Journal of Hospital Infection 131 (2023) 213–220

Available online at www.sciencedirect.com

Journal of Hospital Infection

journal homepage: www.elsevier.com/locate/jhin

European survey on the current surveillance practices, management guidelines, treatment pathways and heterogeneity of testing of *Clostridioides difficile*, 2018–2019: results from The Combatting Bacterial Resistance in Europe CDI (COMBACTE-CDI)

V.F. Viprey [a,*,†], G. Granata [b,‡], K.E.W. Vendrik [c,d,†], G.L. Davis [a], N. Petrosillo [b], E.J. Kuijper [c,d,e], T. Vilken [f], C. Lammens [f], J.J. Schotsman [g], A.D. Benson [a], M.A. Cataldo [b], T.I.I. van der Kooi [d], M.H. Wilcox [a,e,h], K.A. Davies [a,e,h], on behalf of the COMBACTE-CDI consortium[‡]

[a] *Healthcare Associated Infections Research Group, Leeds Institute of Medical Research, University of Leeds, Leeds, UK*
[b] *National Institute for Infectious Diseases "L. Spallanzani", Rome, Italy*
[c] *Leiden University Medical Center, Leiden, the Netherlands*
[d] *National Institute for Public Health and the Environment, Bilthoven, the Netherlands*
[e] *European Society of Clinical Microbiology and Infectious Diseases (ESCMID), Study Group for Clostridioides Difficile (ESGCD)*
[f] *Laboratory of Medical Microbiology, University of Antwerp, Antwerp, Belgium*
[g] *University Medical Centre Utrecht, Utrecht, the Netherlands*
[h] *Department of Microbiology, Leeds Teaching Hospitals NHS Trust, Leeds, UK*

ARTICLE INFO

Article history:
Received 14 September 2022
Accepted 22 November 2022
Available online 1 December 2022

Keywords:
Clostridium difficile
Clostridioides difficile
Guidelines awareness
Diagnosis
Treatment

SUMMARY

Background: Awareness and compliance with international guidelines for diagnosis and clinical management of *Clostridioides difficile* infection (CDI) are unknown.
Aim: To compare the awareness and compliance with the recommended strategies for diagnosis and clinical management of CDI across Europe in 2018–2019.
Methods: Hospital sites and their associated community practices across 12 European countries completed an online survey in 2018–2019, to report on their practices in terms of surveillance, prevention, diagnosis, and treatment of CDI. Responses were collected from 105 hospitals and 39 community general practitioners (GPs).
Findings: Hospital sites of 11 countries reported participation in national surveillance schemes compared with six countries for international schemes. The European Society of Clinical Microbiology and Infectious Diseases (ESCMID)-recommended CDI testing methodologies were used by 82% (86/105) of hospitals, however countries reporting the highest incidence of CDI used non-recommended tests. Over 75% (80/105) of hospitals were aware of the most recent European CDI treatment guidelines at the time of this survey compared

* Corresponding author. Address: Leeds Institute of Medical Research, Old Medical School, Leeds, LS1 3EX, UK. Tel.: +44 113 392 8664.
E-mail address: v.f.viprey@leeds.ac.uk (V.F. Viprey).
† These authors contributed equally to this work and share first authorship.
‡ The members of the COMBACTE-CDI consortium are listed in the Acknowledgements.

https://doi.org/10.1016/j.jhin.2022.11.011

with only 26% (10/39) of surveyed GPs. However, up to 15% (16/105) of hospitals reported using the non-recommended metronidazole for recurrent CDI cases, sites in countries with lower awareness of CDI treatment guidelines. Only 37% (39/105) of hospitals adopted contact isolation precautions in case of suspected CDI.

Conclusion: Good awareness of guidelines for the management of CDI was observed across the surveyed European hospital sites. However, low compliance with diagnostic testing guidelines, infection control measures for suspected CDI, and insufficient awareness of treatment guidelines continued to be reported in some countries.

Introduction

Clostridioides difficile is amongst the most frequently reported micro-organisms in healthcare associated infections in Europe, and is associated with a high disease burden, contributing to significant morbidity and mortality [1,2]. Guidelines produced over the last decade provide recommendations on the management of *C. difficile* infection (CDI) in terms of surveillance, prevention, diagnosis and treatment [3—12]. Standardized surveillance of CDI in hospitals by the European Centre for Disease Prevention and Control (ECDC) started in 2016 [1,13,14]. In 2017, 19 countries had submitted CDI surveillance data to the ECDC [1,15]. It is unknown how many European hospitals and community practices participate in national or local CDI surveillance and to what extent. In addition to national CDI testing policies, the 2016 European Society of Clinical Microbiology and Infectious Diseases (ESCMID) guidance recommended a two-stage approach for CDI diagnosis that should include both the detection of the organism or toxin genes using glutamate dehydrogenase (GDH) or nucleic acid amplification test (NAAT) and *C. difficile* toxin(s) using enzyme immunoassay [4,8]. European guidance documents for *C. difficile* infection control measures published in 2008 and updated in 2018 recommend adoption of isolation contact precautions for patients with confirmed CDI [3,9]. The American Society of Infectious Diseases (IDSA) and Society for Healthcare Epidemiology of America (SHEA) 2018 guidelines and the 2009 ESCMID guidelines also recommend isolation contact precautions for patients suspected of having CDI [5,10]. The ESCMID treatment guidelines published in 2014 strongly recommend against the use of metronidazole for severe primary or recurrent CDIs [7]. It is unknown to what extent physicians, particularly from the community, are aware of these recommended CDI testing and treatment pathways.

Differences in the CDI rate between countries may be due in part to the heterogeneity in the management of CDI and compliance with the recommended strategies. In this study, we present results of a survey questionnaire distributed to hospital sites and associated community practices that took part in the 2018 point-prevalence study of COMBACTE-CDI (Combatting Bacterial Resistance in Europe — CDI), across 12 European countries [16]. We describe the current surveillance practices, CDI testing procedures, and the awareness of and compliance with CDI treatment and testing guidelines and isolation precautions as reported in the questionnaire in 2018—2019.

Methods

Source of information

The Network Management System (NMS) is a web-based application and user-friendly repository for all high-level site information, study participant information, training information, study information of all sites, personnel and studies within COMBACTE, developed by Clin-Net and Lab-Net. The NMS allows invitations to be sent to potential sites to complete feasibility questionnaires and gives an overview of the entry status of each questionnaire. The data from the questionnaires are stored in the data management system Research Online (RO). For this survey, a questionnaire was developed to collect information on practices across Europe for the diagnosis, surveillance management and treatment of CDI. Before finalization and rolling out to sites, this survey was piloted by at least three individuals who have expertise in the field but were not involved in the study. The NMS was used to send out the invitations for completion of the survey, with personalized e-mail links. Besides the NMS System, a general survey link was created for distribution to sites of interest not pre-registered into the NMS. This link was received by the sites via the national co-ordinators [16]. The survey was sent out to 126 sites participating in the established research networks of COMBACTE and the sites investigators provided by national co-ordinators of COMBACTE-CDI, from 12 countries representing European regions defined according to the UN Geoscheme for Europe [16]: Belgium, France, Greece, Ireland, Italy, Netherlands, Poland, Slovakia, Spain, Sweden, Romania and UK. The survey was completed in RO between October 2018 and April 2019. The data distributed for analysis did not contain any personal information, only details about individual sites knowledge and compliance with existing guidelines, and retrospective collection of yearly testing, admission, and bed days (BDs) 2017 data. Each site was given an anonymized study identifier. Ethical approval for the COMBACTE-CDI project was received from every country taking part, and from the University of Leeds for the overarching study (IRAS244784) [16].

Survey analysis

Survey data (Supplementary Table S1) were received from 105 hospital sites in 12 countries (overall response rate of 83.3% for the completion of survey via NMS system) with the answers given on the following aspects of the management of CDI summarized per country and across Europe: (i) surveillance

practices, (ii) CDI notification, (iii) awareness of and compliance with testing guidelines, (iv) awareness of and compliance with treatment guidelines, (v) compliance with contact precautions. In addition, survey data received from 39 community doctors (general practitioners out-patient setting (GPs)), including 32 in Italy and seven in six other countries (the Netherlands, Poland, Romania, Slovakia, Spain) are presented as the proportion of all surveyed GPs, when applicable. It was not possible to ascertain how many GPs received the general email survey link via their national co-ordinators, due to GDPR guidelines, and therefore the rate of acceptance of the survey via the link (and not the NMS) by GPs could not be determined. The type of CDI testing algorithm used by the surveyed hospitals allowed for the calculation of the proportion of sites per country that use only one test to diagnose CDI, at least one toxin assay, or any of the ESCMID-recommended testing assays [8]. The CDI testing frequency and CDI incidence rate per 10,000 BDs were calculated for each hospital site and the median presented by country using data reported in the survey, excluding sites with missing or inconsistent data entry (i.e., where the number of BDs was reported as lower than the number of admissions).

Results

Surveillance practices

Of the 105 surveyed hospitals, 44.8% (47/105) and 12.4% (13/105) reported participation in a national and international surveillance scheme for CDI, respectively (Table I). None of the 39 GPs reported participation in CDI surveillance. Most countries (11/12) had a national surveillance programme for CDI and six participated in international surveillance, including the ECDC-supported surveillance (Table I and Supplementary Table S2). Most hospitals participating in national CDI surveillance included hospital-diagnosed CDI in the surveillance (40/47), while CDI diagnosed in non-inpatient settings were less often reported (ca. one in three sites, Supplementary Table S3). CDI patients were registered on national surveillance schemes when there was either a positive test result irrespective of clinical characteristics, or when there was a combination of a positive test result and clinical characteristics, with the toxin Enzyme Immunoassay (EIA) test the most frequent test required (Supplementary Table S4). Clinical characteristics reported to be collected for national surveillance varied (Supplementary Table S5). Microbiological typing data were reported to be recorded in all countries that participated in national surveillance except Poland, Spain, and Sweden, with polymerase chain reaction (PCR)-ribotyping the most common typing method (Supplementary Table S6). Hospital size/denominator data were reported to be recorded for surveillance in all participating countries except Ireland and Sweden, and CDI testing data were reported in all countries (Supplementary Table S7).

CDI notification

Most hospitals reported notifying CDI cases at a local or national level (84/105, Table I), compared with only a third of surveyed GPs (15/39). No international CDI case notification was reported by any of the surveyed sites.

Awareness of and compliance with testing guidelines

Awareness of national CDI testing policies and guidelines were reported in almost all surveyed hospitals (Table I). Less than a fifth of surveyed GPs were aware of national guidelines (7/39).

The CDI testing and incidence rates reported varied by approximately 10-fold between countries. The median CDI testing frequency was 55.9 tests per 10,000 BDs (interquartile range (IQR) 30.1–118.9) and the median CDI incidence rate was 4.1 cases per 10,000 BDs (IQR 2.7–6.4) (Table II). There was only a moderate correlation between the reported CDI testing and

Table I
Participation in *Clostridioides difficile* infection (CDI) surveillance schemes, CDI notification, awareness of CDI testing policies and treatment guidelines in hospital sites by European country, 2018–2019 survey

Country	Number of hospital sites	Number of sites (%)									
		Participation in international surveillance		Participation in national surveillance		Notification of CDI cases		Awareness of national CDI testing guidelines		Awareness of european CDI treatment guidelines	
		N	%	*N*	%	*N*	%	*N*	%	*N*	%
Belgium	1	1	100.0	1	100.0	1	100.0	1	100.0	1	100.0
France	23	0	0	7	30.4	18	78.3	22	95.7	20	87.0
Greece	2	0	0	0	0	1	50.0	1	50.0	2	100.0
Ireland	1	0	0	1	100.0	1	100.0	1	100.0	1	100.0
Italy	20	4	20.0	5	25.0	16	80.0	15	75.0	14	70.0
Netherlands	3	0	0	2	66.7	0	0	1	33.3	1	33.3
Poland	12	4	33.3	2	16.7	11	91.7	12	100.0	9	75.0
Romania	5	0	0	3	60.0	4	80.0	5	100.0	3	60.0
Slovakia	1	1	100.0	1	100.0	1	100.0	1	100.0	1	100.0
Spain	13	2	15.4	1	7.7	10	76.9	10	76.9	11	84.6
Sweden	4	0	0	4	100.0	1	25.0	4	100.0	4	100.0
UK	20	1	5.0	20	100.0	20	100.0	20	100.0	13	65.0
Total	105	13	12.4	47	44.8	84	80.0	93	88.6	80	76.2

Table II
Clostridioides difficile infection (CDI) testing and incidence rate in hospital facilities by European country in 2017

Country	Number of hospital sites [a]	Median testing frequency per 10,000 BDs (IQR)	Median CDI cases per 10,000 BDs (IQR)	Median number of BDs (IQR)
Belgium	1	67.3 (67.3–67.3)	6.4 (6.4–6.4)	249,489 (249,489–249,489)
France	14	28.9 (24.4–39.1)	2.3 (1.7–2.9)	292,269 (213,826–557,173)
Greece	2	51.6 (47.7–55.5)	2.7 (2.7–2.7)	156,063 (141,408–170,717)
Ireland	1	20.4 (20.4–20.4)	5.9 (5.9–5.9)	238,318 (238,318–238,318)
Italy	11	32.7 (23.9–41.9)	3.8 (2.9–7.0)	110,657 (91,178–163,508)
Netherlands	2	93.9 (81.7–106.2)	2.5 (2.0–3.0)	121,559 (93,709–149,408)
Poland	9	38.4 (29.3–43.9)	5.1 (4.2–8.5)	128,520 (54,221–163,506)
Romania	3	124.1 (66.3–162.1)	39.7 (21.9–39.8)	100,000 (83,521–219,194)
Spain	6	87.9 (67.8–166.1)	6.8 (5.7–7.9)	165,436 (103,668–254,035)
Sweden	4	200.5 (176.5–235.4)	23.9 (22.0–27.8)	101,969 (89,585–177,851)
UK	11	168.0 (114.1–193.9)	3.9 (2.9–4.7)	263,033 (202,882–343,922)
Total	64	55.9 (30.1–118.9)	4.1 (2.7–6.4)	183,068 (99,985–273,649)

The yearly CDI testing and incidence rate were calculated for each hospital separately and the median and interquartile range (IQR) is shown by country. BDs, bed days; CDI, *Clostridioides difficile* infection.
[a] Number of hospital sites with answers on all of the following survey questions for the year 2017: the number of bed days, the number of patients with at least one sample tested for CDI, and the number of patients with a positive CDI test result.

incidence rates ($r = 0.53$, Supplementary Figure S1). Most hospital sites (95.2%, 100/105) used more than one test to diagnose CDI, and 81.9% (86/105) did use an ESCMID-recommended algorithm (Table III). The countries with the highest median incidence of CDI (Sweden, 23.9 cases/10,000 BD; Romania, 39.7 cases/10,000 BD) also had the highest proportion of sites that used a single test to diagnose CDI, against ESCMID guidelines.

Awareness of and compliance with treatment guidelines

Three-quarters of hospitals (80/105) were aware of European CDI treatment guidelines (Table I), compared with only a quarter of GPs (10/39). In accordance with guidelines available at the time of this survey, almost two-thirds of hospitals (63/105) reported using metronidazole to treat a mild/moderate primary CDI case, followed by vancomycin and fidaxomicin (Table IV). Against recommendations, metronidazole was reportedly used by some sites for severe primary or recurrent CDIs (up to 20 sites: Table IV). Both for first severe CDI episodes and first severe recurrence episodes, metronidazole was employed as monotherapy in only three hospitals. Other antimicrobials were also reported to be used. Interestingly, metronidazole use for a severe first episode and for recurrent episodes of CDI, was reported mostly in countries with lower awareness of European CDI treatment guidelines (Figure 1).

Faecal microbiota transplantation (FMT) was reportedly used in over half of hospitals (59/105), either performed on-site (36/105), or through referral to a centre for FMT (23/105). The majority of on-site FMT procedures were performed in selected patients after the first CDI recurrence (21/36), followed by selected patients with severe CDI (11/36). All 12 countries except Greece had at least one site using FMT for CDI. Bezlotoxumab for recurrent CDI was reportedly used in 5.7% (6/105) of hospitals (two sites in Italy, Spain and UK). The main reasons

Table III
Assays used for *Clostridioides difficile* infection (CDI) testing in hospital facilities by European country, 2018–2019 survey

Country	Number of surveyed hospital sites	Number of sites (%)					
		Single assays		At least one toxin detection assay		ESCMID-recommended assays	
		N	%	*N*	%	*N*	%
Belgium	1	0	0	1	100.0	1	100.0
France	23	0	0	14	60.9	14	60.9
Greece	2	0	0	2	100.0	2	100.0
Ireland	1	0	0	1	100.0	1	100.0
Italy	20	2	10.0	18	90.0	16	80.0
Netherlands	3	0	0	3	100.0	3	100.0
Poland	12	0	0	12	100.0	12	100.0
Romania	5	1	20.0	5	100.0	4	80.0
Slovakia	1	0	0	1	100.0	1	100.0
Spain	13	0	0	11	84.6	11	84.6
Sweden	4	2	50.0	2	50.0	2	50.0
UK	20	0	0	19	95.0	19	95.0
Total	105	5	5.0	89	84.8	86	81.9

ESCMID, European Society of Clinical Microbiology and Infectious Diseases.

Table IV
Clostridioides difficile infection (CDI) treatment pathways in hospital sites, Europe, 2018–2019 survey

Type of CDI	Total number of sites (%) reporting to use									
	Metronidazole		Vancomycin, standard regimen		Vancomycin, tapered and pulsed regimen		Fidaxomicin		Other	
	N	%	*N*	%	*N*	%	*N*	%	*N*	%
First CDI episode mild/moderate	63	60.0	40	38.1	0	0	10	9.5	1	1.0
First CDI episode, severe	20	19.0	88	83.8	0	0	17	16.2	2	2.0
First recurrence of CDI, mild/moderate	16	15.2	48	45.7	1	1.0	25	23.8	1	1.0
First recurrence of CDI, severe	16	15.2	73	69.5	1	1.0	33	31.4	5	4.8
Second recurrence of CDI, mild/moderate	7	6.7	36	34.3	4	3.8	26	24.8	5	4.8
Second recurrence of CDI, severe	15	14.3	54	51.4	4	3.8	43	41.0	12	11.4

Severity was classified according to guidelines (Supplementary Table S8).

provided for not using bezlotoxumab was lack of availability in the pharmacy (46/99), and lack of experience (40/99).

Compliance with contact precautions

For confirmed CDI patients, three-quarters of surveyed hospitals (78/105) reported always adopting contact isolation precautions, compared with 37% (39/105) for suspected CDI patients (Figure 2). Strict adherence to contact isolation precautions for confirmed CDI ('always') was the lowest in Romania (2/5). Contact isolation precautions in cases of suspected CDI ('always' or 'often') was the highest in Sweden (4/4), the Netherlands (3/3) and UK (17/20), and was the lowest in Romania (2/5).

Discussion

To the author's knowledge, this is the first multi-centre survey summarizing the surveillance practices and level of awareness and compliance with recommendations for the clinical management and diagnosis of CDI, survey undertaken in 105 hospital sites and 39 community GPs across 12 European countries in 2018–2019.

Of those 12 countries, Greece, Italy and Spain reported not having a national surveillance system as part of a survey conducted by the ESCMID study group for *C. difficile* (ESGCD) in 2017 [15], whereas at least one site in all 12 countries except Greece reported participation in national surveillance schemes in this survey. Hospital-diagnosed CDI cases were the focus of national surveillance, with considerable variation in the inclusion criteria and data reported between and within countries. Sites from five countries reported participating in the ECDC surveillance (Belgium, Italy, Poland, Slovakia and UK), whereas all countries except Sweden did participate in the ECDC surveillance during its launch phase in 2016 [1].

Almost all hospital sites across Europe (95%) reported using more than one test to diagnose CDI, demonstrating that the 2016 ESCMID guidance on not using single-use assays was being

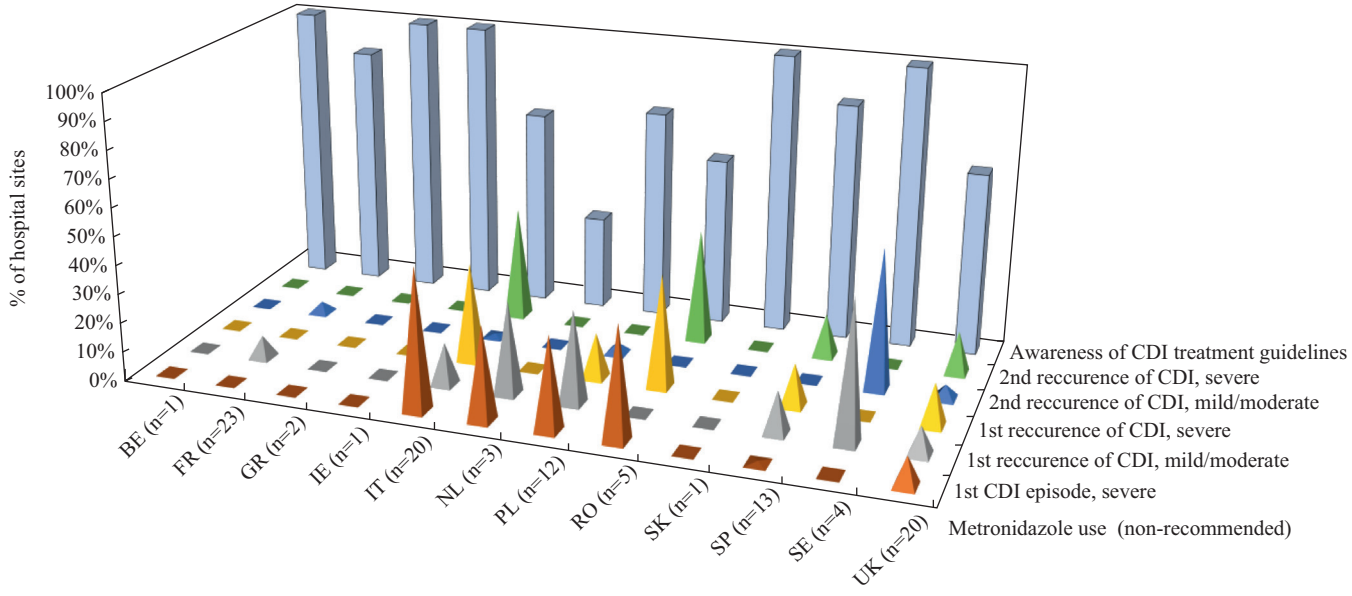

Figure 1. Awareness of European *Clostridioides difficile* infection (CDI) treatment guidelines and use of non-recommended CDI treatment by European country, 2018–2019 survey. BE, Belgium; FR, France; IE, Ireland; IT, Italy; NL, Netherlands; PL, Poland; RO, Romania; SE, Sweden; SK, Slovakia; SP, Spain. The number of surveyed hospital sites per country (equivalent to the number of responders) is shown in brackets.

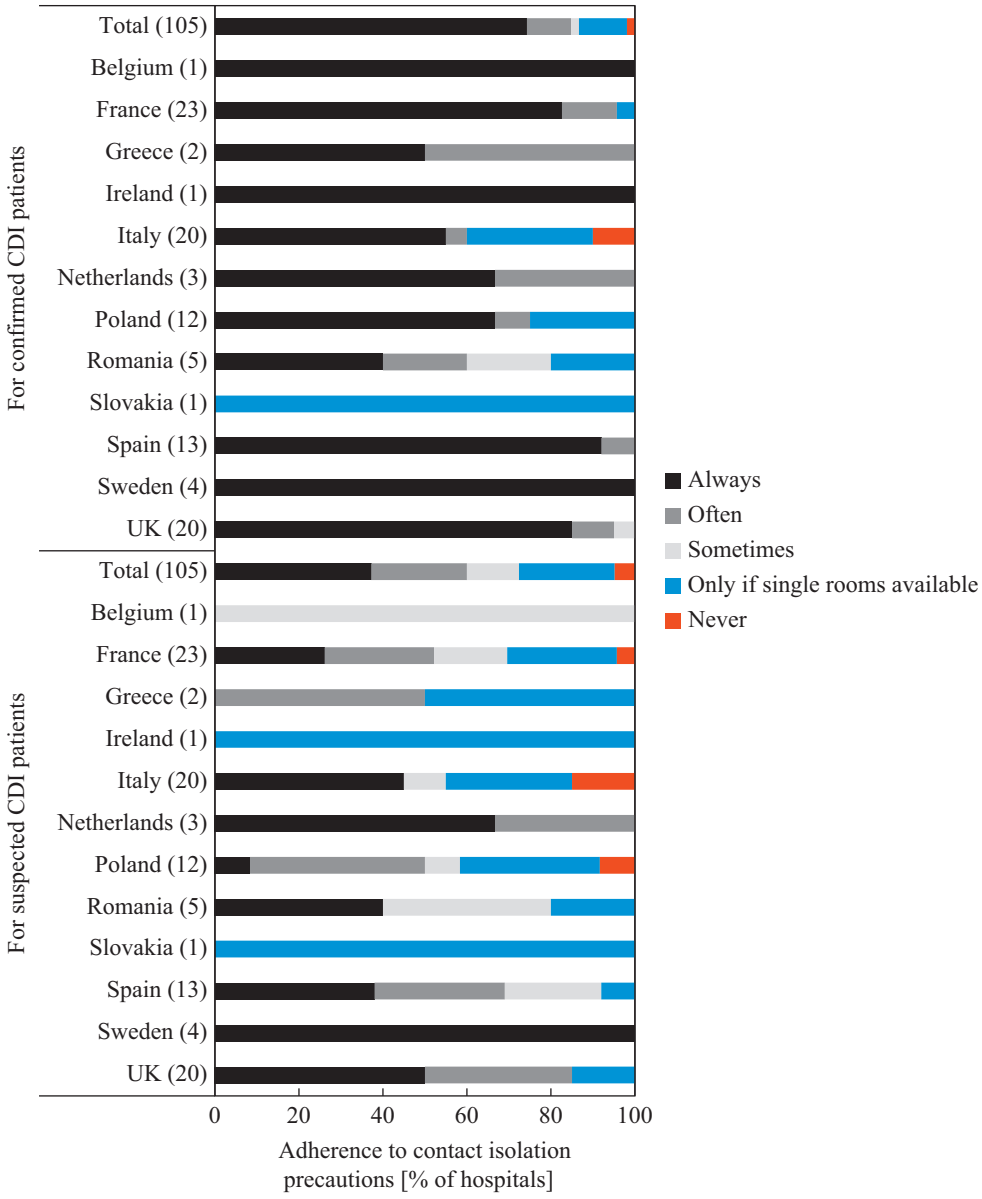

Figure 2. Compliance with infection control measures (contact isolation precautions) in hospital sites by European country, 2018–2019 survey. The number of surveyed hospital sites in each country is indicated in brackets. CDI, *Clostridioides difficile* infection.

followed [8]. Only half of hospital sites across Europe reported using an optimized diagnostic test for CDI in studies conducted in 2012–2013, and only 64% in a 2014–2015 study [17,18]. This 2018–2019 survey shows that more than 80% of hospital sites used an ESCMID-recommended diagnostic algorithm, which is also higher than the proportion of sites that followed those ESCMID recommendations in 2016 (71.5%) [1]. Countries reporting the highest number of CDI cases per 10,000 BDs also had the highest proportion of sites that used a single assay for CDI diagnosis, suggesting that low compliance with the use of recommended methodologies may impact on the reported case rate. Together with the moderate correlation observed between testing rates for CDI and reported incidence rates, these data are in accordance with previous observations, whereby low levels of testing or the use of non-recommended methods of testing were found to both have an effect on the reported incidence rates of CDI (by either masking the true CDI rate or over-diagnosis of cases, e.g., single test could over-diagnose CDI and detects only colonization or asymptomatic carriers) [17,19].

The ESCMID treatment guidelines available at the time of this survey did recommend against the use of metronidazole for a severe first or recurrent episodes of CDI [7], and we observe that metronidazole was indeed still reportedly used for severe or recurrent cases of CDI in those countries with low awareness of European CDI treatment guidelines. Only a quarter of surveyed GPs were aware of European treatment guidelines. The use of 'other' non-traditional CDI treatment antimicrobials was also reported for the treatment of recurrent CDI cases, suggesting that lack of guidelines knowledge could lead to the use of non-traditional treatment (e.g., tigecycline). Most surveyed sites reported not using bezlotoxumab for recurrent CDI due to lack of experience or availability, in line with the recent introduction of this product at the time of this survey

(European Union marketing authorization date of 2017), while fidaxomicin was introduced in the European market late in 2011. The 2014 ESCMID treatment guidance was updated late in 2021, with metronidazole no longer recommended for treatment of initial CDI, and bezlotoxumab to be considered for recurrent CDI and initial CDI with increased risk of recurrence, when fidaxomicin was not available or feasible [11]. A decreased metronidazole use in the USA was observed 18 months following publication of revised 2018 IDSA/SHEA guidelines [10,20], highlighting the impact of revised guidelines on CDI treatment. It is therefore anticipated that introduction of revised European treatment guidelines will influence best practice in Europe over the next couple of years.

While this survey showed a high rate of compliance with contact isolation precautions for patients with confirmed CDI, there is either a lack of awareness of the risk of spread of *C. difficile* by patients with suspected CDI [21], or other logistical issues (e.g., number of single bed occupancy rooms, Supplementary Tables S9, S10), leading to a low number of sites adopting isolation contact precautions for suspected CDI patients. The importance of national guidelines should also be emphasized. We note that compliance with contact isolation precautions in case of suspected CDI is high amongst the 20 surveyed sites in the UK, and that, in alignment with international guidelines, the 2013 UK guidelines strongly recommend isolation of patients while the cause of diarrhoea is being determined [22]. It should be noted that countries with reported high adherence to isolation precautions, but high CDI incidence rate also have the highest proportion of sites using a single assay; single test could over-diagnose CDI as discussed above.

There are some limitations to this study. Some countries were represented with only a few sites, and due to a lack of knowledge on what surveillance is and which sites participate in surveillance, the true participation proportions are difficult to assess. Countries recruited to the point-prevalence study of COMBACTE-CDI were invited to participate in this survey, with some large European countries (e.g., Germany) not included to avoid over-representation of a specific region, as previously discussed [16]. It should also be noted that the number of community doctors with survey data was low, and that although most of the survey was designed with objectives questions (answer options: yes/no, multiple choice; Supplementary Table S1), some of the items in the questionnaire may lead to subjective answers (e.g., isolation contact precautions), limiting the grade of evidence.

In conclusion, data from this survey show good awareness of CDI testing and treatment guidelines in hospital sites across Europe. However, there are still disparities between countries and insufficient awareness of infection control measures for suspected CDI. Lack of knowledge on guidelines for CDI management was found in the community, which is accompanied by underdiagnosis of CDI in this setting [16]. Furthermore, there is a lot of variability in surveillance characteristics between and within countries and a lack of knowledge on the definition of and participation in surveillance. Heterogeneity of sites and the fact that the survey relies on the accuracy of answers (with a mix of objective and some subjective questions) should be emphasized. These data highlight possible areas for improvement in guideline communications to reduce the knowledge gap between countries and between the hospital and the community setting. This study aims to raise awareness of the standardized European treatment guidelines published in 2021 [11] and to reaffirm the importance of adhering to the 2016 European testing guidelines [8] to achieve more accurate CDI incidence rate. It also indicates that a more consistent approach to isolation precautions across Europe is needed. Continued recruitment of hospitals to collect data compatible with the ECDC protocol for CDI surveillance and frequent reporting at both national and European level should be encouraged.

Acknowledgements

The authors thank the COMBACTE-CDI consortium for contribution to study design, the COMBACTE-CDI management board for critical review of the manuscript, and all healthcare professionals who completed the survey. The COMBACTE-CDI Consortium consists of academic partners and European Federation of Pharmaceutical Industries and Associations (EFPIA) partners: M. Bonten (University Medical Center Utrecht, the Netherlands), K. A. Davies (Scientific lead, University of Leeds, UK), M. H. Wilcox (University of Leeds, UK), E. Kuijper (Leiden University Medical Center, the Netherlands), M. Rupnik (National Laboratory of Health, Environment and Food, Maribor, Slovenia), S. Wingen-Heimann (University Hospital of Cologne, Germany), E. Tacconelli (Karls Eberhard University Tübingen, Germany), T. Vilken (University of Antwerp, Belgium), N. Petrosillo (Lazzaro Spallanzani National Institute for Infectious Diseases, Rome, Italy). EFPIA partners: Pfizer Ltd. (UK), GlaxoSmithKline (Belgium), bioMérieux (France), Sanofi Pasteur (France) and Da Volterra (France). COMBACTE-CDI management board: M. Bonten (UMC Utrecht), P. Cleuziat (bioMérieux), C. Webber (Pfizer Ltd), M. Rupnik (NLZOH) and M. Wilcox (University of Leeds).

Author contributions

V.F.V: validation, formal analysis, writing-original draft, writing-reviewing and editing, visualization. G.G: methodology, formal analysis, writing-original draft, writing-reviewing and editing, visualization. K.E.W.V: methodology, formal analysis, writing-original draft, writing-reviewing and editing, visualization. G.L.D: methodology, investigation, resources, writing-reviewing and editing, supervision, project administration, funding acquisition. N.P: conceptualization, methodology, investigation, writing-reviewing and editing, supervision. E.J.K: conceptualization, methodology, investigation, writing-reviewing and editing, supervision. T.V: methodology, investigation, resources, writing-original draft, writing-reviewing and editing. C.L: investigation, resources, writing-reviewing and editing. J.J.S: methodology, software, resources, writing-reviewing and editing. a.d.b: data curation, writing-reviewing and editing, project administration. M.A.C: formal analysis, writing-reviewing and editing. T.I.I.K: formal analysis, writing-reviewing and editing. M.H.W: conceptualization, methodology, investigation, writing-reviewing and editing, supervision, funding acquisition. K.A.D: conceptualization, methodology, formal analysis, investigation, resources, writing-reviewing and editing, supervision, project administration, funding acquisition.

Conflict of interest statement

M.W.H. reports research support grants received by institution from Almirall, Da Volterra, EnteroBiotix, GSK, Merck, MicroPharm, Nabriva, Paratek, Pfizer, Seres, Summit, The

European Tissue Symposium and Tillots. M.W.H. has received consulting fees from AiCuris, Bayer, Crestone, Da Volterra, Deinove, Enterobiotix, The European Tissue Symposium, Ferring, GSK, Menarini, Merck, Nestlé, Paion, Paratek, Pfizer, Phico therapeutics, Opex, Biopharma, Seres, Surface Skins, Summit, Tillotts, and Vaxxilon/Idorsia. M.W.H. has received lecture fees from Merck, Pfizer, Seres, and Tillotts. N.P. has received payment from MSD, Pfizer, ImmuneMed, Novartis, B&D, GSK, J&J, Thermofisher, Roche, and Tillots. K.D. reports grant funding held by institution from Techlab Inc and Cepheid Inc. All authors report funding for the COMBACTE-CDI study as indicated in the funding statement.

Funding statement
The COMBACTE-CDI study was supported by Innovative Medicines Initiative 2 Joint Undertaking under grant agreement no. 777362 resources of which are composed of financial contribution from the European Union's Horizon 2020 research and innovation programme, and EFPIA. The funder contributed financially to study design but did not contribute to data collection, analysis, interpretation, preparation of the manuscript or the decision to publish.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhin.2022.11.011.

References

[1] European Centre for Disease Prevention and Control. Healthcare-associated infections: *Clostridium difficile* infections. In: ECDC. Annual epidemiological report for 2016. Stockholm: ECDC; 2018.
[2] Cassini A, Plachouras D, Eckmanns T, Abu Sin M, Blank HP, Ducomble T, et al. Burden of six healthcare-associated infections on European population health: estimating incidence-based disability-adjusted life years through a population prevalence-based modelling study. PLoS Med 2016;13(10):e1002150.
[3] Vonberg RP, Kuijper EJ, Wilcox MH, Barbut F, Tülle P, Gastmeier P, et al. Infection control measures to limit the spread of *Clostridium difficile*. Clin Microbiol Infect 2008;14(Suppl.5):2—20.
[4] Crobach MJT, Dekkers OM, Wilcox MH, Kuijper EJ. European Society of Clinical Microbiology and Infectious Diseases (ESCMID): data review and recommendations for diagnosis *Clostridium difficile*-infection (CDI). Clin Microbiol Infect 2009;15(12):1053—66.
[5] Bauer MP, Kuijper EJ, van Dissel JT. European Society of Clinical Microbiology and Infectious Diseases (ESCMID): treatment guidance document for *Clostridium difficile* infection (CDI). Clin Microbiol Infect 2009;15(12):1067—79.
[6] Cohen SH, Gerding DN, Johnson S, Kelly CP, Loo VG, McDonald LC, et al. Clinical practice guidelines for *Clostridium difficile* infection in adults: 2010 update by the society for healthcare epidemiology of America (SHEA) and the infectious diseases society of America. Infect Control Hosp Epidemiol 2010;31(5):431—55.
[7] Debast SB, Bauer MP, Kuijper EJ. on behalf of the Committee. European Society of Clinical Microbiology and Infectious Diseases: update of the treatment guidance document for *Clostridium difficile* infection. Clin Microbiol Infect 2014;20(Suppl.2):1—26.
[8] Crobach MJT, Planche T, Eckert C, Barbut F, Terveer EM, Dekkers OM, et al. European Society of Clinical Microbiology and Infectious Diseases: update of the diagnostic guidance document for *Clostridium difficile* infection. Clin Microbiol Infect 2016;22(Suppl.4):S63—81.
[9] Tschudin-Sutter S, Kuijper EJ, Durovic A, Vehreschild MJGT, Barbut F, Eckert C, et al. Guidance document for prevention of *Clostridium difficile* infection in acute healthcare settings. Clin Microbiol Infect 2018;24(10):1051—4.
[10] Mc Donald LC, Gerding DN, Johnson S, Bakken JS, Carroll KC, Coffin SE, et al. Clinical practice guidelines for *Clostridium difficile* infection in adults and children: 2017 update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). Clin Infect Dis 2018;66(7):e1—48.
[11] Van Prehn J, Reigadas E, Vogelzang EH, Bouza E, Hristea A, Guery B, et al. European Society of Clinical Microbiology and Infectious Diseases: 2021 update on the treatment guidance document for *Clostridioides difficile* infection in adults. Clin Microbiol Infect. 27(Suppl.2):S1-S21.
[12] Johnson S, Lavergne V, Skinner AM, Gonzales-Luna A, Garey KW, Kelly CP, et al. Clinical Practice Guideline by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA): 2021 Focused Update Guidelines on Management of *Clostridioides difficile* Infection in Adults. Clin Infect Dis 2021;73(5):e1029—44.
[13] European Centre for Disease Prevention and Control. European Surveillance of *Clostridioides* (*Clostridium*) *difficile* infections. Surveillance protocol version 2.4. Stockholm: ECDC; 2019. https://data.europa.eu/doi/10.2900/60304.
[14] Van Dorp SM, Kinross P, Gastmeier P, Behnke M, Kola A, Delmée M, et al. Standardised surveillance of Clostridium difficile infection in European acute care hospitals: a pilot study, 2013. Euro Surveill 2016;21(29):30293.
[15] Krutova M, Kinross P, Barbut F, Hajdu A, Wilcox MH, Kuijper EJ, et al. How to: Surveillance of *Clostridium difficile* infections. Clin Microbiol Infect 2018;24(5):469—745.
[16] Viprey VF, Davis GL, Benson AD, Duncan E, Spittal W, Vernon JJ, et al. A point-prevalence study on community and inpatient *Clostridioides difficile* infections (CDI): results from Combatting Bacterial Resistance in Europe CDI (COMBACTE-CDI), July to November 2018. Euro Surveill 2022;27(26):2100704.
[17] Davies KA, Longshaw CM, Davis GL, Bouza E, Barbut F, Barna Z, et al. Underdiagnosis of *Clostridium difficile* across Europe: the European, multicentre, prospective, biannual, point-prevalence study of Clostridium difficile infection in hospitalised patients with diarrhoea (EUCLID). Lancet Infect Dis 2014;14(12):1208—19.
[18] Davies K, Davis G, Barbut F, Eckert C, Petrosillo N, Wilcox MH. Variability in testing policies and impact on reported Clostridium difficile infection rates: results from the pilot Longitudinal European Clostridium difficile Infection Diagnosis surveillance study (LuCID). Eur J Clin Microbiol Infect Dis 2016;35(12):1949—56.
[19] Davies K, Davis G, Barbut F, Eckert C, Petrosillo N, Pisapia R, et al. Factors affecting reported *Clostridioides difficile* infection rates; the more you look the more you find, but should you believe what you see? Anaerobe 2020;62:102178.
[20] Clancy CJ, Buehrle D, Vu M, Wagener MM, Nguyen MH. Impact of revised Infectious Diseases Society of America and Society for Healthcare Epidemiology of America clinical practice guidelines on the treatment of *Clostridium difficile* infections in the United States. Clin Infect Dis 2021;72(11):1944—9.
[21] Sunkesula VCK, Kundrapu S, Jury LA, Deshpande A, Sethi AK, Donskey CJ. Potential for transmission of spores by patients awaiting laboratory testing to confirm suspected *Clostridium difficile* infection. Infect Control Hosp Epidemiol 2013;34(3):306—8.
[22] Public Health England. Updated guidance on the management and treatment of *Clostridium difficile* infection. 2013. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/321891/Clostridium_difficile_management_and_treatment.pdf [last accessed April 2021].