September 2020. Prior to developing the NLP component, the original semi-automated algorithm – based on structured data – was validated in KUH. The NLP algorithms were subsequently developed as an 'add-on' component and designed as an additional step following the existing semi-automated algorithm, aiming to eliminate false-positive signals whilst maintaining sensitivity. This sequential design will arguably lower implementation thresholds in the future: hospitals can already start implementing the semi-automated algorithm with structured data and may later add the (more advanced and challenging) NLP component (**Figure 10.1** and **Supplemental Table S10.1**). Model results were compared with the reference standard, which is the traditional manually annotated surveillance. Review and approval for this study was obtained from the Regional Ethical Review Board in Stockholm, Sweden (2018/1030-31).

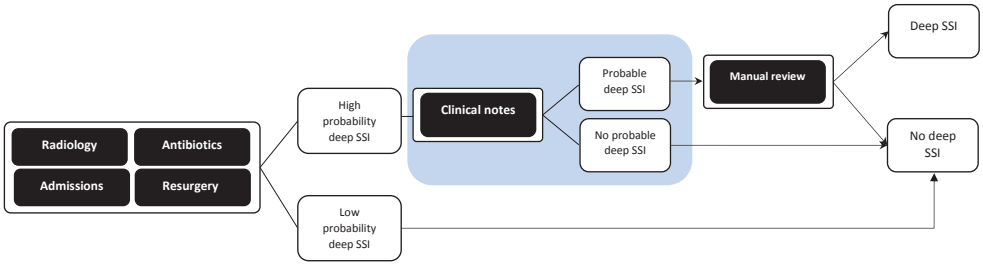

Figure 10.1. Schematic overview of the original semi-automated algorithm comprised of structured data, augmented with unstructured data (clinical notes, in blue frame).

Outcome

The key outcome was a binary indicator of a deep SSI or organ/space SSI, hereinafter referred to as deep SSI, versus no deep SSI (i.e. no SSI or superficial SSI) within 30 days after the colorectal procedure. The outcome was recorded during manual annotation by two experienced infection control practitioners (ICPs) according to the European Centre for Disease Prevention and Control (ECDC) SSI definition and guidelines.[6]

Data sources

In 2020, the Stockholm Proactive Adverse Events REsearch (2SPARE) database was created. 2SPARE is an SQL-based relational database and a duplicate of the data recorded in the EHR system of the KUH, currently containing all patient records over the period January 2010 –August 2021 including data on patient characteristics, hospital admission and discharge records, outpatient records, physiological parameters, medication orders, microbiology-, clinical chemistry-, radiology results, and clinical notes. The clinical notes data includes unstructured, free-text notes such as progress notes, discharge summaries, history and physical examination notes, and telephone encounter notes, all written in Swedish language. We limited the notes to those written by physicians, residents, surgery assistants, and nurses, and to those written within 1 – 30 days post-surgery as these are most likely to contain SSI-relevant information.

Validation of the original semi-automated algorithm

Firstly, prior to developing NLP components, the original semi-automated algorithm based on structured data only was validated. From the 2SPARE database, a random selection of 225 patients undergoing colorectal surgery during the study period (41 deep SSI) were selected as validation cohort to apply the original algorithm on. Model performance results were compared to the reference standard (i.e. manual SSI-ascertainment) **(Figure 10.2**). For the manual SSI-ascertainment, both raters were blinded for the algorithm outcomes and twenty cases of the validation cohort were reviewed in overlap resulting in almost perfect agreement (95%) between them, with a Cohen's Kappa of 0.87 for SSI classification.

Development and validation of the NLP-augmented models

The original semi-automated algorithm was subsequently applied to the remaining colorectal patients in 2SPARE. Next, a random selection of 250 high-probability records were extracted for the development cohort and annotated resulting in 92 deep SSIs. Several NLP components were developed using this development cohort consisting of high-probability individuals. The final NLP-augmented algorithms were validated using the validation cohort as described above (**Figure 10.2**).

Pre-processing of linguistic variables

A list of keywords was compiled by reviewing clinical literature and local case reports, and by expert consultation in the Netherlands and Sweden (i.e. colorectal surgeons, medical

microbiologists, ICPs, infectious disease consultants) (**Figure 10.3**). Next, from the keywords we created a list of lemmatised versions and applied part-of-speech tagging to capture differences in grammatical and spelling versions of the words. This resulted in the overall lexicon list. The keywords given by Dutch experts were translated to Swedish to be able to apply them on Swedish notes, and all keywords were translated to English for the purpose of reporting results.

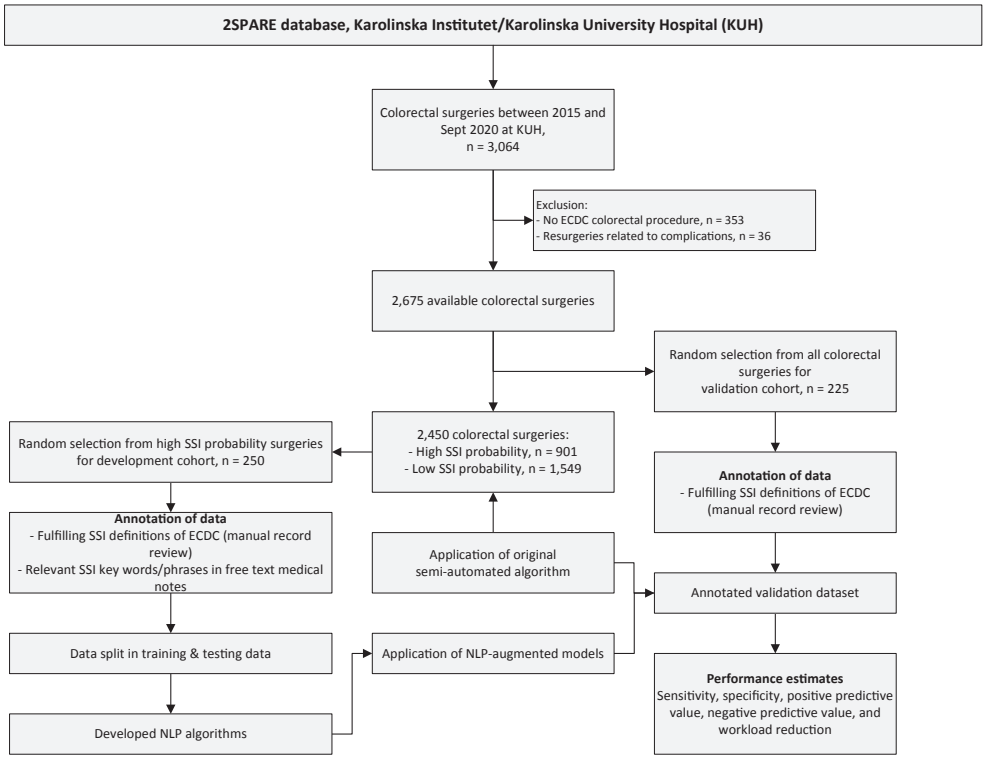

Figure 10.2. Flow chart of the study.
Abbreviations: KUH = Karolinska University Hospital; ECDC = European Centre for Disease Prevention and Control; NLP = natural language processing; SSI = surgical site infection.

Feature selection and algorithm development

The original keywords and their lemmatised versions can be considered as 'features'. All text from the clinical notes were matched with the lexicon list and each feature match was counted. Negation detection using the NegEx algorithm was applied to filter out negated mentions.[27] For example, in case '*no signs of infection*' is written down, the keyword '*infection*' is negated and not counted as a keyword match. Subsequently, three input types were considered: a count

per keyword, a discretised count with four bins, and a binary model indicating the presence or absence of a keyword. Each input type has its pros and cons: a binary representation benefits from its simplicity, however, cannot capture the case when several mentions of the same keyword corresponds to a stronger deep SSI signal. The count per keyword, on the other hand, captures the number of times each keyword is mentioned, but is more sensitive to writing styles and will have fewer examples of each distinct keyword count in the training data. The discretised count can be viewed as a compromise between the binary model and the counts model, since three of the bins represented a count below, within, or above the expected (interquartile) range, and the fourth bin represented no occurrences.

During development, we split the development cohort consisting of high-probability records as classified by the original algorithm into training (80%) and testing data sets (20%) to evaluate parameters of the learning algorithms. Two tree-based classification algorithms, a single decision tree (DT) and a random forest (RF) with 500 trees,[28] were evaluated for their ability to separate between the two classes, deep SSI and no deep SSI.[29,30] A DT has the benefit of being interpretable, since the tree can be understood as one set of rules for classifying future patients as belonging to either class. An RF, on the other hand, is a more complex model with multiple sets of rules and therefore lacks in interpretability, but often outperforms a DT. Each of the classifiers, DT and RF, was applied to each feature representation (raw counts, discretised counts, or binary counts) resulting in six tree-based models.

For application in semi-automated surveillance, a near-perfect sensitivity is required as false-positive cases are corrected during subsequent chart review, whereas false-negative cases will remain unnoticed. To increase the sensitivity when using the DT classifier, ten small decision trees with slightly different characteristics were inferred from the development data. Subsequently, in the validation cohort, a patient was classified as deep SSI if any of these trees classified the patient as such. This ensemble of DT classifiers could be considered as a miniature forest with a decision threshold of 0.1. Within an RF, each tree classifies each patient in the data set. Generally, for an RF with two classes, a majority decision determined class membership, i.e. the class assigned by a majority of the trees will be assigned to the patient. This corresponds to a decision threshold of 0.5, meaning that 50% of the trees are required to consider a patient as belonging to the class deep SSI for the RF to classify it as such. To increase the sensitivity of the RF the conventional decision threshold of 0.5 was lowered, meaning that fewer trees are required to classify a patient as deep SSI, which will however reduce PPV. Multiple decision thresholds were explored using the development cohort, and the thresholds of 0.3 (for model using raw or discretised counts) and 0.35 (model using binary counts) were selected to ensure a high sensitivity (> 0.95 in the development cohort).

Rule-based NLP component

Furthermore, a rule-based NLP component was developed based on keywords reflecting the deep SSI definition (**Supplemental Figure S10.1**). This NLP component is more straightforward as no DT or RF techniques are used: if a keyword match was present for a patient according to the OR/AND-rules as specified in **Supplemental Figure S10.1**, the patient was classified as probable deep SSI by the algorithm (**Figure 10.1**).

Analysis

In total, eight surveillance models were investigated as described above: the original semi-automated model composed of structured data only (model 1); model 1 augmented with the NLP component developed with DT using either raw counts (model 2), discretised counts (model 3) or binary counts (model 4); model 1 augmented with the NLP component developed with RF using either raw counts (model 5), discretised counts (model 6) or binary counts (model 7); and model 1 augmented with the rule-based component (model 8). First, the original semi-automated model (model 1) was applied to the validation cohort and the performance measures sensitivity, specificity, PPV, negative predictive value (NPV) and workload reduction (WR) were calculated as compared to the reference standard. WR was defined as the difference between the total number of surgeries under surveillance and the proportion of surgeries requiring manual review after algorithm application.

Baseline characteristics were compared between the high probability groups – as defined by the original algorithm – of the development and validation cohorts. Heat maps were created from the development cohort to visualise the presence of keywords between the deep SSI group and the group without. The NLP-augmented models (models 2 – 8) were applied to the validation cohort and for each model sensitivity (recall), specificity, PPV (precision), NPV, and WR was calculated with corresponding 95% confidence intervals (95% CI). 2SPARE data acquisition, management and analysis were performed using R statistical software (version 3.6.1) and Python (version 3.7), and in accordance with current regulations concerning privacy and ethics.

RESULTS

The mean age of the validation cohort was 62.6 year (standard deviation 17.2) and 48.9% (n = 110) were female (**Table 10.1**). The majority of patients had a primary surgery (63.6%; n = 143) and most surgeries were open (77.3%; n = 174). In 41.8% (n = 94) of patients a stoma was created.

Table 10.1. Baseline characteristics of the validation cohort of this study.

	Patients in validation cohort (n = 225)
Age in years (mean (SD))	62.6 (17.2)
Sex (n (%))	
Male	115 (51.1)
Female	110 (48.9)
BMI (mean (SD))	26.1 (5.4)
Missing (n (%))	2 (0.9)
ASA grade (n (%))	
Grade I	25 (11.1)
Grade II	96 (42.7)
Grade III	78 (34.7)
Grade IV	4 (1.8)
Grade V	0 (0)
Missing	22 (9.8)
Surgical approach (n (%))	
Closed	51 (22.7)
Open	174 (77.3)
Duration of surgery in minutes (mean (SD))	330.6 (154.0)
Missing (n (%))	65 (28.9)
Wound class (n (%))	
Clean-contaminated (class 2)	171 (76.0)
Contaminated (class 3)	42 (18.7)
Dirty-infected (class 4)	12 (5.3)
Stoma (n (%))	
Yes	94 (41.8)
No	131 (58.2)
30-day mortality (n (%))	
Yes	5 (2.2)
No	220 (97.8)
Malignancy (n (%))	
Yes	173 (76.9)
No	52 (23.1)
Primary procedure (n (%))	
Yes	143 (63.6)
No	82 (36.4)
Surgical site infection (n (%))	
No	165 (73.3)
Yes	60 (26.7)
- Superficial	19 (31.7)
- Deep	41 (68.3)
Anastomotic leakage (n (%))*	
Yes	13 (31.7)
No	28 (68.3)

* Only registered in case of deep surgical site infection.
Abbreviations: n = number; SD = standard deviation; BMI = body mass index; ASA = American Society of Anesthesiologists.

Validation of the original semi-automated algorithm with structured data only

The original semi-automated algorithm (model 1) was applied to the validation cohort. A requested radiology consult and receiving antibiotic therapy for ≥ 3 days were the most common criteria present in patients (**Table 10.2**). Of the 41 patients with a deep SSI, 40 were classified correctly by the algorithm as high probability (sensitivity = 97.6%; 95% CI 87.1% – 100%) (**Table 10.3**). The patient with a deep SSI that was missed by the algorithm had none of the four algorithm components during the follow-up period: the deep SSI was manually ascertained based on a clinical note describing pus from the rectal stump.

Table 10.2. Number of patients per algorithm component (model 1).

Components of model 1	Number of patients (n (%))
Augmented stay	87 (38.7)
Reintervention	40 (17.8)
Radiology	107 (47.6)
Antibiotics	93 (41.3)

Table 10.3. Performance characteristics of the different surveillance models.

	Sensitivity (% (95% CI))	Specificity (% (95% CI))	PPV (% (95% CI))	NPV (% (95% CI))	Workload reduction (%)
model 1	97.6 (87.1 – 100.0)	69.6 (62.4 – 76.1)	41.7 (31.7 – 52.2)	99.2 (95.7 – 100.0)	57.3
model 2	87.8 (73.8 – 95.9)	79.9 (73.4 – 85.4)	49.3 (37.4 – 61.3)	96.7 (92.5 – 98.9)	67.5
model 3	95.1 (83.5 – 99.4)	73.4 (66.4 – 79.6)	44.3 (33.7 – 55.3)	98.5 (94.8 – 99.8)	60.9
model 4	95.1 (83.5 – 99.4)	73.4 (66.4 – 79.6)	44.3 (33.7 – 55.3)	98.5 (94.8 – 99.8)	60.9
model 5	92.7 (80.0 – 98.5)	77.72 (71.0 – 83.5)	48.1 (36.7 – 59.6)	97.9 (94.1 – 99.6)	64.9
model 6	95.1 (83.5 – 99.4)	70.6 (63.5 – 77.1)	41.9 (31.8 – 52.6)	98.5 (94.6 – 99.8)	58.7
model 7	92.7 (80.1 – 98.5)	79.3 (72.8 – 84.9)	50.0 (38.3 – 61.7)	97.9 (94.2 – 99.6)	66.2
model 8	85.4 (70.8 – 94.4)	82.1 (75.8 – 87.3)	51.5 (39.0 – 63.8)	96.2 (91.8 – 98.6)	69.8

Model 1: original algorithm with structured data only.
Model 2: model 1 augmented with the NLP component developed using decision tree and raw counts.
Model 3: model 1 augmented with the NLP component developed using decision tree and discretised counts.
Model 4: model 1 augmented with the NLP component developed using decision tree and binary counts.
Model 5: model 1 augmented with the NLP component developed using random forest and raw counts.
Model 6: model 1 augmented with the NLP component developed using random forest and discretised counts.
Model 7: model 1 augmented with the NLP component developed using random forest and binary counts.
Model 8: Model 1 augmented with a rule-based component.
Abbreviations: 95% CI = 95% confidence interval; PPV = positive predictive value; NPV = negative predictive value; NLP = natural language processing.

Model performance of the semi-automated algorithm augmented with an NLP component

Baseline characteristics between the high-probability patients of the development cohort (n = 250) and the validation cohort (n = 96) were similar, albeit somewhat lower frequency of primary procedures, 55.2% versus 64.8%, and higher frequency of SSIs, 54.2% versus 46.4%, (**Supplemental Table S10.2**).

The distribution of keywords among patients with deep SSI versus no deep SSI differed with regards to frequency and timing (**Figure 10.3**). The keywords 'abscess', 'anastomotic leakage', 'drainage' and antibiotic names appeared more frequently in the clinical notes from deep SSI cases. The other keywords were present in both groups, however more often in the group of patients with deep SSI and between day 15 – 30 post-surgery.

For each NLP-augmented surveillance model, performances are shown in **Table 10.3**. Model 3 and 4 had sensitivity above 95% and 3.6% less records to review manually as compared to the original algorithm based of structured data (model 1). Keywords incorporated in model 3 were: the antibiotic names, 'abscess', 'anastomotic leakage', 'subfebrile', 'fluid', 'intestinal content', 'drainage', 'leakage', 'antibiotics', and 'drained'. For model 4 also the following keywords were included: 'intestinal content', 'serous', and 'echo'. The rule-based component (model 8) had lowest sensitivity. Overall, the models with discretised or binary count input types had better performance estimates than raw counts.

DISCUSSION

In this study, the original semi-automated algorithm achieved 97.6% sensitivity and 57.3% WR. When adding an NLP-component to this algorithm, the number of records to assess manually was decreased by 1.4% – 12.5% at the cost of sensitivity. The NLP component with the best performance yielded seven (3.6%) fewer patients to review manually, thereby lowering the sensitivity with 2.5% (one extra deep SSI missed).

Although the original semi-automated algorithm was developed and validated in other countries than Sweden, also within this country the sensitivity was high. These results confirm the potential of large-scale implementation of this algorithm within Europe and its robustness and adaptability in different clinical settings. The NLP component lowered the number of false positives and thus resulted in WR, however this added value was minimal. These findings are similar to a study of Grundmeier and colleagues,[31] who used a data-driven selection of pre-specified keywords related to SSI from clinical narratives after ambulatory paediatric surgery. By using regular expression matching, keyword occurrence was counted and combined within

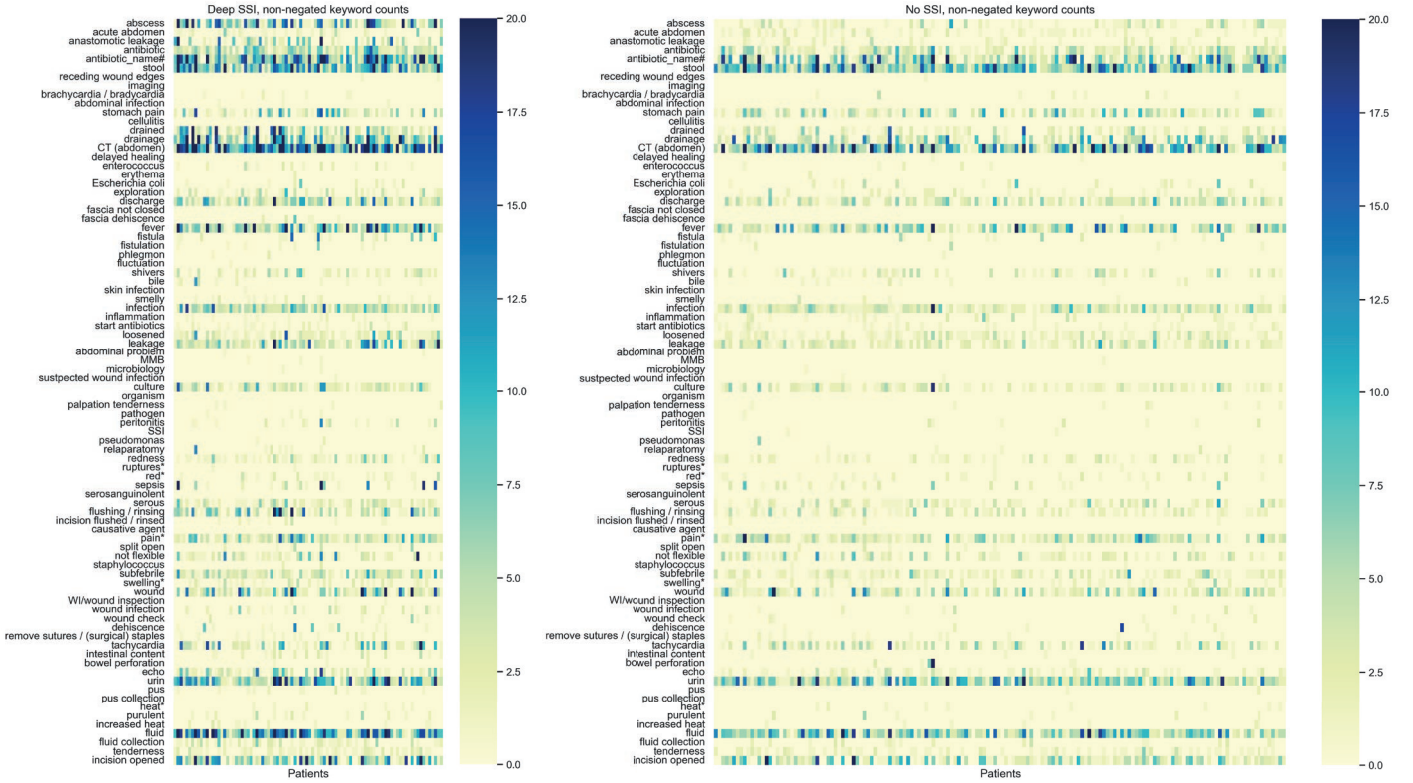

Figure 10.3. Heat map for the distribution of keywords among patients with deep SSI and patients without deep SSI.
* Proximity search, keywords must be within a distance of five words from one of the following locations: incision, operation wound, abdomen, wound, pelvis, duodenum, flank, gall bladder, skin, intra-abdominal, next to anastomosis, colon, liver, pancreas, abdomen/stomach, between small intestines, operation area, operation wound, presacral, rectum, retroperitoneal, incision, intestine, small intestine, under diaphragm, midline incision, midline wound, sutures/stitches/(surgical) staples, stomach.
# The following antibiotics including their brand names: piperacillin-tazobactam, meropenem, imipenem, metronidazole, ciprofloxacin, cefotaxime, trimethoprim-sulfa, cefuroxime, amoxicillin. Abbreviations: SSI = surgical site infection.

an RF model. High sensitivity (90%) was obtained, but the PPV was 23%, which is lower compared to 44.3 – 51.5% for model 2 – 8 in our study. A study who successfully succeeded to discriminate between SSI groups is from Thirukumaran and colleagues.[21] They demonstrated high sensitivity and PPV in a model that combined administrative data (age, sex, race, clinical comorbidities, year of procedure and Clinical Classification diagnosis categories) with clinical notes to detect SSIs after orthopaedic surgery. Although they applied a comparable NLP technique as this current study, it remains uncertain what the value of NLP was in case similar structured clinical care data was used as in this current study. Thereby, SSI diagnosis after abdominal surgeries are more complex compared to the more 'straightforward' orthopaedic surgeries.

Other attempts of NLP surveillance systems from Tvardik et al.,[32] Fitzhenry et al.,[33] Branch-Elliman et al.[22] and Murff et al.[34] had modest performance results with sensitivities reported between 33% and 87%. All these studies used different NLP techniques, different patient populations and had various targets (other post-operative complications or catheter-related urinary tract infections) complicating direct comparisons, and reflects the numerous techniques available that can be applied to process unstructured clinical notes and to build an algorithm.

There may be several reasons for the limited benefit obtained in this study by adding an NLP component. First, the NLP component tries to find the patients with deep SSI in an already pre-selected high-risk group identified by the four components of the original algorithm. These patients have either reoperations, antibiotics, radiology or prolonged hospital stays and certain keywords are therefore expected in all these patients given their clinical course and complications. The lexicon list was developed for distinguishing deep SSI from non-deep SSI by consulting various clinical specialties, however, maybe other keywords and language patterns are required to identify the deep SSI cases in the high-probability group. Second, on practical ground, we have chosen to add the NLP component as the last step in the algorithm. Including the NLP component in the first steps of the algorithm, as often seen in rule-based algorithms that combine structured and unstructured data, may achieve better results.[26] Third, all studies mentioned above used different techniques to process and analyse clinical notes. We did not attempt all possible options because we investigated NLP in semi-automation setting, thereby prioritising sensitivity. Using clinical notes may be more valuable in fully-automated surveillance, in which sensitivity and specificity are balanced instead of focusing on high sensitivity only. However, expectations are tempered as the studies applying other techniques also had modest results. Last, the development of an (NLP) algorithm requires an excellent reference standard of sufficient size to ensure correct classification of patients.[10,11,22] Although the agreement between our raters was good, the sample size for developing the NLP components might have been too small.

Clinical notes are a rich data source, useful for post-discharge surveillance and an extremely important data source in the detection and manual ascertainment of SSI by ICPs.[35] It is therefore a logical step to incorporate this data source in surveillance algorithms. However, aside from the limited incremental benefit in this study, several drawbacks of using this data source for automated surveillance exist. First, medical personnel often describe terms indirectly related to SSI (e.g. *dehiscence, opening incision, removing sutures, rupture*) or describe their observations in terms of smell, colour or shape (e.g., *yellow substance, smelly, not flexible, etc.*) making it difficult to catch important vocabulary. Lexicon libraries with medical synonyms, such as the Unified Medical Language System from the National Library of Medicine, can help to connect alternate names for the same concept or keywords, however are not available for all languages (yet).[36] Second, the frequency of reporting and the vocabulary used varies between individual practitioners, centres and between countries. There is no information available about the generalisability of such algorithms when applied to other languages, and little is known about their robustness – especially when using the count input type – against (local) reporting habits. Third, to the best of our knowledge, there is limited experience with using NLP-augmented surveillance algorithms in daily routines. Given the small benefit that NLP provides in this study, one may wonder whether its development, implementation and maintenance will be cost-effective.[22] Although the digital infrastructure can be expanded to other (post-operative) complications, developing and building NLP models require substantial effort of information technology experts. Last, techniques to build NLP-augmented algorithms are mostly complex and less transparent, lowering the chance of understanding and acceptance of clinicians and hospital staff. We used two methods for feature classification: a DT has the benefit of being interpretable, since the tree can be understood as a set of rules for classifying future patients as belonging to either class. An RF, on the other hand, is more complex and therefore lacks in interpretability, but such classifiers are usually more accurate and less likely to over fit data compared to a DT.[29] For future implementation, there will be a trade-off between optimal case finding techniques versus practical considerations such as acceptability and resources.

To summarise, the original algorithm comprised of structured data only had near-perfect sensitivity, but high number of false positives (i.e. low PPV). Adding an NLP component to incorporate clinical notes as extra data source lowered the number of false positives, however the benefit was minor: the number of records to review manually was reduced by only 1.4% –12.5%. Given the complexity of such systems and the resource-intensive nature of developing NLP, large-scale implementation seems unlikely. However, further research is needed to evaluate whether NLP technology is an appropriate tool for helping to detect deep SSI in semi-automated surveillance systems or their utility in fully automated surveillance.

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SUPPLEMENTARY MATERIAL

Supplemental Table S10.1. Details semi-automated algorithm composed of structured data.

Elements algorithm	Criteria[a]	Specification
(Re)Admissions	Length of stay of index admission ≥ 14 days OR ≥ 1 re-admission OR death	Length of hospital stay of the index admission (i.e., admission during which the colorectal surgery took place) of ≥ 14 days ((discharge date – date of index surgery) +1) OR ≥ 1 readmission(s) for the relevant specialty (i.e. specialty surgery or gastrointestinal oncology surgery), after the index surgery but within FU time OR Mortality within FU time
Resurgery	≥ 1 reoperation by original surgery specialty	Surgeries performed by the department of surgery or gastrointestinal oncology surgery, after the index surgery and within FU time. No further restrictions.
Antibiotics	≥ 3 consecutive days of antibiotics (ATC J01) post-operative, starting from day 2	All antibiotic orders (ATC J01) prescribed from day 2* until end of FU, including outpatient prescriptions but excluding ICU prescriptions. Overlapping episodes count as 1 day (e.g. two antibiotic prescriptions, one for 4 days and one for 2 days of which 1 days overlap result in a total of 5 consecutive days of antibiotic exposure).
Radiology	Ordering CT scan	CT scan order within FU time

* Date of initial, index surgery = day 0.
[a] All criteria should be fulfilled within 45 days after the index surgery (FU time = 45 days).
Abbreviations: FU = follow-up; ICU = intensive care unit.

Pus or **Purulent**

OR

Dehiscence or **remove sutures** AND **fever** or **pain** or **tenderness**

OR

Abscess

OR

Supplemental Figure S10.1. Rule-based component.

Supplemental Table S10.2. Baseline characteristics of high-probability patients in the development and validation cohort.

	High-probability patients development cohort (n = 250)	High-probability patients validation cohort (n = 96)
Age in years (mean (SD))	61.2 (15.4)	64.2 (16.8)
Sex (n (%))		
Male	158 (63.2)	59 (61.5)
Female	92 (36.8)	37 (38.5)
BMI (mean (SD))	25.9 (5.1)	26.3 (5.5)
Missing (n (%))	0 (0.0)	1 (1.0)
ASA grade (n (%))		
Grade I	17 (6.8)	9 (9.4)
Grade II	125 (50.0)	35 (36.5)
Grade III	83 (33.2)	42 (43.8)
Grade IV	4 (1.6)	2 (2.1)
Grade V	0 (0)	0 (0)
Missing	21 (8.4)	8 (8.3)
Surgical approach (n (%))		
Closed	37 (14.8)	12 (12.5)
Open	213 (85.2)	84 (87.5)
Duration of surgery in minutes (mean (SD))	401.4 (176.0)	377.5 (165.5)
Missing (n (%))	70 (28.0)	21 (21.9)
Wound class (n (%))		
Clean-Contaminated (class 2)	184 (73.6)	74 (77.1)
Contaminated (class 3)	50 (20.0)	16 (16.7)
Dirty-infected (class 4)	16 (6.4)	6 (6.3)
Stoma (n (%))		
Yes	139 (55.6)	54 (56.3)
No	111 (44.4)	42 (43.8)
30-day mortality (n (%))		
Yes	6 (2.4)	3 (3.1)
No	244 (97.6)	93 (96.9)
Malignancy (n (%))		
Yes	191 (76.4)	77 (80.2)
No	59 (23.6)	19 (19.8)
Primary procedure (n (%))		
Yes	162 (64.8)	53 (55.2)
No	88 (35.2)	43 (44.8)
Surgical site infection (n (%))		
No	132 (52.8)	44 (45.8)
Yes	118 (46.4)	52 (54.2)
- Superficial	26 (22.0)	12 (23.1)
- Deep	92 (78.0)	40 (76.9)
Anastomotic leakage (n (%))*		
Yes	36 (39.1)	13 (32.5)
No	56 (60.9)	27 (67.5)

* Only registered in case of deep surgical site infection.
Abbreviations: SD = standard deviation; n = number.

General discussion

11

Janneke D.M. Verberk

GENERAL DISCUSSION

Although surveillance is a means, in this thesis it is actually the end. The aim of this thesis was to evaluate current traditional surveillance methods of healthcare-associated infections (HAIs) and to explore the feasibility and generalisability of automated surveillance (AS) methods in different hospitals. We focused on the robustness of semi-automated classification algorithms in different settings with variability in clinical practice, patient populations, electronic health record (EHR) systems and data management skills. The knowledge gained can help in improving AS and will facilitate implementation. This chapter starts with a general discussion on (automated) surveillance of HAIs, based on results obtained within this thesis and findings reported by other studies. Subsequently, the lessons we learned and the remaining challenges are described, followed by considerations regarding AS in the future.

The value of surveillance

HAI surveillance is a means that can be used for two intended purposes: it serves either as a cornerstone of within-hospital infection prevention and patient safety programmes, or can be used as a quality metric.[1,2] For the first purpose, its effectiveness has been generally acknowledged worldwide, as several studies demonstrated that surveillance, or participation in surveillance networks, result in a reduction of HAIs.[3-6] Surveillance increases awareness, provides information for action and targeted interventions can be implemented.[7] Additionally, surveillance results can be used for evaluating interventions (**Chapter 2**) or for monitoring the number of HAIs during unexpected circumstances (**Chapter 3**). Surveillance of infections has not only been proven effective within individual hospitals, but also on the public health level. The recent COVID-19 pandemic illustrated the importance of monitoring infection rates and to share and report data on local, national and international level.[8]

The second purpose, using HAI rates for benchmarking and public reporting, has been applied and mandated increasingly over the past years in several countries.[2,9-11] Nevertheless, there is criticism and attention regarding the methodology, and the accuracy and reliability of traditional surveillance – manual chart review using standardised case definitions – has been questioned by many.[11-14] This criticism concerns subjectivity in case definitions, inter-rater variation, and 'the-more-you-look-the-more-you-find principle', affecting reliable comparability (**Chapter 4 & 5**).[15-17] Apart from these methodological issues, in **Chapter 4** limitations were reported regarding practical aspects of surveillance of catheter-related bloodstream infections (CRBSIs). Examples are the yield of surveillance given low incidences, the lack of resources and organisational support, the high workload, and information technology (IT) problems.[18] These

practical aspects are often overlooked, as the evaluation of surveillance programmes is mostly limited to investigating the effectiveness of a programme to reduce HAIs. These methodological and practical issues motivate to look for alternative ways to conduct surveillance.

The value of automated surveillance

Automated surveillance is considered a possible solution to overcome many of the drawbacks of traditional manual surveillance. It aims to improve efficiency by reducing the number of charts for manual review (in case of semi-automated surveillance, **Chapter 8 – 10**) or by ascertaining the HAI status without any human involvement (in case of fully automated surveillance).[19-25] Especially when HAI incidences are low, time and effort of infection control practitioners (ICPs) can be saved and re-allocated.[26] Second, another main advantage in automation is that (a part of) the surveillance process is standardised by algorithms. If the algorithms are applied correctly, this will increase reliable comparisons between centres. Several studies, including studies in this thesis, showed that automation is even superior to traditional methods as more HAIs are found by using algorithms (**Chapter 8 & 9**).[25,27-31]

In this thesis, we focused mainly on semi-automated surveillance, in particular semi-automated classification models composed of rule-based components. This type of model is considered relatively easy to apply, adjustable to clinical variations, and is understandable for clinicians which will increase acceptance.[2,27,32] Hence, they have the potential for large-scale implementation. Although the final ascertainment still requires human interpretation and thus runs the risk of subjectivity, the selection of high-risk cases is a standardised process and decreases the chance of missing a HAI.[32] Complex models, such as machine learning or natural language processing, are increasingly presented given the increased availability of data sources and techniques. However, how these algorithms work is difficult for clinicians to understand and implementation is hampered as a high level of programming and IT expertise is required (**Chapter 10**).

As we focused in this thesis on semi-automated surveillance, we prioritised sensitivity as most important performance outcome, as false-positive cases will be corrected during subsequent chart review, while false-negative cases will remain unnoticed. However, the intended purpose of the AS system decides which performance outcome, sensitivity, specificity, or positive predictive value will be important: in fully automated surveillance there is usually a trade-off between sensitivity and specificity, while for semi-automated surveillance the main focus is on sensitivity.[32] In addition, in this thesis the large-scale potential of semi-automated surveillance of one of the most common HAI, namely surgical site infections (SSIs), was investigated. Although our findings will generally hold true for semi-automated surveillance of other HAI

targets as well, for every new HAI target or new surveillance population there probably will be additional exceptions or quintessential features, as well as for fully AS methods.

Lessons learned and hurdles to take towards large scale implementation

Many algorithm types are developed, both for semi- and fully automated surveillance, with overall satisfying performances.[20-24,33-35] Despite these promising results, the studies presenting these algorithms are mainly development studies, performed in single (often academic) centres. External validations or actual implementation studies on AS systems are scarce.[36,37] As reported by two systematic reviews, only 23% of the included studies used a separate validation cohort and only 25% of automated methods were used in daily clinical routine.[29,38] Hence, knowledge about generalisability or prerequisites of AS models is limited, and information about the path toward actual implementation is strongly needed. The chapters in this thesis showed that high algorithm performance or successful validation does not guarantee widespread implementation. The points raised below provide a summary of why AS has not been implemented on large scale in the Netherlands as of yet, and what hurdles there are to tackle.

First, the automated selection of the population under surveillance, in other words the denominator, is difficult. The current inclusion rules for SSI surveillance are a challenge to automate: uniform selection of the denominator by all hospitals fails by differences in coding systems, or data needed for denominator selection is currently not recorded in structured format in EHRs (**Chapter 8 & 9**).[39] For example, the inclusion rule 'a primary surgery' could not be fulfilled as automatically distinguishing primary surgeries from revision procedures was not possible with current procedure codes. If we consider changing inclusion rules, there is the risk of a break in trend line and incomparability because of unequal distributions of primary and revision surgeries between centres. A change in procedure coding systems is not desired and difficult to achieve. Also for the CRBSI surveillance, the total number of catheter days (the denominator) cannot be computed automatically as the removal date is often not registered systematically in the EHR systems (**Chapter 4**). Second, organisational aspects hinder implementation. Either because of a lack of support from local boards or governmental bodies, or because of limited knowledge in AS or implementation strategies (**Chapter 7**). Full feasibility or implementation studies are therefore strongly recommended. In addition, organisations need to invest IT capacity and ensure access to programming skills. Especially if implementation of complex models using both structured and unstructured data, which require high level programming and technologic support, is preferred (**Chapter 10**). Third, information about input source data and algorithm specifications in scientific papers is often not detailed enough or non-transparent, making it difficult for others who would like to validate, replicate and

implement this within their own institute. Therefore, in **Chapter 7**, a list of items to report in (scientific) publications of AS is provided. It would be helpful if an organisation such as the EQUATOR (Enhancing the QUAlity and Transparency Of health Research) Network, known from the STROBE, CONSORT and PRISMA guidelines, could provide a guideline for reporting on automated solutions in healthcare, including the items as suggested in **Chapter 7**. Fourth, meaningful comparison of surveillance results – either manually or automatically generated – requires risk-adjustment.[40,41] Several models for risk-adjustment have been developed and refined last years, however, the search for a proper case-mix correction is still ongoing and debated.[11,42-46] In case of AS, data required for risk-adjustment should be obtained in an automated way as well to maintain the benefit of workload reduction gained by AS. However, obtaining variables needed for case-mix automatically is not self-explanatory (**Chapter 9**). Last, in the Dutch setting, patients usually return to the same hospital in case of complications. Follow-up information of HAIs or algorithm data components are therefore available and accessible. HAI detection or wide-spread implementation of AS may be hampered in case follow-up visits and treatments are not in the same hospital. Moreover, in recent years, more and more centres differentiate into highly specialised care centres in one domain, such as oncology, cardiovascular diseases or pulmonology, delivering specialised complex care to patients from all over the country.[47] The lower complexity care and rehabilitation for these patients is provided by local healthcare facilities nearby. This so-called 'shared care' will, most likely, increase in the future. Linking data and EHR systems across healthcare providers will overcome the problem of loss to follow-up, however is not applicable in most countries and complicated by strict data protection regulations (**Chapter 7**). Furthermore, in the context of benchmarking and quality improvement, these developments may hamper correct adjudication of the healthcare facility where a certain infection has been acquired.

Workload reduction and standardisation are mostly brought forward as the advantages of AS. However, these concepts should be discussed and clarified in a broader context. The workload reduction is often expressed in outcomes such as the reduction in number of records to review manually or in time savings of ICPs.[21,35] Automation yields considerable benefits in the data collection and manual case ascertainment by ICPs, however also requires time in terms of efforts for development, validation, implementation and maintenance of AS systems.[26] Therefore, workload reduction as an outcome of AS effectiveness may be misleading and may not be representative as time indicator for applying AS as a whole: the work will be (partly) shifted from ICPs to IT personnel and ICPs' time savings are spend on validation and interpretation.[37,48] Integrating systems, developing data warehouses and establishing an IT infrastructure takes approximately two years, as reported by Apte et al.[49], Wisniewski et al.[50], and in **Chapter 7** of this thesis.[27,37] However, once the infrastructure is established

and the algorithms implemented, the time investment will be largely reduced and limited to maintenance and validation only. Moreover, new algorithms to be implemented, or AS of other outcomes (e.g. complications) will benefit from the already existing infrastructure. Information about time needed for maintenance, running and adaptation of AS systems is unknown and not reported so far for any of the AS methods. Since setting up AS requires a significant time investment, it is valuable to also consider options to reduce the workload of the current traditional surveillance on the short term. In **Chapter 6** we concluded that two out of three investigated variables appeared irrelevant to be collected for surveillance and not essential to report. As collecting information through manual surveillance is time-consuming, the relevance in terms of data interpretation or risk-adjustment of each of the variables required for surveillance should be clear and regularly evaluated.

Standardisation is considered the other main advantage of automation. Uniform methods, and standardised case definitions are needed for meaningful comparison of HAI rates (e.g. high accuracy and discriminative power), together with a proper case-mix correction.[32,51] One may question the uniformity of AS methods if hospitals use different types of surveillance algorithms for the same HAI target, if hospitals slightly modify case definitions of the targeted HAIs for fully automation purposes, or when different input source data is used.[52,53] In the Netherlands, hospitals have different types of EHR systems applying different coding systems.[52,54] The wide landscape of systems used in (Dutch) hospitals and the variety in documenting and structuring information in EHRs results in large variations of input source data for algorithms. We demonstrated that determining clear data specifications and thorough validation largely prevents variations in applying semi-automated surveillance. However, be aware that as long data input or algorithm types are not aligned between hospitals or countries, it is not guaranteed that algorithms will work for every institution, and that meaningful outcomes can be generated and compared.

In this thesis we demonstrated automation benefits over traditional surveillance regarding ICP time, sensitivity and standardisation, however we also conclude that it will not take away current controversies and issues regarding differences in methods and data collection.[9]

What is needed to scale-up? Considerations for future automated surveillance

From all studies published so far, we can conclude that the focus has been on algorithm development and accuracy to detect HAIs. Current efforts are directed towards implementation and use of algorithms with satisfying performance on large scale. To scale up, we need more knowledge in *how* to organise this, and what aspects deserve extra attention before implementation. We think that the following points – either for within-hospital surveillance

purpose or for benchmarking and public reporting – are desired to guide and ensure quality of large scale use of AS systems: 1) commitment and resources of all stakeholders involved; 2) guidance in how to organise AS regarding responsibilities and regulations on local and (inter) national level; 3) AS system requirements; and 4) data standardisation and interoperability. Each of these points is explained in more detail below.

Commitment and resources

In **Chapter 7** of this thesis determinants of successful implementation of AS systems were investigated. The support from hospital management, and commitment and involvement of healthcare workers were considered key for implementation. A study of Grota et al.[36] concluded that 'in hospitals with strong leadership and engagement with patient safety, ICPs in general may feel more supported in implementing AS and overcoming barriers'. Involvement, support and commitment of all stakeholders – from legal specialists, data protection officers to hospital management – is paramount for successful implementation and use of AS.[32] Additionally, also alignment and collaboration with parties outside the healthcare facility is important, for example with national medical specialty societies, e-health initiatives or relevant governmental bodies. AS is a continuous effort, as local IT systems, legislations, clinical practice, and organisation of care are continuously changing. Resources and (financial) commitment are therefore needed for the long term to guarantee quality and reliability of surveillance results.[48]

Responsibilities, regulations, and organisation of automated surveillance

AS systems can be organised and implemented within an individual healthcare facility, or in a network context. If a healthcare facility implements AS individually, it has full responsibility for methods, finance, performance and maintenance of the system and there is no coordinating party such as a network involved. The disadvantage of this individual approach is that algorithm types, surveillance populations, or case definitions for HAI targets may differ between centres, limiting comparability. Therefore, one may wonder whether HAI rates obtained by local, individual AS systems can be accepted as a quality metric or for benchmarking, and participation in a (inter) national network will perhaps be rejected. In addition, this individual implementation approach will probably not lead to large scale implementation of the same AS system in other centres, knowledge building, or financial support from third parties.

The recently established PRAISE network[32] (Providing a Roadmap for Automated Infection Surveillance in Europe) aims to support the transition of AS from the research setting to large-scale implementation and has written a roadmap with comprehensive information how

to achieve this. In this roadmap, two organisational approaches are described in case AS will be implemented within a surveillance network of participating healthcare facilities: this can be either organised locally or centrally. In locally implemented surveillance, the healthcare facility collects the source data and applies the algorithm, utilising specifications and guidance from the coordinating centre. Subsequently, the surveillance results are shared with the central body or institute who coordinates the trend analyses, monitors the quality of the data and ensures periodic validations.[32] Using this approach, hospitals can adapt algorithms to their local situation, as long as they meet the requirements and surveillance protocol. For centrally implemented AS, individual healthcare facilities send their source data to the coordinating centre or institute that applies the algorithms and reports back the results. For hospitals without sufficient resources or knowledge in AS this approach is more accessible, and funding may be easier arranged in a network context.

For both organisational approaches, governance aspects such as legislation, responsibilities of stakeholders, and alignment with local and (inter)national regulatory policies should be agreed upon and documented. For centrally implemented AS it will be more complex to set up an organisational structure and to obtain consensus on the methods and surveillance protocol given the many partners and institutions involved. In addition, a technological solution such as AS brings concerns about data security, proper handling, sharing, and privacy, and the laws on data regulation and protection should be adopted in the implementation strategy.[55] Transparency and clarity in tasks, responsibilities, organisational structure, governance and activities in implementing and running AS systems is needed to enhance and set up large scale implementation.[55]

Requirements for automated surveillance systems

Apart from the organisational and governance aspects as described above, guidance in system requirements is a particular point of attention to prevent meaningless data that cannot be compared between healthcare facilities. A broad variety of surveillance algorithms and methods have been developed and there is large heterogeneity in the degree of automation of the surveillance process (semi- versus fully AS) and in algorithm types (classification models, machine learning, or simple rule-based models mimicking the case definition). For individual, within-hospital surveillance this may not be a problem, but in case of a network context and benchmarking, there is a need for an AS protocol with clear guidelines and requirements for AS systems to comply with. In both approaches, locally or centrally implemented AS, the coordinating centre or institute is most likely to be responsible for the AS design, protocol, and coordination.[32] This ensures quality, validity and comparability of outcomes generated by AS, and separates the wheat from the chaff. Examples are requirements for the algorithm (the

performance such as sensitivity, case definitions, reference standard and requirements for data validation and algorithm validation), or requirements for the system itself, such as technical- and end-user requirements. An example of a technical requirement is that the system should be able to select the surveillance population (the denominator) in an automated way. The flexibility to add or remove records by hand is an example of end-user requirements.

Data standardisation and interoperability

Numerous studies investigated which data sources are most accurate to use in AS algorithms.[29,56-60] Administrative data are easy to collect and therefore widely used, however several studies confirmed their limited quality and validity.[56-58] Clinical routine care data, such as diagnostic testing results, narrative clinical notes, or medico-administrative data on treatments and interventions, are increasingly used for algorithm development, as they provide valuable information necessary to detect HAIs. These data reside in different (sub) systems of a hospitals' IT infrastructure and are often linked together and stored within a clinical data warehouse. The added value of unstructured clinical notes has not yet been firmly established.[61,62] In **Chapter 10** we concluded that the added value of clinical notes to the semi-automated classification algorithm was limited. Given the complexity of such systems, the resource-intensive nature of developing algorithms using natural language processing, and the dependence on reporting habits of clinicians, large-scale implementation of this algorithm seems unlikely. However, the use of clinical notes in AS needs more study, as its utility for both semi- and fully AS is to date still inconclusive.

No studies systematically investigated to what extent data sources needed for automated denominator selection, algorithm application, or case-mix correction are actually available, or available in the same format in healthcare facilities in the same region, nation or even internationally. Large scale implementation starts with standardised data that is uniform and available in hospitals. In addition, AS systems requiring a minimum data set are most likely to succeed.[32]

As described earlier, the lack of standardisation of input source data between healthcare facilities impedes uniform AS implementation, especially when aiming for fully automated surveillance.[37,52,63,64] Each healthcare facility documents information in its own coding language and its own IT (sub)system. For within hospital surveillance this will not be a problem – except for difficulties in linking and aligning data between subsystems – but for sharing (source) data with others, comparability and benchmarking it is. A uniform coding standard will lead to increased standardisation and more easier data exchange. Thereby, universal scripts or solutions may be possible, and standardisation creates opportunities for surveillance of other endpoints

(e.g. complications), near real-time surveillance, outbreak surveillance or prediction. Also from a broader healthcare perspective than surveillance only, there is an increasing demand for standardisation to facilitate information exchange between healthcare providers within the healthcare supply chain and to decrease the burden of registration. Several local, regional and (inter)national initiatives are undertaken to increase standardisation and data exchange in healthcare, each focusing on a different perspective and goal. For example, Santeon, a Dutch network of seven teaching hospitals realised the Health Intelligence Platform Santeon to quickly exchange and compare data[65]; the 'Samenwerkende Algemene Ziekenhuizen' (SAZ), a network of 28 general hospitals started a collaborative centre of expertise in algorithms and artificial intelligence (AI)[66]; the Dutch non-profit foundation Health-RI tries to build an integrated health data research infrastructure[67]; Nictiz is an independent competence centre for electronic information exchange in healthcare that develops, provides and manages standards that can be implemented in the healthcare supply chain[68]; and the European eHealth interoperability roadmap published by the European Committee provides what input and governance processes are needed for decision making in support of eHealth.[69] Also during the COVID-19 pandemic, new attention has emerged to the utility of using and exchanging EHR data rapidly for infection prevention purposes, and the pandemic triggered new collaborative informatics infrastructures.[70]

Ideally, information is documented according to a uniform standard at the earliest point of data creation.[54] In most healthcare facilities, this means that information is registered according to a uniform standard in the EHR directly. However, EHR systems have many functionalities (e.g. order and result management, administrative processes, invoicing and internal logistics). With redesigning EHR systems, the vision and functions of such systems should be reconsidered. Alternatively, instead of demanding EHR systems to document information according to a standard, each healthcare facility can also link the uniform standard afterwards to their own source data structure. Some initiatives for a dictionary with structured terms for data exchange are already there, such as SNOMED CT or LOINC, which are suitable for automation processes.[54,71] However, mapping source data to standardised concepts will costs time, is error prone, and should be repeated for each new application or target.[54] Apart from standardisation of source data or standardisation in delivery output, another option, and perhaps the easiest, is to translate algorithm specifications and data requirements to own source data. Although this option is least standardised because differences in input source data remain, this is perhaps the fastest and most cost-effective approach.

There are also drawbacks of using a highly standardised IT approach. It is hard to create a standard that everyone approves, and there is often no room for exceptions or unique circumstances. Thereby, one party should be responsible for maintaining and updating the

standards and should provide guidance and support in implementation in hospitals' IT systems. Moreover, the use of a uniform standard requires decision-making and consensus on different levels than the standard itself, such as which standard(s) to use, how to use it, where in the care supply chain it is required, and responsibilities and implementation for actual use. All relevant stakeholders are needed to shape such a change, thereby taking into account legislation and political strategies. To ensure that healthcare facilities definitely switch to an (internationally) accepted standard, mandatory rules and systematic funding by political legislators will speed up the development and implementation of a standardised digital health IT structure.[54] This also prevents fragmented initiatives and prevents the development and interchangeable use of multiple standards at the same time.

CONCLUDING REMARKS

Semi-automated classification models with rule-based components are applicable and effective in Dutch and European hospitals. The ability to adapt an algorithm to local clinical practice is essential for successful algorithm performance. Automated surveillance should not be evaluated in terms of workload reduction or sensitivity and specificity only, but also on the feasibility and potential for actual use. The whole process – from denominator selection to interpretation of surveillance results – should be taken into account.

The healthcare landscape changes continuously. Treatments, pathogens, resistance patterns, diseases, or patients, but also organisation of delivery of care, legislations, technologic support and IT systems will change all the time. Ongoing maintenance, validation and updates in AS will always remain a continuing process. Although automation has benefits over the traditional surveillance, it will not take away current controversies and issues regarding differences in methods and data collection. There is a need for guidance and collaboration in how to organise and use AS on large scale to retain quality of surveillance data and surveillance networks.

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APPENDICES

NEDERLANDSE SAMENVATTING

Zorggerelateerde infecties, kortweg zorginfecties genoemd, zijn infecties die ontstaan tijdens een opname of medische behandeling in een zorginstelling. Zorginfecties leiden tot extra opnameduur, ziektelast en kosten. Elke dag hebben in Europa 3,5% – 10,5% van de patiënten in een zorginstelling een zorginfectie. Dit resulteert in ongeveer vier miljoen patiënten met een zorginfectie en 37.000 sterfgevallen per jaar. Surveillance (een doorlopende, systematische verzameling, analyse, en interpretatie van data) speelt een belangrijke rol bij de preventie en bestrijding van zorginfecties. In de meeste ziekenhuizen wordt de surveillance handmatig uitgevoerd: een deskundige infectiepreventie (DI) bekijkt handmatig elk patiëntendossier om te beoordelen of de patiënt voldoet aan de infectiedefinitie. Dit wordt uitgevoerd volgens een nationaal surveillanceprotocol met vooraf vastgestelde inclusie-eisen en infectiedefinities. Hoewel deze traditionele manier van surveillance wordt gezien als de referentiestandaard, wordt het uitvoeren van de surveillance ervaren als arbeidsintensief, zijn de definities subjectief te interpreteren, en is er bewijs voor matige betrouwbaarheid en overeenstemming tussen verschillende beoordelaars. Automatisering wordt gezien als een mogelijke oplossing voor deze nadelen, aangezien bij een geautomatiseerde surveillance een algoritme het selectie- en beoordelingsproces standaardiseert en zo de variabiliteit en subjectiviteit doet verminderen. Daarnaast hoeft de DI minder tijd te besteden aan het handmatig beoordelen van patiëntendossiers omdat het surveillance algoritme bepaalt welke patiënten een zorginfectie hebben (in het geval van volledig geautomatiseerde surveillance) of het algoritme een selectie maakt van patiënten met een hoge kans een zorginfectie te hebben ontwikkeld (in het geval van semi-geautomatiseerde surveillance). In dit laatste geval hoeven alleen nog de patiënten met een hoge kans handmatig door de DI te worden beoordeeld.

De studies in dit proefschrift evalueren de huidige traditionele surveillancemethoden en onderzoeken de haalbaarheid en toepasbaarheid van (semi-)geautomatiseerde surveillance in verschillende ziekenhuizen.

Deel I: Praktijkvoorbeelden van het gebruik van surveillancegegevens

Het eerste deel van dit proefschrift beschrijft twee praktijkvoorbeelden waarin surveillancedata van zorginfecties worden gebruikt. **Hoofdstuk 2** laat zien dat het gebruik van externe ventriculaire drains (EVD's) met een antibioticacoating geen beschermend effect heeft op ventriculostomie-gerelateerde infecties bij neurochirurgische patiënten vergeleken met reguliere EVD's. **Hoofdstuk 3** geeft een overzicht van trends in zorginfecties tijdens de COVID-19-pandemie in vergelijking met pre-pandemische gegevens. De incidentie van

lijnsepsis, beademing-gerelateerde pneumonieën, en infecties aan het gastro-intestinale stelsel en centrale zenuwstelsel was toegenomen tijdens het eerste jaar van de pandemie. In zowel intensive-care (IC-) patiënten met COVID-19 als zonder COVID-19 was een toename in de lijnsepsisincidentie ten opzichte van pre-pandemische gegevens. Mogelijke oorzaken van deze toename in zorginfecties zijn een veranderd infectiepreventiebeleid, andere patiëntenpopulatie, de hoge werkdruk, of de inzet van minder ervaren personeel. Wat de daadwerkelijke factoren zijn die deze toename hebben veroorzaakt moet verder onderzocht worden.

Deel II: Evaluatie van huidige surveillance activiteiten

In **Hoofdstuk 4** wordt de huidige surveillance van lijnsepsis geëvalueerd. Met behulp van focusgroepdiscussies en interviews zijn ervaringen en suggesties voor verbeteringen onderzocht. Het nut van de surveillance werd betwijfeld gezien de tijd die men erin steekt terwijl de lijnsepsisincidentie laag is. Daarnaast wordt de uitvoering bemoeilijkt door automatiseringsproblemen en gebrek aan ondersteuning hierin. Ook gaf men aan dat betrokkenheid en leiderschap wordt gemist in de uitvoering van de surveillance en dat de definities om een lijnsepsis te kunnen scoren niet altijd toepasbaar zijn op alle patiënten. Suggesties voor verbeteringen waren onder andere het versimpelen van inclusiecriteria en infectiedefinities, het langer opvolgen van de patiënten met katheters (ook in de thuiszorg), het aanpassen van de definities voor specifieke patiëntengroepen, en meer gebruik te maken van automatisering.

Waar in hoofdstuk 4 de focus lag op de uitvoering, is in **Hoofdstuk 5** de betrouwbaarheid van de surveillancemethode onderzocht. In deze prospectieve cohortstudie studie voerden zeven Nederlandse ziekenhuizen surveillance uit van postoperatieve wondinfecties (POWI) bij patiënten die een colorectale resectie hebben ondergaan. Voorafgaand aan de uitvoering volgden alle veertien DI's een training om het toepassen van het protocol en de definities te oefenen, en om overeenstemming in niveau en uitvoering te bereiken. Tijdens de uitvoering van de surveillance werden verschillende metingen gedaan waarbij DI's individueel casuïstiek beoordeelden en hierop de infectiedefinitie toepasten: dit waren zowel casussen uit het eigen ziekenhuis als vooraf opgezette casuïstiek. Deze beoordelingen werden met elkaar vergeleken. Het bleek dat DI's consistent waren in het toepassen van de infectiedefinitie (hoge betrouwbaarheid), maar niet altijd de juiste beoordeling gaven (lage validiteit). Hieruit werd geconcludeerd dat de POWI-cijfers reproduceerbaar zijn en dus geschikt voor het volgen van trends binnen het eigen ziekenhuis, maar niet altijd correct en daarom minder geschikt voor een betrouwbare vergelijking tussen de verschillende ziekenhuizen.

Omdat het opzetten, valideren, en implementeren van geautomatiseerde surveillance tijd kost, is het waardevol om op de korte termijn al aanpassingen te doen om de werklast van traditionele surveillance te verminderen. In **Hoofdstuk 6** is onderzocht of drie variabelen het risico op het ontwikkelen van een POWI vergroten, en dus essentieel zijn om te verzamelen voor surveillancedoeleinden. Deze variabelen betreffen een operatie voorafgaand aan de ingreep die wordt gesurveilleerd, een vervolgoperatie tijdens de follow-up periode, of een tweede ingreep tijdens dezelfde operatiesessie als de ingreep die wordt gesurveilleerd. Uit analyse van 115.943 operaties uitgevoerd tussen 2012 – 2015 door 85 ziekenhuizen bleek enkel een vervolgoperatie het risico op het ontwikkelen van een POWI te verhogen. De overige twee variabelen hoeven dus niet meer verzameld en gerapporteerd te worden. Aangezien deze informatie vaak handmatig opgezocht moet worden levert dit tijdswinst op.

Deel III: Op weg naar (semi-)geautomatiseerde surveillance van zorginfecties

In het laatste gedeelte van dit proefschrift is onderzocht of semi-automatische surveillance haalbaar en toepasbaar is binnen (Nederlandse) ziekenhuizen, en welke factoren implementatie bevorderen of belemmeren. In **Hoofdstuk 7** is met behulp van een online vragenlijst de huidige stand van geautomatiseerde surveillance in Europa onderzocht. Negentien respondenten uit elf verschillende Europese landen vulden de vragenlijst in. Twaalf (63%) respondenten rapporteerden een geautomatiseerd surveillancesysteem in gebruik te hebben: vier een volledig geautomatiseerd systeem en zeven een semi-geautomatiseerd systeem. Voor één respondent was het type systeem onbekend. Classificatiemodellen waren het meest gebruikte type algoritme (n = 8), gevolgd door 'machine learning' en regressiemodellen (elk n = 1). Twee respondenten konden geen details geven over het type algoritme. Naast het gebruik van verschillende algoritmen is er ook grote variabiliteit in brondata en in type zorginfecties die worden gesurveilleerd. Implementatie wordt bevorderd door steun en betrokkenheid van zorgprofessionals en directies, en door een goede samenwerking met de informatie technologie (IT) afdeling. De beschikbaarheid van een data warehouse werd ook genoemd als bevorderend voor implementatie. Factoren die implementatie bemoeilijken zijn de wetgeving rondom beveiliging en bescherming van (persoons-)gegevens en het opzetten en onderhouden van geavanceerde IT-infrastructuren.

Hoofdstuk 8 beschrijft de validatie van een semi-automatisch surveillancemodel om patiënten met een hoge kans op een diepe POWI na implantatie van een primaire totale heup- of knieprothese te detecteren. Naast de validatie van het algoritme werd ook onderzocht of de surveillancepopulatie op automatische wijze geselecteerd kon worden. Het algoritme werd toegepast op 9.554 ingrepen uitgevoerd tussen 2012 – 2018 in vier Nederlandse ziekenhuizen,

en algoritme-resultaten werden vergeleken met handmatige surveillance. Alle gevallen van diepe POWI werden door het model geïdentificeerd, met een positief voorspellende waarde tussen de 55.8% – 72.2%. Er werden tevens vijf extra diepe POWI gevonden die bij de handmatige surveillance waren gemist. De surveillancepopulatie kon echter niet automatisch worden geselecteerd: 0.8% – 22.2% van de ingrepen bleek een revisie te betreffen in plaats van een primaire heup- of knieprothese.

In **Hoofdstuk 9** worden twee verschillende surveillancemodellen gevalideerd, een classificatiemodel en een regressiemodel, die colorectale chirurgische patiënten detecteren met een hoge kans op een diepe POWI. Daarnaast wordt beschreven of en hoe ziekenhuizen de surveillancepopulatie automatisch kunnen selecteren, en of ze in staat zijn om casemix variabelen te extraheren uit hun ziekenhuisinformatiesysteem. Het kunnen verzamelen en extraheren van deze gegevens is een voorwaarde voor succesvolle implementatie van semi-automatische surveillance. Beide surveillancemodellen identificeerden alle diepe POWI's, maar het classificatiealgoritme moest worden aangepast omdat bleek dat twee van de vier ziekenhuizen niet structureel een microbiologische kweek afnemen bij patiënten met verdenking op een diepe POWI. Net als in hoofdstuk 8 bleek ook bij colorectale chirurgie de exacte surveillancepopulatie niet automatisch te selecteren en waren niet alle variabelen benodigd voor casemixcorrectie op automatische wijze beschikbaar. Omdat het classificatiemodel makkelijker aan te passen is aan klinische praktijkvariatie en minder ingewikkelde datamanagementtechnieken vereist is dit model meer geschikt voor grootschalige implementatie vergeleken met het regressiemodel.

In klinische aantekeningen (ongestructureerde data) staat vaak waardevolle (klinische) informatie die gebruikt wordt door DI's om een POWI te kunnen scoren. Het originele classificatiemodel zoals beschreven in Hoofdstuk 9 gebruikt enkel gegevens die zijn vastgelegd in gestructureerde velden, maar dit geeft relatief veel vals-positieve resultaten. De hypothese was dat het gebruik van klinische aantekeningen de selectie hoog-risico patiënten kan verfijnen en zo meer werklastreductie kan opleveren. In **Hoofdstuk 10** worden met behulp van 'natural language processing' de klinische aantekeningen geanalyseerd en als algoritme-element toegevoegd aan het originele classificatiemodel. Dit resulteerde in 3.7% minder vals-positieve resultaten, maar er miste daardoor één diepe POWI. Aangezien het opnemen van ongestructureerde data in algoritmes complex en arbeidsintensief is hebben we geconcludeerd dat het voor deze toepassing niet opweegt tegen het geringe voordeel dat het oplevert.

CONCLUSIE

In **Hoofdstuk 11** worden de resultaten van de studies uit dit proefschrift samengevat en in context geplaatst. De studies uit dit proefschrift ondersteunen het standpunt dat semi-geautomatiseerde classificatiemodellen toepasbaar en effectief zijn voor de surveillance van zorginfecties in Nederlandse en Europese ziekenhuizen. De mogelijkheid om een algoritme aan te passen aan de lokale klinische praktijk is essentieel voor succesvolle algoritmeprestaties. Geautomatiseerde surveillance moet niet alleen worden beoordeeld op vermindering van de werklast of sensitiviteit en specificiteit, maar ook op de haalbaarheid en het potentieel voor daadwerkelijk gebruik en implementatie. Het hele surveillanceproces – van automatische patiëntenselectie tot interpretatie van surveillanceresultaten – moet daarbij worden meegenomen.

Het zorglandschap verandert continu. Behandelingen, ziekteverwekkers, resistentie, ziekten of patiënten, maar ook de organisatie van zorgverlening, wetgeving, technologische ondersteuning en IT-systemen zullen voortdurend veranderen. Doorlopend onderhoud, validatie en updates in geautomatiseerde surveillance zullen altijd nodig zijn en een continu proces blijven. Hoewel automatisering voordelen heeft ten opzichte van traditionele surveillance, neemt het de huidige controverses en problemen rondom verschillen in methoden (verschillende soorten algoritmen of infectiedefinities) en gegevensverzameling (verschillen in brondata) niet weg. Er is daarom behoefte aan sturing en samenwerking om geautomatiseerde surveillance op grote schaal te gebruiken, om de kwaliteit van surveillancegegevens te garanderen.

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ABOUT THE AUTHOR

Janneke Verberk was born on April 25th 1992 in Utrecht, the Netherlands. She grew up in Culemborg where she followed secondary education at Lek en Linge. Thereafter, she studied the bachelor Health and Life Sciences at the VU University Amsterdam from which she graduated in 2013. Subsequently, she graduated from the Master Biomedical Sciences, specialisations Infectious Diseases and International Public Health, at the VU University Amsterdam in 2015.

After this, she started working as epidemiologist for the National Immunisation Programme at the National Institute for Public Health and the Environment (RIVM) in Bilthoven, focusing on seroepidemiology (PIENTER-3) and rotavirus vaccination. In August 2018 she started her PhD projects presented in this thesis at the Infection Prevention unit of the University Medical Centre Utrecht (UMCU) in collaboration with the department Epidemiology and Surveillance of the RIVM under supervision of prof. dr. Marc Bonten (UMCU), dr. Maaike van Mourik (UMCU) and dr. Sabine de Greeff (RIVM). She performed several multicentre studies investigating automated surveillance of healthcare-associated infections and spent several weeks as a visiting researcher with the Department of Medicine at Karolinska Institutet Stockholm, Sweden, under supervision of dr. Pontus Nauclér and dr. Suzanne van der Werff. Besides her work as a PhD candidate, she assisted in teaching epidemiology to medical students and infection control practitioners, and advised PREZIES (RIVM) in national implementation strategies of semi-automated surveillance. When in March 2020 the SARS-CoV-2 became a pandemic, she started simultaneously working for the EU-funded project Rapid European COVID-19 Emergency Research Response (RECOVER) and for the seroepidemiological study PIENTER-corona of the RIVM. In November 2021 she was awarded the 'Professor Frits de Waard Penning' for conducting original and excellent epidemiological research.

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