Estimation of the incidence of invasive meningococcal disease using a capture-recapture model based on two independent surveillance systems

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Abstract

Background: Invasive meningococcal disease (IMD) is an urgent notifiable disease and its early notification is essential to prevent cases. The objective of the study was to assess the sensitivity of two independent surveillance systems, the statutory disease reporting system (SDR) and the microbiological reporting system (MRS), and to estimate the incidence of IMD.

Methods: The study was performed in Catalonia, Spain, between 2011 and 2015. The variables collected were age, sex, year of report, size of municipality (< 10,000 and $\geq$ 10,000), clinical form, death, serogroup, country of birth and type of reporting centre (private and public). The capture-recapture analysis and 95% confidence intervals were calculated using the Chapman formula. Multinomial logistic regression was performed for adjusted estimation.

Results: The sensitivity of the two combined surveillance systems was 88.5% (85.0–92.0). SDR had greater sensitivity than the MRS (67.9%; 62.7–73.1 vs. 64.7%; 59.4–70.0). In 2014–2015, the sensitivity of both systems was higher (80.6%; 73.2–87.9 vs. 73.4%; 65.2–81.6) than in 2011–2013 (59.3%; 52.6–66.0 vs. 58.3%; 51.6–65.1). In private centres, the sensitivity was higher for SDR than for MRS (100%; 100–100 vs. 4.8%; -4.4–13.9). The adjusted estimate of cases was lower than that obtained using the Chapman formula (279; 266–296 vs. 313; 295–330). The estimated adjusted incidence of IMD was 0.7/100,000 persons-year.

Conclusions: The sensitivity of enhanced surveillance through the combination of two complementary sources was higher than for the sources individually. Factors associated with under-reporting in different systems should be analysed to improve IMD surveillance.

Background

Invasive meningococcal disease (IMD) continues to be an important cause of morbidity and mortality, mainly in children aged < 4 years and adolescents. [1]

In the European regions, the incidence rate of confirmed IMD cases is around 0.6/100,000 persons, [2] similar to Spain (0.58/100,000 persons). [3] The highest incidence is for meningococcal serogroup B, accounting for 51.5% of confirmed IMD cases. The case fatality rate is around 10–15% [3, 4] and long-term sequelae occur in 10–20% of cases. [5]

IMD is an urgent notifiable disease and its early notification is essential to provide an adequate public health response in patients and their close contacts to prevent further cases. Epidemiological surveillance allows monitoring of the impact of public health interventions, including vaccination programmes. Therefore, a robust epidemiological and microbiological system with timely and accurate surveillance providing information on the frequency of cases and the distribution of circulating serogroups is crucial.

Evaluations of surveillance systems should be conducted regularly to increase their utility. [6–8] There are two reporting systems for the epidemiological surveillance of communicable disease in Catalonia: the statutory disease reporting system (SDR) and the microbiological reporting system (MRS). [9]

The capture-recapture method is a statistical method for estimating the real incidence of diseases in a population with two or more information sources. [10, 11] The method is valid if four conditions are met: 1) the population under study has to be closed, i.e., there should be no changes during the study period; 2) there must be a method of determining whether an individual identified by one source is the same as an individual identified by the other; 3) each individual must have the same probability of being captured by either system; 4) the systems must be independent.

The aim of this study was to assess the sensitivity of the two surveillance systems in Catalonia (SDR and MRS) using the capture-recapture method and to estimate the incidence of IMD.

Methods

Information sources

Catalonia is a region in the northeast of Spain with a population of 7,508,106 in 2015. [12]

The SDR is a passive surveillance system through which health professionals declare all infectious diseases subject to surveillance. The reporting of cases to the Public Health Agency of Catalonia (PHAC) is mandatory and includes confirmed cases of IMD and is regulated by a Decree. [9, 13]

The MRS is a surveillance system that consists of microbiologists notifying laboratory confirmed microorganisms that cause infectious diseases. The main objectives of the MRS are to confirm suspected cases of infectious diseases through the identification of the microorganisms and serogroups involved and to determine trends and changes in epidemiological patterns and microbiological resistance. [14]

The MRS was non-compulsory until 2015 and involved 50 health care centres representing over 83% of acute hospital beds. [15] Confirmed IMD cases were reported by microbiologists including sex, age, clinical presentation, serogroup and diagnostic method.

Both systems belong to the PHAC epidemiological surveillance network and, since 2014, transfer information automatically, but the independence of the sources is maintained.

Cases definition, inclusion, and exclusion criteria

A confirmed case of IMD was defined as laboratory confirmed if at least one of the following criteria was fulfilled: isolation in cultures or detection of *Neisseria meningitidis* DNA by PCR in a normally sterile site, detection of gram-negative diplococci or *N. meningitidis* antigen in cerebrospinal fluid.

Data collection

We made a retrospective study of confirmed IMD cases in Catalonia from January 2011 to December 2015. We extracted all IMD records from the MRS and SDR and linked the databases using the personal identification code (PIC). When the PIC was not available, data on notification, age and sex were used to identify duplicates between the two sources. In cases with inconclusive matching, the hospital was used as a fifth matching criterion.

Estimates were made for the entire 5-year period and by age, sex, year of report, size of municipality (< 10,000 and ≥ 10,000), country of birth, number of hospital beds, clinical form (meningitis, with or without sepsis, sepsis, and others), serogroup, death and reporting centre (private or public).

The study was not submitted for research ethics approval as the activities described were conducted as part of the legislated mandate of the Health Department of Catalonia, the competent authority for surveillance of communicable diseases according to Decree 203/2015 of the 15 September which created the epidemiological surveillance network of Catalonia. [9] All the study activities formed part of public health surveillance and did not require informed consent. Personal data were used only for the matching process and measures to protect the confidentiality of personal data were applied (access to the data restricted to the personnel involved in data analysis, and removal of personal data from the datasets after matching).

Statistical methods

The total number of IMD cases was estimated using the two-source capture-recapture method, which uses Chapman's formula, [16] developed to reduce bias due to small samples:

$$N = \frac{(L1 + 1)(L2 + 1)}{a + 1} - 1$$
$$95\%CI = N \pm 1.96 \sqrt{\frac{(L1 + 1)(L2 + 1)(L1 - a)(L2 - a)}{(a + 1)^2(a + 2)}}$$

where L1 is the number of cases in the SDR dataset, L2 is the number of cases reported to MRS, and **a** is the number of cases captured by both systems. The sensitivity (Se) of case ascertainment by the two sources was also calculated as the proportion of true cases detected by each source, i.e. Se (1) = L1/N for source 1 and Se (2) = L2/N for source 2. The sensitivity of both sources combined was calculated as the proportion of cases detected by one of the two sources or both, i.e., Se (1, 2) = (L1 + L2 - **a**)/N.

The independence of the sources was considered when applying the capture-recapture method. [17, 18] In the two-by-two table, where **a** represents cases reported by two sources or combinations of sources, **b** and **c** cases reported exclusively by either of the two sources and **x** the estimated non-reported cases by either of the sources, the odds ratio (OR = ax/bc) should not differ from one.

A multinomial logit model was used to evaluate patient characteristics and the probability of capture by different sources, which allows more precise estimates of the number of cases. [19, 20] We used a backwards stepwise procedure (using likelihood ratio tests, with a P-value > 0.2 as the criterion for removing variables from the model), [21, 22] starting with a full model including all potential covariates, and we used the parameter estimates from the model to estimate the sizes of population subgroups and their 95% confidence intervals (CI). All analyses were made using R software version 3.0.1.

Results

Patient characteristics

Patient characteristics by source are shown in Table 1. From 2011 to 2015, 212 IMD cases were reported to the SDR and 202 cases to the MRS, representing an incidence of 0.56 and 0.54 /100,000 persons-year, respectively. IMD due to serogroup B was the most-frequently reported serogroup (77.4% and 75.7% in the SDR and MRS, respectively). Around 63% of patients were aged < 15 years; the mean age was 21.4 for the SDR and 20.5 years for the MRS. Male sex was more frequent in the SDR (52.4%) than in the MRS (49%). The SDR presented the most cases in 2015 (48 cases; 22.6%) and the MRS (61 cases; 30.2%) in 2011. The SDR reported that 84% of patients lived in a municipality of ≥ 10,000 people compared with 73% in the MRS. In both sources, the number of cases declared in a hospital of ≥ 200 beds were around 70%. The main clinical form in both sources was meningitis (54.7% and 64.8%, respectively) and sepsis (38.7% and 32.7%, respectively). Reports from private centres represented 10% of cases in the SDR and 0.5% in the MRS. Twenty-two cases (10.4%) cases reported by the SDR died compared with 11 cases (5.4%) reported by the MRS.

Table 1
Sociodemographic, clinical and microbiological characteristics of invasive meningococcal disease cases reported to the SDR and MRS, Catalonia 2011–2015

	SDR (n = 212)	MRS (n = 202)
Age groups		
Mean (SD)	21.4 (27.9)	20.5 (26.7)
Median (IQR)	6 (36)	6 (32.3)
<2 years, n (%)	62 (29.8%)	61 (30.7%)
2–4 years, n (%)	35 (16.8%)	30 (15.1%)
5–14 years, n (%)	34 (16.3%)	35 (17.6%)
15–24 years, n (%)	12 (5.8%)	12 (6.0%)
25–34 years, n (%)	12 (5.8%)	9 (4.5%)
35–44 years, n (%)	10 (4.8%)	12 (6.0%)
45–54 years, n (%)	9 (4.3%)	7 (3.5%)
>55 years, n (%)	34 (16.3%)	33 (16.6%)
NAs	1 (0.5%)	2 (1.0%)
Sex, n (%)		
Male	111 (52.4%)	99 (49.0%)
Female	101 (47.6%)	103 (51.0%)
Year of report, n (%)		
2011	43 (20.3%)	61 (30.2%)
2012	41 (19.3%)	29 (14.4%)
2013	38 (17.9%)	30 (14.9%)
2014	42 (19.8%)	34 (16.8%)
2015	48 (22.6%)	48 (23.8%)
Size of municipality, n (%)		
<10,000 people	27 (12.7%)	28 (13.9%)
≥10,000 people	177 (83.5%)	148 (73.3%)
NAs	8 (3.8%)	26 (12.9%)
Country of birth, n (%)		
Spain	194 (91.5%)	188 (93.1%)
Other countries	18 (8.5%)	14 (6.9%)
Number of hospital beds, n (%)		
<200	60 (28.3%)	65 (32.2%)
≥200	149 (70.3%)	137 (67.8%)
NAs	3 (1.4%)	0 (0.0%)
Clinical form, n (%)		
Meningitis	116 (54.7%)	131 (64.8%)
Sepsis	82 (38.7%)	66 (32.7%)
Other forms	14 (6.6%)	4 (2.0%)
NAs	0 (0.0%)	1 (0.5%)
Serogroup, n (%)		
A	0 (0.0%)	2 (1.0%)

NAs: Not available; SDR: Statutory disease reporting; MDR: Microbiological reporting system

	SDR (n = 212)	MRS (n = 202)
B	164 (77.4%)	153 (75.7%)
C	26 (12.3%)	21 (10.4%)
W135	4 (1.9%)	6 (3.0%)
Y	5 (2.4%)	2 (1.0%)
Y/ W135	1 (0.5%)	1 (0.5%)
Non-groupable	6 (2.8%)	4 (2.0%)
NAs	6 (2.8%)	13 (6.4%)
Type of reporting centre		
Private	21 (10.0%)	1 (0.5%)
Public	190 (90.0%)	201 (99.5%)
NAs: Not available; SDR: Statutory disease reporting; MDR: Microbiological reporting system		

Capture-recapture analysis

The odds ratio (OR) was 1.01 (95%CI 0.62–1.66), reinforcing the independence of the two sources.

During the period studied, 212 and 202 IMD cases were reported by the SDR and MRS, respectively. One hundred thirty-seven cases (43.8%) coincided in both sources and 36 cases (11.5%) were not reported to either source. The estimated number of cases was 313 (95% CI 295–330) (Table 2) and the estimated incidence rate was 0.83/100,000 persons-year.

Table 2
Capture–recapture analysis of two datasets to estimate the total number of invasive meningococcal disease cases, Catalonia 2011–2015

		SDR		
		Identified	Not identified	Total
MRS	Identified	137	65	202
	Not identified	75	36	111
	Total	212	101	313
SDR: Statutory disease reporting				
MRS: Microbiological reporting system				

The sensitivity of the SDR was 67.9% (95%CI 62.7–73.1) and that of the MRS was 64.7% (95%CI 59.4–70.0) ($P<0.001$) (Table 3). The sensitivity increased to 88.5% (95%CI 85.0–92.0) when the datasets were combined.

Table 3

Capture–recapture analysis of all invasive meningococcal disease cases reported to the SDR and MRS stratified by characteristics, Catalonia 2011–2015

	No. records in SDR	No. records in MRS	Matched records	Calculated unreported cases	Estimated total no. of cases (95% CI)	Sensitivity SDR (%) (95% CI)	Sensitivity MRS (%) (95% CI)	Difference in sensitivities (%)	P-value
All cases	212	202	137	36	313 (295, 330)	67.9 (62.7, 73.1)	64.7 (59.4, 70.0)	3.2	< 0.001
Age group									
<15 years	131	126	87	20	190 (177, 203)	69.1 (62.6, 75.7)	66.5 (59.8, 73.2)	2.6	0.468
≥15 years	80	74	49	16	121 (109, 133)	66.4 (58.0, 74.8)	61.4 (52.7, 70.1)	5.0	
Sex									
Male	111	99	71	16	155 (144, 166)	71.8 (64.7, 78.9)	64.0 (56.5, 71.6)	7.8	0.588
Female	101	103	66	20	158 (145, 171)	64.2 (56.7, 71.7)	65.5 (58.1, 72.9)	-1.3	
Year of report									
2011–2013	122	120	71	35	206 (187, 226)	59.3 (52.6, 66.0)	58.3 (51.6, 65.1)	1.0	< 0.001
2014–2015	90	82	66	6	112 (106, 118)	80.6 (73.2, 87.9)	73.4 (65.2, 81.6)	7.2	
Size of municipality									
<10,000 people	27	28	22	2	35 (32, 37)	78.7 (65.0, 92.4)	81.6 (68.7, 94.6)	-2.9	0.100
≥10,000 people	177	148	110	23	238 (225, 252)	74.4 (68.9, 80.0)	62.2 (56.1, 68.4)	12.2	
Country of birth									
Spain	194	188	127	32	287 (271, 304)	67.6 (62.2, 73.0)	65.5 (60.0, 71.0)	2.1	0.696
Other countries	18	14	10	3	25 (20, 30)	72.3 (54.7, 89.9)	56.2 (36.7, 75.7)	16.1	
Number of hospital beds									
<200	60	65	40	13	97 (87, 108)	61.7 (52.1, 71.4)	66.9 (57.5, 76.2)	-5.1	0.514
≥200	149	137	97	22	210 (197, 224)	70.9 (64.7, 77.0)	65.2 (58.7, 71.6)	5.7	
Clinical form									
Meningitis	116	131	84	18	181 (169, 193)	64.2 (57.2, 71.2)	72.5 (66.0, 79.0)	-8.3	0.936
Sepsis	82	66	50	10	108 (99, 117)	75.9 (67.9, 84.0)	61.1 (51.9, 70.3)	14.8	
Type of reporting centre									
Private	21	1	1	0	21 (21, 21)	100 (100, 100)	4.8 (-4.4, 13.9)	95.2	0.002
Public	190	201	136	26	281 (267, 295)	67.7 (62.2, 73.2)	71.6 (66.4, 76.9)	-3.9	
SDR: Statutory disease reporting; MDR: Microbiological reporting system									

There were no differences in sensitivity between in < 15 years and ≥ 15 years age groups (P-value = 0.468) in either source although it was higher in the < 15 years (69.1%;

95%CI 62.6–75.7 in the SDR and 66.5%; 95%CI 59.8–73.2 in the MRS). The age groups with the highest sensitivity were 2–4 years in the SDR, with 80.3% (95%CI 68.5–92.1), and 35–44 years in the MRS, with 80.5% (95%CI 60.4–100.0) (Fig. 1).

In 2011–2013, sensitivity for the SDR and the MRS were 59.3% (95%CI 52.6–66) and 58.3% (95%CI 51.6–65.1), respectively, lower than that in 2014–2015 (80.6%; 95%CI 73.2–87.9, for the SDR and 73.4%; 95%CI 65.2–81.6, for the MRS ($P < 0.001$)) (Table 3). 2014 showed the highest sensitivity for both sources: 91.3% (95%CI 83.2–99.4) for the SDR and 73.9% (95%CI 61.2–86.6) for the MRS (Fig. 2). 2011 was the only year in which the MRS had a higher sensitivity than the SDR (56.4%; 95%CI 47.1–65.8 and 39.8%; 95%CI 30.6–49.0, respectively). In private centres the sensitivity of the SDR was 100% (95%CI 100–100) and that of the MRS was 4.8% (95%CI -4.4–13.9). No differences were found in other characteristics analysed.

For I meningitis, 116 and 131 cases were reported by the SDR and the MRS, respectively. The estimated number of meningitis cases was 181, and 18 cases were not reported by either source. The highest sensitivity was detected in the MRS (72.5%; 95% CI 66–79) compared with the SDR (64.2%; 95%CI 57.2–71.2) ($P < 0.001$) (Table 4). 2014–2015 showed a higher sensitivity in both sources compared with 2011–2013: 82.4% (95%CI 72.7–92) in the MRS and 75.6% (95%CI 64.7–86.5) in the SDR. Public centres had a higher sensitivity in the MRS (77.7%; 95%CI 71.4–84.0) and in the SDR (63.9%; 95%CI 56.6–71.2) ($P < 0.037$).

Table 4
Capture–recapture analysis of meningococcal meningitis reported to the SDR and MRS stratified by characteristics, Catalonia 2011–2015

	No. records in SDR	No. records in MRS	Matched records	Calculated unreported cases	Estimated total no. of cases (95% CI)	Sensitivity SDR (%) (95% CI)	Sensitivity MRS (%) (95% CI)	Difference in sensitivities (%)	P-value
All cases	116	131	84	18	181 (169, 193)	64.2 (57.2, 71.2)	72.5 (66.0, 79.0)	-8.3	< 0.001
Age group									
<15 years	72	81	51	13	115 (104, 125)	63.1 (54.3, 72.0)	71.0 (62.7, 79.3)	-7.9	0.682
≥15 years	43	49	32	6	66 (60, 73)	65.5 (53.9, 77.0)	74.6 (64.1, 85.1)	-9.1	
Sex									
Male	62	69	47	7	91 (84, 98)	68.2 (58.6, 77.8)	75.9 (67.1, 84.7)	-7.7	0.245
Female	54	62	37	12	91 (81, 101)	59.9 (49.8, 70.0)	68.7 (59.2, 78.3)	-8.9	
Year of report									
2011–2013	71	82	47	18	124 (111, 137)	57.5 (48.8, 66.2)	66.4 (58.1, 74.7)	-8.9	0.013
2014–2015	45	49	37	3	60 (56, 64)	75.6 (64.7, 86.5)	82.4 (72.7, 92.0)	-6.7	
Size of municipality									
<10,000 people	19	20	16	1	24 (22, 26)	80.2 (64.1, 96.2)	84.4 (69.8, 99.0)	-4.2	0.165
≥10,000 people	93	93	65	12	133 (124, 143)	70.0 (62.2, 77.8)	70.0 (62.2, 77.8)	0.0	
Country of birth									
Spain	107	120	77	17	167 (155, 179)	64.3 (57.0, 71.5)	72.1 (65.3, 78.9)	-7.8	0.862
Other countries	9	11	7	1	14 (12, 17)	64.3 (39.2, 89.4)	78.6 (57.1, 100.0)	-14.3	
Number of hospital beds									
<200	31	40	23	6	54 (47, 61)	57.7 (44.5, 70.9)	74.5 (62.8, 86.2)	-16.8	0.516
≥200	84	91	61	11	126 (116, 135)	67.1 (58.9, 75.4)	72.7 (64.9, 80.5)	-5.6	
Type of reporting centre									
Private	9	1	1	0	9 (9, 9)	100.0 (100.0, 100.0)	11.1 (-9.4, 31.6)	88.9	0.037
Public	107	130	83	14	168 (158, 178)	63.9 (56.6, 71.2)	77.7 (71.4, 84.0)	-13.7	
SDR: Statutory disease reporting; MDR: Microbiological reporting system									

For sepsis, 82 cases and 66 cases were reported by the SDR and the MRS, respectively. The sensitivity was higher for the SDR (75.9%; 95%CI 67.9–84) than the MRS (61.1%; 95%CI 51.9–70.3) (Table 5). There were 108 estimated cases and 10 cases were not reported by either source. The sensitivity was higher in the < 15 years than in the ≥ 15 years in both sources, but higher in the SDR (81.1%; 95%CI 71.1–91.1 versus 71%; 95%CI 59.4–82.5 for the MRS; P = 0.0036), and higher in 2014–2015 than in 2011–2013 (87.6%; 95%CI 78–97.3 for the SDR and 71.9%; 95%CI 58.7–85.1 for the MRS) (P < 0.015).

Table 5

Capture-recapture analysis of meningococcal septicaemia reported to the SDR and MRS stratified by characteristics, Catalonia 2011–2015

	No. records in SDR	No. records in MRS	Matched records	Calculated unreported cases	Estimated total no. of cases (95% CI)	Sensitivity SDR (%) (95% CI)	Sensitivity MRS (%) (95% CI)	Difference in sensitivities (%)	P-value
All cases	82	66	50	10	108 (99, 117)	75.9 (67.9, 84.0)	61.1 (51.9, 70.3)	14.8	< 0.001
Age at notification, years									
<15 years	48	42	34	4	60 (55, 64)	81.1 (71.1, 91.1)	71.0 (59.4, 82.5)	10.1	0.036
≥15 years	34	23	16	8	49 (40, 58)	70.3 (57.4, 83.1)	47.5 (33.4, 61.6)	22.7	
Sex									
Male	43	27	22	5	53 (47, 59)	81.8 (71.3, 92.2)	51.3 (37.8, 64.8)	30.4	0.315
Female	39	39	28	5	55 (49, 60)	72.0 (60.0, 83.9)	72.0 (60.0, 83.9)	0.0	
Year of report									
2011–2013	43	34	22	11	66 (56, 77)	65.2 (53.6, 76.7)	51.5 (39.5, 63.6)	13.6	0.015
2014–2015	39	32	28	2	45 (42, 48)	87.6 (78.0, 97.3)	71.9 (58.7, 85.1)	15.7	
Size of municipality									
<10,000 people	7	7	5	1	10 (8, 12)	72.2 (44.0, 100.0)	72.2 (44.0, 100.0)	0.0	0.918
≥10,000 people	71	52	43	6	86 (80, 93)	82.9 (74.9, 90.8)	60.7 (50.3, 71.0)	22.2	
Country of birth									
Spain	73	63	47	9	98 (90, 106)	74.7 (66.1, 83.3)	64.5 (55.0, 74.0)	10.2	0.275
Other countries	9	3	3	0	9 (9, 9)	100.0 (100.0, 100.0)	33.3 (2.5, 64.1)	66.7	
Number of hospital beds									
<200	25	23	16	4	36 (31, 42)	70.0 (55.0, 85.1)	64.4 (48.7, 80.1)	5.6	0.831
≥200	56	43	34	6	71 (65, 78)	79.2 (69.7, 88.7)	60.8 (49.4, 72.2)	18.4	
Type of reporting centre									
Private	9	0	0	0	9 (9, 9)	100.0 (100.0, 100.0)	0 (0.0, 0.0)	100	0.988
Public	73	66	50	8	97 (89, 104)	75.9 (67.3, 84.4)	68.6 (59.3, 77.9)	7.3	

SDR: Statutory disease reporting; MDR: Microbiological reporting system

Serogroup B (Supplementary Table 1) showed the sensitivity of the SDR was higher than that of the MRS (74.6%; 95%CI 68.8–80.3 and 69.6%; 95%CI 63.5–75.6, respectively). There were differences according to the period and the type of centre. In 2014–2015, the sensitivity was 87.1% (95%CI 79.7–94.5) for the SDR and 78.3% (95%CI 69.2–87.4) for the MRS ($P < 0.002$). In private centres, the sensitivity in SDR was 100% compared with 7.1% (95%CI -6.4–20.6) ($P = 0.004$) in MRS. The sensitivity was higher for IMD serogroup C cases in SDR than in MRS (76.7%; 95%CI 62.5–90.9 and 62%; 95%CI 45.6–78.3, respectively) (Supplementary Table 2).

All 22 deaths were reported in the SDR (CFR: 10.4%), and the sensitivity of the SDR was higher than that of the MRS (100%; 95CI% 100–100 vs 50%; 95%CI 29.1–70.9, P = 0.104) (Supplementary Table 3).

The results of the multinomial logit model for all cases are shown in Table 6. The variables considered significant in defining the sensitivity of the two sources were year of report (2011–2013 versus 2014–2015) and size of municipality. With these variables in the model, the adjusted estimate of the total number of cases was 279 cases (95%CI 266–296) and the estimated incidence rate was 0.7/100,000 persons-year.

Table 6
Variables defining the sensitivity of the SDR and MRS in detecting invasive meningococcal diseases cases. Multinomial logit model

	OR (95%CI)	<i>p-value</i>
Year of report (2014–2015)	2.29 (1.35, 3.89)	0.002
Size of municipality (≥ 10,000 people)	0.51 (0.23, 1.12)	0.093
OR: odds ratio; n estimate: 279 (266, 296)		

Discussion

The sensitivity obtained by combining the two surveillance system for IMD cases was 88.5%, greater than for each source s (67.9% and 64.7%, respectively). Globally, the SDR showed higher sensitivity than the MDR, mainly for cases of sepsis, I serogroup B and serogroup C, although for meningitis the sensitivity of the MDR was higher than that of the SDR.

Similar studies found greater sensitivities by combining data systems than we did. Baldovin et al. [23] in Italy, reported an overall sensitivity of 94.7% by combining four data sources (mandatory notification system, laboratory surveillance, invasive bacterial surveillance and hospital discharge). Jansson et al. [24], in Sweden, found a global sensitivity of 98.7%, 91.1% for clinical notification and 85.4% for laboratory reporting. In Austria a good agreement between the National Reference Center for meningococci and the hospital discharge was found, although a clinical review of hospital discharge data was necessary to detect false positive cases recorded. [25]

The sensitivity was similar in children aged < 15 years than in persons aged ≥ 15 years in both sources (69.1% for the SDR and 66.5% for the MRS; P = 0.468). Gibson et al., [26] in Australia, analysed IMD sensitivity in children aged < 15 years in three sources: notifiable system, hospitalized patients and mortality data. They found a greater sensitivity (99.5%) than we did, although 15% of hospitalized children were false-positive cases.

We found a greater sensitivity for meningitis in the MRS than in the SDR (72.5% vs 64.2%). A possible explanation is that meningitis is considered a more serious disease and, therefore, microbiologists are more sensitive to its reporting. It is difficult to compare our results with those of other studies, since other sources of information were used or the independence of data sources was presumed but not demonstrated, [25] which is essential when using the capture-recapture method.

Notification of confirmed cases of IMD by laboratories is essential in epidemiological surveillance. [27] Molecular information on circulating serogroups that is required to implement public health measures such as vaccination is essential to control the disease [28] and evaluate the impact of available vaccines.

In the absence of automated electronic reporting, monitoring and increasing the speed of laboratory reports may allow the public health department to administer chemoprophylaxis and vaccination to contacts. [28] Although a higher sensitivity has been reported for electronic reporting than for paper-based reports by some authors, [29] during the study period, electronic surveillance was used in the SDR but not in the MDR, which may explain, at least in part, why the MDR had a lower sensitivity than the SDR. [30]

In the multinomial model, the 2014–2015 period and the size of the municipality show a higher sensitivity in the SDR, suggesting that IMD was well recorded in the two surveillance systems, although 36 cases (11.5%) were not captured by either source. This suggests there was underreporting, despite the clinical severity of the disease. It is very important to improve reporting by all physicians and microbiologists to the SDR and MDR to assess the impact of interventions such as immunization.

The estimated IMD incidence rate of 0.7/100, 000 persons-year found in the multinomial model is less than that found using capture-recapture (0.83/100,000 persons-year) but higher than that calculated using the SDR (0.56/100,000 persons-year) or MDR data (0.54/100,000 persons-year). Other European studies showed incidence rates of between 0.39 [23] and 1.18/100,000 persons-year. [25]

The sensitivity of the two sources were intermediate (67.9% for the SDR and 64.7% for the MRS). The lower sensitivity of the MRS may be due to the fact that the MRS is a sentinel system with a coverage of 82% of acute hospital beds and without private centres. In our series, 21 cases (10%) included in the SDR were reported by private centres, while only one case (0.5%) was reported to the MSR; this patient was finally transferred to a public hospital. The inclusion of cases that have an equal probability of selection in one source might lead to an overestimation. Other authors have reported this limitation when the hospital discharge data set includes probable cases which are not included in the reference centre. [25]

Death was registered in 22 cases (10.5%), similar to that reported in other European countries (ECDC) but slightly lower than that observed in Italy (14%) using the capture-recapture method. [23] All cases were reported to the SDR but only 50% were reported to the MRS, indicating that clinical data are better in

the SDR than in the MRS. Other authors have used mortality data for capture-recapture analysis and concluded that all deaths were reported in notifiable systems. [26]

The sensitivity of the sources studied for the surveillance of IMD cannot be generalized to other diseases because physicians' or microbiologists' perception of the importance of IMD differs from that of other diseases. [29]

The main strength of this study is that the two sources had wide coverage. The SDR is a universal epidemiological surveillance source and, unlike the MDR, is a sentinel source, with a high coverage of 83%. Cases with PIC accounted for 85.5% of all cases reported to detect whether cases were coincident or not. In addition, the independence of the two sources was demonstrated, complying with the premise of the capture-recapture method.

A limitation of the study was that not all cases had the same probability of being selected from a given source. Cases diagnosed in private centres or public centres that did not participate in the MRS could not be reported by this system and this may explain, at least in part, the lower sensitivity than the SDR. This highlights the importance of including public and private centres to increase the robustness of the MRS. Another limitation was that we did not analyse the role of the electronic surveillance system, although a previous study detected greater sensitivity of the SDR when electronic surveillance was introduced. [30]

Conclusions

The sensitivity of enhanced surveillance through the combination of two complementary sources (statutory reporting by physicians and microbiological reporting by microbiologists) was higher than that of the individual sources. These systems are complementary and constitute the basic sources of information necessary for adequate epidemiological surveillance of IMD. Specific studies to estimate the factors associated with under-reporting are needed to reinforce epidemiological surveillance of this disease.

Declarations

Ethics approval and consent to participate

Not applicable

Consent of publication

Not applicable

Availability of data and materials

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

Competing interests

The authors declare that they have no competing interests.

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Author's contributions

PC analyzed and interpreted data, studied conception and design of the study and writes the manuscript; MV and NS did statistical analysis; GC revised and collected data; TG,SH,LR collected data; MJ revised the study and AD did critical revision and got funding.

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Figures

Figure 1

Sensitivities of the SDR and MRS stratified by age groups. Catalonia 2011-2015

Figure 2

Sensitivities of the SDR and MRS stratified by year of reporting, Catalonia 2011-2015

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