

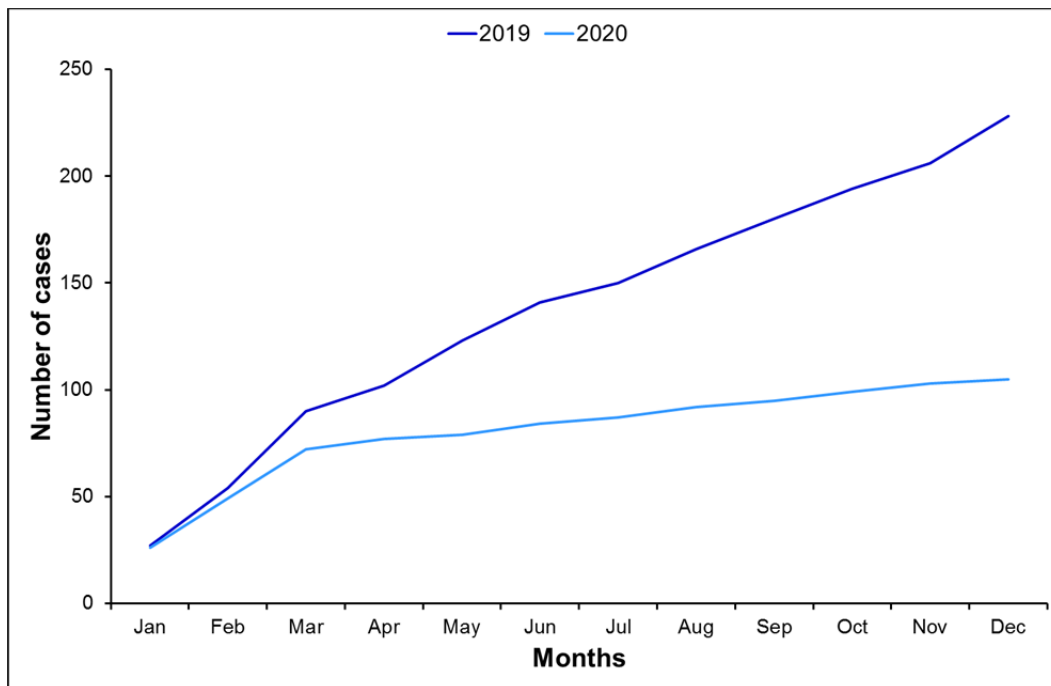
Data of the laboratory surveillance of meningococci at the NRZMHi (2020)

Introduction

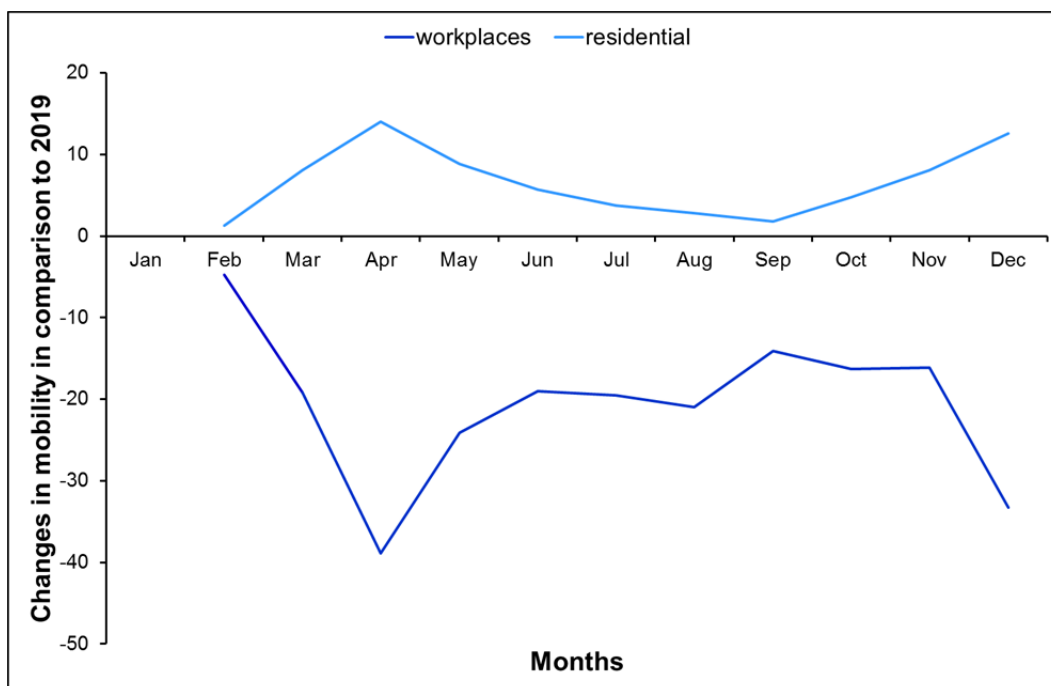
The German National Reference Centre for Meningococci and *Haemophilus influenzae* (NRZMHi) supports integrated molecular surveillance of both the Robert-Koch-Institute and the ECDC as well as surveillance of antimicrobial susceptibility of meningococci from invasive meningococcal disease (IMD). In 2020, 186 samples from 163 individuals were analysed for meningococci. The NRZMHi confirmed *Neisseria meningitidis* in 138 patients, in 105 of them from primarily sterile compartments (latter figure corresponds to the number of cases with invasive disease). In 29 patients (27.6% out of 105) detection of meningococci was carried out using molecular techniques only. During the same period, 138 cases of IMD were notified to the RKI (data as of 04.03.2021, SurvStat@RKI). Given that all processed cases of IMD were notified retrospectively, one can assume a 77% coverage of IMD by NRZMHi (89% in 2019).

In 2020, the incidence of IMD in Germany (0.17/100,000) was significantly lower than in 2019 (0.31/100,000) (data as of 04.03.2020, SurvStat@RKI). The implementation of social distancing measures, mask wearing mandates and school closures during the COVID-19 pandemic caused not only a national but a world-wide reduction of infectious diseases (Epid Bull 2021;7:3-7; Brueggemann et al., Lancet Digit Health 2021 Jun;3(6):e360-e370). The resulting reduction of cases of invasive meningococcal disease as well as mobility changes are shown in the following graphs.

Trend of IMD cases in the course of the COVID-19 pandemic 2020



Cumulative graph of the number of IMD cases processed at the NRZMHi in 2020 in comparison to the number of cases in 2019

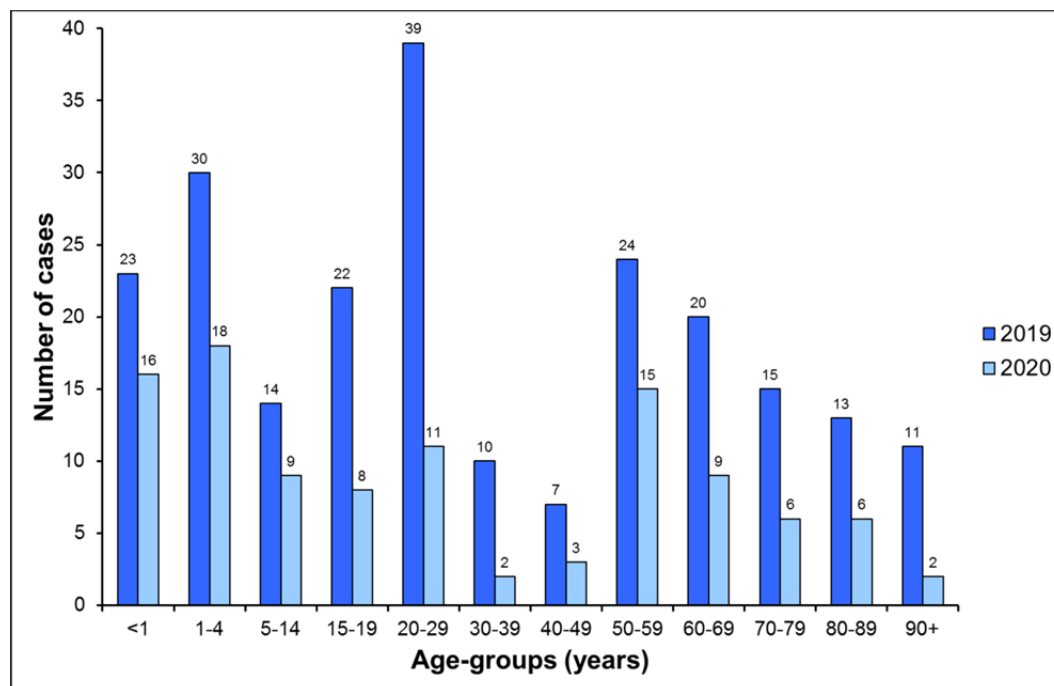


Mobility changes of visitors to workplaces and visitors to residential areas in Germany between 2019 and 2020

The data were retrieved from Google COVID-19 mobility reports (<https://www.google.com/covid19/mobility/>) which are based on aggregated, anonymized sets of data from Google users who have turned on the location history setting.

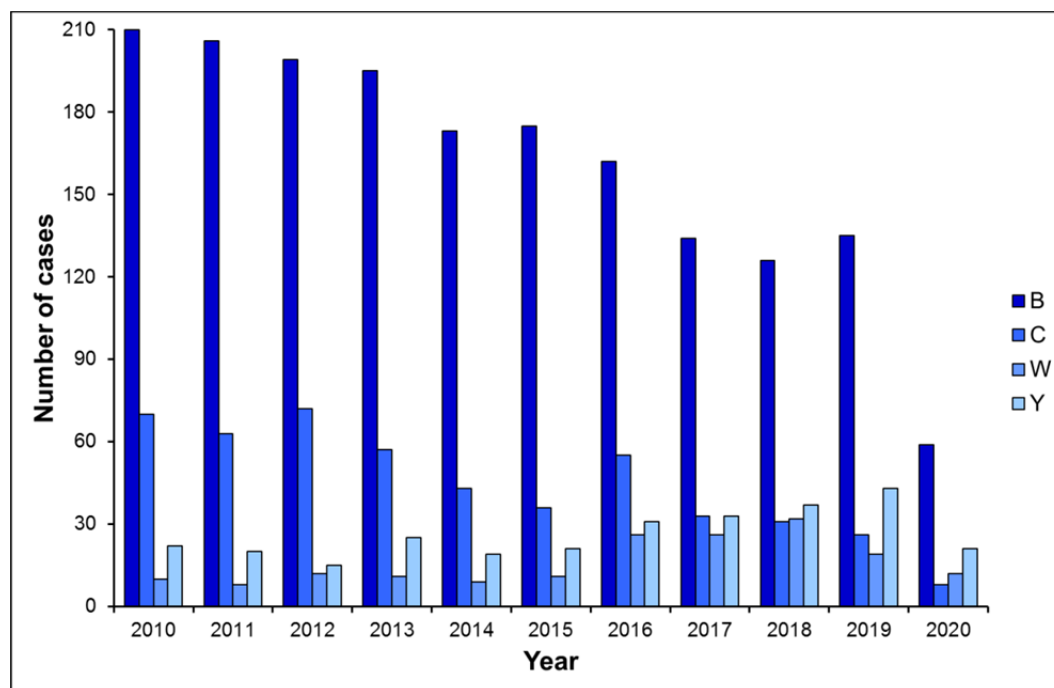
With the beginning of the first national lockdown in March 2020 the number of IMD cases processed at the NRZMHi decreased significantly in parallel to the notified cases at the RKI. Changes in mobility due to contact restrictions as well as the implementation of social distancing rules and the obligation to wear face masks obviously efficiently prevented the spread of meningococci and subsequently the occurrence of infections.

IMD cases according to age groups (2019 and 2020)



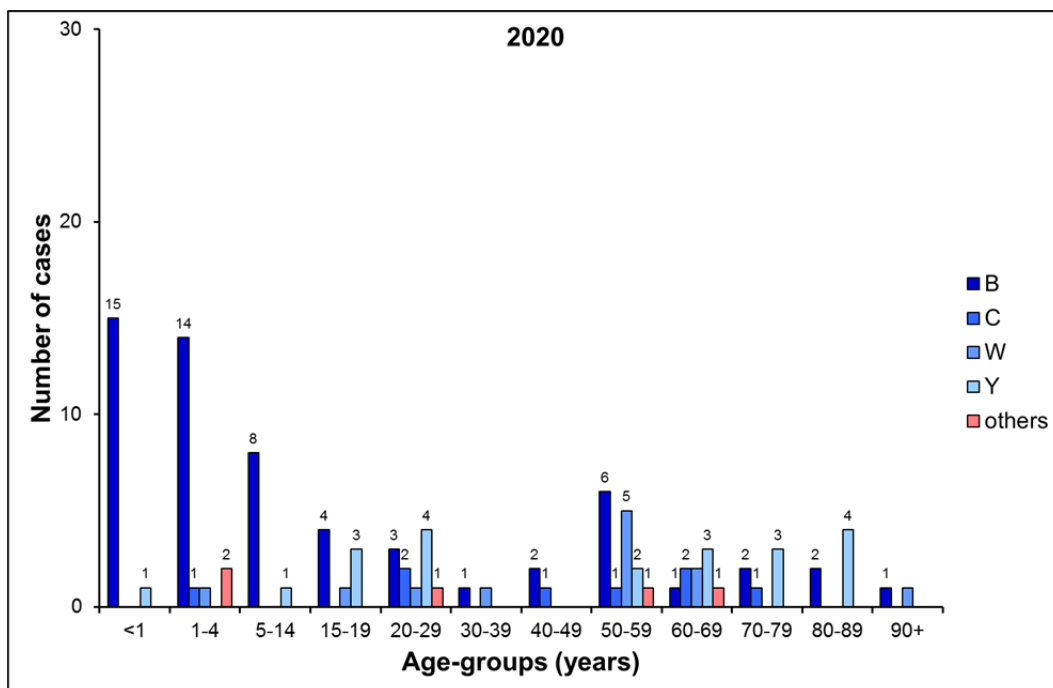
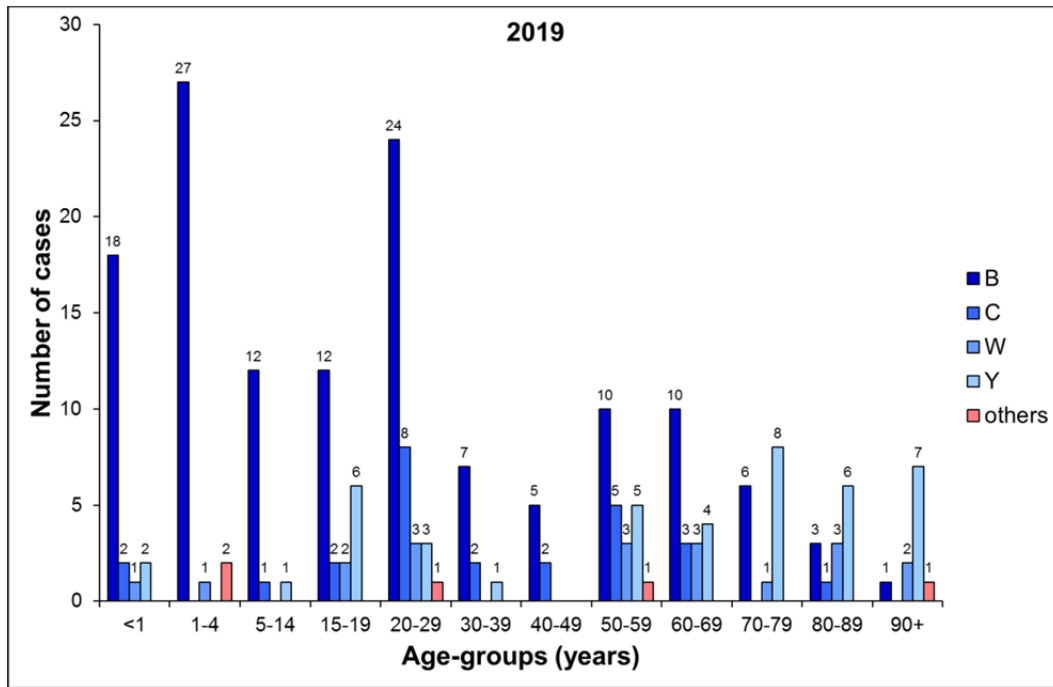
The number of IMD cases processed at the NRZMHi in 2020 decreased in all age-groups. The relatively smallest decline was observed in infants, whereas the largest decline was observed among 20 to 39 year olds.

Frequency of serogroups B, C, W and Y (2010-2020)



Most likely due to the COVID-19 infection control measures, significantly less isolates of all serogroups were submitted to the NRZMHi. The relative distribution of the four serogroups did not change in comparison to 2019.

Serogroups according to age groups (2019 and 2020)



As previously, most cases occurred in patients aged 20 years or above. The proportion of serogroup B disease in children aged less than one year was 2020 significantly higher than 2019.

Serogroups according to federal states (2020)

Serogruppe	BW	BY	BE	BB	HH	HE	MV	NI	NW	RP	SN	ST	SH	TH	unkn	abr
B	12	7	5	2	1	5	1	2	10		1	1	3	1	7	1
C	1	1				1			3	1					1	
E		1														
W	6	2	1			1			2							
Y	6	4		1				1	5	1	1	1			1	
NG	1	2							1							
IMD cases analysed at NRZMHi	26	17	6	3	1	7	1	3	21	2	2	2	3	1	9	1
incidence/100,000	0,25	0,19	0,27	0,20	0,22	0,14	0,06	0,14	0,16	0,10	0,02	0,14	0,14	0,1		

BW: Baden-Wuerttemberg, BY: Bavaria, BE: Berlin, BB: Brandenburg, HH: Hamburg, HE: Hesse, MV: Mecklenburg-Western Pomerania, NI: Lower Saxony, NW: North Rhine-Westphalia, RP: Rhineland-Palatinate, SN: Saxony, ST: Saxony-Anhalt, SH: Schleswig-Holstein, TH: Thuringia, abr: abroad.
No cases occurred in Bremen and Saarland.

For four invasive cases, the serogroup could not be determined (NG).

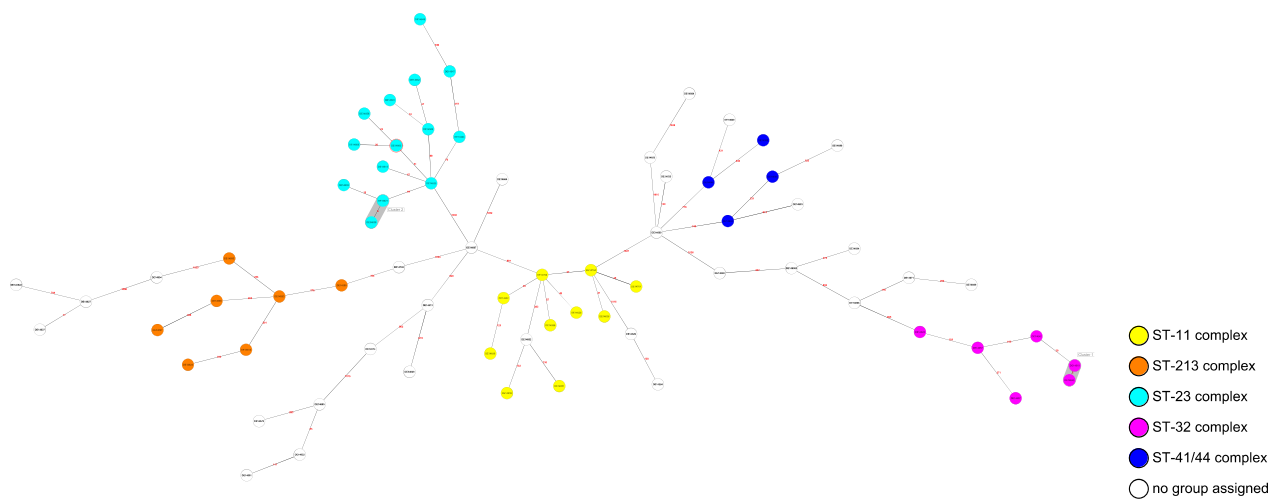
Most common finetypes (2020)

Feintype	No. of cases	% of cases
Y:P1.5-1,2-2:F5-8	13	13.5
W:P1.5,2:F1-1	9	9.4
B:P1.22,14:F5-5	7	7.3
B:P1.7,16:F3-3	3	3.1
C:P1.5,2:F3-3	3	3.1
B:P1.17,9:F1-7	2	2.1
B:P1.21,16:F4-1	2	2.1
B:P1.5-1,10-4:F1-2	2	2.1
B:P1.17-1,23:F1-5	2	2.1
B:P1.18-1,3:F1-5	2	2.1
B:P1.7-2,4:F5-9	2	2.1
W:P1.5-2,10-1:F5-8	2	2.1
Y:P1.5-1,10-1:F4-1	2	2.1

The three most frequent finetypes in 2020 were already among the six most frequent finetypes in 2019.

Meningococcal clusters based on whole genome sequencing

Whole genome sequencing was applied to 71 meningococcal isolates and sequence differences were analysed by core genome multi-locus sequence typing bases on 1248 genes.



Isolates high-lighted in different colours represent the most common clonal complexes according to multi-locus sequence typing.

A cluster is defined by no more than six differences between two isolates. Two clusters were detected in 2020 (shaded in grey).

Cluster	Allele differences	Date of sampling	Age-group (years)	county	Federal state	finetype	clonal complex
1	2	February 2020	15-19	Alb-Donau	BW	B:P1.7-2,30-4:F3-3	ST-32
		February 2020	5-14	Ravensburg	BW	B:P1.7-2,30-2:F3-3	ST-32
2	6	February 2020	0	Düsseldorf	NW	Y:P1.5-1,2-2:F5-8	ST-23
		February 2020	15-19	Cloppenburg	NI	Y:P1.5-1,2-2:F5-8	ST-23

The isolates of cluster 1 belonged to spatio-temporal linked cases, whereas a spatial linkage was lacking in cluster 2. Of note, both clusters occurred before the first lock-down.

Genome sequencing highlighted the abundant diversity of meningococcal isolates and an almost complete lack of signals for transmission between to cases of invasive disease.

Potential coverage of the meningococcal isolates from 2020 by the serogroup B vaccines Bexsero® und Trumenba®

Based on the Meningococcal Deduced Vaccine Antigen Reactivity (MenDeVAR) (Rodrigues et al. 2020)

Serogroup	Number of cases	Reactivity	Bexsero®		Trumenba®	
			Number of cases	% of cases	Number of cases	% of cases
B	38	exact match	12	31.6	4	10.5
		cross-reactivity	7	18.4	25	65.8
C	5	exact match	1	20		
		cross-reactivity	1	20	2	40
W	11	exact match				
		cross-reactivity	10	90.9	1	9.1
Y	16	exact match				
		cross-reactivity	1	6.25	14	87.5

Antigens of serogroup B vaccines are present in almost all meningococci, thus they are not serogroup-specific. However, the antigen sequences are highly variable and therefore, not all antigen variants are covered by the respective vaccines.

Among the German serogroup B (MenB) isolates, a higher proportion is covered by Trumenba®, whereas the proportion of covered MenC isolates is identical for both vaccines. The MenW isolates are predominantly covered by Bexsero® and the MenY isolates by Trumenba®.

An exact match is based on the presence of the vaccine antigens variant, whereas cross-reactivity is deduced from experimental data (Rodrigues et al. 2020, J. Clin. Microbiol. 59(1):e02161-20).

Antimicrobial susceptibility of invasive meningococcal isolates

(according to EUCAST breakpoints 2020)

Antibiotics	susceptible	intermediate	resistant
Penicillin	45	28 (36.8%)	3 (3.9%)
Cefotaxime	76		
Ciprofloxacin	76		
Rifampicin	76		

A trend to an increase of the proportion of penicillin intermediate susceptible isolates from 30.6% (95 % CI; 24.5–37.6) (2019) to 36.8% (95 % CI; 26.9–48.1) (2020) was seen, whereas the proportion of penicillin resistant isolates declined from 5.9% (95 % CI; 3.3–10.3) (2019) to 3.9% (95 % CI; 1.4–11.0) (2020).

Disclaimer

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