The accuracy of fully automated algorithms for surveillance of healthcare-onset Clostridioides difficile infections in hospitalized patients

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Abstract

We developed and validated a set of fully automated surveillance algorithms for healthcare-onset CDI using electronic health records. In a validation data set of 750 manually annotated admissions, the algorithm based on International Classification of Disease, Tenth Revision (ICD-10) code A04.7 had insufficient sensitivity. Algorithms based on microbiological test results with or without addition of symptoms performed well.

(Received 4 January 2022; accepted 8 February 2022)

Clostridioides difficile infections (CDI) pose a problem within healthcare worldwide. In Europe, nearly 190,000 patients are hospitalized with CDI every year. The most dominant risk factor for CDI is previous treatment with antibiotics, but CDI outbreaks also occur in healthcare institutions. Effective surveillance is important to register adverse events, enable quick response to outbreaks, and to evaluate control measures. However, most surveillance is based on time-consuming and resource-intensive manual review of patient records, which is also prone to subjective interpretation and surveillance bias.

In this study, we developed and evaluated the performance of a set of fully automated rule-based surveillance algorithms, including free-text analysis, for healthcare-onset (HO) CDI in hospitalized patients using electronic health record (EHR) data.

Methods

In this observational study, we used prospectively entered EHR data from the Karolinska University Hospital which is stored in a research infrastructure called Health Bank–Swedish Health Record Research Bank at DSV/Stockholm University, as previously described. The study was approved by the Regional Ethical Review Board in Stockholm under permission no. 2016/2309-32.

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Cite this article: van der Werff SD, Fritzing M, Tanushi H, Henriksson A, Dalianis H, Ternhag A, Färnert A, and Nauclér P. (2022). The accuracy of fully automated algorithms for surveillance of healthcare-onset Clostridioides difficile infections in hospitalized patients. Antimicrobial Stewardship & Healthcare Epidemiology, https://doi.org/10.1017/ash.2022.32

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previous positive stool sample.\textsuperscript{6,7} Other CDI episodes were regarded as new infections.

The performance of the algorithms was assessed in a validation data set of 750 randomly selected admissions during 2012 and 2013. The validation data set was created by sampling 3 groups: (1) admissions with at least 1 positive stool sample for \textit{C. difficile} (\(n = 287\) of 756); (2) admissions with only negative stool samples for \textit{C. difficile} (\(n = 213\) of 4,916); and (3) admissions with no stool samples analyzed for \textit{C. difficile} (\(n = 250\) of 173,459). The 750 admissions were manually annotated via medical record review to determine whether patients fulfilled the ECDC CDI definition. These 750 admissions added up to 983 potential CDI episodes (within the 3 groups 470, 263 and 250 possible CDI-episodes, respectively) (Fig. 1).

Algorithm performance was evaluated by assessing the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). To obtain performance estimates of the algorithms in the total hospital population, estimates were extrapolated to all patients hospitalized during 2012–2013 based on the sampling proportions within the 3 groups described above.\textsuperscript{5} The confidence interval (CI) for the extrapolated estimates were calculated as the 2.5th and 97.5th percentiles of point estimates obtained from 10,000 bootstrap samples for each of the 3 groups. To account for uncertainty, the bootstrapping was performed before extrapolating the proportions from the validation dataset to the validation period cohort. Analyses were performed using R version 3.6.1 software (R Foundation for Statistical Computing, Vienna, Austria).

**Results**

The 750 hospital admissions within the validation cohort comprised 719 patients (641 adults and 78 children), of whom 253 (35.2%) had a CDI. Moreover, 225 (35.1%) of 641 adults had a CDI, and 28 (35.9%) of 78 children had a CDI. Compared to patients without CDI, patients with a CDI were older (median age, 69 vs 58 y), had a longer length of stay (median days, 17 vs 5), had a higher Charlson comorbidity index (median, 2 vs 1), and had a higher in-hospital mortality rate [9.5%, (24 of 253) versus 1.9% (9 of 466); all \(P < .001\)].

According to the manual record review of the 983 potential CDI episodes present within the 750 admissions 351 were confirmed CDI episodes: 260 (26.4%) were new, 60 (6.1%) were ongoing, and 31 (3.2%) were recurrent (Fig. 1). For the algorithm performance only the new CDI episodes were used. Algorithm 1, based on ICD-10 code A04.7, had a sensitivity of 0.442 (95% CI, 0.381–0.504) in correctly identifying CDI episodes (Table 1). Algorithms 2 and 3 had sensitivities of 1.000 (95% CI, 0.999–1.000) and 0.992 (95% CI, 0.980–1.000), respectively, and both had a specificity of 1.000 (95% CI, 0.999–1.000). Using algorithm 2, 12 patients in the validation set were misclassified as positive compared to 6 patients using algorithm 3, and algorithm 3 misclassified 2 patients as negative (for details see footnote Table 1).

**Discussion**

Fully automated algorithms based on microbiological data with or without free-text analysis of symptoms performed well for surveillance purposes in detecting CDI, whereas an algorithm based on ICD-10 code had insufficient sensitivity. This inadequacy was related to poor recording of the CDI ICD-10 code despite positive stool tests and symptoms for CDI. The algorithm based on only microbiological tests tended to slightly overestimate the prevalence of CDI, and the algorithm that also included analyses of free text slightly reduced false positives. However, this improvement came at the expense of being computationally more challenging and would also require adaptation to local EHR systems. The small difference between the algorithms based on microbiological data
Infection According to the ECDC Definition

Among 983 Potential CDI Episodes in 750 Admissions in the Validation Period (n = 180,715)

- **True Positives**: 115
- **False Positives**: 69
- **False Negatives**: 145
- **True Negatives**: 654

| Algorithm   | Sensitivity (95% CI) | Specificity (95% CI) | PPV (95% CI) | NPV (95% CI) | AUC (95% CI) |
|-------------|----------------------|----------------------|--------------|--------------|--------------|
| Algorithm 1a | 0.442 (0.381–0.504)  | 0.999 (0.998–1.000)  | 0.998 (0.998–1.000) | 0.720 (0.701–0.739) | 1.000 (0.999–1.000) |
| Algorithm 2a | 0.992 (0.980–1.000)  | 0.996 (0.993–1.000)  | 0.956 (0.932–0.978) | 0.978 (0.954–0.992) | 0.956 (0.932–0.978) |

C. difficile during admission were regarded as potential CDI-episodes, and each admission without stool samples analyzed for C. difficile counted as one potential CDI-episode. The extrapolated results of the algorithms from the validation data set to the validation period cohort (2012–2013) were based on the sampling proportion of potential CDI episodes from the 3 different groups: (1) admissions with a positive stool sample for C. difficile; (2) admissions with only negative stool samples for C. difficile analyzed for C. difficile; (3) admissions without an available stool sample.

The strengths of our study included the extensive availability of EHR data, which enabled us to simulate the performance of epidemiological surveillance using real-world, real-time data, and the application of the same testing guidelines and diagnostic methods for CDI throughout the entire study period. Our study also had limitations. We used data from only 1 hospital over a limited period, so the applicability of the algorithms to other acute-care settings, especially in regard to different testing strategies over time and across institutions, may limit the generalizability of our results. For example, during the study period, immunoassays (EIAs) or nucleic acid amplification tests (NAATs) were not used as diagnostic methods, which reduced the risk of overdiagnosis in our study. However, the introduction of NAAT might lead to the overdiagnosis of CDI, both by algorithms and manual annotation, which should be considered when implementing this algorithm during later periods or at other institutions.

In conclusion, algorithms based on microbiological test results only are likely to perform well in hospitals with symptom indications for C. difficile testing, while free-text analysis of medical notes could improve surveillance algorithm performance if more liberal indications for C. difficile testing are used.

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**Financial support.** The work was supported by Sweden’s Innovation Agency (Vinnova grant no. 2016-00563). P.N. was supported by a Region Stockholm clinical research appointment.

**Conflicts of interest.** All authors report no conflicts of interest relevant to this article.
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