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Accidental hypothermia in Denmark: A nationwide cohort study of incidence and outcomes

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ABSTRACT

Objectives To investigate the incidence of accidental hypothermia (AH) in a nationwide registry and the associated outcomes.

Design Nationwide retrospective cohort study

Participants and settings All patients at least 18 years old, admitted to hospitals in Denmark with a diagnosis of AH, with an International Classification of Diseases, 10th edition code of T689, from January 1996 to November 2016. Other recorded diagnoses were included in the analyses.

Primary and secondary outcome measures The primary outcome was 1-year mortality.

Results During the inclusion period, 5242 patients were admitted with a diagnosis of AH, corresponding to a mean annual incidence of 4.4±1.2 (range by calendar year: 2.9–6.4) per 100 000 inhabitants. A total of 2230 (43%) had AH recorded as the primary diagnosis without any recorded secondary diagnoses (primary AH), 1336 (25%) had AH recorded as the primary diagnosis with other recorded secondary diagnoses (AH+2° diagnosis), and 1676 (32%) had AH recorded as a secondary diagnosis with another recorded primary diagnosis (1° diagnosis+AH). Alcohol intoxication was the most common diagnosis associated with AH. Overall 1-year mortality was 27%. In patients with primary AH, 1-year mortality was 22%, compared with 26% in patients with secondary AH type I, and 35% in patients with secondary AH type II ($p_{log\text{-}rank}$<0.001).

Conclusions The present study investigated the incidence of AH, associated comorbidities and mortality after AH in Denmark from 1995 to 2016. The diagnosis is associated with a high comorbidity burden and a considerable 1-year mortality. In the high proportion of patients with associated comorbidities, establishing whether AH or the comorbidities are the drivers of mortality remains difficult. This complicates our understanding of AH and makes it difficult to find modifiable factors associated with both AH and outcomes. Future prospective studies are needed elucidate the causal relationship between AH and associated comorbidities.

Strengths and limitations of this study

- ► Large contemporary study to investigate the incidence, comorbidity burden and outcome in patients diagnosed with accidental hypothermia.
- ► Data originated from a national cohort of patients.
- ► The registry data limited the data granularity to what has been presented in the present paper.
- ► The presented incidences are likely to be significantly different in other countries, depending on climate, demography and so on.

INTRODUCTION

Accidental hypothermia (AH), defined as an involuntary drop in core temperature below 35°C, is a serious condition with considerable mortality.[1 2] AH can result from isolated cold exposure (primary hypothermia) or in association with acute or chronic illness (secondary hypothermia).[2] The severity of hypothermia can be graded into three stages based on core temperature: 32°C–35°C (mild AH), 28°C–32°C (moderate AH) and <28°C (severe AH).[3–6] In-hospital mortality after severe hypothermia has been reported to be as high as 30%. It is estimated that approximately 1500 people die from hypothermia every year in the USA.[1 4] Few previous studies have investigated the incidence and outcome after AH, however, the studies represent heterogenous populations from different climate zones and different time periods.[7–10] Accordingly, our knowledge of the contemporary incidence, demographics and outcomes after AH remains sparse.

The aim of this study was to investigate the incidence of AH in a Danish nationwide registry, and the associated outcomes in adult patients.

Geography

Denmark covers a relatively small area of 4 300 000 hectares but has a comparatively long coastline. The highest point is 173 m above sea level. Denmark is located on the 55th to 57th parallel north in the temperate climate zone. Mean temperatures range from 0°C in January and February to 15.7°C in August. The population was about 5.8 million

as of 1 January 2016. About 1.8 million (about 31% of the population) lived in the capital, Copenhagen.

METHODS

The present study is a nationwide retrospective cohort study including all adult patients admitted to hospitals in Denmark with a diagnosis of AH from January 1996 to November 2016. The primary outcome was 1-year mortality after diagnosis. We chose a priori to include only those cases with a first-time diagnosis of AH. The rationale behind this decision was to ensure that a patient with multiple hospital admissions for AH only counted once in the analysis.

All Danish residents are given a personal identification number at the time of birth or immigration. This number is used in all contacts with the healthcare system, and it is used as identifier in national registries. Data were extracted from the Danish National Patient Register (NPR) to identify all patients admitted with a discharge diagnosis of AH, defined by the International Classification of Diseases, 10th edition (ICD-10, which has been used in Denmark since 1993) code T689.

Patients were stratified into three groups based on whether AH was recorded as the only diagnosis (primary AH), whether AH was recorded as the primary diagnosis with other recorded secondary diagnoses (AH+2° diagnosis), or whether AH was recorded as a secondary diagnosis (1° diagnosis+AH) for a given admission.

The primary diagnosis is defined as the diagnosis primarily causing the need for the admission, while the secondary diagnoses are defined as other conditions that required attention during a given admission. Main treatment categories, such as 'intensive care admission', and 'respirator treatment' were also extracted from the NPR. The AH diagnosis was linked to survival (ie, the primary outcome) using the nationwide Danish Register of Causes of Death.

Patient and public involvement

Patients or the public were not involved in the design of the present study.

Statistical analyses

Throughout, categorical variables are presented as counts (%), normally distributed continuous variables are presented as mean±SD and skewed continuous variables are presented as median (25th percentile to 75th percentile). Normality was assessed visually by QQ plots prior to analyses. Associations between baseline variables and AH types were tested by the χ^2 test for categorical variables and with the one-way analysis of variance for continuous variable.

To give an overview of common comorbidity, a list of associated ICD-10 diagnoses with a prevalence higher than 1% in patients with AH was presented. This overview was stratified by whether AH was recorded as the primary diagnosis (AH+2° diagnosis) or whether AH was recorded as a secondary diagnosis (1° diagnosis+AH).

The annual incidence of AH per calendar year was plotted for the total cohort as well as after stratification by AH type. The mean annual incidence±SD with range was presented. To assess if the incidence of AH was changing over time, linear models were applied with calendar year being included as a continuous covariate assuming a linear trend. The absolute change in AH incidence per calendar year±SD was presented. The distribution of AH diagnoses per calendar months were displayed along with mean outside temperatures. The mean annual incidence±SD of AH after stratification by age group was presented.

We presented crude 1-year mortality rates for the total cohort, as well as after stratification by AH type, by sex and by age group. We presented 1-year mortality after stratification by sex and age group. Differences in mortality between females and males, stratified by age group, were analysed by application of the χ^2 test.

For each patient in the cohort, the date of entry (ie, the date of AH diagnosis) as well as the date of death was recorded in the registries. The Kaplan-Meier estimator was applied to visualise time to death within 1 year from admission, stratified by AH type, sex and age group. The log-rank test was applied to assess possible differences between strata.

To analyse time to death between groups, we applied Cox proportional hazard models adjusting for AH type, sex, age at admission and calendar year. We presented HRs with 95% CIs. A significance level of <0.05 was applied throughout. SAS software, V.9.4 (SAS Institute) was used for all statistical analysis.

RESULTS

Over the inclusion period of almost 22 years, the Danish Health Care System received a total of 5242 adult patients admitted with a diagnosis of AH. A total of 2230 (43%) had AH recorded as the final primary diagnosis without any recorded secondary diagnoses (primary AH), 1336 (25%) had AH recorded as the final primary diagnosis with other recorded secondary diagnoses (AH+2° diagnosis), and 1676 (32%) had AH recorded as a final secondary diagnosis with another recorded primary diagnosis (1° diagnosis+AH).

A total of 1981 (38%) of the patients admitted with AH were women. The mean age was 61±21 years. Female sex was slightly less prevalent among patients with primary AH compared with patients with AH+2° diagnosis and patients with 1° diagnosis+AH (35% vs 39% vs 40%, p<0.001). Patients with primary AH were slightly younger compared with patients with AH+2° diagnosis and patients with 1° diagnosis+AH (59±22 years vs 62±20 years vs 62±20 years, p<0.001).

Comorbidity

Both AH+2° diagnosis and 1° diagnosis+AH were associated with a significant comorbidity burden. A list of

Table 1 List of associated ICD-10 diagnoses with a prevalence higher than 1% in patients with accidental hypothermia

List of secondary ICD-10 diagnoses in patients with AH+2° diagnosis (n=1336)			List of primary ICD-10 diagnoses in patients with 1° diagnosis+AH (n=1676)		
Diagnosis	**ICD-10**	**n (%)**	**Diagnosis**	**ICD-10**	**n (%)**
Acute alcohol intoxication	DF100	198 (15)	Acute alcohol intoxication	DF100	153 (9.1)
Alcohol dependence syndrome	DF102	118 (8.9)	Respiratory insufficiency	DJ969	74 (4.4)
Harmful use of alcohol	DF101	96 (7.2)	Sepsis	DA419	61 (3.6)
Pneumonia	DJ189	87 (6.5)	Acute respiratory insufficiency	DJ960	58 (3.5)
Dementia	DF039	74 (5.5)	Hypoglycaemia	DE162	55 (3.3)
Hypertension	DI109	59 (4.4)	Pneumonia	DJ189	48 (2.9)
Atrial fibrillation or flutter	DI489	57 (4.3)	Dehydration	DE869	33 (2.0)
Dehydration	DE869	52 (3.9)	Drowning/non-fatal submersion	DT751	32 (1.9)
Traumatic ischaemia of muscle	DT796	29 (2.2)	Cardiac arrest	DI469	28 (1.7)
Type II diabetes	DE119	27 (2.0)	Concussion	DS060	28 (1.7)
COPD	DJ449	24 (1.8)	Multiple lesions	DT079	29 (1.7)
Hypoglycaemia	DE162	23 (1.7)	Stroke	DI649	27 (1.6)
Anaemia	DD649	21 (1.6)	Traumatic ischaemia of muscle	DT796	25 (1.5)
Hypokalaemia	DE876	21 (1.6)	Alcohol dependence syndrome	DF102	20 (1.2)
Cardiac arrest	DI469	22 (1.6)	Harmful use of alcohol	DF101	17 (1.0)
Complication after stroke	DI694	22 (1.6)	Septic shock	DR572	17 (1.0)
Bacterial pneumonia	DJ159	20 (1.5)	–	–	–
Urinary tract infection	DN390	20 (1.5)	–	–	–
Sepsis	DA419	16 (1.2)	–	–	–
Type I diabetes	DE109	16 (1.2)	–	–	–
Epilepsy	DG409	16 (1.2)	–	–	–
Hypotension	DI959	15 (1.1)	–	–	–
Schizophrenia	DF209	14 (1.0)	–	–	–

AH+2° diagnosis: AH recorded as primary diagnosis with one or more recorded secondary diagnoses.
1°diagnosis+AH: AH recorded as a secondary diagnosis with another recorded primary diagnosis.

associated diagnoses with a proportion higher than 1% is provided in table 1. The most frequent diagnosis associated with AH was alcohol intoxication (table 1).

A total of 816 (16%) patients with AH received care in an intensive care unit (ICU). A total of 305 (5.8%) were treated with vasopressors and/or inotropic agents, 397 (7.6%) received ventilator treatment, and 479 (9.1) received dialysis. A total of 21 (0.4%) patients were treated with extracorporeal circulation.

Incidence

The mean annual incidence of AH was 4.4±1.2 per 100 000 inhabitants with a range from 2.9 to 6.4 per 100 000 inhabitants (figure 1). The overall incidence of AH increased from 2000 to 2016 (absolute increase 0.16±0.02 per 100 000 inhabitants per calendar year, p<0.001).

The annual incidence of AH was 4.3±1.6 per 100 000 in inhabitants from 18 to 20 years, 2.3±0.55 per 100 000 in inhabitants from 21 to 40 years, 4.8±1.1 per 100 000 in inhabitants from 41 to 60 years, 7.2±2.6 in inhabitants from 61 to 80 years, and 28±11 in inhabitants older than 80 years.

The incidence of AH followed a seasonal trend, with the highest per cent of AH occurring in January (16%) and the lowest percent of AH occurring in August (3.0%, figure 2). Of all AH diagnoses, 29% were recorded in the Danish capital region inhabited by 31% of the total Danish population.

Outcome

Overall mortality within the first 7 days of admission was 11%, increasing to 16% at 30 days, and 27% at 1 year. One-year mortality was 22% in patients with primary AH, 26% in patients with AH+2° diagnosis and 35% in patients with 1° diagnosis+AH (p<0.001, figure 3). The higher mortality in patients with comorbidities remained unchanged after adjustment for confounding factors (table 2).

Increasing age was significantly associated with increased 1-year mortality (table 2). One-year mortality increased from 1.6% in patients between 18 and 20 years to 45% in patients older than 80 years (p<0.001, table 2).

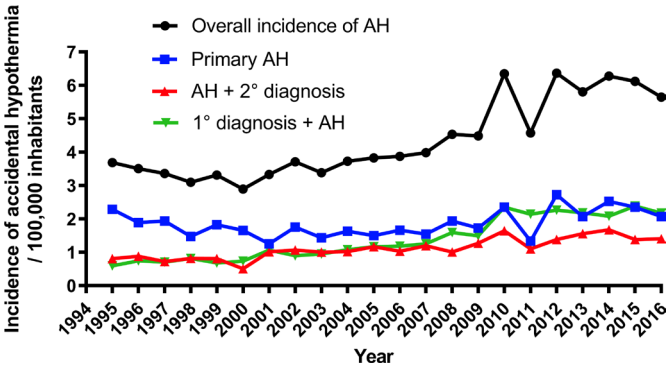

Figure 1 Incidence of accidental hypothermia per 100 000 inhabitants per calendar year. Primary AH: AH recorded as primary diagnosis without any recorded secondary diagnoses. AH+2° diagnosis: AH recorded as primary diagnosis with one or more recorded secondary diagnoses. 1° diagnosis+AH: AH recorded as a secondary diagnosis with another recorded primary diagnosis. AH, accidental hypothermia.

One-year mortality was higher in females compared with males (31% vs 25%, p<0.001, table 2), corresponding to a HR of 1.3 (1.2 to 1.4). In contrast, we found a significantly lower mortality in females older than 80 years compared with men older than 80 years (41% vs 52%, p<0.001), but no significant differences between the sexes in other age groups (table 3). A significantly higher proportion of females were older than 80 years compared with men (39% vs 14%, p<0.001, table 3). The higher overall mortality in women was caused by a higher proportion of women compared with men being older than 80 years. Female sex was associated with a lower mortality compared with male sex after adjustment for confounding factors including age (HR 0.89 95% CI 0.80 to 0.99, table 2).

Calendar year was not associated with outcome in univariate analysis, however, after adjustment, calendar year was associated with slightly decreased mortality with a HR of 0.98 (0.98 to 0.99, p<0.001) per year (table 2).

DISCUSSION

We chose to stratify patients into three groups (primary AH, AH+2° diagnosis and 1° diagnosis+AH). The rationale behind this stratification was to distinguish patients

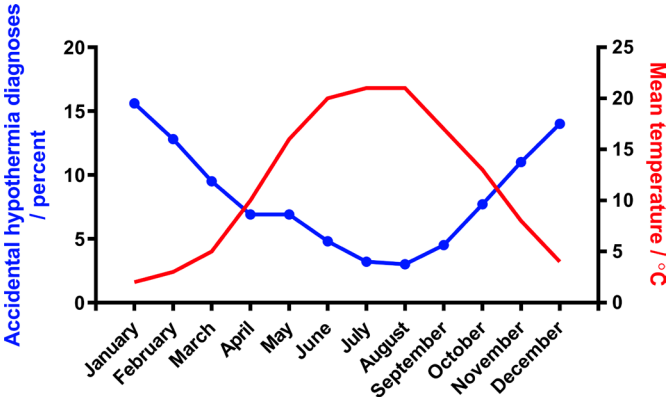

Figure 2 Distribution of accidental hypothermia diagnoses per calendar month.

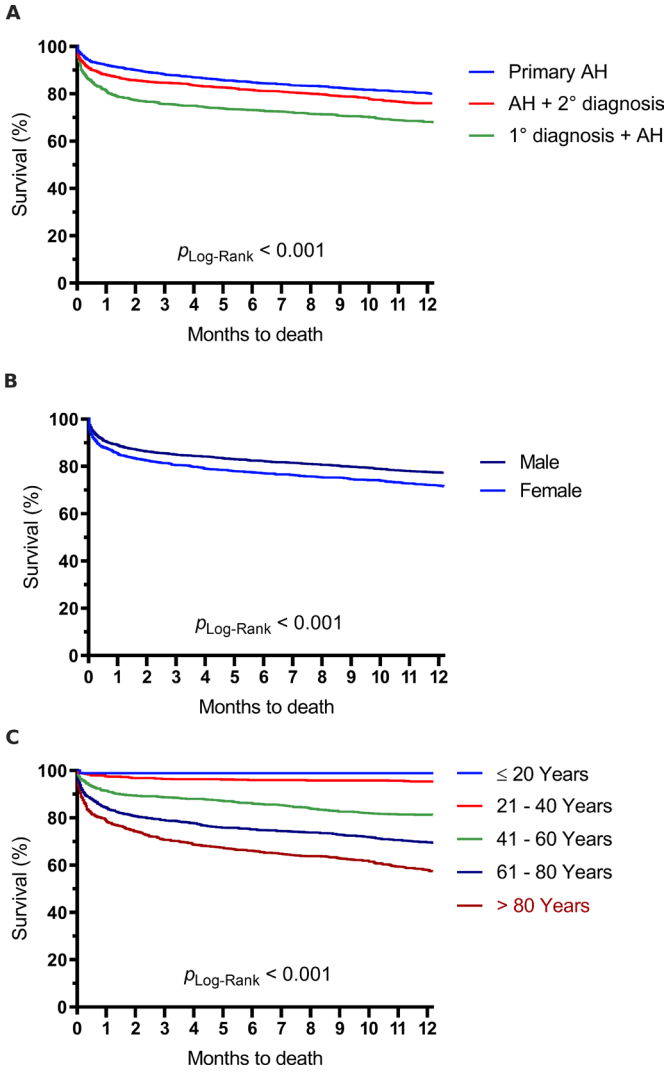

Figure 3 One-year survival in accidental hypothermia patients stratified by AH type (A), men versus women (B) and by age at admission (C). Primary AH: AH recorded as primary diagnosis without any recorded secondary diagnoses. AH+2° diagnosis: AH recorded as primary diagnosis with one or more recorded secondary diagnoses. 1° diagnosis+AH: AH recorded as a secondary diagnosis with another recorded primary diagnosis. AH, accidental hypothermia.

with isolated AH and no comorbidity vs patients with comorbidities, when the admitting physician believed that the AH diagnosis was the primary cause of the admission versus patients with comorbidities, when the admitting physician believed that the AH diagnosis was a secondary cause of admission.

The annual incidence of AH was 4.4 per 100 000 in this study. A study from the Netherlands reported an incidence of AH of 1.1 cases per 100 000 per year from 1987 to 1990.[8] However, in this cohort, trauma was the primary cause of AH suggesting a significantly different population compared with the present study.[8] A study from four counties with 900 000 inhabitants in the northern part of Sweden reported 3.4 cases of AH per 100 000 per year in from 2000 to 2007.[9] In contrast to the present study from a temperate climate zone, the Swedish study was

Table 2 Associations between covariates and mortality within 1 year

	Patients per group	Mortality n (%)	Univariate models HRs (95% CI)	P value	Multivariate model* HRs (95% CI)	P value
AH type†						
Primary AH	2230	496 (22)	ref.		ref.	
AH+2° diagnosis	1336	352 (26)	1.2 (1.1 to 1.4)	<0.001	1.2 (1.0 to 1.3)	0.04
1° diagnosis+AH	1676	582 (35)	1.7 (1.5 to 2.0)	<0.001	1.7 (1.5 to 2.0)	<0.001
Sex						
Female	1981	615 (31)	ref.		ref.	
Male	3261	815 (25)	1.3 (1.2 to 1.4)	<0.001	0.89 (0.80 to 0.99)	0.04
Age at admission						
18–20 years	181	3 (1.7)	ref.		ref.	
21–40 years	753	43 (5.7)	3.5 (1.1 to 11)	0.03	3.4 (1.0 to 11)	0.04
41–60 years	1571	337 (21)	15 (4.7 to 45)	<0.001	14 (4.4 to 43)	<0.001
61–80 years	1512	490 (32)	24 (7.6 to 74)	<0.001	24 (7.6 to 73)	<0.001
>80 years	1225	557 (45)	36 (12 to 113)	<0.001	38 (12 to 117)	<0.001

Results presented as crude mortality rates as well as HRs after application of Cox proportional hazard models, including time to death within 1 year as the outcome variable.
Primary AH: AH recorded as primary diagnosis without any recorded secondary diagnoses.
AH+2° diagnosis: AH recorded as primary diagnosis with one or more recorded secondary diagnoses.
1°diagnosis+AH: AH recorded as a secondary diagnosis with another recorded primary diagnosis.
*Adjusted for AH type, sex, age and calendar year.
†Accidental hypothermia (AH).

conducted in a subartic region. However, the Swedish study reported a lower incidence of AH. The Swedish study found an approximate twofold increase in the incidence of AH during the study period. The authors suggest that this may be caused by increased physician awareness and increased reporting.[9] A study from New Zealand reported an AH incidence of 6.9 per 100 000 per year from 1977 to 1986.[7]

There was no clinically significant increase in the incidence of AH during our study period. More males were admitted with AH compared with women. This is consistent with the results of other studies.[11–15]

The incidence of AH was low during summer and increased during the winter months. The likely explanation is that Denmark has a temperate climate with a cold fall and winter. The increased incidence of AH during the winter is consistent with findings from other studies of AH in cold climates.[9–11 16–18]

We found an overall 30-day mortality of 16% and 1-year mortality of 27%. A study from Japan previously reported a high in-hospital mortality of 24% in a population with AH from 2011 to 2016.[10] One difference between the two studies was that a significantly higher proportion of patients in the Japanese study were admitted to an ICU

Table 3 Mortality within 1 year stratified by age group and sex

Age group	Total number in each age group	Female sex 1981	Male sex 3261	P value
18–20 years	Female, n=40 Male, n=141	0 (0)	3 (2.1)	1.0
21–40 years	Female, n=159 Male, n=594	10 (6.3)	33 (5.6)	0.72
41–60 years	Female, n=419 Male, n=1152	87 (21)	250 (22)	0.69
61–80 years	Female, n=597 Male, n=915	201 (34)	289 (32)	0.40
>80 years	Female, n=766 Male, n=459	317 (41)	240 (52)	0.0002

P values for χ^2 test (or Fisher's exact test) for difference in mortality between sexes.

(49% vs 16%). The difference in short-term mortality may be explained by different patient characteristics.

In the present study, older age was associated with both increased incidence of AH and with increased mortality consistent with previously reported data.[8 19 20] The Swedish study also found a higher proportion of older women with AH.[9] In our study, women and men had comparable mortality in all age groups with the exception of patients older than 80 years. Women older than 80 years had a significantly lower mortality than men. This may be explained by the long follow-up and the longer life expectancy of women.

We found that the diagnosis of AH was associated with a burden of comorbidities. Having other recorded diagnoses was associated with a significantly higher mortality compared with having AH as the only recorded diagnosis (ie, primary AH). The association between comorbidity and mortality is consistent with previous studies in AH populations.[10 19]

As with our study, previous studies have also used registry data to address some of the same research questions. The incidence and outcomes of AH depend on climate, geography and socioeconomic factors.

AH is a relatively rare diagnosis, and may be overlooked; especially in the case of mild AH presenting with associated diagnoses such as sepsis. Patients with AH constitute a highly heterogenous group depending on the cause of AH. Whether AH or associated diagnoses are the drivers of ensuing morbidity or mortality remains poorly understood. Future studies on AH should ideally be prospective. Eligibility criteria should be based on body temperature measured on admission. Clinical signs on admission should be reported to validate current classification methods of AH stages.[6] Data collection should include a brief description of the circumstances associated with the event, for example, water accident. Associated diagnoses should be reported, and the treating clinician should ideally record, whether AH was the driver of any associated diagnoses, whether an associated diagnosis was the driver of AH, or whether AH and associated diagnoses were considered unrelated. Endpoints should include readmissions after index-admission and all-cause mortality.

Limitations

A primary limitation of the present study was caused by data originating from national registries. This limited the data granularity to what has been presented in the present paper. While the diagnosis of AH likely has a high specificity, a lower sensitivity may have resulted in underreporting of patients with hypothermia, especially in presence of competing diagnoses. The incidence of secondary AH may be higher than we reported. However, hospitals are reimbursed based on correct reporting of diagnoses, and accordingly, the registry has a high accuracy for most diagnoses.[21] While diagnoses were classified by treating physicians as primary or secondary, it is unknown to what extent this classification corresponds to primary AH (AH from isolated cold exposure) and secondary AH (AH in relation to acute or chronic illness).[2] However, patients whose only diagnosis was AH most likely had primary hypothermia. Excluding additional admissions of patients admitted more than once with a diagnosis of AH might have caused underestimation of the true incidence of AH.

CONCLUSIONS

The present study investigated the incidence of AH, associated comorbidities, and mortality after AH in Denmark from 1995 to 2016. The diagnosis is associated with a high comorbidity burden and a considerable 1-year mortality. In the high proportion of patients with associated comorbidities, establishing whether AH or the comorbidities are the drivers of mortality remains difficult. This complicates our understanding of AH and makes it difficult to find modifiable factors associated with both AH and outcomes. Future prospective studies are needed elucidate the causal relationship between AH and associated comorbidities.

Contributors Author MW initiated the project. SW, AFM, JK, CH and MW were involved in planning the study including the statistical analyses. Authors SW and AFM wrote the first draft of the manuscript. SW, AFM, JK, CH and MW were all involved in the production of the final manuscript.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval The study was approved by the Danish Patient Safety Authority (Institutional review board, ref. no. 3-3013-1906/1/) and was conducted consistent with the Declaration of Helsinki. As we conducted a national retrospective study over a time period of 21 years, the Danish Patient Safety Authority approved the study without need for obtaining consent from each individual.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data may be obtained from a third party and are not publicly available. Data were extracted from national Danish registries. Accordingly, assess to data can be obtained by application to the relevant Danish authorities.

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