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# Estimation of the incidence of invasive meningococcal disease using a capture–recapture model based on two independent surveillance systems in Catalonia, Spain

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## ABSTRACT

**Objectives** 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 and to estimate the incidence of IMD.

**Design** We used capture–recapture model based on two independent surveillance systems, the statutory disease reporting (SDR) system and the microbiological reporting system (MRS) of the Public Health Agency of Catalonia, between 2011 and 2015. The capture–recapture analysis and 95% CIs were calculated using the Chapman formula. Multivariate vector generalised linear model was performed for adjusted estimation.

**Measures** The variables collected were age, sex, year of report, size of municipality (<10 000 and ≥10 000), clinical form, death, serogroup, country of birth and type of reporting centre (private and public).

**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 IMD 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.

## STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The use of two surveillance sources as universal statutory disease reporting system based on passive reporting and sentinel microbiological reporting system (MRS) covering 83% of acute hospital beds, offer a wide coverage.
⇒ The independence of the two sources was demonstrated by complying with the premise of the capture–recapture method.
⇒ Not all centres participate in the MRS, thus not all cases diagnosed had the same probability of being selected from a given source.
⇒ The role of the automated electronic reporting of data that might be associated to a greater sensitivity was not analysed.

## 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 was 0.62/100 000 persons-year in 2018,[2] and in Spain it was 0.86/100 000 persons.[3] Six serogroups (A, B, C, W, X, Y) currently cause almost all cases of this life-threatening disease worldwide. Case fatality rate is about 10% in developed countries,[4–6] and 40%–65% present with meningitis, but meningococcemia and pneumonia are also frequent,[4] being the serogroup involved related both with the case fatality rate[7] and the predominant clinical form.[8] Serogroup B causes more than a third part of IMD,[4 9] but in some countries or population groups the proportion is even higher.[10 11] In Spain, from 2009 to 2018, serogroup B accounted for 64% of IMD cases.[12] A high proportion, up to 60%[13] of IMD cases, are

affected by a range of sequelae and health-related impairment in the quality of life of survivors and their families.[14]

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.[15–17] There are two reporting systems for the epidemiological surveillance of communicable disease in Catalonia: the statutory disease reporting (SDR) system and the microbiological reporting system (MRS).[18]

The capture–recapture method is a statistical method for estimating the real incidence of diseases in a population with two or more information sources.[19 20] The method is valid if four conditions are met: (1) the population under study has to be closed, that is, 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.[21]

The SDR is a passive surveillance system through which health professionals report 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.[18 22]

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.[23]

The MRS was non-compulsory until 2015 and involved 50 healthcare centres representing over 83% of acute hospital beds.[24] Confirmed IMD cases were reported by microbiologists including sex, age, clinical presentation (meningitis, bacteraemia of unknown focus and other clinical presentations), 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).

### Ethics statement

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 15 September which created the epidemiological surveillance network of Catalonia.[18] 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).

### Patient and public involvement

No patient involved.

### Statistical methods

The total number of IMD cases was estimated using the two-source capture–recapture method, which uses Chapman's formula,[25] developed to reduce bias due to small samples:

$$N = \frac{(L1+1)(L2+1)}{a+1} - 1$$

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

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, that is, 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, that is, Se (1, 2) =(L1+L2-a)/N.

The independence of the sources was considered when applying the capture–recapture method.[26 27] 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 OR (OR=ax/bc) should not differ from one.

As a multivariate model, a vector generalised linear model (VGLM) from the generalised additive model framework[28] was used to evaluate patient characteristics and the probability of capture by the different sources taking into account the covariates: age (<15 vs ≥15), gender, year of notification (2011–2013 vs 2014–2015), size of the municipality (<10 000 vs ≥10 000), country of birth (Spain vs other), number of hospital beds (<200 vs ≥200) and diagnosis (meningitis vs septicaemia). The outcome for the model is a two column matrix with 0 and 1 indicating if the record is identified by SDR or MRS. 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)[29 30] to eliminate covariates, starting with a full model including all described covariates, and we used the parameter estimates from the model to estimate the sizes of population subgroups and calculate incidence rates. The 95% confidence intervals (CI) were calculated, allowing for uncertainty in the total number of cases estimated. For each of the described covariates, VGLM with source notification as outcome was used to test differences in sensitivities. All analyses were made using R software V.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

**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%) |
| 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%) |
| Septicaemia | 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%) |
| 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%) |

Continued

Table 1 Continued

| | SDR (n=212) | MRS (n=202) |
|---|---|---|
| Type of reporting centre | | |
| Private | 21 (10.0%) | 1 (0.5%) |
| Public | 190 (90.0%) | 201 (99.5%) |

MRS, Microbiological reporting system; NAs, Not available; SDR, Statutory disease reporting.

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. Overall, 22 cases (10.4%) reported by the SDR died compared with 11 cases (5.4%) reported by the MRS.

### Capture–recapture analysis

The OR was 1.01 (95% CI 0.62 to 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. Overall, 137 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 to 330) (figure 1) and the estimated incidence rate was 0.83/100 000 persons-year.

The sensitivity of the SDR was 67.9% (95% CI 62.7% to 73.1%) and that of the MRS was 64.7% (95% CI 59.4% to 70.0%) (p<0.001) (table 2). The sensitivity increased to 88.5% (95% CI 85.0% to 92.0%) when the datasets were combined.

There were no differences in sensitivity between in <15 years and ≥15 years age group (p value=0.468) in either source, although it was higher in the <15 years (69.1%;95% CI 62.6% to 75.7% in the SDR and 66.5%; 95% CI 59.8% to 73.2% in the MRS). The age groups with the highest sensitivity were 2–4 years in the SDR, with


Figure 1 Venn diagram of the capture–recapture analysis of two datasets to estimate the total number of invasive meningococcal disease cases, Catalonia 2011–2015. MRS, microbiological reporting system; SDR, statutory disease reporting.

80.3% (95% CI 68.5% to 92.1%), and 35–44 years in the MRS, with 80.5% (95% CI 60.4% to 100.0%) (figure 2).

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

For 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% to 79%) compared with the SDR (64.2%; 95% CI 57.2% to 71.2%) (p<0.001) (table 3). Years 2014–2015 showed a higher sensitivity in both sources compared with 2011–2013: 82.4% (95% CI 72.7% to 92%) in the MRS and 75.6% (95% CI 64.7% to 86.5%) in the SDR. Public centres had a higher sensitivity in the MRS (77.7%; 95% CI 71.4% to 84.0%) and in the SDR (63.9%; 95% CI 56.6% to 71.2%) (p<0.037).

For septicaemia, 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% to 84%) than the MRS (61.1%; 95% CI 51.9% to 70.3%) (table 4). 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% to 91.1% vs 71%; 95% CI 59.4% to 82.5% for the MRS; p=0.036), and higher in 2014–2015 than in 2011–2013 (87.6%; 95% CI 78% to 97.3% for the SDR and 71.9%; 95% CI 58.7% to 85.1% for the MRS) (p<0.015).

Serogroup B (online supplemental table 1) showed the sensitivity of the SDR was higher than that of the MRS (74.6%; 95% CI 68.8% to 80.3% and 69.6%; 95% CI 63.5% to 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% to 94.5%) for the SDR and 78.3% (95% CI 69.2% to 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% to 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% to 90.9% and 62%; 95% CI 45.6% to 78.3%, respectively) (online supplemental table 2).

All 22 deaths were reported in the SDR (Case fatality rate: 10.4%), and the sensitivity of the SDR was higher than that of the MRS (100%; 95 CI% 100% to 100% vs 50%; 95% CI 29.1% to 70.9%, p=0.104). No differences

**Table 2** Capture–recapture analysis of all invasive meningococcal disease cases reported to the SDR and MRS stratified by characteristics, Catalonia 2011–2015

| | Records in SDR, n | Records in MRS, n | Matched records | Calculated unreported cases | Estimated total number 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 to 330) | 67.9 (62.7 to 73.1) | 64.7 (59.4 to 70.0) | 3.2 | <0.001 |
| Age group | | | | | | | | | |
| <15 years | 131 | 126 | 87 | 20 | 190 (177 to 203) | 69.1 (62.6 to 75.7) | 66.5 (59.8 to 73.2) | 2.6 | 0.468 |
| ≥15 years | 80 | 74 | 49 | 16 | 121 (109 to 133) | 66.4 (58.0 to 74.8) | 61.4 (52.7 to 70.1) | 5.0 | |
| Sex | | | | | | | | | |
| Male | 111 | 99 | 71 | 16 | 155 (144 to 166) | 71.8 (64.7 to 78.9) | 64.0 (56.5 to 71.6) | 7.8 | 0.588 |
| Female | 101 | 103 | 66 | 20 | 158 (145 to 171) | 64.2 (56.7 to 71.7) | 65.5 (58.1 to 72.9) | −1.3 | |
| Year of report | | | | | | | | | |
| 2011–2013 | 122 | 120 | 71 | 35 | 206 (187 to 226) | 59.3 (52.6 to 66.0) | 58.3 (51.6 to 65.1) | 1.0 | <0.001 |
| 2014–2015 | 90 | 82 | 66 | 6 | 112 (106 to 118) | 80.6 (73.2 to 87.9) | 73.4 (65.2 to 81.6) | 7.2 | |
| Size of municipality | | | | | | | | | |
| <10 000 people | 27 | 28 | 22 | 2 | 35 (32 to 37) | 78.7 (65.0 to 92.4) | 81.6 (68.7 to 94.6) | −2.9 | 0.100 |
| ≥10 000 people | 177 | 148 | 110 | 23 | 238 (225 to 252) | 74.4 (68.9 to 80.0) | 62.2 (56.1 to 68.4) | 12.2 | |
| Country of birth | | | | | | | | | |
| Spain | 194 | 188 | 127 | 32 | 287 (271 to 304) | 67.6 (62.2 to 73.0) | 65.5 (60.0 to 71.0) | 2.1 | 0.696 |
| Other countries | 18 | 14 | 10 | 3 | 25 (20 to 30) | 72.3 (54.7 to 89.9) | 56.2 (36.7 to 75.7) | 16.1 | |
| Hospital beds, n | | | | | | | | | |
| <200 | 60 | 65 | 40 | 13 | 97 (87 to 108) | 61.7 (52.1 to 71.4) | 66.9 (57.5 to 76.2) | −5.1 | 0.514 |
| ≥200 | 149 | 137 | 97 | 22 | 210 (197 to 224) | 70.9 (64.7 to 77.0) | 65.2 (58.7 to 71.6) | 5.7 | |
| Clinical form | | | | | | | | | |
| Meningitis | 116 | 131 | 84 | 18 | 181 (169 to 193) | 64.2 (57.2 to 71.2) | 72.5 (66.0 to 79.0) | −8.3 | 0.936 |
| Sepsis | 82 | 66 | 50 | 10 | 108 (99 to 117) | 75.9 (67.9 to 84.0) | 61.1 (51.9 to 70.3) | 14.8 | |
| Type of reporting centre | | | | | | | | | |
| Private | 21 | 1 | 1 | 0 | 21 (21 to 21) | 100 (100 to 100) | 4.8 (−4.4 to 13.9) | 95.2 | 0.002 |
| Public | 190 | 201 | 136 | 26 | 281 (267 to 295) | 67.7 (62.2 to 73.2) | 71.6 (66.4 to 76.9) | −3.9 | |
| Serogrup | | | | | | | | | |
| B | 164 | 153 | 114 | 17 | 220 (209 to 231) | 74.6 (68.8 to 80.3) | 69.6 (63.5 to 75.6) | 5.0 | 0.636 |
| C | 26 | 21 | 16 | 3 | 34 (29 to 39) | 76.7 (62.5 to 90.9) | 61.9 (45.6 to 78.3) | 14.8 | |

MRS, microbiological reporting system; SDR, statutory disease reporting system.

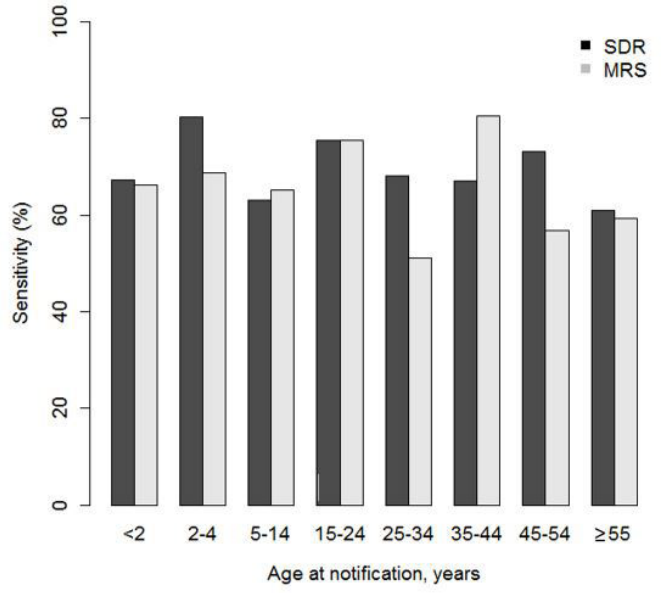


**Figure 2** Sensitivities of the SDR and MRS stratified by age groups. Catalonia 2011–2015. MRS, microbiological reporting system; SDR, statutory disease reporting.

were found in other characteristics analysed (online supplemental table 3).

The results of the multivariate model for all cases are shown in table 5. The variables considered to define the sensitivity of the two sources were year of report (2011–2013 vs 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 to 296) and the estimated incidence rate was 0.7/100 000 persons-year.

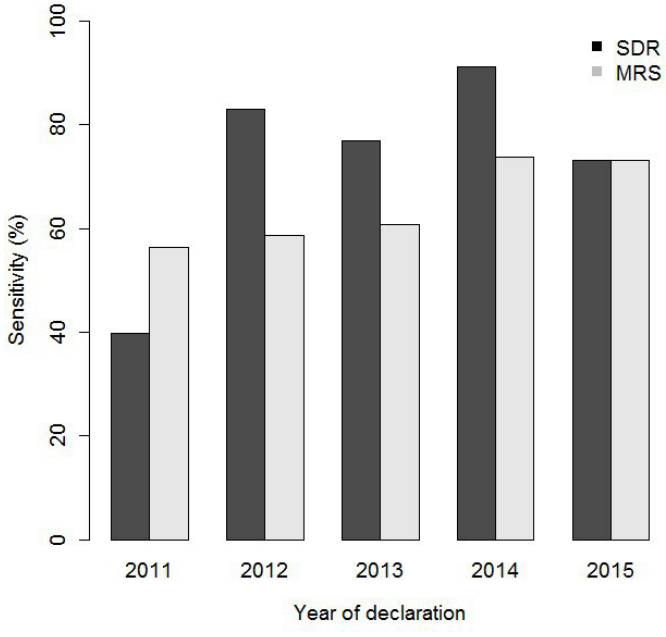


**Figure 3** Sensitivities of the SDR and MRS stratified by year of reporting, Catalonia 2011–2015. MRS, microbiological reporting system; SDR, statutory disease reporting.

## DISCUSSION

The sensitivity obtained by combining the two surveillance system for IMD cases was 88.5%, greater than for each source. Globally, the SDR showed higher sensitivity than the MRS, mainly for cases of sepsis, serogroup B and serogroup C, although for meningitis the sensitivity of the MRS was higher than that of the SDR.

Sensitivity of SDR was 67.9%, very close to that of 66.5% found by Andrianou *et al* in Italy in a study carried out in 2018 using the hospital discharge records system as the external source.[31]

Other studies found greater sensitivities by combining data systems than we did. Baldovin *et al*[32] 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*,[33] 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.[34]

Globally, 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). The differences could be because there is greater sensibilisation to declare paediatric cases than adult cases or because there are differences on IMD incidence according to age.[9] Gibson *et al*[35] in Australia analysed IMD sensitivity in children aged<15 years in three sources: notifiable system, hospitalised patients and mortality data. They found a greater sensitivity (99.5%) than we did, although 15% of hospitalised children were false-positive cases.

Sensitivity was higher in 2014–2015 than in 2011–2013 for both sources (SDR and MRS). SDR had overall higher sensitivity for IMD cases, septicaemia cases as well as serogroup B and C cases, but not for meningitis cases for which MRS had higher sensitivity. The improvement in notification in the years 2014–2015 may be due to different causes, one could be that there is greater awareness for the notification of infectious diseases to public health surveillance systems, although it should be analysed in subsequent studies. In a different way, Andrianou *et al*[31] compared the surveillance of the Italian IMD with the registry of hospital discharges, and found a lower sensitivity in 2018 compared with 2015–2017. This yearly evaluation allows the detection of problems in the notification process.

We found a greater sensitivity for meningitis in the MRS than in the SDR (72.5% vs 64.2%) but not for septicaemia (61.1% vs 75.9%). Multiple reasons could explain this fact. A possible explanation is that meningitis has a specific section in MRS for reporting, while septicaemia is reported in bacteraemia of unknown focus section and it could be confused. It is important to determine the reason for this lower sensitivity to septicaemia in order to improve the completeness of MRS reporting.

**Table 3** Capture–recapture analysis of meningococcal meningitis reported to the SDR and MRS stratified by characteristics, Catalonia 2011–2015

| | Records in SDR, n | Records in MRS, n | Matched records | Calculated unreported cases | Estimated total number 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 to 193) | 64.2 (57.2 to 71.2) | 72.5 (66.0 to 79.0) | −8.3 | <0.001 |
| Age group | | | | | | | | | |
| <15 years | 72 | 81 | 51 | 13 | 115 (104 to 125) | 63.1 (54.3 to 72.0) | 71.0 (62.7 to 79.3) | −7.9 | 0.682 |
| ≥15 years | 43 | 49 | 32 | 6 | 66 (60 to 73) | 65.5 (53.9 to 77.0) | 74.6 (64.1 to 85.1) | −9.1 | |
| Sex | | | | | | | | | |
| Male | 62 | 69 | 47 | 7 | 91 (84 to 98) | 68.2 (58.6 to 77.8) | 75.9 (67.1 to 84.7) | −7.7 | 0.245 |
| Female | 54 | 62 | 37 | 12 | 91 (81 to 101) | 59.9 (49.8 to 70.0) | 68.7 (59.2 to 78.3) | −8.9 | |
| Year of report | | | | | | | | | |
| 2011–2013 | 71 | 82 | 47 | 18 | 124 (111 to 137) | 57.5 (48.8 to 66.2) | 66.4 (58.1 to 74.7) | −8.9 | 0.013 |
| 2014–2015 | 45 | 49 | 37 | 3 | 60 (56 to 64) | 75.6 (64.7 to 86.5) | 82.4 (72.7 to 92.0) | −6.7 | |
| Size of municipality | | | | | | | | | |
| <10 000 people | 19 | 20 | 16 | 1 | 24 (22 to 26) | 80.2 (64.1 to 96.2) | 84.4 (69.8 to 99.0) | −4.2 | 0.165 |
| ≥10 000 people | 93 | 93 | 65 | 12 | 133 (124 to 143) | 70.0 (62.2 to 77.8) | 70.0 (62.2 to 77.8) | 0.0 | |
| Country of birth | | | | | | | | | |
| Spain | 107 | 120 | 77 | 17 | 167 (155 to 179) | 64.3 (57.0 to 71.5) | 72.1 (65.3 to 78.9) | −7.8 | 0.862 |
| Other countries | 9 | 11 | 7 | 1 | 14 (12 to 17) | 64.3 (39.2 to 89.4) | 78.6 (57.1 to 100.0) | −14.3 | |
| Hospital beds, n | | | | | | | | | |
| <200 | 31 | 40 | 23 | 6 | 54 (47 to 61) | 57.7 (44.5 to 70.9) | 74.5 (62.8 to 86.2) | −16.8 | 0.516 |
| ≥200 | 84 | 91 | 61 | 11 | 126 (116 to 135) | 67.1 (58.9 to 75.4) | 72.7 (64.9 to 80.5) | −5.6 | |
| Type of reporting centre | | | | | | | | | |
| Private | 9 | 1 | 1 | 0 | 9 (9 to 9) | 100.0 (100.0 to 100.0) | 11.1 (−9.4 to 31.6) | 88.9 | 0.037 |
| Public | 107 | 130 | 83 | 14 | 168 (158 to 178) | 63.9 (56.6 to 71.2) | 77.7 (71.4 to 84.0) | −13.7 | |
| Serogrup | | | | | | | | | |
| B | 91 | 100 | 70 | 9 | 130 (122 to 138) | 70.1 (62.2 to 77.9) | 77.0 (69.7 to 84.2) | −6.9 | 0.641 |
| C | 16 | 16 | 11 | 2 | 23 (19 to 27) | 69.3 (50.4 to 88.1) | 69.3 (50.4 to 88.1) | 0 | |

MRS, Microbiological reporting system; SDR, Statutory disease reporting.

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

| | Records in SDR, n | Records in MRS, n | Matched records | Calculated unreported cases | Estimated total number 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 to 117) | 75.9 (67.9 to 84.0) | 61.1 (51.9 to 70.3) | 14.8 | <0.001 |
| Age at notification, years | | | | | | | | | |
| <15 years | 48 | 42 | 34 | 4 | 60 (55 to 64) | 81.1 (71.1 to 91.1) | 71.0 (59.4 to 82.5) | 10.1 | 0.036 |
| ≥15 years | 34 | 23 | 16 | 8 | 49 (40 to 58) | 70.3 (57.4 to 83.1) | 47.5 (33.4 to 61.6) | 22.7 | |
| Sex | | | | | | | | | |
| Male | 43 | 27 | 22 | 5 | 53 (47 to 59) | 81.8 (71.3 to 92.2) | 51.3 (37.8 to 64.8) | 30.4 | 0.315 |
| Female | 39 | 39 | 28 | 5 | 55 (49 to 60) | 72.0 (60.0 to 83.9) | 72.0 (60.0 to 83.9) | 0.0 | |
| Year of report | | | | | | | | | |
| 2011–2013 | 43 | 34 | 22 | 11 | 66 (56 to 77) | 65.2 (53.6 to 76.7) | 51.5 (39.5 to 63.6) | 13.6 | 0.015 |
| 2014–2015 | 39 | 32 | 28 | 2 | 45 (42 to 48) | 87.6 (78.0 to 97.3) | 71.9 (58.7 to 85.1) | 15.7 | |
| Size of municipality | | | | | | | | | |
| <10000 people | 7 | 7 | 5 | 1 | 10 (8 to 12) | 72.2 (44.0 to 100.0) | 72.2 (44.0 to 100.0) | 0.0 | 0.918 |
| ≥10000 people | 71 | 52 | 43 | 6 | 86 (80 to 93) | 82.9 (74.9 to 90.8) | 60.7 (50.3 to 71.0) | 22.2 | |
| Country of birth | | | | | | | | | |
| Spain | 73 | 63 | 47 | 9 | 98 (90 to 106) | 74.7 (66.1 to 83.3) | 64.5 (55.0 to 74.0) | 10.2 | 0.275 |
| Other countries | 9 | 3 | 3 | 0 | 9 (9 to 9) | 100.0 (100.0 to 100.0) | 33.3 (2.5 to 64.1) | 66.7 | |
| Hospital beds, n | | | | | | | | | |
| <200 | 25 | 23 | 16 | 4 | 36 (31 to 42) | 70.0 (55.0 to 85.1) | 64.4 (48.7 to 80.1) | 5.6 | 0.831 |
| ≥200 | 56 | 43 | 34 | 6 | 71 (65 to 78) | 79.2 (69.7 to 88.7) | 60.8 (49.4 to 72.2) | 18.4 | |
| Type of reporting centre | | | | | | | | | |
| Private | 9 | 0 | 0 | 0 | 9 (9 to 9) | 100.0 (100.0 to 100.0) | 0 (0.0 to 0.0) | 100 | 0.988 |
| Public | 73 | 66 | 50 | 8 | 97 (89 to 104) | 75.9 (67.3 to 84.4) | 68.6 (59.3 to 77.9) | 7.3 | |
| Serogrup | | | | | | | | | |
| B | 66 | 51 | 43 | 4 | 78 (73 to 84) | 84.4 (76.4 to 92.4) | 65.2 (54.7 to 75.8) | 19.2 | 0.661 |
| C | 8 | 4 | 4 | 0 | 8 (8 to 8) | 100 (100 to 100) | 50.0 (15.4 to 84.7) | 50.0 | |

MRS, microbiological reporting system; SDR, statutory disease reporting system.

Table 5 Variables defining the sensitivity of the statutory disease reporting system and microbiological reporting system in detecting invasive meningococcal diseases cases. Multivariate model.

| | OR (95% CI) | P value |
|---|---|---|
| Year of report (2014–2015) | 2.29 (1.35 to 3.89) | 0.002 |
| Size of municipality (≥10 000 people) | 0.51 (0.23 to 1.12) | 0.093 |

n estimate: 279 (266, 296).

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,[34] which is essential when using the capture–recapture method.

Notification of confirmed cases of IMD by laboratories is essential in epidemiological surveillance.[36] Molecular information on circulating serogroups that is required to implement public health measures such as vaccination is essential to control the disease[37] 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.[27] Although a higher sensitivity has been reported for electronic reporting than for paper-based reports by some authors,[38] during the study period, automated electronic reporting was used in the SDR but not in the MRS, which may explain, at least in part, why the MRS had a lower sensitivity than the SDR.[39]

In the multivariate 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 under-reporting, despite the clinical severity of the disease. Other authors have also found under-reporting of this disease.[40] It is very important to improve reporting by all physicians and microbiologists to the SDR and MRS to assess the impact of interventions such as immunisation.

The estimated IMD incidence rate of 0.7/100 000 persons-year found in the multivariate 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 MRS data (0.54/100 000 persons-year). Other European studies showed incidence rates of between 0.39[32] and 1.18/100 000 persons-year.[34]

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 83% 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 1 case (0.5%) was reported to the MRS; 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.[34]

Death was registered in 22 cases (10.5%), similar to that reported in other European countries,[2] but slightly lower than that observed in Italy (14%) using the capture–recapture method.[32] 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.[34]

The sensitivity of the sources studied for the surveillance of IMD cannot be generalised to other diseases because physicians' or microbiologists' perception of the importance of IMD differs from that of other diseases.[38]

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 MRS, 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.[39]

## 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.

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**Contributors** PC is the guarantor and analysed 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 and LR collected data. MJ revised the study and AD did critical revision and got funding.

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