swissnoso

Nationales Zentrum
für Infektionsprävention

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Final Report on StAR-2: Surveillance for *C. difficile* infections in Switzerland

1. Summary

The project "Surveillance for *C. difficile* infections in Switzerland" represents a collaborative effort by experts in the field of infectious diseases and epidemiology within the national campaign against antibiotic-resistance “StAR-2” by the Federal Office of Public Health (FOPH). This report summarizes the findings and achievements and recommendations for future action. The main aim of this project is to address the critical gap in the surveillance of *Clostridioides difficile* infections (CDI) within Switzerland and to present possibilities for the strengthening of *C. difficile* Surveillance in Switzerland by establishing a continuous monitoring system for *C. difficile* infections (CDI). Most European countries report the incidence of *C. difficile*, with Irland, UK, and Germany having mandatory reporting.

In the absence of a coordinated framework for data collection and analysis for CDI, Switzerland has faced challenges in understanding the true burden of this infection. This project recognized the need to improve this situation and initiated three interrelated projects to comprehensively assess CDI in the Swiss healthcare landscape.

The project submitted to the FOPH focused on laboratory surveillance in collaboration with ANRESIS, and was successfully completed in 2020. However, very few laboratories participated despite the fact, that we financed some of the interfaces e.g., for the commonly used software “DORNER”. Therefore, we extended the project with alternative approaches to meet the goals of the project submitted to the FOPH, even when the submitted project was successfully completed.

1. **Surveillance based on laboratory data from ANRESIS**
   This surveillance approach is based on automated data collection of microbiological results on *C. difficile* testing and aggregated data summary plus individual reporting of positivity rates. For this, Swissnoso in collaboration with ANRESIS initiated the expansion of the dataset to include laboratory data on CDI within the ANRESIS platform. Data collection is standardized, but highly dependent on the initiative of laboratories to enable the data transfer. ANRESIS has a solid record for collection and analysis of antibiotic resistance data and recently expanded to collect antibiotic consumption data amongst others. This method provides unique opportunities to use CDI-rates as a surrogate marker for antibiotic consumption and as a tool for detection and rapid feedback on possible outbreaks within institutions.

2. **Surveillance based on clinical data, following the European Centre for Disease Control & Prevention (ECDC) model**

   This clinically oriented ECDC model is the traditional standard for data collection within the hospitals and further for the calculation of incidence rates for CDI. For this, a nationwide survey was conducted by Swissnoso and administered to Swiss acute care hospitals. Data collection was standardized and included administrative and diagnostic parameters. Analysis of the data provided an overview of current standard of practice and allowed for a representative estimate of CDI incidence of 3.8 CDI episodes/ 10,000 patient days for 2022.

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3. **Surveillance based on routinely collected data by the Swiss Federal Statistical Office (FSO)**

   This approach leverages the dataset based on mandatory data reported to the FSO. For this, Swissnoso analyzed a subset of anonymized data from the Swiss medical statistics of hospitals (MedStat) including one of the codes for CDI (based on ICD-code A04.7) data and publicly available data on Swiss hospital statistics. This enabled the calculation of annual CDI-incidence rates, demonstrating stable infection rates with a mean rate of 3.7 / 10,000 patient days between 2014 and 2021. In addition to the epidemiologic insights, this dataset includes outcome and hospitalization data, revealing a high rate of rehospitalization for recurrent CDI. Surveillance based on this administrative data therefore revealed valuable insights into the epidemiology and an estimate of the added cost by prolonged hospitalization.

Results

The findings from these approaches illuminated the CDI landscape in Switzerland. We learned that the burden of CDI in Switzerland is underestimated. From the survey, a striking heterogeneity in surveillance activities, diagnostic approaches, and infection control strategies became evident. The laboratory-based surveillance offers additional advantages beyond monitoring of CDI-rates, a potential for synergy that is currently untapped. The analysis of the MedStat dataset added another dimension to our understanding of CDI in Switzerland. Collectively, these results underscore the urgent need for a unified national surveillance system for CDI in Switzerland.

Recommendations and conclusion

The project team recommends the Federal Office of Public Health (FOPH) to continue to support the implementation of a national surveillance system for CDI in Switzerland.
The routine data based surveillance – laboratory data and MedStat – would allow to get a quite reasonable overview of *C.difficile* incidence without additional workload for hospitals.
Mandatory reporting would facilitate laboratory-based surveillance
The Swissnoso board has voted to include *C.difficile* not as top priority, given the fact that they are unable to provide human resources for an additional module of surveillance.

Therefore, we recommend

1. To continue with Laboratory surveillance, finances and scientific support is granted by resources of ANRESIS. Swissnoso can support ANRESIS to motivate more laboratories for participation
2. To consider to add *C.difficile* to the pathogens with mandatory reporting
3. To yearly analyse *C.difficile* data from FSO, to stratify *C.difficile* colonization and infection, and to reduce bias by the laboratory method used to diagnose *C.difficile*

In conclusion, the project goal of *C.difficile* surveillance has been successfully completed despite major challenges of the pandemic. The ECDC protocol likely exceeds human resources on the hospital level.

2. Introduction and scope of report

In Switzerland, there is a notable absence of a nationwide surveillance system for *Clostridioides difficile* infections (CDI), setting it apart from many other European countries. This project aims to address this gap by providing multiple approaches for continuing a comprehensive CDI surveillance system. Within the project we have explored different surveillance approaches, including a lab data based approach, an approach based on the ECDC model, and an approach based on routine data (MedStat: the dataset of SFO). ,. The results indicate a consistent CDI-rate during the last decade, for 2022 our analysis of hospital data / survey indicates an incidence of 3.8 CDI episodes per 10,000 patient days in Swiss acute care hospitals. This report lays the groundwork for a standardized CDI surveillance.

Background

Clostridioides difficile (*C. difficile*) is the most common gastrointestinal hospital-acquired infection (HAI) worldwide, placing a significant burden on healthcare systems and patient well-being [1] .The spectrum of *C. difficile* infection (CDI) comprises a wide range of clinical presentations, from mild diarrhea to life-threatening conditions such as toxic megacolon. With the potential to cause significant morbidity, mortality, and associated healthcare costs, CDI presents a serious challenge to healthcare providers worldwide [2,3].

Traditionally perceived as primarily a hospital-acquired infection, CDI is increasingly being recognized in ambulatory care settings [4]. Fundamental factors underlying the development of CDI include the acquisition of *C. difficile* e.g., from the environment, exposure to antibiotic therapy, and a host susceptible to infection: Risk factors include older age, multiple comorbidities, chemotherapy or immunosuppressive treatments, recent surgery, and proton pump inhibitor therapy.

Even after receiving adequate treatment, up to 30% patients experience recurrent infections [5,6]. Therefore, CDI surveillance is critical not only for understanding the complex dynamics of infection rates, but it also serves as the foundation for designing targeted intervention programs to reduce the incidence of CDI. These interventions focus primarily on the two modifiable components: antibiotic exposure and *C. difficile* acquisition. Antibiotic stewardship programs address both factors and have demonstrated the potential to reduce infection rates by up to 30%, with even greater impact when combined with robust infection control measures [7,8].

C. difficile occupies a special position among the most relevant antibiotic-resistant pathogens. Its importance stems not primarily from the emergence of antimicrobial resistance, but from the bacteria's intrinsic resistance to antimicrobials due to its ability to form spores and thrive in the gastrointestinal tract. Like other antibiotic-resistant bacteria, it often plays a role in infections following antibiotic exposure. Studies have shown the correlation between antibiotic consumption and the prevalence of *C. difficile* infections [7,8]. This finding has paved the way for the use of *C. difficile* infection rates as a surrogate marker for antibiotic use and as an adjunct in antibiotic stewardship programs.

In this context, *C. difficile* has been defined as a pathogen of priority for antimicrobial resistance by the centers for disease control CDC [9]. Its importance is further underlined by the fact that the European centers for disease control ECDC coordinates a multinational surveillance program in place across Europe [10]. Switzerland currently lacks such a system, despite its active participation in *C. difficile* research and development of national and European guidelines. This stands in contrast to the recommendations formed in these guidelines, that advocate for surveillance of *C. difficile* infections [11]. To improve this gap, *C. difficile* was chosen as one of three priority projects by Swissnoso within the Swiss initiative against antimicrobial Resistance (StAR-2) coordinated by the Federal Office of Public Health (FOPH).

The initial proposal for the project was to integrate *C. difficile* data into the database of ANRESIS, the Swiss Centre for Antibiotic Resistance, leveraging on the synergy between surveillance of infection

rates, antibiotic stewardship programs and infection surveillance, national antibiotic stewardship programs and hospital infection control. However, we experienced unforeseen challenges within the project. As the COVID-19 pandemic began to unfold, the entire healthcare system struggled to cope, and the diagnostic laboratories forced to prioritize essential diagnostic services over other activities. As a result, our project experienced significant delays, prompting the project team to explore alternative approaches to data collection. However, this adversity created unexpected opportunities for growth and knowledge expansion. We began to recognize the potential value of tapping into alternative data sources. Despite the hurdles posed by the pandemic, we have made significant progress. In this report, we present the results and lessons learned from our activities. In the following sections, we present the most up-to-date estimate of the national burden of CDI in Swiss acute care hospitals, aiming to establish a foundation for a continuous, standardized surveillance system. Implementing this standardized surveillance system holds the potential to address the current heterogeneity in CDI surveillance, diagnosis, and control strategies across Switzerland, thereby facilitating disease monitoring as well as targeted interventions.

While we are unable to implement a continuous operating surveillance system within the available timeframe, we have laid the foundation to continue the surveillance activities from now on. We have discovered new approaches for harvesting existing data pools for CDI. In this report, we present the basis for future projects, extending beyond *C. difficile*. The summary of our activities, findings, and the recommendations drawn from the project are intended to serve as a resource for future activities related to *C. difficile* surveillance in Switzerland and beyond.

3. Project Approach and Methodology

In this section, we outline the three surveillance approaches for a national surveillance of *C. difficile*.

Surveillance based on laboratory data from ANRESIS:

The data collection with automated transfer of laboratory-results is a fundamental component of the project. This approach was initiated in collaboration with ANRESIS at the outset of our efforts to establish a surveillance for *C. difficile*. It holds significant appeal due to its automation capabilities, rapid feedback, and synergies with antimicrobial consumption and outbreak detection. But the participation of laboratories is essential to realize this project. ANRESIS visited laboratories on-site and Swissnoso promoted the integration of the data to the hospitals and infection prevention teams, offering support and financial compensation to institutions for this data expansion.

On the technical side, substantial adjustments were necessary to adapt the ANRESIS platform to include non-cultural results. This entailed defining relevant variables and integrating them into the current interface. This then further needs an additional adjustment from each participating laboratory. The database now enables the import of positive *C. difficile* test results and the methodology used for detection. ANRESIS has further developed a dashboard, including *C. difficile* data, that can be reported back to the participants and linked to the institution's antibiotic consumption data.

However, our initial plan to expand data import from larger laboratories to ANRESIS was hampered by resource constraints within the labs, due to the COVID-19 pandemic. As a result, Swissnoso took significant steps to independently advance the project, which led to the two other approaches described here. With the survey we have gathered the data regarding the most common diagnostic methods used and the number of tests performed. We have analyzed the conformity with current diagnostic guidelines for *C. difficile*. To enable validation of data quality and the effect on the incidence rate with laboratory-based surveillance, we have offered a comparative analysis of infection rates with clinical surveillance and laboratory surveillance to all participants.

The participation rate of labs remained too low to allow for calculation of national infection rates for CDI. Nonetheless, ANRESIS has demonstrated the proof of concept that a correlation exists between antibiotic consumption and the incidence of *C. difficile* and continues its work on the subject. The prerequisites for this endeavor have been established to the best of Swissnoso's knowledge.

Surveillance based on clinical data, following the European Centre for Disease Control & Prevention (ECDC) model:

Surveillance based on the ECDC model serves as a cornerstone for establishing a comprehensive surveillance system for *C. difficile*. This model, employed as standard practice in other surveillance programs internationally, not only provided a robust foundation for our study. It also served as a reference for international comparisons.

Dataset

A reporting form for CDI-Surveillance was developed by Swissnoso and pretested in several hospitals. The parameters of interest were the number of CDI diagnoses, the current measures for management of CDI in addition to general hospital parameters and the testing algorithm and frequency of *C. difficile* testing. Diagnostic criteria for CDI followed definitions outlined by ECDC and the Centers for Disease Control & Prevention (CDC, Atlanta, USA). They were adapted to the Swiss hospital setting, while still allowing for comparison with the minimal surveillance protocol of the ECDC [10,12]. The web-based survey with SurveyMonkey [13] was sent to all Swiss acute care hospitals participating in the Swissnoso surveillance system [14]. Long-term care facilities, psychiatric hospitals and maternity hospitals were excluded from the survey. Local infection control teams were asked to provide the

information for their institution for the entire year from 01.01.2022 to 31.12.2022 according to predefined definitions. Participation in the electronic questionnaire was possible via link in German or French during a ten-week period. CDI was defined as a positive test result for toxigenic *C. difficile*. “Lab-based CDI” refers to diagnoses based on laboratory-results alone, while the term “CDI episode” would be used for symptomatic patients with CDI. We asked for the total number of patients affected and for recurrences. Repeated tests within 14 days of CDI diagnosis were considered duplicates and not counted as separate CDI cases. Data entry was possible for individual institutions as well as cumulative data for a whole hospital group.

Information was submitted to Swissnoso by trained infection control practitioners or infectious disease physicians in aggregate form, without patient-specific data. All participants were provided with instructions and explanations of key parameters and were given the opportunity to seek professional support directly from the investigators or to provide written feedback through the survey.

Method

Submitted data were collected in SurveyMonkey and extracted into Excel, followed by plausibility checks and data cleaning. Descriptive statistical analyses were carried out using Stata version 16.1 (College Station, TX: StataCorp LLC) by a professional biostatistician (AS).

Depending on local procedures, the completeness of the responses varied. While some participants were able to provide information on all questions and variables, other answers were incomplete. Accounting for this variability, we analyzed the responses for each question separately. Questionnaires with incomplete responses were excluded in the respective analyses. We have calculated in total 9 different incidences. 95% Poisson confidence intervals were calculated for the incidence rate. We have used the definitions as outlined in the reference guidelines [15,16]. The incidence expressed as number of *C. difficile* episodes / 10,000 patient-days was used for comparison with our other calculations and to express mean incidence rates. Where appropriate, we stratified the answers to the following hospital categories: tertiary care hospitals, primary care hospitals and hospitals specialized in surgery.

Surveillance based on routinely collected data by the Swiss Federal Statistical Office (FSO):

The use of administrative data for surveillance marks an innovative stride in our project, as it integrates Diagnosis-Related Group (DRG) data analysis into the framework, opening new horizons for a data-driven perspective on *C. difficile* surveillance.

Dataset

We have received the dataset MS Standard Dataset DRG TYPOL from the Swiss medical statistics of hospitals (MedStat) collected by the Swiss Federal Statistical Office (FSO). Our dataset included all hospitalizations between 2005 and 2021 with a *C. difficile* infection (CDI) as side or main diagnosis (based on ICD-code A04.7). The variables are described in a document provided by the FSO).

Method

For further analysis, we have restricted the dataset to the following hospital categories: tertiary care hospitals, primary care hospitals and hospitals specialized in surgery. This restriction makes the dataset comparable to the Swissnoso *C. difficile* survey performed in spring 2023. To calculate the incidence of CDI, we have merged the MedStat dataset with the public available data “Key figures for Swiss hospitals” published by the FOPH. From the FOPH dataset, we have extracted the number of patient days and the number of discharges. We were able to merge data on the level of the hospital category

(primary care, tertiary care, specialized hospitals). It was not possible to do the merge on a hospital level because hospitals are anonymized in the MedStat dataset. The definition of patient days in the FOPH dataset changed several times since 2005. The last large change was in 2013, thus we have limited our analysis to the time period 2014-2021 to avoid a measurement bias, although another small change took place in 2020 (long-term stays are not considered anymore in the calculation of patient days).

The incidence was calculated as number of hospitalizations with a code for CDI infection divided by 10,000 patient days, and 1,000 discharges, respectively. 95% Poisson confidence intervals were calculated for the incidence rate. We have used the OECD definition for the duration of the hospital stay. Statistical analysis was done in Stata (version 16.1).

4. Results and Findings

Surveillance based on laboratory data from ANRESIS:

Key achievements:

- Successful integration of microbiological data for *C. difficile* in the ANRESIS platform.
- Implementation of an automated reporting system based on laboratory criteria, including diagnostic methods.
- Potential for automated infection rate reporting and correlation with antibiotic use.

Our collaborative efforts in the laboratory-based approach have yielded significant achievements. We have achieved the integration of microbiological data for *C. difficile* in the ANRESIS platform. Notably, an automated system was developed for feedback of infection rates. This system has the potential to streamline infection rate reporting and link it with antibiotic usage data by ANRESIS.

However, it's important to note that the success of this approach hinges on the cooperation of individual laboratories to adapt to automated data transfer—an area where Swissnoso's influence is limited. Our ongoing goal is to expand upon the proof of principle that links antibiotic consumption with *C. difficile* incidence, ultimately enhancing antibiotic stewardship efforts across affiliated hospitals. We stand ready to further assist participating hospitals and ANRESIS in this process as needed.

Surveillance based on clinical data, following the European Centre for Disease Control & Prevention (ECDC) model:

Key achievements:

- Development of a tailored survey instrument for CDI surveillance in Switzerland.
- Establishment of a baseline for CDI-incidence rate (mean incidence rate of 3.83 CDI-episodes per 10,000 patient days in 2022), providing a vital standard for comparative analysis.
- Highlighted the lack of nationwide consistency in surveillance and infection control measures.
- Demonstrated a 10% increase in CDI incidence rates by using an alternative case definition (Lab-CDI diagnoses) for surveillance.
- Provided insights into laboratory testing practices, with an average of 76.5 tests per 10,000 patient days per hospital and a mean positivity rate of 9.2%.

From the survey responses, we were able to gain insights into the current landscape of *C. difficile* infections in Swiss acute care hospitals. We successfully calculated a first national rate of the incidence of CDI and revealed significant variation in standard procedures nationwide.

Results

The survey was sent to 129 acute care hospitals or hospital networks in March 2023 from which 67 participated (52%) (Figure 1). Ten respondents provided cumulative data for a hospital group; therefore,

the actual number of participating institutions may be higher than indicated. Two children's hospitals were excluded from the subsequent analyses. The response rate varied by hospital type: 77% of tertiary care hospitals participated in the survey (34/44 invited hospitals), followed by 42% of primary care hospitals (21/50 invited hospitals), and specialized hospitals with 34% (12/35 invited hospitals). Compared to the official hospital statistics by the office of public health (FOPH) our sample covers 51% of all acute care hospitals from all regions of Switzerland.

CDI incidence

Because of the different monitoring practices, not all participants were able to provide the data for the different case definitions. 49 participants provided data regarding the number of patients with CDI.

The participants reported in total 1593 patients with CDI. In 2022 the mean incidence rate of CDI-episodes per hospital was 3.8 /10,000 patient days (Poisson 95% CI: 3.2-4.5). We observed significant variation in CDI incidence rates between hospital types (Figure 1 und Table 1). Notably, calculating the incidence in terms of Lab-CDI diagnoses, the rate was 4.2 Lab-CDI/ 10,000 patient days per hospital (Poisson 95% CI: 3.3-5.1), indicating an increase by more than 10%, only by using another case definition in the numerator, which has already been demonstrated in other studies [17].

Based on the data, we calculated a recurrence rate of 10.7% (153/1425 patients).

29 hospitals stratified by community-acquired CDI and hospital-acquired CDI. Thereby almost all used a simplified definition for HAI with hospitalization duration of more than 48h as a cut off to for the two categories: with this definition 50.4% of CDI were classified as community-acquired infections (442 of 860 CDI).

Prevention, control, and clinical management of CDI

In our sample, surveillance and infection control related measures were often institution-specific and lacked nationwide consistency. Of note, isolation practices differed from international guidelines that generally recommend single-room isolation [23]. Instead, in Switzerland a risk-adapted approach is widely used with half of the respondents indicating the use of additional individual criteria for isolation - mainly for infection with hypervirulent ribotypes or for uncooperative and incontinent patients.

Laboratory diagnosis of CDI: microbiological stewardship and test algorithms

Two thirds of the participants (43/65) provided numbers of laboratory tests for *C. difficile* in 2022. The mean number of tests performed was 76.5 per 10,000 patient days per hospital, with a mean positivity rate of 9.2%. (Table 2). Different diagnostic algorithms were reported: Overall, 58% of the laboratories followed internationally recommended diagnostic algorithms [18]. The most common screening test (used by 18/26 participants) was a glutamate dehydrogenase (GDH)-based enzyme immunoassay (EIA), either alone or in combination with toxin EIA, followed by nucleic acid amplification test NAAT for discordant results. NAAT-based initial screening with toxin EIA was reported by 5 of 26 respondents. Toxigenic culture and susceptibility testing is available only in a minority of hospitals (11,1%).

Surveillance based on routinely collected data by the Swiss Federal Statistical Office (FSO):

Key achievements:

- Integration of routinely collected Diagnosis-Related Group (DRG) data for comprehensive healthcare analysis.

- In-depth data analysis to calculate CDI incidence rates, track temporal trends, and assess resource utilization patterns.
- Seamless integration with national CDI surveillance efforts, bridging clinical epidemiology with healthcare economics.
- Has the potential to be expanded to monitoring of other infections beyond CDI.

We successfully integrated Diagnosis-Related Group (DRG) data, a rich source of healthcare information in Switzerland, into our project. This integration opened a new dimension in the surveillance, as it allowed us to accurately identify CDI cases with standardized criteria and integrate severity and outcome data and to track temporal trends.

Results

Between 2014 and 2021, a total of 22,414 hospitalizations with a CDI took place, 83.4% from tertiary care hospitals, 15.7% from primary care hospitals and 0.9% from specialized hospitals. The patients' median age was 74 [IQR: 62-83] and 55.3% were women. CDI was the main reason for hospitalization in 28.0% of the cases (see Figure 3).

The median duration of the hospital stay was 14 days [IQR: 7-24]. The hospital stay was longer when CDI was a side diagnosis: 17 days [IQR: 10-29] compared to 7 days [4-12] when CDI was the main diagnosis. The severity of the CDI is coded since 2017. (See Table 3) 7.8% (1,752 of 22,414) of the patients with CDI died during the hospital stay. 2.5% (n=160) of patients with CDI as main diagnosis and 9.9% (n= 1592) of patients with CDI as side diagnosis. 18.5% of the patients had more than one hospitalization with a CDI (3274 of 17669 patients). Most of the re-hospitalizations were within two months after discharge (67.5%, 3,201 of 4,745 re-hospitalizations).

Between 2014 and 2021, the mean incidence was 3.7 per 10,000 patient days and 2.2 per 1,000 discharges, respectively. There was no significant increase or decrease of the incidence over time (Figure 4). The incidence was highest in tertiary care hospitals 3.9 per 10,000 patient days compared to 3.2 and 0.9 in primary care hospitals and specialized hospitals, respectively.

5. Discussion and Recommendations

The analysis of Clostridioides difficile (*C. difficile*) infections in Switzerland, as undertaken in this project, provides valuable insights into the epidemiology, clinical aspects, and management of CDI. This analysis provides the first nationwide estimate on the incidence of CDI in Switzerland using the most current data available. Our results are consistent with the official database of the Federal Statistical Office, indicating that our sample adequately represents the burden of infections in Swiss healthcare. In the most recent publication, ECDC reported a crude incidence rate of CDI 3.48 cases/10,000 patient-days, which is similar to the rate of 3.83 CDI episodes /10,000 patient days in our survey. Like the Swiss data (Figure 2) tertiary care hospitals had the highest rates of 3.87 cases/10,000 patient-days, and the heterogeneous group of 'specialized' hospitals had the lowest rates of infections. The European recurrence rate was 12%, which is similar our recurrence rate of 10.7% (data from questionnaire) and 18% (MedStat data). Both rates are lower than the recurrence rate of 20-30% reported in the literature [5,6,19,20] and may reflect the low perception of the problem in Swiss hospitals.

Diagnostic algorithms for *C. difficile* detection:

Different tests are available for detection of *C. difficile* and the approach to testing varied across the participants: Overall, 58% followed one of the internationally recommended multistep algorithms for diagnosis [18](Lower compared to the ECDC-report with 76,8% [21]). Compliance to guidelines was best in tertiary care hospitals with 73.3% (22/30), as compared to 25% in primary care hospitals (3/12). The most common screening test is an enzyme immunoassay (EIA), often used with other testing methods if needed. EIA are rapid, simple, and inexpensive and, as part of a multistep algorithm, accurate tests for the diagnosis of *C. difficile* infection. Participants with non-guideline-recommended testing strategies were more likely to rely on NAAT alone for diagnosis of CDI. NAAT are accurate tests for CDI but with the potential for overdiagnosis and substantially higher costs, they should be interpreted only in context with other parameters for CDI-diagnoses. Toxigenic culture remains the reference test for *C. difficile* infections and is a prerequisite for susceptibility testing and molecular typing of *C. difficile* strains, which is uniformly recommended across international surveillance programs. This expertise is limited to only a few laboratories in our sample.

As the diagnostic approach significantly influences detection rates, the diversity of the diagnostic algorithms used makes interpretation of the results difficult. With the use of suboptimal testing, both under- and overreporting are of concern, as demonstrated in previous studies and ESCMID-guidelines [18,22]. Adequate patient selection can improve diagnostic accuracy and is accordingly recommended in the guidelines. Here, only 3 hospitals have testing restrictions in place (restricting testing to unformed stool sample and refusing to retest patient with recent positive test results).

Prevention, control, and management of CDI

The lack of uniform national recommendations explains the heterogeneity in management of CDI. Even larger hospitals use individual case definitions, with some tracking symptomatic patients while others count only patients with a first CDI and others use automatic surveillance with positive test results (Lab-CDI). Most hospitals get notifications for positive *C. difficile* test results, while only 15.8% (9/57 responses) would routinely investigate for nosocomial transmission of CDI in their hospital (5 tertiary care, 3 primary care hospitals, 1 specialized hospital). Two participants (both tertiary hospitals) had episodes with increased infection rates (clusters and/or outbreaks) during the observation period.

Limitations

Consideration of several limitations is required for interpretation of these results: First, our sample does not include all hospitals: however, we had a high participation rate among larger hospitals. As these are the facilities caring for most patients with CDI, our analysis represents the care of CDI patients very well.

Additionally, our results are consistent with our analyses of the DRG-dataset. As infection rates are known to be significantly influenced by many factors, we have considered a rough estimate to be still of value in the absence of other reliable data. Second, the test algorithm was not reported from all participants, which could have possibly altered our results. Third, we do not have any clinical or outcome data for the survey, therefore we could not calculate mortality, risk factors or the proportion of preventable infections. We estimate that, by strict adherence to antibiotic stewardship and consequent infection control measures, up to half of the infections could have been avoided (assuming a preventable proportion of 30% by antibiotic stewardship coupled with >20% reduction by adequate infection control) [7,8].

In conclusion, the survey results highlight the continuing need for standardized CDI surveillance in Switzerland. The diversity in diagnostic and control practices, as well as case definitions, underscores the importance of a consistent methodology. Establishing a nationwide surveillance system, as outlined by the European Center for Disease Control & Prevention (ECDC), would provide a valuable tool for benchmarking and tailored interventions to reduce CDI rates. Moreover, such surveillance can have an immediate impact on patient outcomes and healthcare institutions. The use of an automated laboratory-based surveillance system, as previously proposed by Swissnoso and ANRESIS, holds promise for timely outbreak detection and correlation of infection rates with antibiotic consumption, further supporting antibiotic stewardship efforts.

Implications for Future National Surveillance for CDI

The establishment of a nationwide surveillance program would bring Switzerland in line with many European countries that already have comprehensive CDI monitoring programs. The considerably high infection rates and in regard of both economic and medical aspects, it is evident that a nationwide monitoring system for CDI is not only sensible but also necessary.

Ideally, such a system is including:

1. Standardization: A standardized methodology for diagnosis, data collection, and reporting would enhance comparability across healthcare institutions, regions, and even with international benchmarks.

2. Patient Benefits: Reduction of CDI incidence through effective surveillance and intervention measures would directly benefit patient care by minimizing the risk of CDI-associated morbidity and mortality.

3. Resource Optimization: By implementing strategies based on surveillance data, healthcare institutions can optimize resource allocation, ultimately reducing the economic burden of CDI.

4. Synergy: Timely Outbreak Detection, Use of infection rates as a parameter in antibiotic stewardship programs, Assessment of the effectiveness of targeted intervention strategies.

6. Conclusion

In conclusion, the comprehensive analysis of *Clostridioides difficile* infections (CDI) in Switzerland through the three integrated projects has yielded valuable insights into the current landscape of CDI surveillance, epidemiology, and associated factors. The findings from each project provide critical information that can inform future public health strategies and local healthcare practices in Switzerland.

The incidence rates estimated through our nationwide survey provide critical benchmarks for understanding the burden of CDI in Switzerland. A rate of 3.8 CDI episodes per 10,000 patient days in 2022, slightly exceeding the mean incidence rate reported in the European surveillance, highlights the relevance of CDI in our healthcare system.

The analysis of the MedStat dataset supplements our understanding of CDI in Swiss hospitals. Notably, CDI emerged as a significant reason for hospitalization. Furthermore, the recurrence rates of 10-18% among our analyses underscore the pressing need for robust preventive measures to mitigate the impact of CDI on patient outcomes. The stability of CDI incidence rates between 2014 and 2021 suggests that CDI remains a persistent challenge in Swiss healthcare. However, this also implies an opportunity for sustained intervention and improvement.

Achievements of the Project

The high participation rate in our survey suggests a willingness among Swiss hospitals to contribute to CDI surveillance efforts. The high rates of CDI in tertiary care hospitals and the significant proportion of community-acquired cases challenge conventional assumptions about the epidemiology of CDI. This project serves as a foundation for building a more robust and unified CDI surveillance system in Switzerland, with the potential to reduce infection rates, improve patient care, and lessen the burden on healthcare institutions. While the laboratory-based approach holds the highest potential for synergy with other relevant parameters and timely information, this method is heavily hampered by the persistent low participation rate, what hinders the establishment of a national surveillance for CDI. Considering this obstacle, we believe that in the current state, the continuation of the statistical surveillance with the DRG-dataset is the most promising approach for a continuous surveillance of CDI. This surveillance could be easily extracted from the data routinely collected by the Federal Statistical Office. Swissnoso has the acquired the insights and expertise to continue and even improve the surveillance based on this dataset.

Therefore, the Swissnoso team proposes to continue the CDI-surveillance with the statistical approach outlined here.

Members of the Swissnoso project team

Scientific collaborator:	Dr. med. Ana Durovic
Scientific collaborator:	PD Dr. Alexandra U. Scherrer
Project management:	Vinciane Vouets
Project lead:	Prof. Dr. med. Andreas F. Widmer

7. Appendices and References

Figures and Tables

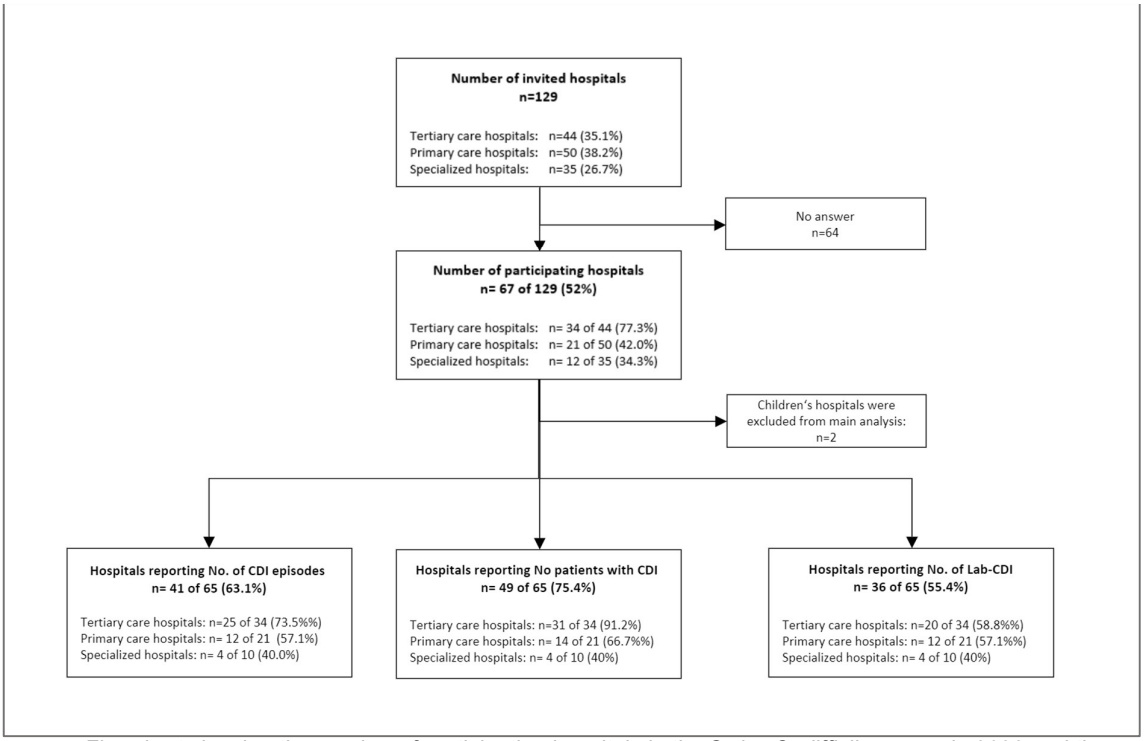

Figure 1 Flowchart showing the number of participating hospitals in the Swiss C. difficile survey in 2022 and the response rate to key measurements.

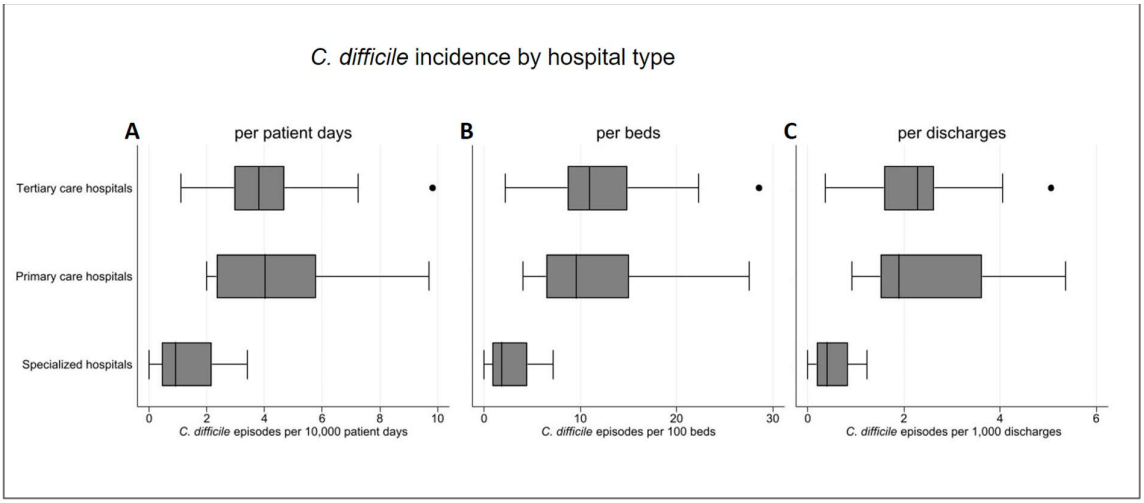

Figure 2 The incidence of C. difficile stratified by different hospital types. A) C. difficile episodes per 10,000 patient days, B) C. difficile episodes per 100 beds and C) C. difficile episodes per 1,000 discharges.

Measured indicator	Incidence per 10,000 patient-days (95% CI)	Incidence per 1,000 discharges (95% CI)	Incidence per 100 beds (95% CI)
C. difficile episodes	3.8 (3.2- 4.5)	2.1 (1.7-2.6)	10.8 (9.8-11.9)
Patients with *C. difficile*	3.4 (2.9-4.0)	1.9 (1.6-2.4)	10.0 (9.1-10.9)
Positive test results for *C. difficile*	4.2 (3.3-5.1)	2.4 (1.9-3.0)	11.6 (10.6-12.8)

Table 1 C. difficile incidence rate in Swiss acute care hospitals in 2022.
(95% CI); 95% Poisson confidence interval

		Number of tests per 10,000 patient days per hospital		Positivity rate (no. positive tested samples/no. tested samples) in %	
Hospital type	No. of hospitals	Mean test rate	Median [IQR]	Mean positivity rate	Median [IQR]
All	43	76.5	72.7 [49.0-87.6]	9.2%	7.1% [4.9-9.4]
Tertiary care hospitals	29	71.7	73.5 [50.0-86.5]	7.3%	7.1% [5.9-8.0]
Primary care hospitals	12	98.5	72.4 [50.6-128.1]	5.4%	4.2% [3.0-7.5]
Specialized hospitals	2	13.2	13.2 [0.9-25.5]	60%	60% [20-100]

Table 2 Testing rate of C. difficile samples and positivity rate stratified by hospital type in Swiss acute care hospitals in 2022
IQR: interquartile range

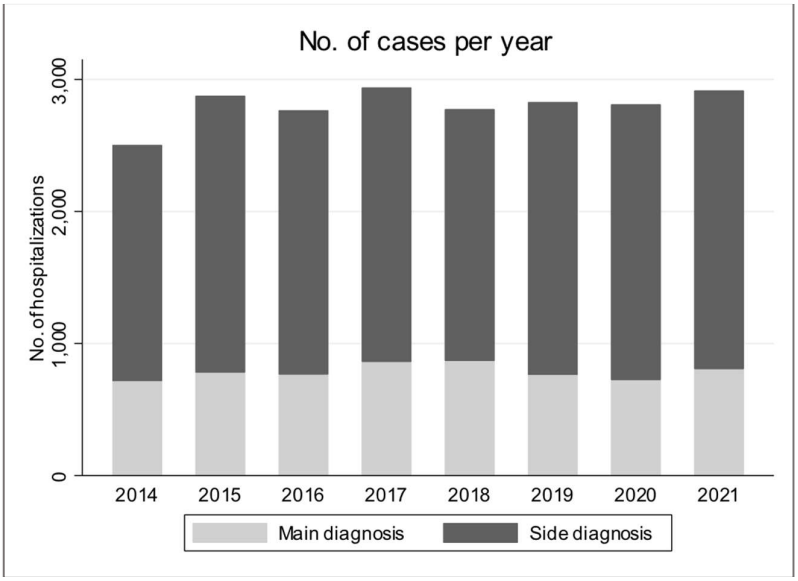

Figure 3: Number of hospitalizations with a C. difficile infection based on MedStat dataset stratified by C.difficile as main or side diagnosis.

Severity	No. of cases (%)
A04.70 Enterokolitis durch Clostridium difficile ohne Megakolon, ohne sonstige Organkomplikationen	7,157 (66.8%)
A04.72 Enterokolitis durch Clostridium difficile mit Megakolon, ohne sonstige Organkomplikationen	420 (3.92%)
A04.71 Enterokolitis durch Clostridium difficile ohne Megakolon, mit sonstigen Organkomplikationen	100 (0.9%)
A04.73 Enterokolitis durch Clostridium difficile mit Megakolon, mit sonstigen Organkomplikationen	50 (0.5%)
A04.79 Enterokolitis durch Clostridium difficile, nicht näher bezeichnet	2,980 (27.8%)

Table 3: ICD-10 codes describing the severity of C. difficile infections.

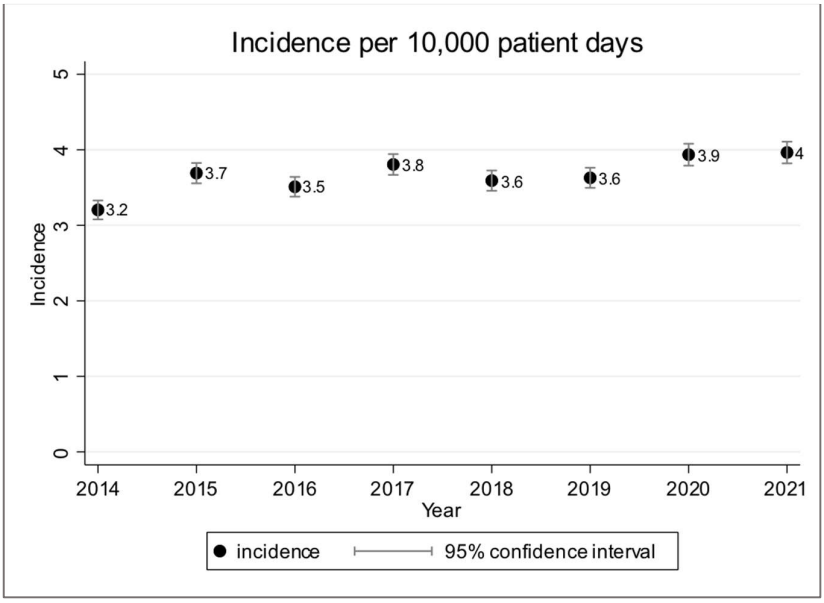

Figure 4: Incidence of C. difficile infections over time based on the MedStat dataset.

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Questionnaire

Swissnoso-Surveillance von Clostridioides difficile Infektionen 2022

Einleitung

Wir laden Sie ein, an der Erhebung von Clostridioides difficile Infektionen (CDI) in Schweizer Akutspitälern 2022 teilzunehmen. Die Durchführung dieser Erhebung ist Teil der Strategie StAR des Bundesamtes für Gesundheit und soll einen Beitrag zur Qualitätsverbesserung erzielen.

Wir bitten Sie höflich, den Fragebogen zur Inzidenz von CDI in ihrem Spital auszufüllen. Ihre Teilnahme hilft, die Datengrundlage für wichtige Entscheidungen in der Infektionsprävention in Akutspitälern zu verbessern. Die Daten Ihres Betriebs werden vertraulich behandelt und nicht namentlich publiziert.

Bitte beziehen Sie die Angaben auf das Jahr 2022 (1. Januar bis 31. Dezember 2022).

Verwenden Sie beim Ausfüllen die im Fragebogen aufgeführten Definitionen für die Bestimmung von CDI - insbesondere für die Fragen in Teil 1.

Falls Sie Fragen haben oder Unterstützung bei der Dateneingabe benötigen, zögern Sie nicht, Ana Durovic (ana.durovic@swissnoso.ch) zu kontaktieren.

Haben Sie vielen Dank für das Beantworten des Fragebogens bis zum 22. April 2023.

Freundliche Grüße

Swissnoso Team

Swissnoso-Surveillance von Clostridioides difficile Infektionen 2022

Definitionen zur CDI-Statistik

Dieser Abschnitt enthält Definitionen und Einschluss-/Ausschlusskriterien als Referenz.

CDI: Clostridioides-difficile-Infektion oder C. difficile-Infektion.

Patient mit CDI: ("Patienten-ID-Nummer") hospitalisierter Patient mit C. difficile-Infektion
Für diesen Bericht sind nur die folgenden Patienten zu berücksichtigen:

- Patienten im Alter von ≥2 Jahren
- Dauer des Krankenhausaufenthalts >24h
- Krankenhausaufenthalt in Akutkrankenhäusern/Abteilungen
- Nachweis von toxigenem C. difficile (Toxin-negative C. difficile-Stämme werden nicht berücksichtigt)

Probe: ("Proben-ID-Nummer") Stuhl/Rektalabstriche mit Testung auf C. difficile
- Zählen Sie jede entnommene und untersuchte Probe als 1 Probe
- Zählen Sie die Probe als 1 Probe, auch wenn mehrere Tests mit derselben Probe durchgeführt wurden

Labor-CDI: (laborbasierte Definition) positiver Labortest auf C. difficile mit Nachweis von toxigenen C. difficile. (Duplikate ausschließen!)

CDI-Episode: (klinische Definition) Nachweis von C. difficile bei einem symptomatischen Patienten. (Labor-CDI + kompatible Symptome, Duplikate ausschließen!)

Duplikat: wiederholte positive Tests **<14d** nach der Erstdiagnose (Labor-CDI und CDI-Episoden) als dieselbe Infektion betrachten!

Rezidiv: wiederholte positive Tests **≥ 2 Wochen und <8 Wochen** nach dem letzten positiven Test gelten als CDI-Rezidiv. (Als neue Labor-CDI/ CDI-Episode zu zählen)

Swissnoso-Surveillance von Clostridioides difficile Infektionen 2022

Teil 1: Überwachung von C. difficile-Infektionen in Ihrem Krankenhaus im Jahr 2022

1. **Bitte geben Sie das Spital an, auf welches sich die Kennzahlen in Frage 3 bzw. in Frage 4 beziehen:**

Name des Betriebs (ggfs. Standorts):	
Adresse:	
PLZ / Ort:	
Kanton:	

2. **Gehört dieses Spital zu einer Spitalgruppe?**

- ◯ Ja
- ◯ Nein

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3. **Auf welchen Standort beziehen sich die Kennzahlen in Frage 4 ?**

- ◯ Alle Standorte der Spitalgruppe
- ◯ Nur angegebener Spitalstandort

4. **Bitte geben Sie für Ihr Spital die folgenden Kennzahlen für das Jahr 2022 an:**

Geben Sie bitte eine Zahl ein. Dezimalstellen, Prozentwerte und nicht numerische Zeichen sind nicht zulässig.

Anzahl Austritte	
Anzahl Pflegetage	
Anzahl Betten	
Anzahl CDI-Episoden insgesamt	
Anzahl Patienten mit CDI	
Anzahl CDI-Episoden, die als Rezidiv eingestuft wurden	
Anzahl Lab-CDI (Duplikate ausschließen)	

5. **Haben Sie die beigelegten Definitionen verwendet?**

- ◯ Ja
- ◯ Nein

6. **Unterscheidet ihr Spital routinemässig zwischen ambulant bzw. spitalerworbenen CDI ?**

- ◯ Ja
- ◯ Nein

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7. **Bitte geben Sie die Anzahl der CDI-Fälle gemäss ihrer Klassifikation für das Jahr 2022 an.**

Anzahl der CDI-Episoden, die als ambulant erworbene CDI eingestuft wurden

Anzahl der CDI-Episoden, die als spitalerworbene CDI eingestuft wurden

Welche Definitionen verwenden Sie für die beiden Kategorien?

8. **Welche Definitionen verwenden Sie für die Klassifizierung ?**

- [ ] Spitalerworbene CDI bei Hospitalisationsdauer von >3d
- [ ] Keine Angaben möglich

>

- [ ] Andere Definitionen, bitten angeben:
  (maximum 100 Zeichen)

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Teil 2: Infektionskontrolle und -prävention für C. difficile in Ihrem Spital im Jahr 2022 in Nicht-Ausbruchssettings

9. **Welche dieser Optionen spiegelt die Massnahmen Ihres Spitals am besten wieder?**
(Mehrfachnennungen möglich)

- ☐ Keine routinemäßige Erfassung von C. difficile-Infektionen
- ☐ Meldung aller positiven Testergebnisse auf C. difficile an das PCI-Team
- ☐ Meldung aller toxin-positiven Testergebnisse auf C. difficile an das PCI-Team
- ☐ Meldung nur bei Infektion bei hypervirulentem C. difficile Stamm (vermuteter oder nachgewiesener Ribotyp 078 und 027)

10. **Führt ihr Spital routinemässige Untersuchungen auf mögliche Übertragungen von C. difficile im Krankenhaus durch (z. B. Screening von Kontaktpersonen, Typisierung von Stämmen)?**

- ◯ Ja, inklusive Ribo-Typisierung
- ◯ Ja, ohne Ribo-Typisierung
- ◯ Nein

11. **Gab es im Jahr 2022 Episoden ungewöhnlicher Häufungen/Ausbrüche von C. difficile?**

- ◯ Ja
- ◯ Nein

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12. **Welche Optionen entsprechen am ehesten dem Vorgehen in Ihrem Spital bei Nachweis von C. difficile?**
(Mehrfachnennungen möglich).

- [ ] Kontaktisolationfür asymptomatische und symptomatische Patienten bei Nachweis von Toxin-positivem C. difficile
- [ ] Kontaktisolation aller symptomatischen Patienten mit Toxin-positivem C. difficile)
- [ ] Kontaktisolation für alle symptomatischen Patienten mit C. difficile Nachweis, auch wenn Toxin-negative C. difficile nachgewiesen wurde
- [ ] Kontaktisolation nur bei hypervirulenten C. difficile (vermutete und/oder bestätigte Ribotypen RT027 oder RT078) und allgemeine Vorsichtsmaßnahmen bei nicht-hypervirulenten C. difficile-Stämmen

>

- [ ] Individuell, je nach Schwere der Erkrankung. Bitte Kriterien angeben:
(maximal 100 Zeichen)

13. **Was ist die Standardbehandlung für Patienten mit einer ersten unkomplizierten Episode einer C. difficile-Infektion in Ihrem Krankenhaus?**

- ◯ Metronidazol p.o.
- ◯ Vancomycin p.o.
- ◯ Fidaxomicin p.o.
- ◯ Keine Standardbehandlung / Sonstiges
- ◯ Unbekannt

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Teil 3: Mikrobiologische Diagnosestandards für C. difficile für Ihr Labor im Jahr 2022

Bei den folgenden Fragen geht es um die diagnostischen Standards in Ihrem Labor im Jahr 2022.

14. **Wie viele Tests auf C. difficile wurden 2022 in Ihrem Labor durchgeführt?**

Geben Sie bitte eine Zahl ein. Dezimalstellen, Prozentwerte und nicht numerische Zeichen sind nicht zulässig.

Gesamtzahl der auf C. difficile getesteten Proben

Gesamtzahl der als "positiv für toxigenes C. difficile" gemeldeten Proben

15. **Welche der folgenden Optionen beschreibt <u>am besten</u> die diagnostischen Routinetests, die in Ihrem Labor im Jahr 2022 verwendet werden?**
(Mehrfachnennungen möglich)

Erklärungen zu Abkürzungen:

Toxin A/B EIA: Enzymimmunoassay zum Nachweis von C. difficile Toxinen A/B

GDH EIA: Enzymimmunoassay zum Nachweis von C. difficile-Glutamatdehydrogenase (C. difficile Antigen)

NAAT / PCR: «Nucleic Acid Amplification Test»

	Screening/Initialer Test	Bestätigungstest/zweiter Test	optionaler Test oder zusätzlicher Bestätigungstest	unbekannt
Toxin A/B EIA	☐	☐	☐	☐
GDH EIA	☐	☐	☐	☐
NAAT/ PCR	☐	☐	☐	☐
Screening auf hypervirulente Stämme	☐	☐	☐	☐
toxigene Kultur	☐	☐	☐	☐

16. **Gab es in Ihrem Labor Einschränkungen in Bezug auf die Testung auf C. difficile im Jahr 2022?**

- ◯ Ja
- ◯ Nein
- ◯ Unbekannt

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17. **Bitte geben Sie die vom Labor angewandten Kriterien für Tests auf C. difficile an:**

- [ ] Nur Untersuchung von ungeformtem Stuhl
- [ ] Keine wiederholten Tests von kürzlich positiven Proben
- [ ] Unbekannt

>

- [ ] Sonstiges, bitte angeben
  (maximal 100 Zeichen)

18. **Gab es 2022 Änderungen in der Labortestung von C. difficile?**

- ◯ Ja
- ◯ Nein
- ◯ Unbekannt

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19. **Bitte geben Sie die Änderungen in der Labortestung an:**
(Mehrfachnennungen möglich)

- [ ] Änderung der mikrobiologischen Diagnostik (Prüfalgorithmus/Prüfmethode)
- [ ] Änderung des Screenings/der Indikation für den Test
- [ ] Unbekannt

>

- [ ] Sonstiges, bitte angeben
(maximal 100 Zeichen)

Swissnoso-Surveillance von Clostridioides difficile Infektionen 2022

Teil 5: Abschluss

20. **Falls Sie allfällige Kommentare haben, bitte nutzen Sie dieses Feld:**
(maximal 300 Zeichen)

21. **Bitte geben Sie eine Ansprechperson an:**

Die Angabe einer Ansprechperson erleichtert es Swissnoso, bei allfälligen Rückfragen Kontakt aufzunehmen. Im Idealfall wird diejenige Person angegeben, welche den Fragebogen ausgefüllt hat.

Name der Ansprechperson:

Telefonnummer:

E-Mail Adresse:

Herzlichen Dank für Ihre Teilnahme.