



## Original Contribution

# Long-Term Mortality in Patients Diagnosed With Pneumococcal Meningitis: A Danish Nationwide Cohort Study

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The objective of the study was to determine the long-term mortality and the causes of death in patients diagnosed with pneumococcal meningitis. The authors performed a nationwide, population-based cohort study including all Danish patients diagnosed with pneumococcal meningitis from 1977 through 2006 and alive 1 year after diagnosis. Data were retrieved from medical databases in Denmark. The absolute and relative risks of all-cause and cause-specific death were analyzed by using Kaplan-Meier survival curves, Poisson regression analysis, Cox regression analysis, and cumulative incidence functions. The authors identified 2,131 pneumococcal meningitis patients and an age- and gender-matched, population-based cohort of 8,524 individuals. Compared with the background population, the pneumococcal meningitis patients had an increased long-term mortality varying from an 8-fold increased mortality in the age category 0–<20 years to a 1.5-fold increased mortality in those aged 60–<80 years. The increased risk of death stemmed from neoplasms, liver diseases, and nervous system diseases. The excess mortality due to neoplasms stemmed mainly from a 5-fold increased risk of death due to hematologic neoplasms. To improve survival in patients surviving the acute phase of pneumococcal meningitis, physicians should meticulously screen this patient population for neurologic sequelae and comorbidity predisposing to the disease.

cause of death; cohort studies; meningitis, pneumococcal; mortality; multiple myeloma

Abbreviations: CI, confidence interval; ICD, *International Classification of Diseases*.

*Streptococcus pneumoniae* and *Neisseria meningitidis* are the main infectious agents causing bacterial meningitis in Western countries (1). Currently, almost half of the cases of community-acquired bacterial meningitis in Denmark are caused by *S. pneumoniae* (2). The main risk factors for pneumococcal meningitis are age (<2 years and >65 years), immunodeficiencies, chronic illnesses, neoplasms, smoking, and alcohol abuse (3–5). Despite antibiotic therapy, adjunctive dexamethasone treatment, and modern intensive care facilities, the case fatality rate of acute pneumococcal meningitis in adults remains high (14%–30%) (6–9), and several studies have reported high rates of neurologic sequelae in adult survivors (30%–41%) (8, 9).

The long-term mortality in patients surviving pneumococcal meningitis is poorly documented and described in only 1 previous study (10). In this study that included 162 pneumo-

coccal meningitis patients, an increased risk of death during the first 4 years following diagnosis of bacterial meningitis was found, whereas the risk of death declined to that of the background population from the fifth year of discharge.

We performed a nationwide cohort study to determine whether patients surviving the first year after pneumococcal meningitis have increased mortality compared with an age- and gender-matched population control cohort and if these patients were at increased risk of any specific causes of death.

## MATERIALS AND METHODS

### Setting

The population of Denmark on January 1, 2008, was 5.5 million inhabitants (11). In 2007, the incidence rate of

**Table 1.** Characteristics of Pneumococcal Meningitis Patients and Population Controls, Denmark, 1977–2006

	Patients <sup>a</sup>			Population Controls <sup>a</sup>			P Value
	No.	%	Median (Interquartile Range)	No.	%	Median (Interquartile Range)	
Study participants	2,131			8,524			
Males	1,140	53.5		4,560	53.5		
Age, years, at diagnosis of pneumococcal meningitis <sup>b</sup>			44.3 (2.8–62.8)			44.3 (2.8–62.8)	
Age at diagnosis of pneumococcal meningitis <sup>b</sup>							
0–<20 years	717	35.6		3,028	35.6		
20–<40 years	233	10.9		932	10.9		
40–<60 years	508	23.8		2,032	23.8		
60–<80 years	561	26.3		2,244	26.3		
≥80 years	72	3.3		288	3.3		
Calendar period at diagnosis of pneumococcal meningitis <sup>b</sup>							
1977–1986	641	30.1		2,564	30.1		
1987–1996	737	34.6		2,948	34.6		
1997–2006	753	35.3		3,012	35.3		
Observation time, years	24,563			105,620			
Emigration during study period	16	0.8		112	1.3		
Lost to follow-up during study period	1			2			
Study subjects with inpatient admission in the period 2 years prior to the date of pneumococcal meningitis diagnosis <sup>b</sup>	916	43.0		3,086	36.2		<0.001
Patients admitted with the following diagnostic categories in the period 2 years prior to the date of pneumococcal meningitis diagnosis							
Infectious diseases	39	1.8		80	0.9		<0.001
Neoplasms <sup>c</sup>	137	6.4		326	3.8		<0.001
Blood/immune diseases	22	1.0		16	0.2		<0.001
Endocrine diseases	28	1.3		68	0.8		0.024

Table continues

pneumococcal meningitis in Denmark was 1.9/100,000 (12). Throughout the study period, tax-paid health care has been provided and free of charge to all Danish citizens.

#### Data sources

We used the unique 10-digit Central Person Registration number assigned to all Danish citizens at birth or immigration to avoid multiple registrations and to track individuals in the following registers.

The Danish National Hospital Register was initiated in 1977 and contains information on all patients discharged from Danish nonpsychiatric hospitals. The records for each inpatient admission include the Central Person Registration number, hospital department, dates of admission, and dis-

charge diagnosis as coded by the attending physician according to the *International Classification of Diseases* (ICD), Eighth Revision, until the end of 1993 and the ICD, Tenth Revision, thereafter. Discharge diagnoses are classified as 1 primary and up to 19 secondary discharge diagnoses (13). From this register, we extracted the date of pneumococcal meningitis diagnosis, along with data on inpatient admissions prior to the diagnosis of pneumococcal meningitis.

The Danish Civil Registration System is a national register established in 1967 that contains the demographic data and vital status of all Danish citizens (14). From this register, we extracted data on birth, gender, date of immigration and emigration, loss to follow-up, and date of death.

Table 1. Continued

	Patients <sup>a</sup>			Population Controls <sup>a</sup>			P Value
	No.	%	Median (Interquartile Range)	No.	%	Median (Interquartile Range)	
Mental disease/drug abuse	6	0.3		28	0.3		0.73
Nervous system diseases	32	1.5		39	0.5		<0.001
Diseases of the sensory organs	44	2.1		66	0.8		<0.001
Cardiovascular diseases	62	2.9		230	2.7		0.59
Respiratory diseases	82	3.8		178	2.1		<0.001
Digestive system diseases	70	3.3		197	2.3		0.01
Skin diseases	11	0.5		32	0.4		0.36
Rheumatologic diseases	53	2.5		124	1.5		0.001
Genitourinary diseases	34	1.6		142	1.7		0.82
Neonatal and congenital diseases	59	2.8		143	1.7		0.001
Pregnancy-related diseases	22	1.0		77	0.9		0.58
Injury, poisoning, and external causes of morbidity	98	4.6		212	2.5		<0.001
Abnormal findings not classified otherwise	63	3.0		165	1.9		0.004
Contacts with health services not classified above	484	22.7		1,928	22.6		0.93

<sup>a</sup> If not stated otherwise, data are the number and percentage of pneumococcal meningitis patients or population controls.

<sup>b</sup> For population controls at the matching date (date of meningitis diagnosis in the corresponding pneumococcal meningitis patient).

<sup>c</sup> Admitted with a cancer diagnosis prior to the pneumococcal meningitis diagnosis.

The Danish Register of Causes of Death contains information from all Danish death certificates since 1943, and registration is currently complete through 2006. Causes of death are coded according to the Danish version of the ICD, Eighth Revision, from 1972 until the end of 1993 and the ICD, Tenth Revision, from 1994 through 2006. The causes of death are registered by the attending physician on the death certificate as primary (immediate cause of death), secondary, or tertiary and an underlying cause of death (15). From this register, we extracted the specific causes of death as recorded as the underlying cause of death.

The Danish Cancer Register is a population-based register and contains information on incident cancers diagnosed in Danish citizens since 1943 (16, 17). The cases of cancer are coded according to the ICD, Seventh Revision, for all years and according to the *International Classification of Diseases for Oncology* from 1978.

### Study population

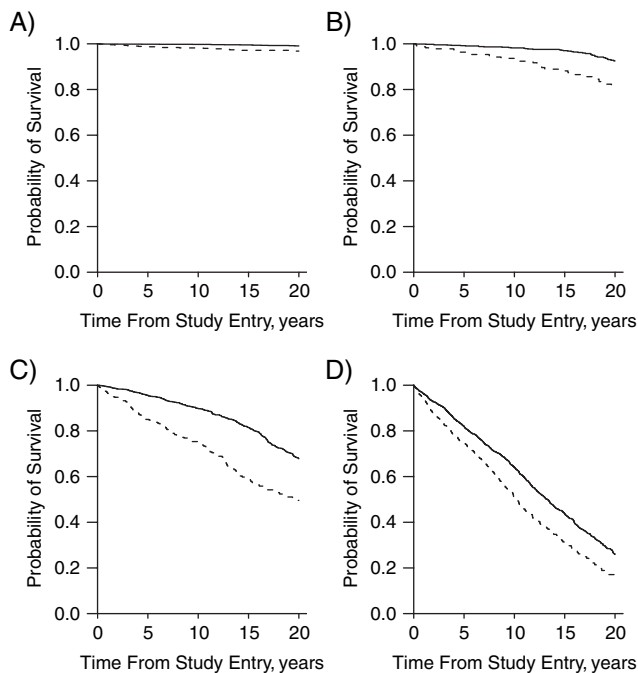
**Pneumococcal meningitis patients.** From the Danish National Hospital Register, we identified all patients who were registered during the period from January 1, 1977, to December 31, 2006, for the first time with a primary or secondary diagnosis of pneumococcal meningitis (ICD, Eighth

Revision, code 320.19 or ICD, Tenth Revision, code G00.1). Patients were excluded when they died, emigrated, or were lost to follow-up within the first year after the diagnosis of pneumococcal meningitis and when they were diagnosed with other infections of the central nervous system (as specified in Web Appendix 1) prior to pneumococcal meningitis, did not live in Denmark at the date of the pneumococcal meningitis diagnosis, or were born outside Denmark. (Web Appendix information is supplementary to the text and can be found on the *Journal's* website (<http://aje.oxfordjournals.org/>)). The index date of these individuals was defined as 1 year after the date of first pneumococcal meningitis diagnosis.

**Population control cohort.** From the Danish Civil Registration System, we identified 4 population controls for each pneumococcal meningitis patient matched on gender and date of birth, who were born in Denmark, alive, and living in Denmark at the index date of the corresponding pneumococcal meningitis patient.

### Outcome

The primary study outcome was time from the index date to death. The secondary outcome was time from the index date to the date of specific underlying cause of death as registered in the Danish Register of Causes of Death. The



**Figure 1.** Kaplan-Meier survival curves of patients with pneumococcal meningitis (dashed line) and population controls (solid line), Denmark, 1977–2006. Age at diagnosis: 0–<20 years (A), 20–<40 years (B), 40–<60 years (C), and 60–<80 years (D).

specific underlying causes of death were categorized by ICD codes as listed in Web Appendix 2.

### Statistical analysis

Time was calculated from the index date to the date of death, emigration, loss to follow-up, or January 1, 2008, whichever came first. In the analyses of cause-specific mortality, time was censored at January 1, 2007, as the Danish Register of Causes of Death was complete only through 2006. Kaplan-Meier analyses were used to construct survival curves. Poisson regression analysis was used to estimate mortality rate ratios in categories defined by age (0–<20, 20–<40, 40–<60, 60–<80, and 80 years of age or older) and follow-up time (in 10-year intervals). As the mortality rate ratio estimates for the follow-up times 10–<20 and 20–<30 years after the index date were not substantially different, we report only 1 follow-up estimate for the 10–<30 year period. The estimates were adjusted for calendar periods (introduced as design variables grouped in the 3 time periods 1977–1986, 1987–1996, and 1997–2006), days of inpatient admissions (number of inpatient admissions in the 2 years prior to pneumococcal meningitis diagnosis, continuous variable), diagnosis other than cancer registered in the Danish National Hospital Register in the 2 years prior to the date of pneumococcal meningitis diagnosis (grouped in 18 ICD categories as listed in Web Appendix 3 and introduced as design variables), and previous diagnosis of cancer (any cancer diagnosis vs. no previous diagnosis of cancer). We computed the

cumulative incidence of specific causes of death, taking into account that these were competing risks (18). Cox regression analysis was used to calculate mortality rate ratios for specific causes of death adjusted for calendar periods, inpatient admission prior to diagnosis of pneumococcal meningitis, and previous cancer diagnoses as described above. Schoenfeld plots confirmed that the proportional hazard assumptions were fulfilled.

We repeated the Poisson regression analyses restricting the study sample to patients (and corresponding population controls) with pneumococcal meningitis as the primary diagnosis. We also repeated the Poisson regression analyses in a study sample excluding patients who had been admitted to a nonpsychiatric hospital within a period of 2 years prior to the date of pneumococcal meningitis diagnosis or were diagnosed with cancer at any time prior to pneumococcal meningitis diagnosis. These analyses were further adjusted for gender and age at diagnosis.

The study was approved by the Danish Data Protection Agency. SPSS, version 15.0, software (SPSS, Inc., Chicago, Illinois), STATA, version 8.0, software (Stata Corporation, College Station, Texas), and R software, version 2.8.1, were used for data analysis.

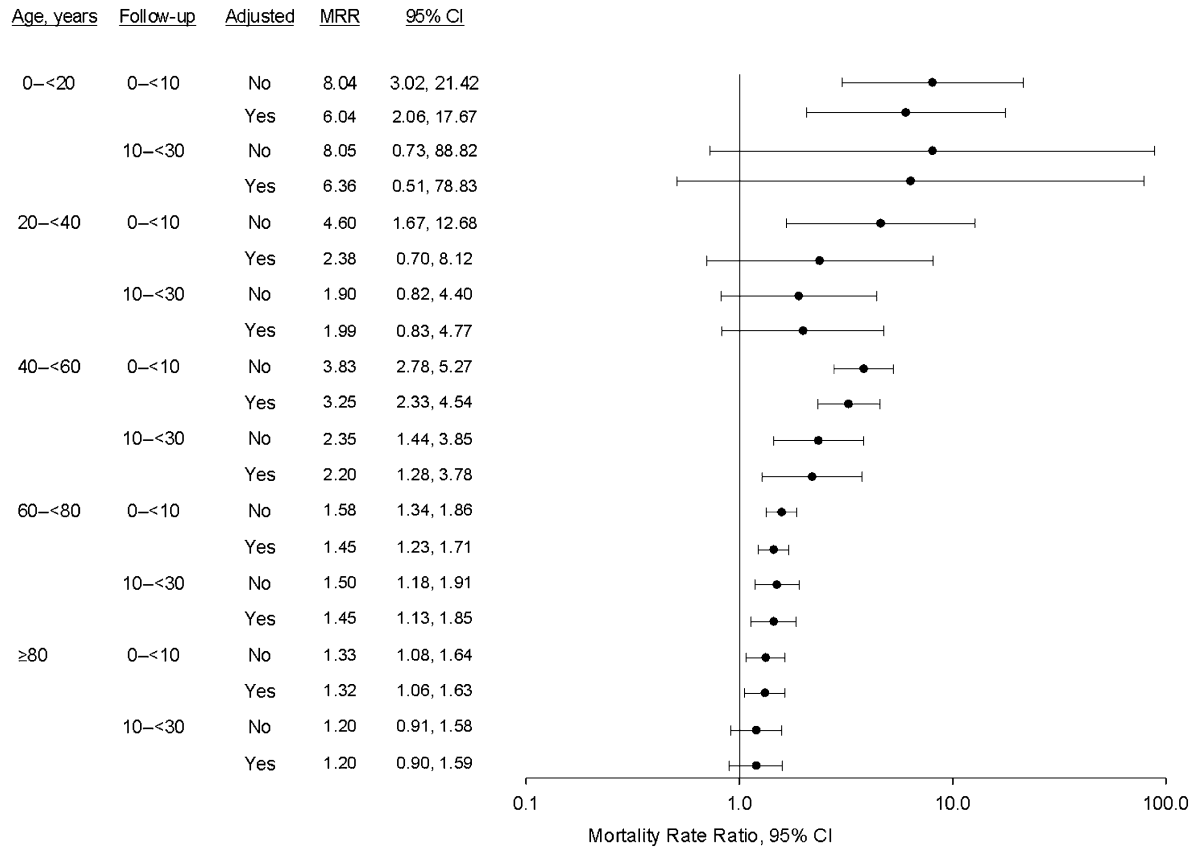
## RESULTS

### Characteristics of the study population

We identified 2,848 patients diagnosed with pneumococcal meningitis in the period 1977–2006. Within the first year of diagnosis of pneumococcal meningitis, 716 (25.1%) patients died, 1 emigrated, and none was lost to follow-up, leaving a total of 2,131 patients (1,976 patients (92.7%) with a primary diagnosis and 155 patients (7.3%) with a secondary diagnosis of pneumococcal meningitis) and 8,524 population controls in the study (Table 1). The median age of patients included in the study at diagnosis of pneumococcal meningitis was 44.3 years (interquartile range, 2.8–62.8 years), and 53.5% were males; 30.1% of the patients had pneumococcal meningitis in the period 1977–1986, 34.6% from 1987–1996, and 35.3% from 1997–2006. More pneumococcal meningitis patients than population controls had been admitted to a hospital in the period of 2 years prior to the date of pneumococcal meningitis diagnosis (43.0% vs. 36.2%). During the same period, pneumococcal meningitis patients were diagnosed with the majority of the diagnosis categories more frequently than population controls (Table 1).

### All-cause mortality

A total of 584 (27.4%) pneumococcal meningitis patients and 1,739 (20.4%) population controls died in the observation period. Figure 1 presents Kaplan-Meier survival curves for pneumococcal meningitis patients and corresponding population controls in 20-year age intervals. Pneumococcal meningitis patients were at increased risk of death throughout the study period. We saw no major change in the mortality rate ratio between genders in the subanalysis including only patients with pneumococcal meningitis registered as



**Figure 2.** Unadjusted and adjusted mortality rate ratios for patients with pneumococcal meningitis compared with population controls, Denmark, 1977–2006. Adjusted for inpatient admission prior to pneumococcal meningitis. CI, confidence interval; MRR, mortality rate ratio.

the primary diagnosis or in the subanalysis in which individuals were excluded if they had either been hospitalized in the 2-year period prior to meningitis diagnosis, or were diagnosed with cancer prior to the meningitis episode (data not shown). The impact of pneumococcal meningitis on the relative risk of death was highest in the youngest age categories with a more than 8-fold increased long-term mortality in the age category 0–<20 years (Figure 2). The absolute increase in mortality was highest in those diagnosed with pneumococcal meningitis after 20 years of age (Figure 1).

**Cause-specific mortality**

Pneumococcal meningitis was associated with an increased risk of death due to neoplasms, digestive system diseases, and nervous system diseases (Table 2; Figure 3).

The risks of death due to neoplasms of the oropharynx and hematologic neoplasms were more than 3 and 5 times higher, respectively, in the pneumococcal meningitis patients (Table 2).

The risks of death due to multiple myeloma and chronic lymphatic leukemia were especially increased in the patients with pneumococcal meningitis. The 10-year risk of death due to multiple myeloma was 2.9% (95% confidence interval (CI): 1.4, 5.3) in patients diagnosed with

pneumococcal meningitis after the age of 50 years compared with 0.1% (95% CI: 0.0, 0.2) in population controls (Figure 4). Of the patients who died of multiple myeloma, only 6 of 23 were diagnosed with the disease prior to hospitalization for pneumococcal meningitis. In contrast, 6 of 8 patients were diagnosed with chronic lymphatic leukemia prior to the pneumococcal meningitis diagnosis.

The increased risk of death due to digestive system diseases was seen exclusively in patients diagnosed with pneumococcal meningitis after 30 years of age, except from 1 individual who had pneumococcal meningitis as an infant and died from a peptic ulcer perforation at the age of 25 years. The increased risk of death in this group was observed exclusively for deaths related to liver diseases. In both cohorts, the majority of liver-related deaths were alcohol related (9 of 16 and 10 of 15, respectively).

We observed a trend toward an increased risk of death due to cardiovascular and respiratory diseases, although these associations were not statistically significant (Table 2).

During follow-up, 32 patients with pneumococcal meningitis died from neurologic causes, of whom 5 patients died from pneumococcal meningitis with a median of 5.8 years from the initial episode. Seven patients died of unspecified bacterial meningitis, 7 died of acquired hydrocephalus, and 4 died from sequelae of inflammatory diseases of the central nervous system.

**Table 2.** Mortality Rate Ratios for Cause-specific Death in Pneumococcal Meningitis Patients Compared With Population Controls, Denmark, 1977–2006

Causes of Death <sup>a</sup>	Unadjusted MRR	95% CI	Adjusted <sup>a</sup> MRR	95% CI	No. of Pneumococcal Meningitis Patients Who Died From the Specific Cause <sup>b</sup>	No. of Population Controls Who Died From the Specific Cause <sup>b</sup>
Infectious diseases	2.33	0.93, 5.84	2.43	0.95, 6.18	7	13
Neoplasms	1.62	1.35, 1.94	1.62	1.35, 1.95	158	419
Oropharynx	3.53	1.08, 11.58	3.88	1.18, 12.74	5	6
Digestive organs	1.30	0.89, 1.89	1.24	0.84, 1.82	35	116
Respiratory and intrathoracic organs	1.25	0.83, 1.90	1.33	0.88, 2.02	29	99
Breast	1.38	0.65, 2.92	1.34	0.62, 2.87	9	28
Female genital organs	1.15	0.50, 2.64	1.25	0.54, 2.91	7	26
Male genital organs	1.05	0.46, 2.39	1.11	0.48, 2.54	7	29
Urinary tract	1.13	0.46, 2.78	1.13	0.45, 2.81	6	23
Hematologic neoplasms	5.16	3.21, 8.29	5.18	3.20, 8.38	38	31
Multiple myeloma	19.34	7.35, 50.88	20.71	7.81, 54.90	23	5
Chronic lymphatic leukemia	6.59	2.16, 20.14	6.99	2.27, 21.58	8	5
Endocrine diseases	1.51	0.85, 2.66	1.23	0.67, 2.26	16	46
Mental disease/drug abuse	1.11	0.57, 2.15	0.99	0.50, 1.95	11	43
Nervous system diseases	3.81	2.37, 6.13	3.58	2.20, 5.82	32	36
Inflammatory diseases of the central nervous system					17	0
Cardiovascular diseases	1.17	0.99, 1.38	1.10	0.92, 1.30	171	629
Respiratory diseases	1.24	0.91, 1.71	1.32	0.96, 1.83	51	152
Digestive system diseases	2.42	1.61, 3.63	1.92	1.25, 2.95	36	64
Gastrointestinal tract diseases	1.67	0.95, 2.92	1.29	0.72, 2.30	17	44
Liver diseases	4.53	2.24, 9.16	3.46	1.64, 7.33	16	15
Diseases of gallbladder, biliary tract, and pancreas	2.59	0.62, 10.82	2.76	0.66, 11.60	3	5
Genitourinary diseases	1.62	0.63, 4.14	1.49	0.56, 3.96	6	16
Injury and poisoning	1.25	0.78, 2.01	1.12	0.69, 1.83	22	75
Ill-defined causes	1.34	0.86, 2.07	1.11	0.70, 1.76	26	84

Abbreviations: CI, confidence interval; MRR, mortality rate ratio.

<sup>a</sup> Adjusted for calendar periods and for inpatient admission prior to pneumococcal meningitis.

<sup>b</sup> The Danish Register of Causes of Death was complete through 2006. In 2007, 35 pneumococcal meningitis patients and 134 population controls died, and these deaths were not included in the analysis of causes of death.

Only 20 deaths were observed in the patients diagnosed with meningitis before the age of 20 years, of which 6 deaths were due to nervous system diseases (adjusted mortality rate ratio = 8.28, 95% CI: 1.56, 44.00). Because of the small number of deaths, we were not able to further stratify the causes of death in this age group.

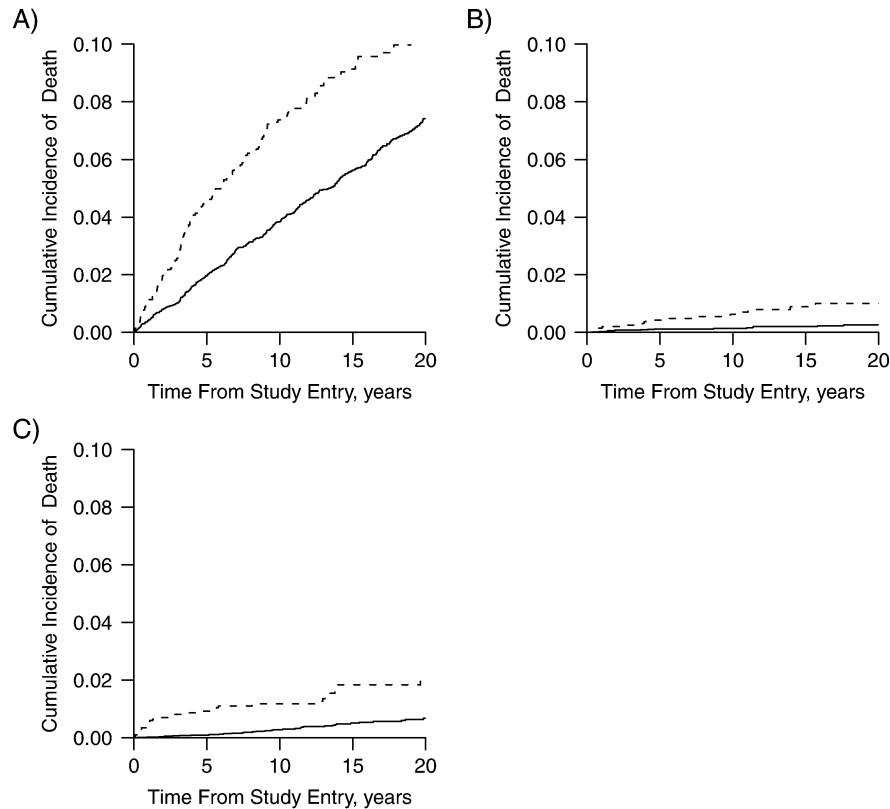
## DISCUSSION

In this nationwide, population-based cohort study, we found a substantially increased mortality up to 30 years after patients were diagnosed with pneumococcal meningitis. The pneumococcal meningitis patients had an increased risk

of death due to neoplasms, liver diseases, and nervous system diseases. To our knowledge, this is the first study to describe the long-term mortality in pneumococcal meningitis patients on a nationwide scale.

## Strengths

The major strengths of the study are its large sample size, the population-based design, and the complete follow-up. The unique Danish Civil Registration System enabled us to identify a large population control cohort of individuals well matched in terms of gender, age, and country of birth. Through the Danish national registers, we had access to



**Figure 3.** Cumulative incidences of death due to neoplasms (A), liver diseases (B), and nervous system diseases (C) for pneumococcal meningitis patients (dashed line) and population controls (solid line), Denmark, 1977–2006. As the Danish Register of Causes of Death was complete only through 2006, follow-up was terminated at January 1, 2007, and patients with an index date in 2007 were not included in these analyses.

complete data on date of death, comorbidity, cancer diagnosis, and causes of death and, importantly, these data were obtained from the same data sources for both cohorts.

### Limitations

We relied on register-based discharge diagnoses that may not be accurate. However, the registration of meningococcal meningitis in the Danish National Hospital Register has been shown to be substantially valid (19), and a similar high sensitivity for the pneumococcal meningitis diagnoses can be assumed. In addition, the number of pneumococcal meningitis patients retrieved from the Danish National Hospital Register was consistent with the annual surveillance reports of pneumococcal meningitis from the Statens Serum Institut (20). From the patient's point of view, the main interest is the long-term prognosis according to the discharge diagnosis. We therefore believe that our study not only adds to the understanding of the medical aspects of pneumococcal meningitis but also is of considerable relevance to the patients, who are diagnosed with pneumococcal meningitis and have a natural interest in knowing their long-term prognosis.

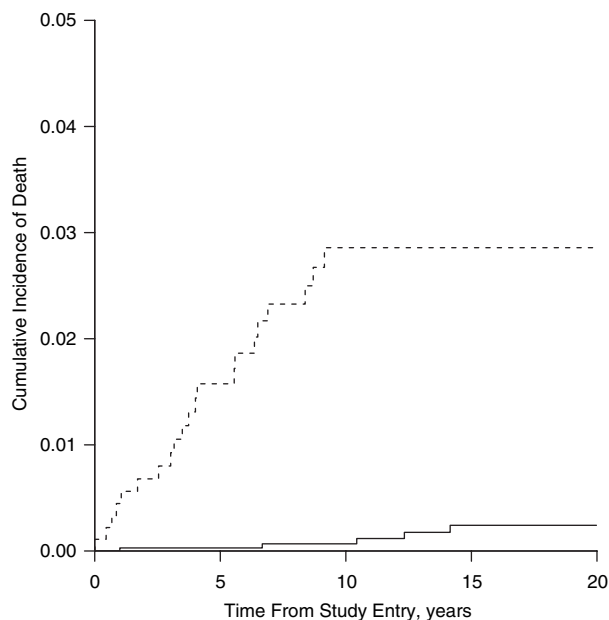
Because of the nature of our study with an inclusion period of 30 years and inclusion of pneumococcal men-

ingitis patients diagnosed at all hospitals in Denmark, we did not have access to clinical and paraclinical data obtained during the hospitalizations. Our data thereby do not allow identification of clinical predictors of long-term mortality or information on neurologic sequelae in the pneumococcal meningitis patients. We also were not able to control for confounding from smoking, alcohol consumption, educational level, or socioeconomic status.

### Discussion of our own results and the literature

In the only previous study addressing the long-term prognosis in pneumococcal meningitis patients, Kjersem et al. (10) found an increased risk of death during the first 4 years following diagnosis of bacterial meningitis. The risk of death declined to that of the background population from the fifth year after the meningitis episode. Of the 875 meningitis patients included, only 162 cases were due to pneumococcal meningitis, the follow-up was short, and preexisting comorbidity was not accounted for.

Initiating this study, we hypothesized that some of the risk factors leading to pneumococcal meningitis (e.g., chronic illness, neoplasms, smoking, and alcohol abuse) (3, 21, 22) and neurologic sequelae from the disease were likely



**Figure 4.** Cumulative incidence of death due to multiple myeloma for patients diagnosed with pneumococcal meningitis after the age of 50 years (dashed line) and population controls (solid line), Denmark, 1977–2006. As the Danish Register of Causes of Death was complete only through 2006, follow-up was terminated at January 1, 2007, and patients with an index date in 2007 were not included in these analyses.

to explain an increased long-term mortality in this patient population. Our data supported this hypothesis.

First, patients diagnosed with pneumococcal meningitis had an increased mortality from neoplasms and a higher proportion of prevalent neoplasms at study inclusion than the population controls. Of interest, the pneumococcal meningitis patients were 5 times more likely to die from hematologic neoplasms, mainly due to a 20 times increased mortality from multiple myeloma. In accordance with our study, Gregersen et al. (23) demonstrated a standardized incidence rate ratio for a subsequent diagnosis of multiple myeloma of 83.2 (95% CI: 22.6, 214.8) in 77 patients older than 40 years of age diagnosed with pneumococcal meningitis. Presumably, the patients at the time of diagnosis of pneumococcal meningitis already housed an unrecognized hematologic neoplasm making them prone to invasive bacterial infection. With an approximately 3% 10-year risk of death from multiple myeloma, it may be cost-effective to screen the pneumococcal meningitis patient population above 50 years systematically for this malignant disease. We also observed an increased risk of death from neoplasms of the oropharynx and presume that this observation stems from an increased risk of pneumococcal meningitis in patients in whom the anatomy in the region of close proximity to the central nervous system has been changed by a tumor.

A second support for our hypothesis was the finding of an increased risk of death due to diseases of the liver. Although we did not have access to data on alcohol consumption, more than half of these deaths were registered as alcohol

related. The increased risk of death from liver diseases in the pneumococcal meningitis patients therefore most likely stems from an association with alcohol abuse.

Nevertheless, the analysis, excluding individuals hospitalized in the 2 years prior to meningitis diagnosis or diagnosed with neoplasms, demonstrated essentially the same increased mortality as found for the complete study population. We were, however, only able to adjust for comorbidity in case it led to hospitalization, and these analyses are probably hampered by unmeasured and residual confounding.

A final support of our hypothesis is our observation of increased long-term mortality due to nervous system diseases, of which several died from known sequelae to pneumococcal meningitis as, for example, hydrocephalus. In accordance with this observation, several studies have demonstrated that patients surviving pneumococcal meningitis have a high risk of suffering from neurologic sequelae (8). In the first nationwide cohort study to address the long-term mortality in survivors of meningococcal meningitis, our group likewise observed a higher risk of death due to nervous system diseases in these patients (24).

In summary, patients diagnosed with pneumococcal meningitis have a substantially increased long-term mortality, mainly due to neoplasms (primarily hematologic neoplasms), liver diseases, and nervous system diseases. We presume that the increased risk stems from neurologic sequelae and comorbidity predisposing to pneumococcal meningitis, but not recognized prior to the primary meningitis episode. To improve survival in patients surviving the acute phase of pneumococcal meningitis, physicians should meticulously examine this patient population for neurologic sequelae and screen for comorbidity predisposing to the disease.

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Conflict of interest: none declared.

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