

# PRIMARY RISK ASSESSMENT

Increase number of *Neisseria meningococcal* infections in the Netherlands

Date of the signal	Date of the RA	Signal provider	Experts consultation	Method
2018	06/11/2018	Request from Cabinet Ms De Block	<b>Permanent members:</b> Dr Valeska Laisnez (AZG), Dr Romain Mahieu (CCC-GGC), Dr Carole Schirvel (AViQ), Ms Mireille Thomas (Ost Belgien), Dr Paul Pardon (FOD-SPF), Dr Patrick Demol (CSS-HGR)  <b>Experts:</b> W. Mattheus (NRC meningo), Dr C. Wyndham-Thomas and Tine Grammens (Sciensano)	Email consultations
Date of update	Closing date			

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**PRIMARY RISK ASSESSMENT  
OF POTENTIAL PUBLIC  
HEALTH EVENT**

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<b>Signal</b>		<p>As of 1 October 2018, the Netherlands launched a vaccination campaign inviting all teenagers (14 years old between 1 May and 31 December 2018) to be vaccinated with ACWY conjugated vaccine. This decision is an answer to the increase of the invasive meningococcal diseases (IMD) due to the serogroup W, clone Cc11 observed between 2015 (4 cases, 0.03 per 100,000 persons) and 2018 (84 cases up to September, 0.66 per 100,000 persons). The clinical presentation with this clone is associated with a 12% fatality rate.</p> <p>Is there a risk the clone will spread in Belgium? Should additional measures be taken?</p>	
Description		Score	Description / arguments
1	Cause known?		Meningococcal infection is caused by <i>Neisseria meningitidis</i> . Based on the polysaccharides in the capsule, twelve serogroups are distinguished, among which in Belgium and in the Netherlands mainly B and further C, W135, Y occur. Besides these serogroups, types, subtypes and immunotypes are distinguished, based on proteins and oligosaccharides in the membrane.
2	Unexpected/unusual		Variations in circulating serotypes are not frequent but expected. In the early's 2000, an increase of infections caused by the serogroup C was observed and followed by a vaccination campaign and the inclusion of the vaccine in the immunisation schedule in Belgium. <i>See more details in Annexes.</i>
3	Severity		Rare diseases (about 100 cases a year in Belgium) but invasive meningococcal diseases (IMD) (eg.: septicaemia and meningitis) are associated with high morbidity (long-term disability +/- 20%) and case fatality rate (5-15%). A 12% case fatality rate is described in the Netherlands with this specific clone.
4	Dissemination (Low/Medium/High)		The serogroup W Cc11 strain that is causing the current increase of IMD in the Netherlands, emerged in Brazil in 2003, spread to Argentina and Chile before emerging in the UK in 2009 and in the Netherlands in 2012. Since 2015, other European countries like Denmark, France, Spain and Sweden experience an increase in this serogroup although the magnitude is still limited. The increase in the Netherlands has been observed over a three years-period (2015-2018) [2].
5	Risk of national spread		The National reference centre (NRC) for <i>Neisseria meningitidis</i> identified 4 cases of serogroup W Cc11 in 2016, 6 cases in 2017 and 10 cases in 2018. Belgium may also see a further increase, and public health actions including vaccination could then be considered.
<b>Preparedness and response</b>			
6	Preparedness		IMD have to be notified to federated entities since control measures for the contacts have to be taken. Each entity has a procedure for contacts management.

			The diagnostic and therapeutic capacity does exist in Belgium where there is also a national reference centre in charge of following the circulating strains and the antibiotic susceptibility.
7	Specific control measures (surveillance, control, communication)		<p>Between 1997 and 2001, an important increase of Meningo C infections was observed in Belgium, mainly in Flanders, reaching as many cases as serogroup B. This change motivated the introduction of a vaccine against serogroup C in the vaccination schedule in 2002 while catch up campaigns were organised in the Flemish Community (all children between 1 and 18 y, from December 2001 until 2004) and in the French Community (all children born between 1996 and 2001, between June 2002 and December 2002).</p> <p>The vaccination coverage for toddlers (18-24 months) is estimated at 89,4 % in Brussels (2012), 91,2 % in Wallonia (2015) and 93,7 % in Flanders (2016).</p> <p>In 2014, the KCE evaluated that the introduction of a generalised vaccination against meningococcus B in Belgium would not be cost effective [3] and the HGR-CSS concluded in March 2017 that there was not enough epidemiological arguments to introduce this vaccine in the routine vaccination in infants [4].</p>
<b>Public health impact</b>			
A	Public health impact in Belgium (Low/Medium/high)	Medium	<p><b>Epidemiological situation is different in the Netherlands and Belgium:</b> There is no abrupt increase of cases. The incidence of IMD in Belgium is quite stable since 2011 with a median incidence of 1.14 cases/100.000 [range 0.97 to 1.44 cases/100.000 inhabitants]. No geographical cluster of cases identified in 2018.</p> <p>There is actually no outbreak and case management procedure of the Federated Entities already includes post exposure prophylaxis and vaccination.</p> <p><b>Microbiological situation is different in the Netherlands and Belgium even if an evolution in the serogroups repartition is also observed in Belgium:</b> the serogroup W in Belgium is not as much frequent as serogroup B. Nevertheless, the microbiological situation is also evolving with an increase of serogroups Y and W in the past 5 years which represented respectively about 20% and 9.5% of the identified serogroups in 2017 while the serogroup B remained the most frequent one with more than 60%.</p> <p>On the provisional results of 2018, the proportion of patients infected by serogroup CWY is nearly as high as the proportion of serougroup B in Belgium. If this convergence is already observed in Flanders, it is not yet the case in Wallonia where serogroup B is still representing &gt;60%. Serogroups do not affect the same age groups, it must be taken into account in the interpretation of the results (<i>See more details in Annexes</i>).</p> <p>Historical time trends of meningococcal disease show natural fluctuations in meningococcal disease. Nevertheless the microbiological situation must be closely monitored because the dissemination of specific pathogenic clones has been also observed in other EU countries since 2013 and IMD are</p>

			associated with high mortality while a vaccine is available.
B	Recommendations (surveillance, control, communication)		<p>Systematic identification of the serogroups identified in IMD patient by the NRC remains essential in order to</p> <ul style="list-style-type: none"> <li>-support the case management procedure</li> <li>-consider in time a vaccination campaign with ACWY.</li> </ul> <p>Considering the higher level of mortality associated with the incriminated clone Cc11 for serogroup W in the Netherlands, a close follow up of each patient is recommended for all suspected cases, specifically those identified with serogroup W.</p> <p>Adaptations to existing guidelines for contact management should be described in order to ensure a common approach in the federated entities.</p> <p>Active and specific communication is not recommended for the moment.</p>
C	Actions		<p>No additional action for case management at this stage. Federated entities will continue to apply their routine procedure for case management including a.o. :</p> <ul style="list-style-type: none"> <li>Invite laboratories to systematically send the strain to the NRC especially if W serogroup (<i>or at least to communicate the serogroup if a laboratory is performing the analyse by its own</i>).</li> <li>Collect systematically additional information on the clinical presentation, outcome and some specific factors like recent travel.</li> </ul> <p>Together with federated entities Sciensano will:</p> <ul style="list-style-type: none"> <li>Communicate on the situation in Belgium in the flash.</li> <li>Compile data from mandatory notification, NRC and sentinel laboratories in order to be able to detect a signal requiring a specific public health response.</li> <li>Request update on European epidemiological situation from ecdc.</li> </ul> <p>The NRC continues to perform a complete genome sequencing (WGS) on all invasive strains to follow the serogroup/clone circulation in Belgium.</p> <p>The HGR-CSS</p> <ul style="list-style-type: none"> <li>Has already planned to revise the recommendation for meningococcal vaccination. The need for a MenACWY vaccination in adolescents, the possibility of replacing the infant MenC vaccine by the MenACWY vaccine, and the option to add MenB vaccination in the child vaccine calendar are all to be considered, evaluated and discussed.</li> </ul> <p>Is requested to give an opinion on the best practices for contact management including vaccination of contacts.</p>

## ANNEXES

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### SITUATION IN THE NETHERLANDS [5], [6]

**Incidence** since 2002 varies between 0.5- 1.0 per 100,000 per year.

**Serogroups circulation:** Natural fluctuations in meningococcal disease have always been observed.

Group B-meningococcus has historically been the most important cause of meningococcal disease up to 1997 when an increase of group C-meningococcosis started leading to the introduction of MenC vaccination in 2002. The number of cases of MenC disease has then fallen sharply from almost 300 in 2001 to less than 10 per year.

A decreasing trends in B meningococcal disease was observed since the late 1990s and currently there are about 70 cases per year due to type B. Epidemic elevations of group B meningococcal disease occur regularly at intervals of 10 to 25 years (van der Ende 2011).

Since October 2015 an increase in the number of patients with meningococcal disease serogroup W is observed.

2015: 4 cases (0.03 per 100,000 persons)

2018: 84 cases (0.66 per 100,000 persons)

### SITUATION IN BELGIUM

**Incidence** median between 2001 and 2017: 1.14 cases/100.000 [range 0.97 to 1.44 cases/100.000 inhabitants)

**Serogroups circulation:** Natural fluctuations in meningococcal disease have always been observed.

Group B-meningococcus has historically been the most important cause of meningococcal disease up to 1997 when an increase of group C-meningococcosis started leading to the introduction of MenC vaccination in 2002. The number of cases of MenC disease has then fallen sharply from almost 179 in 2001 to 4 in 2018.

A decreasing trends in B meningococcal disease was observed since begin 2000 and currently there are about 60 cases per year due to type B.

Type Y meningococcal disease has been increasing since 2011 (n=3 in 2005, n=9 in 2011, n=24 in 2018).

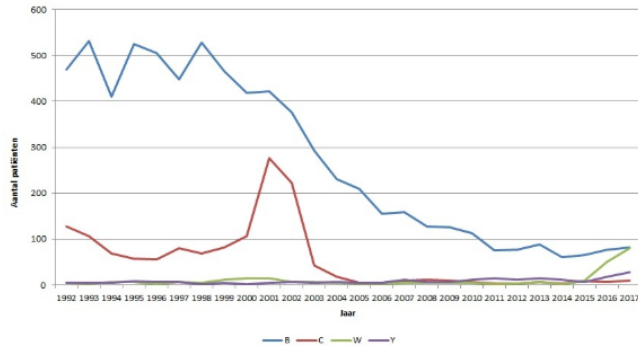
Type W is increasing slightly since 2015.

2015: 8 cases (0.07/100.000)

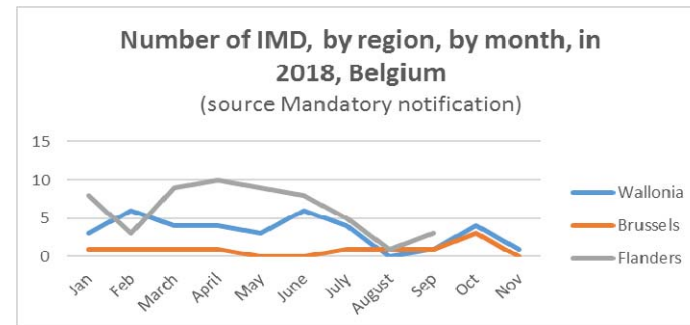
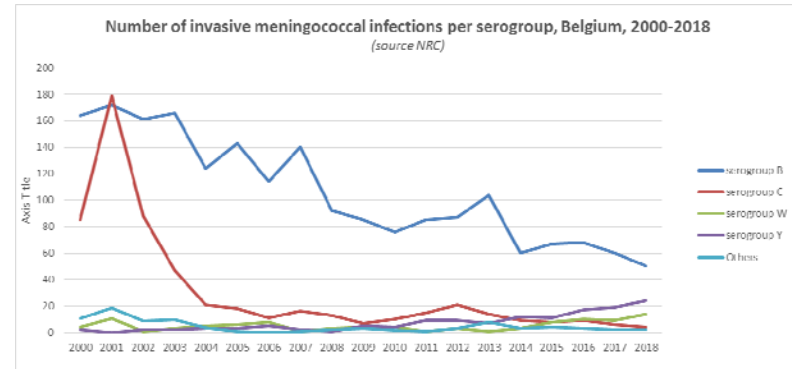
2018: 15 cases (0.13/100.000).

The proportion of W and Y serogroups is about 18% in Belgium for the period 2011-2018 but is reaching about 42% in 2018. The same evolution is observed at regional level even if some variations among the regions are described, *see page 8*.

Aantal gevallen van invasieve meningokokkenziekte per jaar



Figuur 1. Aantal patiënten met invasieve meningokokkenziekte veroorzaakt door type B, C, W en Y, 1992-2017.



### Case fatality rate

5 to 10%, up to 20-50% in case of fulminant sepsis. [6]

12% among serogroup W infections.

### Case fatality rate

2 to 5% (from data mandatory notification). In 2018 (*incomplete data*): Brussels 10 cases, no death. Wallonia, 36 cases, 2 deaths (5.5%). Flanders: 56 cases, 3 deaths (5.3%). Among the 17 serogroup W cases in 2018, 2 deaths (+/- 12% case fatality rate).

### Agegroup:

The most affected age groups differ based on the serogroup:

For B, there are two peaks:

- more than 30% among the < 5 years of age 15-19 age group

The incidence of the Y meningococcal diseases is high

- in children under 5 years and adolescents

from ~50 years onwards

### Seasonality

The peak incidence for serogroup B is in winter and early spring.

### Geographical repartition

No geographical cluster of the Y meningococcal diseases cases

### Agegroup:

The most affected age groups differ based on the serogroup:

The mean proportion for the period 2011-2018,

For B, there are two peaks:

- < 5 years of age: 40.5%
- 15-19 y: 15%

For Y:

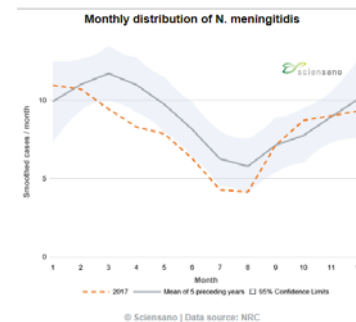
- 0-9 y: 15.5%
- 15-19 y: 15.5%
- 75-85 y: 22%

For W:

- 0-4 y: 41%
- 15-24 y: 26%

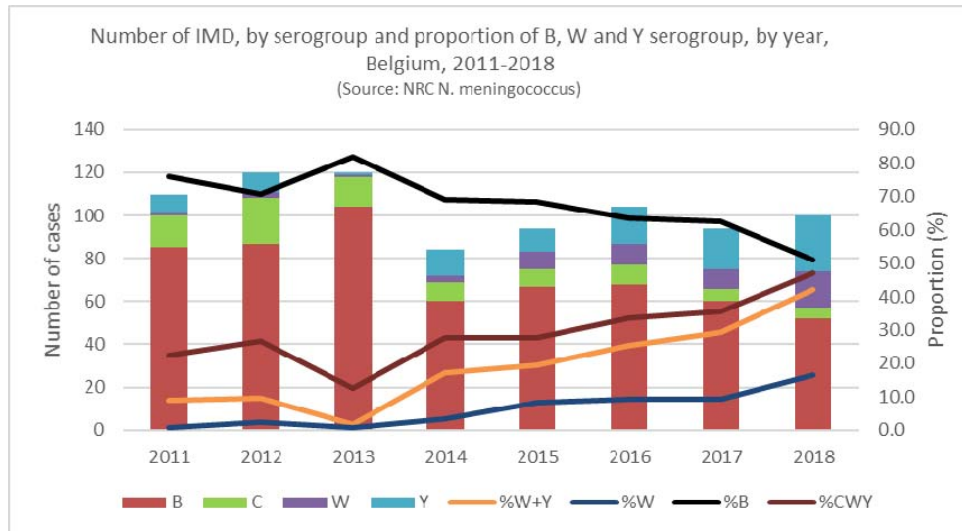
### Seasonality

The peak incidence for serogroup B is in winter and early spring.



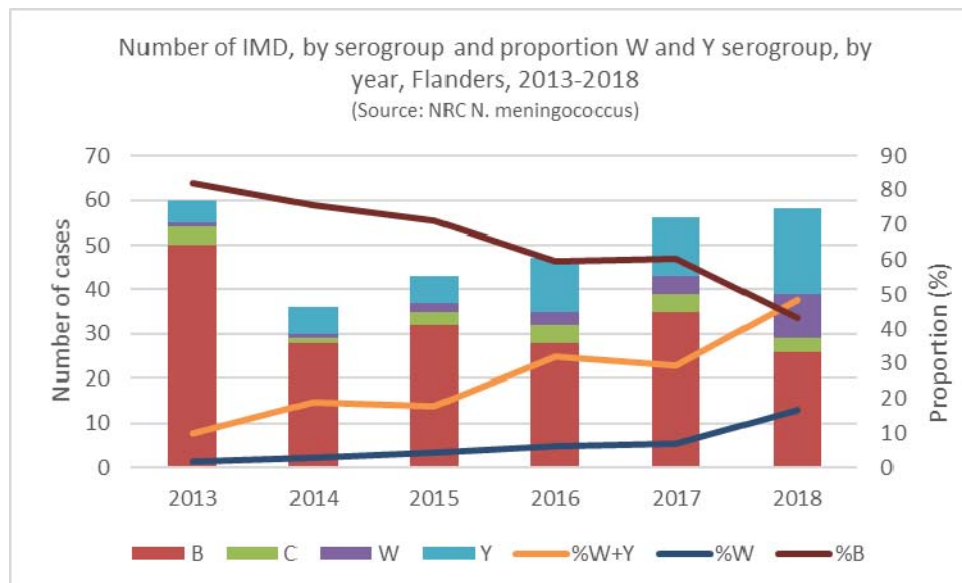
## Geographical repartition of *N. meningitidis* serogroups in Belgium

The graphs below are showing the evolution of the number of IMD by serogroup, for Belgium 2011-2018 and by region, 2013-2018, data from NRC.

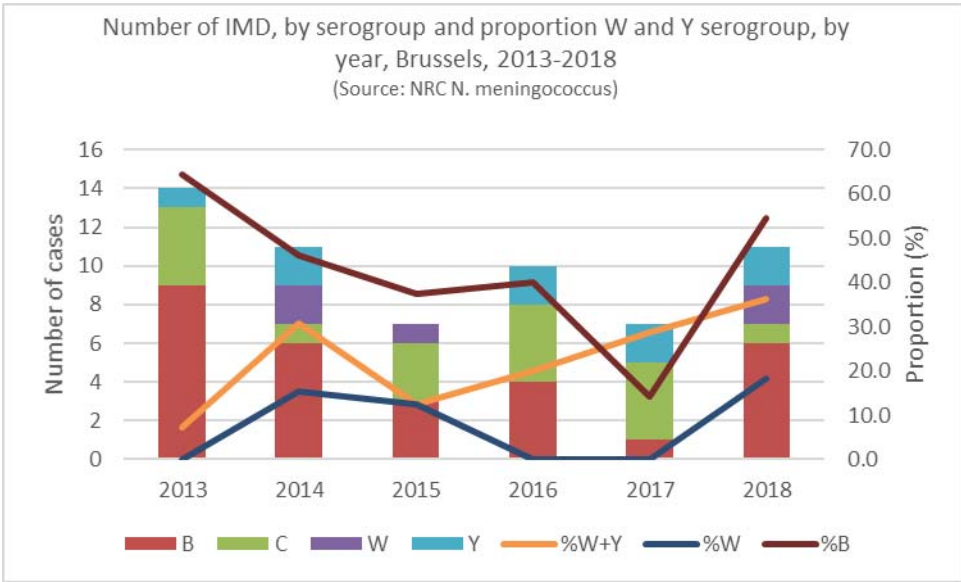
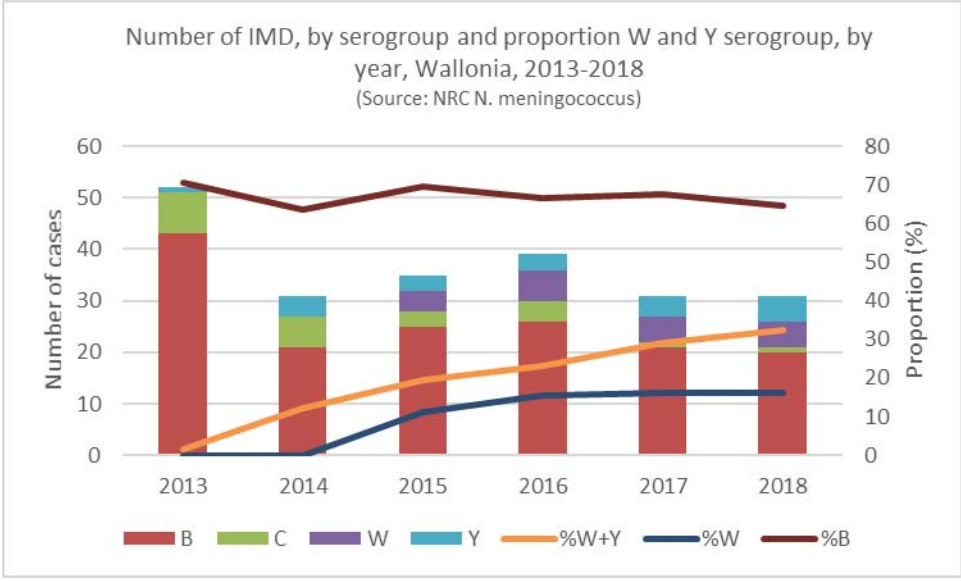


In 2018, the serogroup B remains the most frequent one in Belgium but if we compare the proportion of the serogroup B to the serogroups covered by the ACWY vaccine, we have respectively 51% and 47% of the circulating strains what should be certainly consider in the vaccine strategy mainly if we have some attention for the regional repartition.

In Flanders there are already as many serogroup W/Y cases than serogroup B in 2018. It is not yet the case in Wallonia where the serogroup B remains predominant with 64.5% of the circulating strains. In Brussels the very small number of cases does not allow interpretation of trends.







***Geographical repartition, by province, Belgium, 2011-2017, serogroup, data from the National reference centre***

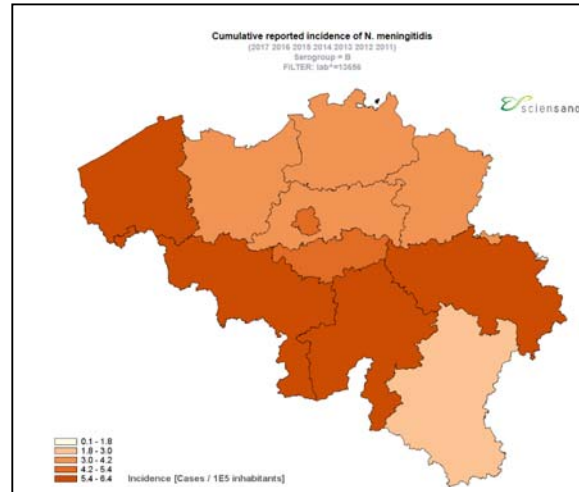
For the same period:

Incidence of serogroup Y

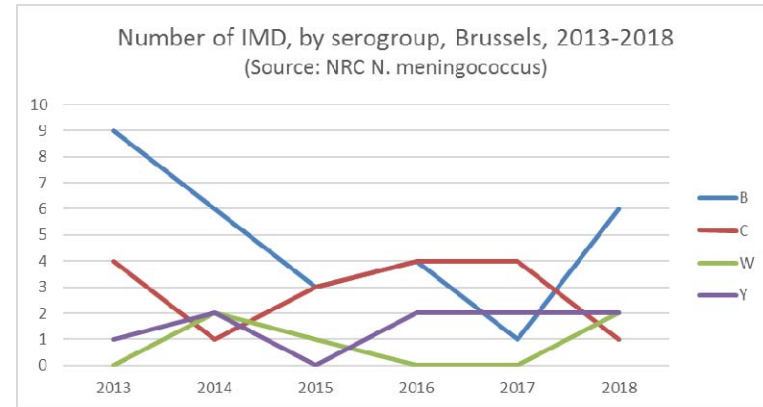
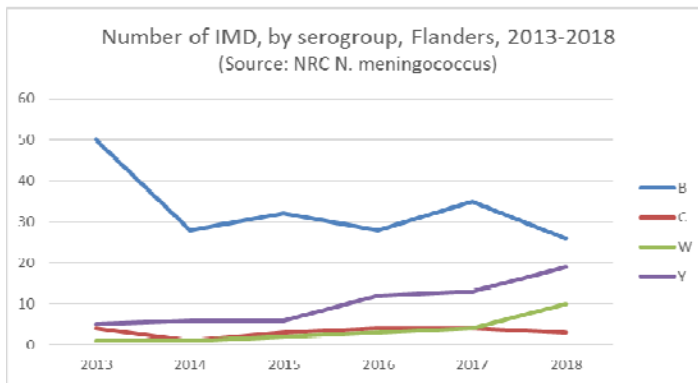
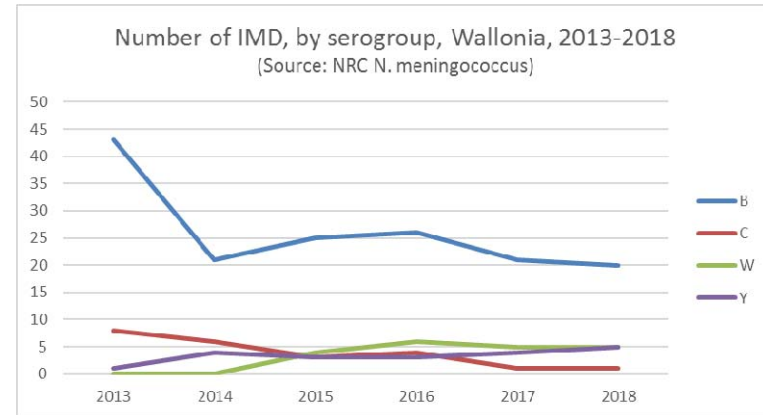
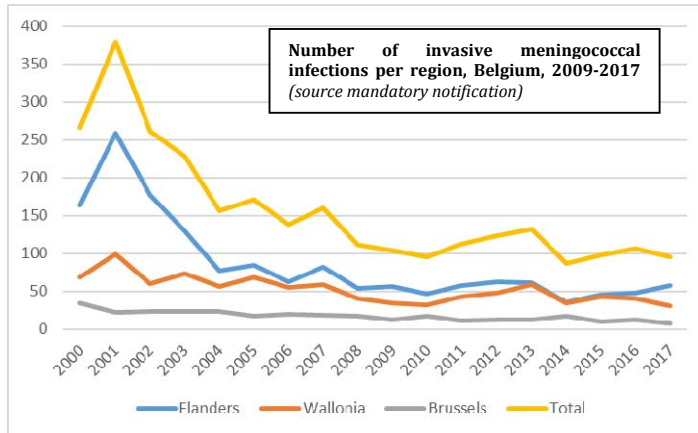
0.1-1.8/100.000 in all provinces except Luxembourg.

Incidence of serogroup W

0.1-1.8/100.000 in all provinces.



## ADDITIONAL GRAPHS - BELGIUM



## REFERENCES

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- [2] Implementation of MenACWY vaccination because of ongoing increase in serogroup W invasive meningococcal disease, the Netherlands, 2018. Mirjam J Knol et al. *Eurosurveillance*, Rapid communications, 19 Apr 2018.
- [3] Un vaccin quadrivalent contre le méningocoque de groupe B : analyse coût-efficacité. G. Hanquet et al. <https://kce.fgov.be/fr/un-vaccin-quadrivalent-contre-le-m%C3%A9ningocoque-de-groupe-b-analyse-co%C3%BBt-efficacit%C3%A9>
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- [5] Toename meningokokkenziekte serogroep W sinds oktober 2015. [https://www.rivm.nl/Onderwerpen/M/Meningokokken/zieook/Toename\\_meningokokkenziekte\\_serogroep\\_W\\_sinds\\_oktober\\_2015](https://www.rivm.nl/Onderwerpen/M/Meningokokken/zieook/Toename_meningokokkenziekte_serogroep_W_sinds_oktober_2015)
- [6] Meningokokken-meningitis en –sepsis. <https://www.rivm.nl/Onderwerpen/M/Meningokokken>