ecdc

**EUROPEAN CENTRE FOR
DISEASE PREVENTION
AND CONTROL**

Surveillance and outbreak reports

NATION-WIDE PROSPECTIVE SURVEILLANCE OF CLOSTRIDIUM DIFFICILE INFECTIONS IN HOSPITALS IN BELGIUM, JULY 2007-JUNE 2008

M L Lambert (mllambert@iph.fgov.be)[1], K Mertens[1], I Ramboer[1], M Delmée[2], C Suetens[1,3]
1. National Surveillance of Infections in Hospitals (NSIH), Epidemiology Unit, Institute of Public Health, Brussels, Belgium
2. National reference laboratory for Clostridium difficile, St Luc Hospital, Catholic University Leuven, Brussels, Belgium
3. Current address: European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden

We report here baseline data from the first year of compulsory surveillance of *Clostridium difficile* infections (CDI) in hospitals in Belgium. Between 1 July 2007 and 30 June 2008, 2,704 CDI were reported: 12% were recurrent and 66% were hospital-associated (half of which occurred 15 days or more after admission). CDI was considered the cause of death (direct or indirect) for 10% of the episodes. The median incidence of CDI was 1.5 per 1,000 admissions and 1.9 per 10,000 hospital-days for all cases, and 0.9 per 1,000 admissions, and 1.1 per 10,000 hospital-days for hospital-associated cases. Further investigation of risk stratification by average length of stay in the reporting hospitals is warranted as a way to improve the comparability of indicators across hospitals and surveillance systems. In spite of methodological issues, the surveillance of CDI in Belgian hospitals has been able to produce robust baseline data that should allow monitoring of trends at hospital and national level, and provide a basis for international comparisons. Remaining challenges are to define and monitor targets for the control of CDI, and to improve the individual feed-back of data at hospital level.

Introduction

Clostridium difficile associated infection (CDI) is now recognised as a major cause of morbidity and mortality in hospitals [1]. Robust data are key for setting accurate targets to control the disease and for monitoring how these targets are achieved, but to our knowledge, no incidence data originating from prospective nation-wide surveillance systems have yet been published in peer-reviewed journals.

In this article, we report baseline data from the first year of compulsory surveillance of CDI in hospitals in Belgium in the period from July 2007 to June 2008. These data include a basic description of CDI and the distribution of incidence rates across reporting hospitals. The essence of a surveillance system is to provide comparable data, i.e. data that can be compared over time, between hospitals and between surveillance systems. We also discuss methodological issues such as the importance of declaring zero cases and the risk stratification of hospitals per length of stay.

Materials and methods

Prospective surveillance of CDI in hospitals in Belgium started in July 2006 and has since 1 July 2007 been compulsory by federal law for all hospitals, with the exception of psychiatric hospitals and hospitals providing chronic care of less than 150 beds (although their voluntary participation is encouraged). Hospitals are requested to report all their CDI over at least one six-month period per year (termed in this article first and/or second "semester").Therefore the unit of our analyses is a "hospital semester", although some hospitals contributed data for the entire year. Registration and data entry are web-based and are separate processes. There is no explicit requirement to declare zero cases, making it impossible to differentiate between "no cases" and "no reporting".

Case-definitions for CDI, hospital-associated (HA) case and recurrent case follow recommendations from the European Working Group on *C. difficile* [2]. Hospital data are limited to denominators from which the average length of stay can be calculated (number of admissions per number of hospital-days). Incidences are computed as number of CDI per 1,000 admissions (or cumulative incidence), and as number of CDI per 10,000 hospital-days (or incidence density).

Stata 10 statistical package was used for data analysis.

Results

From 1 July 2007 to 30 June 2008, 130 hospitals registered 2,704 CDI over 229 surveillance semesters. We excluded 31 of the 229 (14%) surveillance semesters, for which no denominator data were available. This left 198 surveillance semesters (120 hospitals) for the analysis of incidence rates.

Description of cases

Of 2,704 CDI 58% occurred in female patients, 12% were recurrent cases and 66% occurred more than two days after admission (hospital-associated CDI). CDI was considered as cause of death (direct or indirect) for 10% of the cases. Median age was 78 years, 75% of cases were in patients 65 years-old or older.

Most CDI occur late in the course of the hospital stay: 75% of HA cases occurred eight days or more after admission (Figure 1).

Description of hospital-semesters

Table 1 shows the distribution of 198 hospitals semesters in terms of size of the hospitals (number of beds, admissions), length of stay and total hospital-days during the surveillance period. There are clear outliers in the distribution.

For 37 of the198 hospital-semesters (19%), no cases were reported. CDI being a rare event, it is plausible for small hospitals to have zero cases over six months, but less so for larger hospitals. However 20 (54%) of the 37 hospital-semesters without cases were in hospitals reporting more than 30,000 hospital-days for the semester.

Incidences

The distributions across hospital-semesters are shown in Table 2 and Figure 2 (note that many hospitals contributed data for the full year).

The median incidence of HA-CDI across hospitals in Belgium was 1.1 cases per 10,000 hospital-days, but the figure shows clearly that the mode was below one case per 10,000 hospital days, which is partly due to the large number of hospitals not reporting cases (whether zero case, or not reporting). It further shows *outliers*, which presumably reflect outbreaks, including a very severe one (12 cases per 10,000 hospital-days).

We compared characteristics of hospital-semesters and incidences of HA CDI across hospital-semesters, categorised according to their average length of stay.

F I G U R E 1

Time from hospital admission to beginning of CDI in hospital-associated cases (n=1,794 cases occurring more than two days after admission)
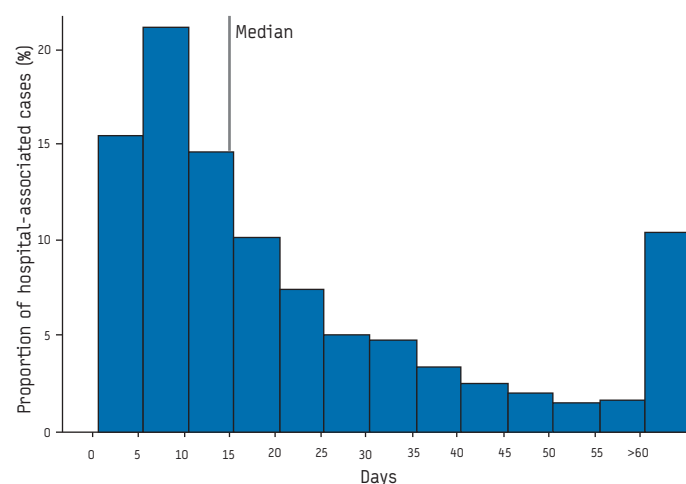
CDI: *Clostridium difficile* infections

T A B L E 1

Characteristics of hospitals contributing data for CDI surveillance in Belgium, July 2007-June 2008 (n=198 hospital-semesters)

Percentiles	P10	P25	P50	P75	P90	Max
Beds	126	197	294	467	822	1,809
Average length of stay [days]	6.2	6.8	7.8	9.6	13.7	127.5
Admissions	1,170	3,168	5,040	7,758	13,871	32,145
Hospital-days	17,488	27,389	37,706	59,962	106,774	248,112

CDI: *Clostridium difficile* infections

This table shows that hospitals with patients staying for an average period of 14 days or more tend to be smaller than those with a length of stay shorter than 14 days. They more often do not report CDI cases, but when they do, report higher rates.

Discussion

The median incidence of all CDI across Belgian hospitals in the period from July 2007 to June 2008 was 1.5 per 1,000 admissions, an incidence higher than the median of 1.1 per 1,000 admissions reported in the first European survey (212 laboratories in eight countries surveyed in the year 2000) [3]. By contrast, the median incidence of all CDI in 35 hospitals in Germany in 2007 was 5.6 per 10,000 hospital-days [4], compared to 1.9 in Belgium (July 2007-June 2008). In Germany, the proportion of hospital-associated cases was 73%, compared to 66% in Belgium. In England, the mean incidence of all CDI in patients 65 years-old or older ranged from 17.5 to 27.4 per 10,000 hospital-days in 2007, depending on the region [5]. In a representative sample of community hospitals in the United States, the mean CDI incidence was 1.3 CDI per 1,000 discharges in 2005 (ICD_9 code 0845) [6]. Overall, the data available for comparisons (i.e. data from a representative sample of hospitals) are rather scarce.

It is noteworthy that 50% of HA cases occurred more than 15 days after admission, reflecting not only the risk associated with a longer exposure [7], but also presumably the fact that a longer period of stay is a proxy for the severity of the condition of the hospitalised patients, in itself a risk factor for CDI.

Since there is no requirement to explicitly report zero cases, hospitals that do not report at all are included in the evaluation as reporting zero cases. CDI being a rare event (in the absence of outbreaks), having zero cases over a period of six months is plausible in small hospitals but less likely in larger hospitals, and our data are therefore an underestimation of the real rates, because for these hospitals reporting no case more likely indicates no reporting. This shows the importance of explicit reporting of zero cases, which we are now implementing in Belgium (hospitals registering online for a new surveillance period, will be requested to actively declare closure of the previous reporting period, with or

T A B L E 2

Incidences of CDI in hospitals in Belgium, July 2007-June 2008 (for 198 hospital-semesters)

	All cases		Hospital- associated cases	
	per 1,000 admissions	per 10,000 hospital-days	per 1,000 admissions	per 10,000 hospital-days
Mean of means				
	2.5	2.3	1.9	1.5
95% CI	1.8-3.3	2.0-2.5	1.2-2.5	1.3-1.7
Percentiles				
P10	0.0	0.0	0.0	0.0
P25	0.6	0.7	0.3	0.4
P50	1.5	1.9	0.9	1.1
P75	2.8	3.4	1.9	2.3
P90	4.8	4.5	3.1	3.3
Maximum				
	56.4	13.9	46.7	12.0

CDI: *Clostridium difficile* infections; CI: confidence interval.

without cases). On the other hand, given that surveillance of CDI in Belgium is compulsory for only one half of a year, we cannot exclude that hospitals would prefer to report on semesters with higher CDI incidence, or outbreak. This would lead to an overestimation of the real rates at national level. In Belgium, hospitals with a longer average period of stay tend to be smaller than those with a shorter stay: our data show that they are more likely not to report cases, but they are also more likely to report high rates when reporting cases, supporting the hypothesis of a bias towards reporting in case of outbreaks. Finally, 13% of surveillance semesters were excluded from the calculation of rates because of missing denominator data, but we do not know if this created a bias, or not.

An issue particularly important for international comparisons is the different mix of hospitals contributing to the computation of national CDI incidence estimates. In Belgium, "acute" hospitals accommodate a varying number of beds for chronic patients. In that respect, stratifying hospitals based on patients' average length of stay might be more appropriate than a stratification of acute versus chronic hospitals based on administrative definitions at national level. We intend to investigate further whether risk stratification by average length of stay of the reporting hospital is a way to improve the comparability of indicators across hospitals, and across surveillance systems.

Conclusions

Although it raises methodological issues, such as the need for an explicit reporting of zero cases, the surveillance of CDI in hospitals in Belgium has been able to produce robust baseline data that can improve our understanding of the epidemiology of the disease. It should also allow for a monitoring of trends at hospital and national level and provide a basis for international comparisons. Remaining challenges are to define and monitor targets for the control of CDI, and to improve the usefulness of data at hospital level through result-oriented individual feed-back.

References

1. Suetens C. Clostridium difficile: summary of actions in the European Union. Euro Surveill. 2008;13(31):pii=18944. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=18944
2. Kuijper EJ, Coignard B, Tüll P; ESCMID Study Group for Clostridium difficile; EU Member States; European Centre for Disease Prevention and Control. Emergence of Clostridium difficile-associated disease in North America and Europe. Clin Microbiol Infect. 2006;12 Suppl 6:2-18.
3. Barbut F, Delmée M, Brazier JS, Petit JC, Poxton IR, Rupnik M, et al. A European survey of diagnostic methods and testing protocols for Clostridium difficile. Clin Microbiol Infect. 2003;9(10):989-96.
4. KISS Krankenhaus-Infektions-Surveillance-System. Modul CDAD-KISS. [KISS Hospital Infections Surveillance System. Module CDAD-KISS]. Berlin: National Reference Centre for Surveillance of Nosocomial Infections; 2008 Sept 9. Availabe from: http://www.nrz-hygiene.de/dwnld/CDAD_Referenzdaten_2007.pdf. [In German].
5. Health Protection Agency. Surveillance of Healthcare Associated Infections Report: 2008. London: Health Protection Agency; July 2008. Available from: http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1216193833496
6. Zilberberg MD, Shorr AF, Kollef MH. Increase in adult Clostridium difficile–related hospitalizations and case-fatality rate, United States, 2000–2005. Emerg Infect Dis. 2008;14(6):929-31.
7. Barbut F, Petit JC. Epidemiology of Clostridium difficile-associated infections. Clin Microbiol Infect. 2001;7(8):405-10.

Figure 2

Incidences of hospital-associated CDI in hospitals in Belgium, July 2007-June 2008 (n=198 hospital-semesters)
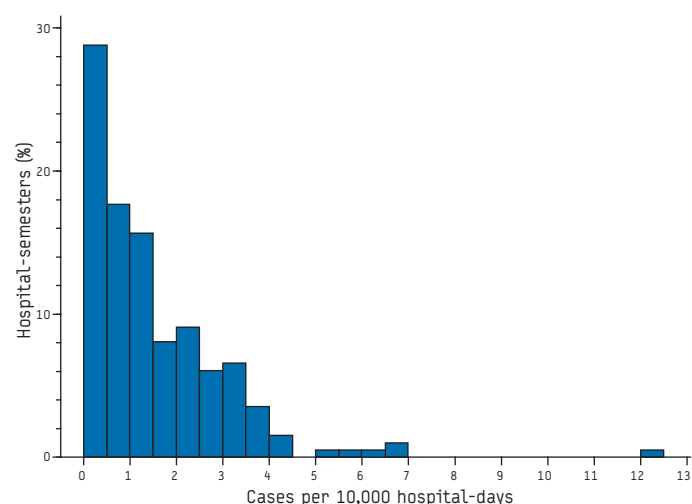
CDI: *Clostridium difficile* infections

Table 3

Hospital characteristics and incidence of CDI , by average length of stay of reporting hospitals. Belgium, July 2007-June 2008

Average length of stay	< 14 days	³14 days	
Hospital-semesters (n)	181	17	
Hospital-semesters not reporting cases (n)	31 (17%)	6 (35%)	Chi²=3.4, p=0.07
Number of beds, median	319	166	
Number of admissions, median	5,239	503	
Number of hospital-days per semester, median	39,357	20,350	
HA CDI per 10,000 hospital-days			
P25	0.4	0.0	
P50	1.1	1.1	
P75	2.2	3.5	
Hospital-semesters with more than three HA cases per 10,000 hospital-days	23 (13%)	6 (35%)	Chi²=6.3, p=0.01

CDI: *Clostridium difficile* infections; HA: hospital-associated.

Research articles

EVALUATION OF A PATIENT REFERRAL CONTACT TRACING PROGRAMME FOR HEPATITIS B AND C VIRUS INFECTION IN DRUG INJECTORS

D D Brewer (interscientific@yahoo.com)[1], H Hagan[2]
1. Interdisciplinary Scientific Research, Seattle, United States
2. National Development and Research Institutes, Inc., New York City, United States

Effective contact tracing for hepatitis B virus (HBV) and hepatitis C virus (HCV) infection could enhance disease control, especially in populations with low HBV vaccination rates and high prevalence of untreated HCV infection. We evaluated a low-cost approach to HBV/HCV contact tracing in injection drug users (IDUs). Index cases (n=26) were IDUs who seroconverted to HBV and/or HCV during a prospective cohort study in Seattle. Interviewers elicited index cases' recent injection partners and administered recall cues and other techniques to boost recall. Index cases received vouchers for free hepatitis testing, which they were to give to locatable partners. Persons redeeming vouchers also received small monetary incentives. Most (26/40) seroconverters participated in the paid contact interviews. Index cases reported many partners (mean=17), and in the aggregate, index cases indicated they could refer more than one third of their elicited partners for testing. Overall, only 17 persons were ultimately referred and just eight of these were confirmed as partners sought for referral. The supplementary elicitation techniques, and especially the recall cues, increased reporting of injection partners substantially. The injection network constructed from reported partnerships was mostly connected and cyclic. Successful contact tracing in IDUs likely requires active involvement by public health staff to locate and notify exposed injection partners.

Introduction

The two basic approaches to contact tracing for infectious disease are provider referral and patient referral [1,2]. In provider referral, health workers elicit infected persons' contacts, obtain identifying and locating information on those contacts, and then locate them to notify them of their exposure and provide counselling, testing, treatment and/or vaccination. In patient referral, infected persons are instructed by health workers to notify their contacts and refer them for testing, treatment and/or vaccination.

Contact tracing for hepatitis B and C viruses (HBV and HCV) in most communities defaults to patient referral or even no contact tracing at all. In some communities, contact tracing may also be initiated by public health staff in response to a case report or a request from a clinician or patient, but such efforts may be quite limited due to the extremely low rate of HBV/HCV case reporting, particularly for injection drug users (IDUs) [3,4]. Health departments in a few communities, however, have implemented routine, proactive HBV control programmes that include tracing index cases' sexual and household contacts [5,6]. To our knowledge, no routine contact tracing programmes have been described in the literature for HBV in IDUs or for HCV in any population.

Nevertheless, there are potential disease control benefits of effective HBV/HCV contact tracing programmes for IDUs. IDUs have low rates of HBV vaccination (in recent studies, 4-22% of IDUs without active or past infection had been vaccinated [7-9]) and contact tracing offers an opportunity to vaccinate susceptibles who have had risky contact with infected persons. Also, through HCV contact tracing, many HCV-infected IDUs can be identified and evaluated for treatment of their infections. IDUs treated for HCV infection, including those who continue to inject, show effective sustained virologic responses comparable to patients without a history of illicit drug injection, even over long post-treatment follow-up periods [10].

In this article, we report an evaluation of a patient referral contact tracing programme for HBV and HCV infection in IDUs. We also describe the impact of supplementary interviewing techniques for eliciting contacts and assess epidemiologically relevant aspects of the injection network ascertained through the programme.

Methods
Participants

Participants were IDUs who seroconverted to HBV or HCV during a prospective cohort study of incident HCV infection conducted in Seattle, United States (US), between 2004 and 2006. IDUs were recruited into the cohort study from the county jail, two needle exchange programmes, street locations where IDUs were present, and by referral from another research study and from eligible participants. Individuals who had injected drugs at least once in the previous six months, spoke English, were 15 years of age or older and tested negative for HCV antibody were eligible for the cohort study. Cohort study participants were scheduled for HBV and HCV antibody testing and counselling every six months during the study period. Sera were screened for HCV antibody (anti-HCV) with a third generation enzyme immunoassay (Abbott Laboratories, Chicago). Sera were screened for hepatitis B core antibody (anti-HBc) using an enzyme immunoassay (Abbott Laboratories, Chicago). Anti-HBc-seronegative participants, some of whom may have been previously

vaccinated, were referred to free HBV vaccination services near the study office. (None of the study staff were licensed nursing or medical providers and consequently were legally prohibited from vaccinating participants.) Seroconversion was determined by the appearance of anti-HCV or anti-HBc in a previously seronegative individual.

A total of 211 IDUs completed at least one of the follow-up assessments. During the course of the cohort study, 36 participants seroconverted to HBV and/or HCV, and 23 (64%) agreed to participate in the contact tracing study, which was formally separate from the cohort study. (Unfortunately, we did not collect data on reasons for not participating in the contact tracing study.) All seroconverters were referred to a hepatitis clinic for free medical evaluation. Four additional IDUs with prevalent HCV infection at baseline were also invited, inadvertently, to participate in the contact tracing study; three of them agreed to participate. For ease of presentation, we group these additional cases with the prospectively identified seroconverters. Thus, the overall participation rate in the contact tracing study was 65% (26/40). Participants in the contact tracing study received USD 20 for their participation, and all provided written informed consent. The University of Washington Human Subjects Review Committee approved the study.

Interviewing procedures

Four trained study staff served as interviewers for this study (including one who had served as an interviewer in a prior HCV contact tracing study [11]). At the beginning of the interview, interviewers explained to index cases the purposes of contact tracing and how the interview related to those goals. Interviewers then asked index cases to recall their injection partners during the 12 months preceding the interview, a period which encompassed most or all of the time after index cases had seroconverted. Injection partners were defined as persons who had injected drugs together with an index case, regardless of whether they had shared needles and including persons who injected the index case and persons whom the index case injected.

Interviewers began eliciting partners by asking index cases to list their partners freely. When index cases indicated they did not have or could not recall any more partners, interviewers prompted non-specifically (e.g. "who else did you inject drugs with …?"). Interviewers prompted in this way until the index case insisted he or she could recall no additional partners. Next, interviewers slowly read the list of elicited partners back to the index case to ensure the partners were correctly recorded, and then prompted non-specifically again.

At this point, interviewers briefly explained to index cases that our past research showed that people often forget some of their partners. Interviewers then administered location and network recall cues to elicit additional injection partners [12-14]. We used the same 17 locally-relevant and empirically-derived location cues for enhancing recall of injection partners that we had used previously with Seattle IDUs [13,14]. For the location cues, interviewers asked index cases to think of all the people they had met or injected with at a particular place (e.g. a motel) during the recall period, and to list any additional partners if they had forgotten to mention them earlier. For the network cues, interviewers read back the list of partners elicited so far in the interview. For each partner, the interviewer asked the index case to think of other people who interact with or know that partner and to list those with whom the index case had injected during the recall period but whom they had forgotten to mention earlier.

After elicitation, index cases indicated those partners whom they knew how to locate and those whom they planned to refer to the contact tracing study. Interviewers collected first names or street nicknames for all elicited partners.

Referral procedures

Index cases received numbered vouchers to give to the partners whom they agreed to refer to the study for testing. Each voucher indicated that it could be redeemed for USD 5-15 for participation in a confidential study on drug use and health, and listed a telephone number for scheduling an appointment. Interviewers coached index cases how to refer their partners. Index cases were to emphasise that hepatitis was highly prevalent in IDUs and that study participation involved free hepatitis testing, and they were also to highlight the benefits of such testing. Index cases were not instructed to report their seroconversions to their partners or notify them of specific potential exposure to HBV and/or HCV.

When referred persons scheduled their appointments by telephone or came to the study site to redeem their vouchers, interviewers determined whether they matched any of the partners whom the corresponding index cases had agreed to refer. Matching was based on the voucher redeemer's name, voucher number and name of the person the redeemer said they had been referred by. Referred persons who did not appear to match the sought partners were still eligible to participate. Voucher numbers were not required for participation, if the index case accompanied the referred person to the study site. Each referred person was paid USD 5 for redeeming the voucher and was then offered free counselling and antibody testing for HBV and HCV. Those who received counselling and testing were paid an additional USD 10. Persons testing anti-HBc-negative were referred for free HBV vaccination and those testing positive for HBV or HCV were referred to the hepatitis clinic for free medical evaluation.

Statistical analysis

We computed descriptive univariate statistics on index cases' characteristics, contact tracing outcomes, and the number of partners recalled at different stages in the interview, as well as proportional increases in the number elicited during different stages. To assess the representativeness of participating seroconverters, we compared them with seroconverters who did not participate in the contact tracing study in terms of demographics, drug use and injection risk behaviours, using appropriate measures and tests of association. We also calculated Pearson correlations for selected predictors of the number of additional partners elicited by the supplementary techniques. In addition, we computed Pearson correlations for each index case between whether a partner was elicited before or by the recall cues and whether a partner was locatable. We summarised these coefficients with the mean correlation weighted by the number of partners elicited and the associated cumulative Z score [15]. Finally, we produced a graph of the injection network with a spring embedder algorithm as implemented in NetDraw 2.4 (Analytic Technologies, Lexington) (we manually repositioned a few nodes for clarity). In a Note at the end of this article, we describe procedures for identifying elicited partners uniquely.

Results

Index case characteristics

There were no meaningful or statistically significant differences between seroconverters who participated in contact tracing and those who did not in terms of age, sex, race, education, employment, welfare, marital status, homelessness, recent incarceration, hepatitis B vaccination, hepatitis A vaccination, depression, behavioural sexual orientation, recent mental health treatment, current methadone treatment, age at first injection, recent needle exchange participation, or estimated numbers of recent injection partners/needle or syringe sharing partners/injection partners with whom other injection paraphernalia were shared. Twenty-two index participants seroconverted to HCV and four seroconverted to HBV; one seroconverted to both HBV and HCV at the same assessment. Index cases included 20 men and six women, and their mean age was 31 years (median=30, range=17-46). Seventy-two percent of index cases were white, 12% were American Indian or Alaskan Native, and 16% belonged to another ethnic/racial group.

Contact tracing outcomes

Index cases reported a mean of 17 (median=16, range=2-58) injection partners. Twenty-three of the 26 index cases agreed to refer one or more partners. Of the 447 elicited partners, 160 (36%) were sought for referral. (One index case was interviewed on the second to last day of the study, and therefore was not asked to refer his eight partners). Seventeen (10%) referral vouchers, linked to nine index cases, were redeemed. Only eight of those vouchers were matched with confidence to a partner sought for referral by the corresponding index case, although two of these redeemers denied being current injectors. The available evidence suggested a further three persons redeeming vouchers were probably partners of the corresponding index case. Ten of 16 tested contacts were anti-HCV positive, and three of 14 were anti-HBc-positive. There were no meaningful differences in HCV or HBV prevalence between contacts matched to sought partners and those presenting vouchers who were not matched to sought partners. Some index cases spontaneously indicated why they would not refer partners. The reasons included the belief that most partners were already HCV infected (n=2 index cases), court order to stay out of a drug area where most partners

were located (n=1), refusal to "hunt down" partners (n=1), partner in inpatient drug treatment or hospital (n=2), and a dying partner who posed no transmission risk (n=1).

Impact of supplementary elicitation techniques

Index cases listed a mean of nine and median of eight injection partners before the supplementary elicitation techniques were administered. The Table shows that each supplementary elicitation technique elicited a noteworthy number and proportion of additional injection partners beyond those elicited in prior stages of the interview. Non-specific prompting and reading back the list each elicited additional injection partners from approximately half of the index cases. The additional partners reported in each of these stages represented 11-20% increases in the number of partners elicited on average. Most index cases listed additional injection partners in response to the location and network cues, and each set of these additional partners boosted the number elicited by 14-29% on average. The supplementary techniques, in combination, elicited additional injection partners from 89% of index cases, and resulted in a mean of eight additional partners reported (essentially doubling the number elicited, on average).

The location cues were moderately more potent than the network cues. For the typical index case, 0.21 additional injection partners were elicited per location cue and 0.14 additional partners were elicited per network cue.

The number of partners index cases recalled before administration of the recall cues correlated positively with the number recalled in response to the location cues (r=.45, p<.05) and network cues (r=.26, p>.05). The number of freely recalled partners, however, was only weakly related to the number of additional partners elicited from nonspecific prompting (r=.13, p>.05) and reading back the list (r=.15, p>.05).

Eighteen index cases recalled partners both before the cues and by the cues; the two groups varied in locatability. Partners elicited by the cues tended to be somewhat less likely to be locatable or sought for referral (weighted mean r= -0.27, cumulative Z= -4.3, p<.001, median = -.20, range = -.82 to .68; 83% negative). In

Effectiveness of the supplementary elicitation techniques

Stage of elicitation	% listing partners	Mean number listed (SD)	Mean % increase (SD)[a]
Free recall	100	9.4 (8.1)[b]	---
Supplementary techniques			
Non-specific prompting	62	1.5 (1.8)	20 (26)
Reading back the list	42	1.2 (2.0)	11 (19)
Location cues	73	3.5 (3.2)	29 (27)
Network cues	58	1.6 (3.0)	14 (26)
Combined	89	7.8 (6.3)[c]	96 (87)[d]
Total	100	17.2 (12.2)[e]	---

Note: Summary based on 26 index cases.
[a]Percent increase over partners elicited up to that point in interview;
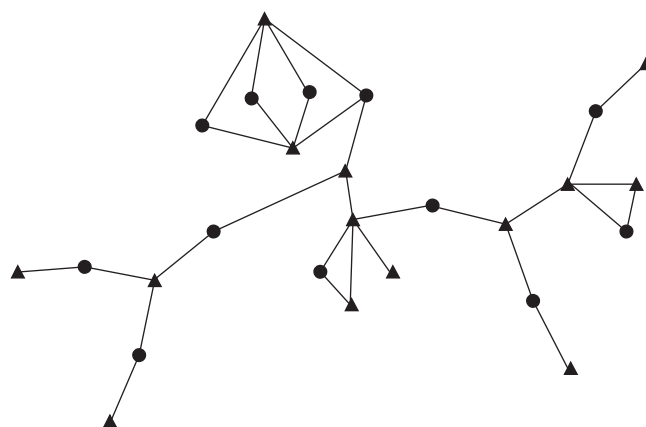[b]Median = 8, range = 1 to 43;
[c]Median = 8, range = 0 to 20;
[d]Median = 78, range = 0 to 360;
[e]Median = 15.5, range = 2 to 58.
SD: standard deviation.

Main component of injection network among index cases

Triangles: index cases; circles: partners (who did not also participate as index cases).

the aggregate, for all 26 index cases, injection partners elicited by the supplementary techniques were somewhat less likely to be locatable or to be sought for referral than those elicited during free recall (27% versus 47%).

Description of injection network

The Figure shows the main component (set of persons connected directly or indirectly by reported injection contact) of the injection network, based on reports from all 26 index cases. Index cases are represented as triangles, and partners who did not also participate as index cases are shown as circles. The main component includes 14 of the 26 index cases; other index cases were not linked to each other directly or indirectly, as far as we could determine. We excluded 76% of elicited partners from our analysis of the injection network because we could not identify them uniquely (the partners' first names were not rare, we judged their street nicknames not to be unique, or index cases referred to them with descriptions only). For clarity, partners mentioned by only one index case are not represented in the Figure, even if they had a rare first name or unique nickname.

Despite the severe restrictions on the data included for analysis, the measured network is fairly connected and cyclic (a cycle is a path involving more than two nodes that starts and ends at a particular node and, when it is traversed, each node is visited only once). However, index cases' recall periods were only 38% concurrent. That is, the sum of the pair-wise temporal overlap between index cases' date-specific recall periods was 38% of the sum of the maximum possible overlap of index cases' recall periods (i.e. if all index cases had been interviewed on the same day). This means that some of the connectedness (and corresponding transmission potential) shown in the Figure might not have been present had the timing of partnerships been considered.

Discussion

Most IDUs who had recently seroconverted to HBV and/or HCV agreed to participate in patient referral contact tracing. Index cases reported many partners in contact interviews, and in the aggregate, index cases indicated they could refer more than one third of their elicited partners for testing. However, very few persons were ultimately referred and only half of them were confirmed as partners sought for referral. The supplementary elicitation techniques, and especially the recall cues, increased reporting of injection partners substantially. In all respects, our results mirrored prior evaluations of these techniques in other studies [13,14], and the evidence of the techniques' effectiveness is now strong enough to make these techniques part of the standard interviewing practice for eliciting injection and sex partners [12]. Although partners elicited by the techniques were less likely to be locatable in the present study, technique-elicited partners are as likely as freely recalled partners to be infected with HCV [14]. The observed injection network was significantly connected and cyclic, as in previous studies of injection networks [11,16,17]. These structural characteristics are associated with epidemic spread of HBV, HCV, human immunodeficiency virus (HIV), and other sexually transmitted diseases [11,17-23]. The degree of connectivity and cyclicity we observed represents a minimum; with more complete data, network connectivity and cyclicity could only increase.

Our contact tracing procedures differed from conventional patient referral approaches in several ways that could have influenced the outcome. Index cases referred their partners for testing without notifying them of their specific exposure to HBV and/or HCV, although index cases were instructed to emphasise the high rate of infection among IDUs. Nonetheless, partners might not have appreciated the urgency for testing given this less personalised notification. Also, we paid index cases to participate in a contact interview. Many public health officials might not choose to make such payments for routine contact tracing, and it is unknown whether infected injectors would be willing to participate in contact tracing without such remuneration. Similarly, we paid referred partners for testing, and that might have increased the chance that a referred partner presented for testing. Furthermore, after completing the baseline interview in the cohort study, participants could refer other IDUs (regardless of whether they had injected together) to the cohort study. Referred persons were screened for eligibility and paid incentives, and index cases also received a "bounty" payment for each person successfully referred. Participants could make such referrals only at this initial point in the cohort study. We lacked sufficient resources in the contact tracing study to make payments to index cases for each partner referred. Index cases may have been less motivated to refer partners after having had the opportunity earlier to refer more easily located persons (any drug injectors) and earn additional money for doing so.

Despite these limitations, our contact tracing results are likely applicable to the investigation of any infectious disease in IDUs. To our knowledge, all prior successful contact tracing efforts with IDUs have been based on provider referral [17,24-29]. The spontaneous comments from some of our index cases about why they would not refer partners indicate that practical barriers to successful patient referral may be common among IDUs. Nonetheless, IDUs are willing to participate in contact tracing, but generally prefer that health workers locate and notify partners [25]. Our results suggest that provider referral is an essential ingredient of any contact tracing effort in IDUs. Moreover, highly connected injection networks imply that HBV/HCV transmission still might be controlled – to some extent – through contact tracing, even if some infected IDUs do not participate [30].

We identified index cases and reported partners as uniquely as possible by:

1. Partner nicknames mentioned multiple times that we judged to be uncommon (e.g. names similar to "Dragon", "Twist", and "Crocodile") and thus very likely to refer to the same person in this local setting;

2. Partner first names mentioned multiple times that were rare in the general population and thus very likely to refer to the same person (<0.1 persons expected to have a particular first name among the total number of partners mentioned by the index cases, as estimated from the Social Security Administration's first name database stratified by decade of birth (http://www.ssa.gov/OACT/babynames/), weighting by the frequency of index cases by birth decade, and accounting for whether a name was used for females or males; birth decade weighting was based on decades of index cases' births, because Seattle IDUs tend to inject with similar age partners [11]);

3. Rare first names (by the same criterion) mentioned by index cases as partner names and which also were the names of other index cases.

By these criteria, the 16 reported partners included in analysis were uniquely identified by five nicknames, seven male first names, and four female first names. We performed simulations in which we randomly sampled first names from the Social Security Administration database with replacement for sample sizes equal to that of named partners in our study. Most simulation trials yielded no rare (<0.1 expected mentions) first names that were sampled two or more times, indicating our criterion was conservative (simulation details available on request).

References

1. Toomey KE, Cates W Jr. Partner notification for the prevention of HIV infection. AIDS. 1989;3(Suppl 1):S57-S62.

2. Potterat JJ, Rothenberg R. The case-finding effectiveness of a self-referral system for gonorrhea: a preliminary report. Am J Public Health. 1977;67(2):174-6.

3. Hagan H, Snyder N, Hough E, Yu T, McKeirnan S, Boase J, et al. Case-reporting of acute hepatitis B and C among injection drug users. J Urban Health. 2002;79(4):579-85.

4. Crofts N, Jolley D, Kaldor J, van Beek I, Wodak A. Epidemiology of hepatitis C virus infection among injecting drug users in Australia. J Epidemiol Community Health. 1997;51(6):692-7.

5. Gunn RA, Weinberg MS, Borntrager D, Murray PJ. Partner notification for persons with chronic hepatitis B virus infection: use of a syphilis model service. Sex Transm Dis. 2006;33(7):437-40.

6. van Steenbergen JE, Baayen D, Peerbooms PG, Coutinho RA, Van Den Hoek A. Much gained by integrating contact tracing and vaccination in the hepatitis B antenatal screening program in Amsterdam, 1992-1999. J Hepatol. 2004;40(6):979-85.

7. Altice FL, Bruce RD, Walton MR, Buitrago MI. Adherence to hepatitis B virus vaccination at syringe exchange sites. J Urban Health. 2005;82(1):151-61.

8. Kuo I, Sherman SG, Thomas DL, Strathdee SA. Hepatitis B virus infection and vaccination among young injection and non-injection drug users: missed opportunities to prevent infection. Drug Alcohol Depend. 2004;73(1):69-78.

9. Ompad DC, Galea S, Wu Y, Fuller CM, Latka M, Koblin B, et al. Acceptance and completion of hepatitis B vaccination among drug users in New York City. Commun Dis Public Health. 2004;7(4):294-300.

10. Grebely J, deVlaming S, Duncan F, Viljoen M, Conway B. Current approaches to HCV infection in current and former injection drug users. J Addict Dis. 2008;27(2):25-35.

11. Brewer DD, Hagan H, Sullivan DG, Muth SQ, Hough ES, Feuerborn NA, et al. Social structural and behavioral underpinnings of hyperendemic Hepatitis C virus transmission in drug injectors. J Infect Dis. 2006;194(6):764-72.

12. Brewer DD, Potterat JJ, Muth SQ, Malone PZ, Montoya PA, Green DA, et al. Randomized trial of supplementary interviewing techniques to enhance recall of sexual partners in contact interviews. Sex Transm Dis. 2005;32(3):189-93.

13. Brewer DD, Garrett SB. Evaluation of interviewing techniques to enhance recall of sexual and drug injection partners. Sex Transm Dis. 2001;28(11):666-77.

14. Brewer DD, Hagan H, Hough ES. Improved injection network ascertainment with supplementary elicitation techniques. Int J STD AIDS. 2008;19(3):188-91.

15. Rosenthal R. Meta-analytic procedures for social research. Newbury Park (CA): Sage Publications; 1991.

16. Rothenberg RB, Potterat JJ, Woodhouse DE, Muth SQ, Darrow WW, Klovdahl AS. Social network dynamics and HIV transmission. AIDS. 1998;12(12):1529-36.

17. Vogt TM, Perz JF, Van Houten CK Jr, Harrington R, Hansuld T, Bialek SR, et al. An outbreak of hepatitis B virus infection among methamphetamine injectors: the role of sharing injection drug equipment. Addiction. 2006;101(5):726-30.

18. Friedman SR, Neaigus A, Jose B, Curtis R, Goldstein M, Ildefonso G, et al. Sociometric risk networks and risk for HIV infection. Am J Public Health. 1997;87(8):1289-96.

19. Rothenberg RB, Sterk C, Toomey KE, Potterat JJ, Johnson D, Schrader M, et al. Using social network and ethnographic tools to evaluate syphilis transmission. Sex Transm Dis. 1998;25(3):154-60.

20. Potterat JJ, Phillips-Plummer L, Muth SQ, Rothenberg RB, Woodhouse DE, Maldonado-Long TS, et al. Risk network structure in the early epidemic phase of HIV transmission in Colorado Springs. Sex Transm Infect. 2002;78(Suppl 1):i159-63.

21. Potterat JJ, Muth SQ, Rothenberg RB, Zimmerman-Rogers H, Green DL, Taylor JE, et al.. Sexual network structure as an indicator of epidemic phase. Sex Transm Infect. 2002;78(Suppl 1):i152-8.

22. Potterat JJ, Rothenberg RB, Muth SQ. Network structural dynamics and infectious disease propagation. Int J STD AIDS. 1999;10(3):182-5.

23. Rothenberg R, Kimbrough L, Lewis-Hardy R, Heath B, Williams OC, Tambe P, et al. Social network methods for endemic foci of syphilis. Sex Transm Dis. 2000;27(1):12-8.

24. Barata LC, Andriguetti MT, de Matos MR. Outbreak of malaria induced among users of injectable drugs. Rev Saude Publica. 1993;27(1):9-14. [In Portuguese].

25. Levy JA, Fox SE. The outreach-assisted model of partner notification with IDUs. Public Health Rep. 1998;113(Suppl 1):160-9.

26. Munday PE, McDonald W, Murray-Sykes KM, Harris JRW. Contact tracing in hepatitis B infection. Br J Vener Dis. 1983;59(5):314-6.

27. Poulin C, Gyorkos TW, MacPhee J, Cann B, Bickerton J. Contact-tracing among injection drug users in a rural area. Can J Public Health. 1992;83(2):106-8.

28. Poulin C, Gyorkos T, Joseph L, Schlech W, 3rd, Lee S. An epidemic of hepatitis B among injection drug users in a rural area. Can J Public Health. 1992;83(2):102-5.

29. Mercedes L, Heymans T, Saavedra J, Martimo J, Hooker C. Investigation of a cluster of acute hepatitis C virus (HCV) infections in injecting drug users (IDU), Minnesota, 2001. National STD Prevention Conference; 2002 March; San Diego, United States.

30. Potterat JJ, Muth JB, Murray C. Partner notification. Ann Intern Med. 1990;113(6):481.

Letters

PREVENTION OF CONGENITAL RUBELLA AND CONGENITAL VARICELLA IN EUROPE

R M Martin (rma@euro.who.int)[1]
1. Targeted Diseases and Immunization Team, Communicable Diseases Unit, World Health Organization Regional Office for Europe, Copenhagen, Denmarkl

To the editor: The World Health Organization Regional Office for Europe would like to express our appreciation to the authors of the Eurosurveillance article "Prevention of congenital rubella and congenital varicella in Europe" [1]. We agree with the authors on the importance of identifying congenital rubella syndrome (CRS) cases and the importance of increasing rubella immunity among women of childbearing age through the use of rubella-containing vaccines. In 2005, the World Health Organization (WHO) Regional Committee for Europe adopted the 2010 goal of regional elimination of measles and rubella and prevention of congenital rubella infection (using CRS as an indicator) [2].

Pandolfi et al. stated in their article that to reach these goals the WHO Regional Office for Europe advocates strategies including strengthening surveillance for CRS and achieving and maintaining high immunisation coverage with measles and rubella-containing vaccines. The article does not mention, however, that the key strategies also include establishing and strengthening rubella surveillance activities in all Member States of the WHO European Region. Rubella surveillance relies on identification and investigation of suspected cases, including laboratory testing; and monthly case-based reporting (i.e. reporting of individual case information) of rubella to the central government (national public health and surveillance institutions) and to the WHO Regional Office for Europe. These activities are crucial in reaching the goal of preventing congenital rubella infection and monitoring and verifying such achievements in the Region.

Two key indicators in reaching the 2010 rubella elimination and congenital rubella infection prevention goals are annual rubella incidence of <1 indigenous case per 1,000,000 population and CRS incidence of <1 per 100,000 live births. Pandolfi et al. accurately point out the difficulties in obtaining reliable data on the incidence of CRS for various reasons, including the asymptomatic nature of rubella infection, the time lapse before infants with CRS may display symptoms (such as hearing impairment), and weaknesses in surveillance systems. At a national level, well-established rubella surveillance provides better information on the extent of rubella virus transmission and associated morbidity, allows for the identification of groups in which additional disease control efforts are needed, and augments information on population susceptibility from serosurvey results like the ones described by the authors. Prompt disease reporting to local and national authorities is crucial for case investigation and implementation of control measures to prevent additional cases of rubella and CRS.

We believe that high-quality rubella surveillance and disease reporting needs to be emphasised more strongly than is done in the Pandolfi article. Although the authors state that rubella surveillance is in place in all of the WHO European Region countries, the WHO and EUVAC.NET surveillance systems assessment suggests this is not the case [WHO unpublished data 2008; 3]. While most countries have systems for rubella surveillance, there are large, highly-populated countries in the WHO European Region without national rubella surveillance, and many others that do not report rubella cases to national levels. Many others are not in a position to report rubella cases on a monthly basis [3]. Because of the continued circulation of rubella virus in many parts of the world, even with high routine coverage of rubella-containing vaccine among children, there may still be cases of congenital rubella infection given the potential for rubella susceptibility in cohorts of women of childbearing age. We agree with the authors that supplemental immunisation programmes that include susceptible cohorts, who may not have been vaccinated through routine use or supplemental immunisation activities, must be maintained. It is estimated that without rubella immunity among women of childbearing age, even with high routine-use coverage, it could take up to 35 years to eliminate congenital rubella infection [4].

The WHO Regional Office for Europe is committed to eliminate rubella and prevent congenital rubella infection, and encourages its Member States to continue establishing and strengthening rubella and CRS surveillance systems and activities. Without this, reaching the regional goals for elimination of rubella and prevention of congenital rubella infection by 2010 will be endangered.

References

1. Pandolfi E, Chiaradia G, Moncada M, Rava L, Tozzi AE. Prevention of congenital rubella and congenital varicella in Europe. Euro Surveill. 2009;14(9):pii=19133. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19133
2. World Health Organization. Strategic plan for measles and congenital rubella infection in the European Region of WHO. Copenhagen: WHO Regional Office for Europe; 2003. Available from: http://www.euro.who.int/document/e81567.pdf
3. EUVAC.NET. Rubella in Europe: Preliminary results 2000-2007. In: Report of the 6th Annual Meeting, Copenhagen, 29-30 May 2008. Copenhagen: Statens Serum Institut; 2008.
4. Reef SE, Cochi SL. The evidence for rubella and congenital rubella syndrome in the United States: A public health achievement. Clin Infect Dis. 2006;43 Suppl 3:S123-5.

Letters

Authors' reply: Prevention of congenital rubella and congenital varicella in Europe

E Pandolfi (pandolfi.elisabetta@gmail.com)[1]
1. Epidemiology Unit, Bambino Gesù Paediatric Hospital, Rome, Italy

To the editor: We thank the World Health Organization (WHO) Regional Office for Europe for the comments on our article, which add significant details that we may have missed. Obviously, we strongly agree that surveillance represents the basic milestone of prevention strategies, that a lot has to be done, and that surveillance should be enhanced in order to achieve the goal of congenital rubella elimination within the expected time.

Although we may have put more emphasis on the need of high quality surveillance for rubella in the WHO European Region, we tried to underline how prevention strategies should rely on the integration of different activities at different levels. In addition to the enhancement of the existing surveillance systems, surveillance of congenital rubella syndrome (CRS) may benefit from the cooperation with congenital defects registries, which may be explored more deeply.

The role of health providers in informing and recommending appropriate preventive actions is crucial and may be practiced during every medical encounter in the frame of prevention of adverse outcomes of pregnancy. Combining surveillance activities and operative recommendations for clinicians in preconception care will bring the goal of rubella elimination closer and will likely allow achieving other important prevention objectives.