

Supplementary Online Content

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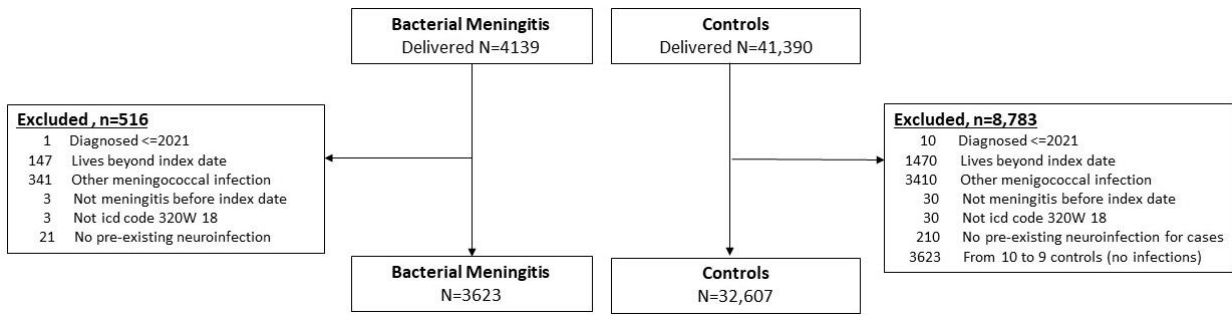
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This supplementary material has been provided by the authors to give readers additional information about their work.

eFigure 1. Flowchart (Sequential Exclusions)

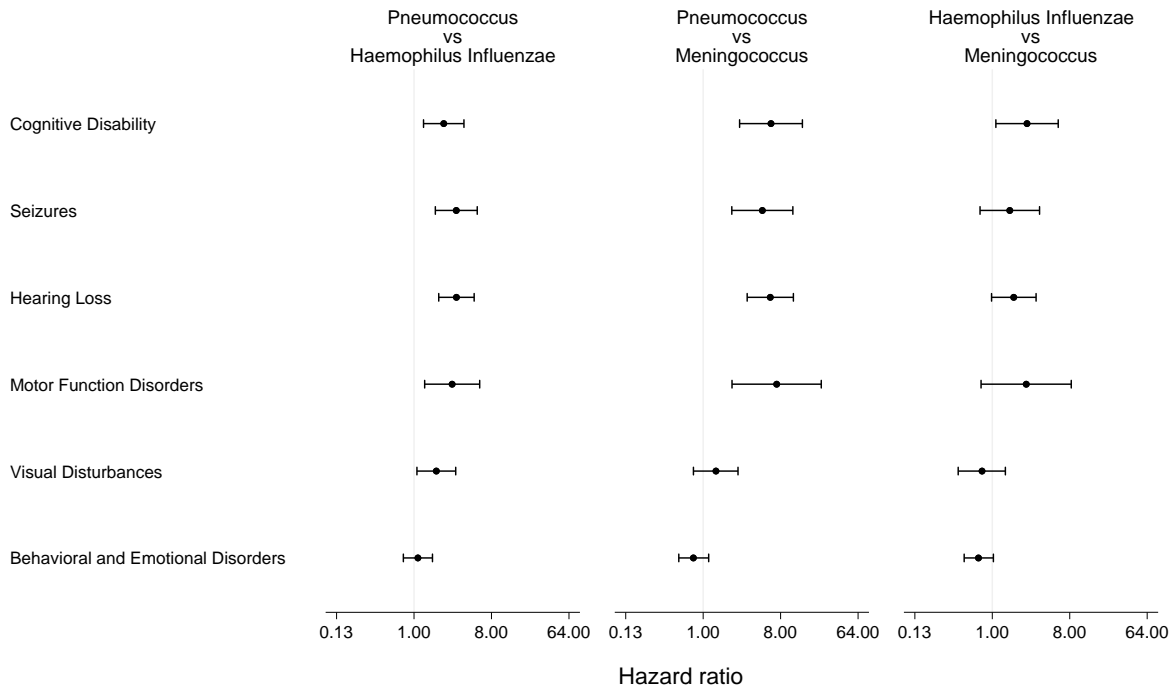


The original cohort delivered to the study team included 4149 cases with bacterial meningitis or meningococcal infection (ICD-9 codes 320 and 036; ICD-10 codes G00 and A39) and 10 matched general population controls. We made the following changes to the cohort:

- Dropped 1 case (and 10 associated controls) diagnosed in 2022 with no follow-up data.
- Dropped 147 cases (and 1470 associated controls) who died on the index date.
- Dropped 341 cases (and 3410 associated controls) with a meningococcal infection other than meningococcal meningitis.
- Dropped 3 cases (and 30 associated controls) who had bacterial meningitis before the index date.
- Dropped 3 cases (and 30 associated controls) with an invalid ICD-9 code “320W 18”.
- Dropped 21 cases (and 210 associated controls) with an infection of the central nervous system prior to the index date.
- Dropped 3623 controls (1 out of 10) including all controls with an infection of the central nervous system prior to the index date.

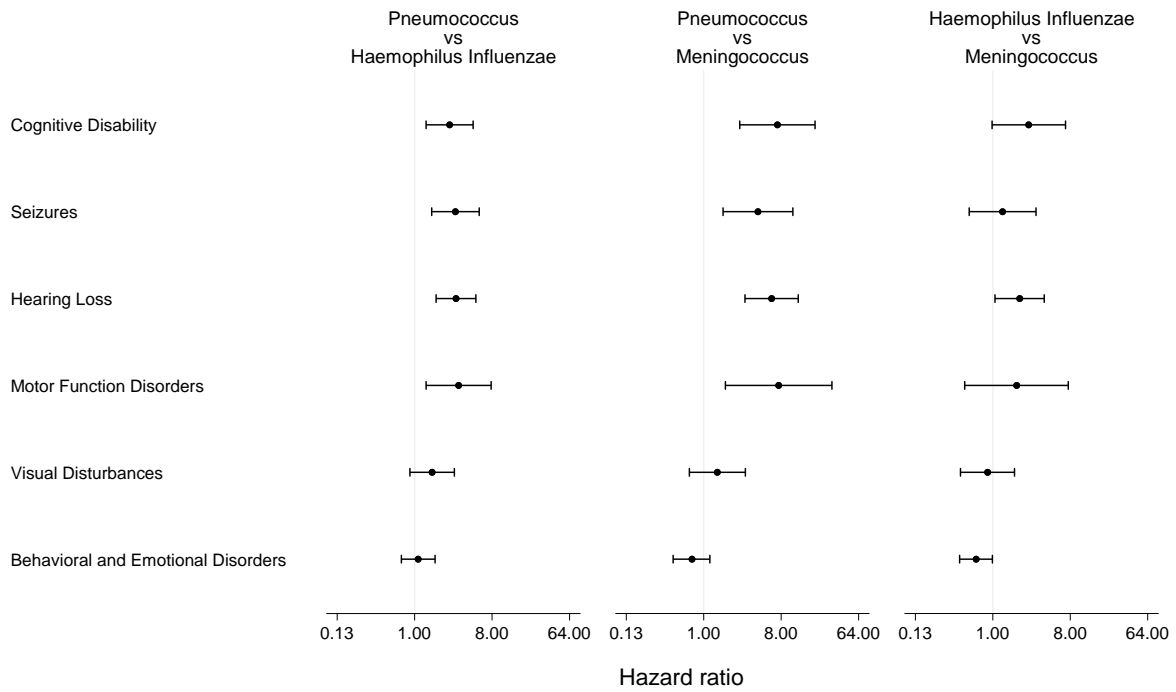
This gave us a final cohort with 3623 cases and 32,607 general population controls (9 controls per case).

eFigure 2. Differences in Risk of Disabilities by Type of Infection



This forest plot shows estimated interaction terms for pairwise differences in the risk of disabilities by bacterial pathogen (an interaction between exposure and type of infection). Reference type of infection is Haemophilus Influenzae (left column) and Meningococcus (middle and right columns). Covariates included in the Cox regression model are age at the index date, the index year, sex, education of mother, education of father, birth characteristics (5-minute Apgar score, birth weight, head circumference), and seven pre-existing conditions (malignancies, perinatal complications, mental and behavioral disorders, diseases of the nervous system, congenital disabilities, traumatic injuries, and operations in the nervous system).

eFigure 3. Differences in Risk of Disabilities by Type of Infection (Year of Diagnosis Before 2005)



This forest plot shows estimated interaction terms for pairwise differences in the risk of disabilities by bacterial pathogen (an interaction between exposure and type of infection) among cases and controls diagnosed before 2005. Reference type of infection is Haemophilus Influenzae (left column) and Meningococcus (middle and right columns). Covariates included in the Cox regression model are age at the index date, the index year, sex, education of mother, education of father, birth characteristics (5-minute Apgar score, birth weight, head circumference), and seven pre-existing conditions (malignancies, perinatal complications, mental and behavioral disorders, diseases of the nervous system, congenital disabilities, traumatic injuries, and operations in the nervous system).

eTable 1. ICD Codes for Preexisting Infections of the Central Nervous System

Description	ICD-10 Codes	ICD-9 Codes
Tuberculosis	A15-A19	010-018
Listeriosis	A32	027
Viral Central Nervous System Infections	A80-A89	046-049, 061-066, 071, 078.8, 079.9, 323
Herpesviral Infections, Varicella, Zoster	B00.3, B00.4, B01.0, B01.1, B02.0, B02.1	052.0, 052.1, 053.0, 053.1, 054.3, 054.7
HIV	B20-B24	042-044, 279
Malaria with Cerebral Complications	B50	084
Neurocysticercosis	B69.0	123.1
Late Complications due to Severe Infections	B90-B94	137-139

eTable 2. ICD Codes for Disabilities

Disability	Description	ICD-10 Codes	ICD-9 Codes
Cognitive Disabilities	Mild cognitive disorder, intellectual disabilities, disorders of speech and language, disorders of scholastic skills	F06.7, F70-F79, F80.0, F81.0, F81.2, F81.8, F81.9	315.A, 315.B, 315.D, 315.W, 315.X, 317-319
Seizures	Epilepsy and recurrent seizures	G40	345
Hearing Loss	Conductive and sensorineural hearing loss, adjustment of implanted device for special senses, presence of otological and audiological implants, presence of external hearing aid	H90.3-H90.5, H90.7	389.B-389.C
Motor Function Disorders	Disorders of motor function, dystonia, other extrapyramidal and movement disorders, cerebral palsy, abnormalities of gait and mobility, ataxia, dependent on wheelchair	F82, G24.9, G25.3, G25.5, G25.9, G80, G81.1, G82.1, G83.0-G83.3, R26-R27	315.E, 333.C, 333.F, 333.W, 333.X, 342.B, 343, 344.A-344.F, 781.C-781.D
Visual Disturbances	Disorders of optic nerve and visual pathways, disorders of ocular muscles, binocular movement, accommodation and refraction, visual disturbances and blindness, adjustment of implanted device for special senses, presence of intraocular lens	H47, H49-H51, H53.0, H53.2, H53.4, H54.4-H54.7	368.A, 368.C, 368.E, 369.G-369.H, 369.W, 377-378
Behavioral and Emotional Disorders	Behavioral and emotional disorders with onset in childhood and adolescence	F90-F98	307, 309, 312-314
Intracranial Structural Injuries	Hydrocephalus, mechanical complications of ventricular intracranial shunt	G91.1-G91.2, T85.0	331.E, 996.C

eTable 3. ICD Codes for Preexisting Conditions

Pre-existing Condition	Description	ICD-10 Codes	ICD-9 Codes
Malignancies and Tumors	Malignant tumors	C00-C97	140-208
	Benign tumors central nervous system	D32-D33	225
	Unknown tumors central nervous system	D42-D43	237, 239.6-239.7
Perinatal Complications		P00-P96	760-779
Mental and Behavioral Disorders		F00-F99	290-319
Diseases of the Nervous System		G00-G99	320-389
Congenital Disabilities		Q00-Q99	740-759
Traumatic Injuries	Cranial nerves	S04, T90.3	907, 950-951
	Intracranial injuries	S06, T90.5	850-854, 907
	Spinal cord injuries	S14.0-S14.1, S24.0-S24.1, S34.0-S34.1, T91.3	907, 952

eTable 4. Medical Procedure Codes for Operations in the Nervous System

Medical Procedure	Classification of Care (KVÅ)	Classification of Care (KOP)
Operations in the Nervous System	AA-AW	0100-0699

eTable 5. ICD Codes for Types of Infection

Bacterial Pathogen	ICD-9	ICD-10
Haemophilus Meningitis	320A	G00.0
Pneumococcal Meningitis	320B	G00.1
Meningococcal Meningitis	036A	A390
Streptococcal Meningitis	320C	G00.2
Staphylococcal Meningitis	320D	G00.3
Other Bacterial Meningitis	320H, 320W	G00.8, G00.8A, G00.8B, G00.8W
Bacterial Meningitis, Unspecified	320, 320X	G00.9

eTable 6. Follow-Up Time

Disability	Bacterial Meningitis Median (p25-p75) years	Controls Median (p25-p75) years
Cognitive Disability	23.8 (11.7-30.5)	24.5 (13.2-30.6)
Seizures	23.8 (11.2-30.5)	24.5 (13.2-30.6)
Hearing Loss	23.1 (10.9-30.3)	24.5 (13.3-30.6)
Motor Function Disorders	24.1 (11.3-30.6)	24.6 (13.3-30.6)
Visual Disturbances	23.8 (11.0-30.5)	24.4 (13.0-30.6)
Behavioral and Emotional Disorders	23.3 (11.1-30.4)	23.8 (12.4-30.4)
Intracranial Structural Injuries	24.3 (12.1-30.6)	24.7 (13.4-30.7)

eTable 7. Unadjusted Cumulative Incidence of Disabilities at 15 and 30 Years of Follow-Up

Disability	Bacterial Meningitis	Controls	Bacterial Meningitis	Controls
	15 years	15 years	30 years	30 years
<u>Full Cohort</u>				
Cognitive Disability	5.91	1.14	8.01	1.99
Seizures	6.59	0.90	8.00	1.62
Hearing Loss	7.43	0.76	10.0	1.40
Motor Function Disorders	5.84	0.69	6.42	0.95
Visual Disturbances	7.68	2.00	9.12	3.15
Behavioral and Emotional disorders	8.21	5.05	13.7	9.61
Intracranial Structural Injuries	3.33	0.06	3.66	0.08
<u>No Pre-existing Conditions</u>				
Cognitive Disability	3.68	0.80	5.21	1.55
Seizures	4.18	0.67	5.53	1.32
Hearing Loss	6.56	0.62	9.03	1.22
Motor Function Disorders	3.41	0.49	3.70	0.69
Visual Disturbances	4.79	1.66	5.76	2.75
Behavioral and Emotional disorders	6.82	4.39	12.1	8.94
Intracranial Structural Injuries	1.42	0.02	1.54	0.03

eTable 8. Adjusted Hazard Ratios With No Preexisting Conditions and in Alternative Matched Cohort

Disability	Matched Cohort^a HR (95% CI)	No Pre-existing Conditions^a HR (95% CI)	Alternative Matched Cohort^a HR (95% CI)
	(# cases = 3623)	(# cases = 2711)	(# cases = 3228)
Cognitive Disability	3.23 (2.71-3.85)	3.63 (2.94-4.49)	4.24 (2.96-6.09)
Seizures	4.14 (3.46-4.96)	4.76 (3.85-5.87)	4.69 (3.29-6.70)
Hearing Loss	7.90 (6.68-9.33)	8.82 (7.32-10.6)	9.00 (6.16-13.1)
Motor Function Disorders	4.65 (3.72-5.80)	5.68 (4.37-7.38)	7.04 (4.28-11.6)
Visual Disturbances	2.37 (2.04-2.74)	2.33 (1.94-2.81)	2.90 (2.18-3.85)
Behavioral and Emotional Disorders	1.42 (1.26-1.59)	1.45 (1.27-1.65)	1.41 (1.18-1.67)
Intracranial Structural Injuries	26.0 (15.5-43.7)	50.1 (21.4-117)	17.4 (5.30-57.1)

^a This table shows the estimated adjusted hazard ratios for seven disabilities. The left column displays the results in the matched cohort, the middle column removes cases and controls with any pre-existing condition (see eTable3 and eTable4 for codes), and the right column shows results for the alternative matched cohort. Covariates included in the Cox regression model are age at the index date, the index year, sex, education of mother, education of father, birth characteristics (5-minute Apgar score, birth weight, head circumference), and seven pre-existing conditions (malignancies, perinatal complications, mental and behavioral disorders, diseases of the nervous system, congenital disabilities, traumatic injuries, and operations in the nervous system).

eTable 9. Participant Characteristics Alternative Matched Cohort

Characteristic	Bacterial Meningitis (n=3228) Cases, No., %	Controls (n=3228) Controls, No., %
Female	1444 (44.7)	1445 (44.8)
<u>Age at Diagnosis of Bacterial Meningitis</u>		
Age (years), Mean (SD)	3.9 (5.0)	4.1 (5.1)
Age (years), Median (p25-p75)	1.4 (0.4-5.6)	1.5 (0.5-5.9)
Age 0 Years	1308 (40.5)	1220 (37.8)
Age 1 Years	561 (17.4)	586 (18.2)
Age 2-4 Years	494 (15.3)	530 (16.4)
Age 5-17 Years	865 (26.8)	892 (27.6)
<u>Education of Mother</u>		
Primary School	373 (11.6)	360 (11.2)
High School	1469 (45.5)	1494 (46.3)
University	1367 (42.3)	1355 (42.0)
Education Missing	19 (0.6)	19 (0.6)
<u>Education of Father</u>		
Primary School	548 (17.0)	566 (17.5)
High School	1572 (48.7)	1585 (49.1)
University	1056 (32.7)	1015 (31.4)
Education Missing	52 (1.6)	62 (1.9)
<u>Birth Characteristics</u>		
Apgar 5 Min, Mean (SD)	9.7 (0.8)	9.7 (0.9)
Birth Weight (g), Mean (SD)	3485 (636)	3496 (609)
Head Circumference (cm), Mean (SD)	34.6 (1.9)	34.7 (1.7)
<u>Pre-existing Conditions</u>		
Malignancies	1 (0.0)	1 (0.0)
Perinatal Complications	264 (8.2)	264 (8.2)
Mental and Behavioral Disorders	21 (0.7)	21 (0.7)
Diseases of the Nervous System	104 (3.2)	104 (3.2)
Congenital Disabilities	106 (3.3)	106 (3.3)
Traumatic Injuries	31 (1.0)	31 (1.0)
Operation in Nervous System	153 (4.7)	153 (4.7)

eTable 10. Frequency of Infections by Type of Bacterial Pathogen

Bacterial Pathogen	Frequency	Percent (%)
Haemophilus Meningitis	888	24.5
Pneumococcal Meningitis	571	15.8
Meningococcal Meningitis	497	13.7
Streptococcal Meningitis	317	8.7
Staphylococcal Meningitis	106	2.9
Other bacterial Meningitis	448	12.4
Bacterial Meningitis, Unspecified	796	22.0
Total	3623	100.0

eTable 11. Year of Diagnosis by Type of Bacterial Pathogen

Bacterial Pathogen	Median	IQR (p25-p75)	Min	Max
Haemophilus Meningitis	1990	1988-1992	1987	2021
Pneumococcal Meningitis	2000	1993-2007	1987	2021
Meningococcal Meningitis	1997	1991-2005	1987	2021
Streptococcal Meningitis	2007	1997-2014	1987	2021
Staphylococcal Meningitis	2004.5	1994-2014	1987	2020
Other bacterial Meningitis	1996	1992-2011	1987	2021
Bacterial Meningitis, Unspecified	2000	1993-2009	1987	2021

eTable 12. P Values for Pairwise Comparison of Adjusted Hazard Ratios by Type of Infection

Disability	Pneumococcus vs Haemophilus Influenzae^a	Pneumococcus vs Meningococcus^a	Haemophilus Influenzae vs Meningococcus^a
Cognitive Disability	0.004	<.001	0.03
Seizures	<.001	<.001	0.25
Hearing Loss	<.001	<.001	0.06
Motor Function Disorders	0.007	0.001	0.14
Visual Disturbances	0.02	0.26	0.39
Behavioral and Emotional Disorders	0.60	0.22	0.07

^a This table shows p-values for interaction terms between bacterial meningitis and type of infection in estimated Cox regression model used to test for pairwise differences in the relative risk of disabilities between types of infections. Covariates included in the Cox regression model are age at the index date, the index year, sex, education of mother, education of father, birth characteristics (5-minute Apgar score, birth weight, head circumference), and seven pre-existing conditions (malignancies, perinatal complications, mental and behavioral disorders, diseases of the nervous system, congenital disabilities, traumatic injuries, and operations in the nervous system).

eTable 13. Adjusted Hazard Ratios for Disabilities by Age at Diagnosis

Disability	Age Below Median^a HR (95% CI)	Age Above Median^a HR (95% CI)	P-value (Difference = 0)
Cognitive Disability	4.67 (3.77-5.78)	1.73 (1.29-2.32)	<.001
Seizures	5.43 (4.32-6.83)	2.87 (2.15-3.83)	0.004
Hearing Loss	8.42 (6.68-10.6)	7.39 (5.77-9.45)	0.29
Motor Function Disorders	5.91 (4.58-7.63)	2.88 (1.90-4.36)	0.06
Visual Disturbances	2.37 (1.97-2.85)	2.28 (1.78-2.92)	0.81
Behavioral and Emotional Disorders	1.67 (1.45-1.93)	1.11 (0.91-1.35)	0.002
Intracranial Structural Injuries	54.8 (25.0-120)	9.79 (4.53-21.2)	0.003

^a This table shows the estimated adjusted hazard ratios for seven disabilities by age at diagnosis (above or below median age conditional on cause of bacterial meningitis [ICD codes in eTable 5]), adjusting for age at the index date, the index year, sex, education of mother, education of father, birth characteristics (5-minute Apgar score, birth weight, head circumference), and seven pre-existing conditions (malignancies, perinatal complications, mental and behavioral disorders, diseases of the nervous system, congenital disabilities, traumatic injuries, and operations in the nervous system). The right column displays p-values for an interaction term between bacterial meningitis and age at diagnosis used to test for differences between children diagnosed when young or old (a difference between the estimated coefficients in the two columns labelled age below median and age above median).

eTable 14. Median Follow-Up Time for Cases and Controls by Age at Diagnosis

Disability	Age Below Median Years	Age Above Median Years
Cognitive Disability	23.6	24.9
Seizures	23.7	24.9
Hearing Loss	23.7	24.9
Motor Function Disorders	23.8	25.0
Visual Disturbances	23.5	24.9
Behavioral and Emotional Disorders	22.8	24.5
Intracranial Structural Injuries	24.0	25.0

eTable 15. Number of Disabilities

Number of Disabilities	Bacterial Meningitis (n=3623) No., %	Controls (n=32,607) No., %
Mean (SD)	0.49 (0.96)	0.14 (0.42)
0 disabilities	2571 (71.0)	28,672 (87.9)
1 disability	654 (18.1)	3379 (10.4)
2 disabilities	207 (5.7)	446 (1.4)
3 disabilities	100 (2.8)	88 (0.3)
4 disabilities	59 (1.6)	17 (0.1)
5 disabilities	26 (0.7)	5 (0.0)
6 disabilities	4 (0.1)	0 (0.0)
7 disabilities	2 (0.1)	0 (0.0)