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Research Article

Altered Mental Status in Danish Emergency Department Patients: A Cohort Study of Aetiology and Mortality

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Abstract

Objective: Altered Mental Status (AMS) is a common presentation of patients in emergency departments, and it is associated with a high mortality rate. This study aimed to examine the aetiologies and outcomes in emergency department patients with AMS.

Methods: This was a single-centre retrospective cohort study. All patients (age ≥18 years) presenting to the emergency department at Aarhus University Hospital with the chief complaint of AMS from July 2016 to June 2017 was included. Primary end points were aetiology and 30-day mortality. Patients were stratified by age group (18-59 years/+60 years) and hospital admission (yes/no) for further analysis.

Results: A total of 554 patients were included. The most common cause of AMS was unspecific *R-diagnosis* (22.2%). Among younger adults (18–59 years), *intoxication* was the most common aetiology, whereas *infection* was the most common cause in older patients (≥60 years). The total 30-day mortality rate was 10.8%. The odds of dying within 30 days after admission were significantly higher for patients with *system/organ dysfunction* compared to the rest of the study population (OR: 6.2, 95% CI: 3.0 to 12.6; p<0.001).

Conclusion: Non-neurological disorders appear dominant at all ages. *Intoxication* was primarily seen among younger adults (18–59 years), while *infection* was a more common cause among the elderly (>60 years). AMS is associated with a high 30-day mortality rate. Patients with *system/organ dysfunction* had significantly higher odds of dying within 30 days compared to the rest of the study population.

Keywords: Altered mental status; Impaired consciousness; Emergency department; Danish Emergency Process Triage (DEPT)

Abbreviations: ADAPT: Adaptive Process Triage; AMS: Altered Mental Status; ATS: Australasian Triage Scale; AUH: Aarhus University Hospital; CNS: Central Nervous System; CPR: Civil Personal Registration Number; Computed Tomography Scan: CT-Scan; CTAS: Canadian Triage And Acuity Scale; DEPT: Danish Emergency Process Triage; ECG: Electrocardiogram; ED: Emergency Department; GCS: Glasgow Coma Scale; ICD-10: International Classification Of Diseases, 10th Revision; MTS: The Manchester Triage System; UTI: Urinary Tract Infection

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Introduction

Altered Mental Status (AMS) is a common presentation of patients in Emergency Departments (ED) [1]. AMS is a broad term used to describe any alteration in a patient's baseline level of cognitive ability, level of awareness, or responsiveness to surroundings [2,3]. Acute changes in mental status can be the first sign of a potentially life-threatening condition that requires fast diagnostic workup and rapid decision-making [3]. Often, these patients pose a great diagnostic challenge to ED physicians due to the numerous neurological (e.g., stroke, brain tumour, or neuro infection) and non-neurological (e.g., infection, intoxication, or metabolic disorders) differential diagnoses [1-3]. Moreover, AMS is a concurrent condition associated with other primary complaints [4-6]. Generally, the patient manifests with vague symptoms with no obvious underlying aetiology, and the initial evaluation is based on limited patient information [1]. Workup strategies also lack standardisation; hence, a broad range of diagnostic tests are usually performed in the ED (e.g., CT scans, ECG, etc.) [7].

Previous studies of AMS patients in ED shave reported high mortality rates ranging from 8.1% to 11.5% [1,7-10]. In particular, the elderly have been found to be at an increased risk of adverse outcomes [7-11]. A bimodal distribution of age has been described, and aetiologies vary significantly with age [1,7]. Intoxication and trauma have been described as common causes of AMS among younger adults, whereas neurological disorders and organ dysfunction are more frequent among the elderly [1,7]. However, the results vary between studies, indicating that aetiologies and mortality rates are not consistent in all regions [7]. Furthermore, current knowledge within the field is mainly based on small sample sizes. In general, more knowledge of the underlying aetiologies, mortality rates, and distribution by age is warranted.

Therefore, the primary aim of this study was to examine aetiologies and 30-day mortality in patients admitted to the ED at Aarhus University Hospital with AMS as the chief complaint. Second, we aimed to compare the distribution of aetiologies among age groups and the mortality risk of different aetiologies.

Materials and Methods

Study Design and Setting

This single-centre retrospective cohort study is based on data on all adult patients presenting with AMS upon admission to the ED at Aarhus University Hospital (AUH) in the period from 1 July 2016 to 30 June 2017.

AUH is the largest hospital in the Central Denmark region. The hospital catchment population is around 350,000 inhabitants, and the ED has approximately 45,000 contacts per year. AUH manages all medical emergencies in the local area. Moreover, it functions as a referral hospital, thus receiving patients with major traumas from the entire region. In the inclusion period, all acute patients entered the hospital through the ED, except parturient women, psychiatric patients, and patients suspected of either ST-elevation myocardial infarction or stroke [12].

The ED contains an emergency room for minor surgical or medical injuries, two short-term medical units, and a specialised trauma centre [13]. Patients are initially triaged by an experienced nurse using the Danish Emergency Process Triage system (DEPT) [14]. In short, DEPT is a five-level triage system based on vital signs and one (or two) symptom-based cards (e.g., *dyspnoea*) related to the patient's chief complaint [12,14]. The patients are triaged after urgency listing from red (life-threatening condition, requires immediate treatment) through to orange, yellow, green (stable condition, no urgency), and blue (minor injuries). The system is used to determine the priority of patients' treatments in similarity to other modern triage systems, such as the Manchester Triage system (MTS), the Australasian Triage Scale (ATS), the Canadian Triage and Acuity Scale (CTAS), and Adaptive Process Triage (ADAPT) [15-17].

Selection of Participants

This study included all ED patients' ≥18 years of age who were triaged with the chief complaint of AMS. Only patients with a Danish personal identification number (CPR number) were included. Patient's triaged with a blue cardor no triaged colour were excluded. If a patient had multiple visits, only the first contact was included in the analysis.

Data Source

Patient data were retrieved from the regional data warehouse, containing all registered patient-related data (e.g., personal identification, diagnoses, vital signs, and triage level). Vital status was obtained from the Danish Civil Registration System, which enabled the complete follow-up of all included patients.

Outcome Measures

The primary outcomes were the causative aetiologies of AMS and 30-day mortality rates. *Aetiology* was measured as the final discharge diagnosis (i.e., action diagnosis), or the last diagnosis given in the case of in-hospital death. Diagnoses were reported in accordance with the International Classification of Diseases (ICD-10) guidelines. *Mortality* was defined as all-cause mortality within 30 days after admission. Second, a comparison of the distributions of aetiologies and their mortality risks in different age groups was conducted. The patients were divided into two subgroups: younger adults (aged 18–59 years) and the elderly (aged 60 or higher). Aetiologies were categorised as either primary neurological or non-neurological, with each classification containing several subgroups.

Analysis

Categorical variables are presented as numbers and percentages. Continuous variables are presented as medians with an interquartile range. To assess the differences in the distribution of the categorical variables between groups, Pearson's chi-square test or Fischer's exact test were used as appropriate. The Wilcoxon rank sum test was used for the comparison of continuous variables. Mortality data are presented as the cumulative number of events and incidence proportions with 95% confidence intervals. Multivariate logistic regression, adjusted for sex and age groups, was used to determine the odds ratios. Cumulative mortality was depicted using Kaplan–Meier survival curves, and distributions were compared using the log-rank test. The level of significance was set at $P<0.05$. All analyses were performed using STATA version 15 (Stata Corp., College Station, Texas, USA).

Ethical Approval

This study was approved by the Danish Data Protection Agency (case no. 1-16-02-317-18) and the Danish Patient Safety Authority (case no. 3-3013-2615). In accordance with Danish law, ethical approval from the Regional Ethics Committee was not required, as this is a register-based study.

Results

Patient Characteristics

During the inclusion period, 38,934 acute contacts were registered at the ED, of which 1.6% were due to AMS (*n*=607). A total of 554 patients were included in the study, as they fulfilled the inclusion criteria (Figure 1).

Patient Characteristics

The patient characteristics are listed in Table 1. The data tended to be constituted by clusters of patients within different age groups. A cluster of patients aged 18–59 years (young adults), and a cluster of patients ≥60 years (elderly) was observed (Supplemental digital content, Figure 1). Upon admission, 189 patients were aged 18–59 years (34.1%) and 365 patients were ≥60 years (65.9%). Patients were triaged as follows: 14.6% red, 56.9% orange, 27.6% yellow, and 1% green.

Aetiology

The causative composition of AMS patients stratified by age groups is illustrated in (Figure 2).The most common discharge diagnoses among AMS patients were *R-diagnoses* (22.2%), *infection* (19.0%), *intoxication* (13.4%), and *system/organ dysfunction* (8.5%). AMS was the result of primary neurologic disorders in 15.5% of cases (*n*=86), with *cerebrovascular disease* as the most frequent disorder, accounting for 4.3% of cases (*n*=24). Aetiologies differed significantly between age groups ($p<0.001$). Infectious diseases were the most common cause in the elderly, while intoxication was more frequent in younger adults, with alcohol as the most frequently abused drug. See Supplemental Digital content table 1 for the exact numbers, frequencies, and further description of the subtypes within the categories. Aetiologies in patients discharged directly from the ED unit differed from those in hospitalised patients (Figure 3). Overall, unspecific diagnoses within the ICD-10 chapters 'symptoms and signs' (*R-diagnoses*) and 'factors influencing health status'(*Z-diagnoses*) were often used; patients discharged from the ED unit with these diagnoses accounted for 83.7% and 77.5% of cases, respectively. Patients suspected of *system/organ dysfunction*, *sepsis, seizures,* or *cerebrovascular diseases* were generally hospitalized, while most *trauma* and *intoxication* cases were managed in the ED.

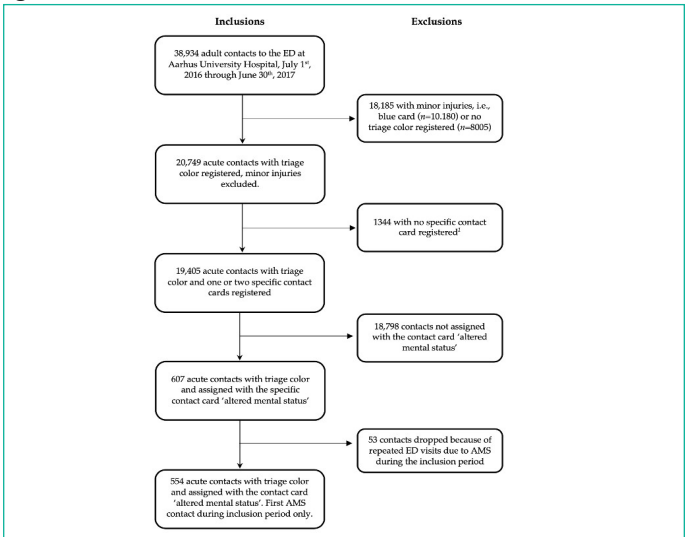

Figure 1: Flowchart for study inclusion.
If a patient was assessed with AMS more than once during the inclusion period, only the first contact was included. [1]Patients with no specific contact card registered included some of the most acute patients, such as patients with major trauma or medical emergencies who were received by a specialised team, immediately taken to the trauma bay, and thus not triaged.

Table 1: Patient characteristics.

	All patients *(n=554)*	Age group		*Significance (P-value)*
		<60 years *(n=189)*	≥60 years *(n=365)*	
Age at contact start, *years, median* (IQR)	70 (51-81)	44 (28-51)	78 (70-86)	-
Sex, *n* (%) Male	266 (48.0)	95 (50.3)	171 (46.9)	0.446
Triage priority, *n* (%)				<0.05
Red	81 (14.6)	17 (9.0)	64 (17.5)	
Orange	315 (56.9)	113 (59.8)	202 (55.3)	
Yellow	153 (27.6)	56 (29.6)	97 (26.6)	
Green	5 (0.9)	3 (1.6)	2 (0.6)	
Level of consciousness, *n* (%)[a]				0.146
GCS 15	231 (41.7)	90 (47.6)	141 (38.6)	
GCS 13-14	195 (35.2)	58 (30.7)	137 (37.5)	
GCS 9-12	78 (14.1)	22 (11.6)	56 (15.3)	
GCS 3-8	47 (8.5)	17 (9.0)	30 (8.2)	
Radiologic exams, *n* (%) CT-cerebrum Chest x-ray	254 (45.8) 186 (33.6)	68 (36.0) 27 (14.3)	186 (51.0) 159 (43.6)	≤0.001 ≤0.001
Time in the ED, *hours, median* (IQR)	5.7 (2.8-21.1)	3.9 (2.4-9.1)	7.9 (3.0-25.4)	≤0.001
Patients hospitalized[b]**,** *n (%)*	227 (41.0)	51 (27.0)	176 (48.2)	≤0.001
Time in hospital[c]**,** *days, median* (IQR)	5.8 (3.3-9.8)	4.9 (1.4-9.5)	5.9 (3.9-9.8)	0.071
Need of intensive care, *n* (%)	24 (4.3)	9 (4.8)	15 (4.1)	0.721

Note: [a]Level of consciousness measured by Glasgow Coma Scale (GCS). Data missing on six patients. [b]Patients admitted to other hospital wards from the short-stay ED. [c]Median hospital length of stay of all patients admitted to other hospital wards.
Abbreviations: *n,* number of patients; IQR, interquartile range (illustrated as 25th and 75th percentiles).

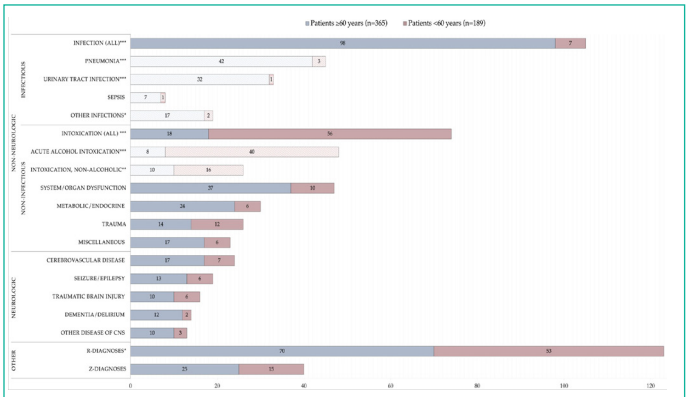

Figure 2: *Aetiologies of AMS cases in the ED stratified by age group* (*n* = 554).
Note: Rows with striped lines represent subcategories within the above-listed filled row. *Intoxication* includes the use and abuse of alcohol or drugs (illicit and medicinal) and withdrawal symptoms. *System/organ dysfunction* includes kidney failure (acute or chronic) and dysfunction of the cardiovascular, gastrointestinal, and respiratory systems. *Miscellaneous* includes different extracranial diagnoses within ICD-10 chapters I-XIV, including oncologic diseases and psychiatric diseases. Primary brain tumours, brain metastases, and infections of the brain and meninges were included in *other diseases of CNS*. *R-diagnoses* refer to 'symptoms, signs and abnormal clinical and lab findings' (Chapter XVIII, ICD-10) and *Z-diagnoses* refer to 'factors influencing health status and contact with health services' (Chapter XXI, ICD-10). *P*-values indicating statistical significance between age groups; *$p < 0.05$, **$p \leq 0.01$, ***$p \leq 0.001$.

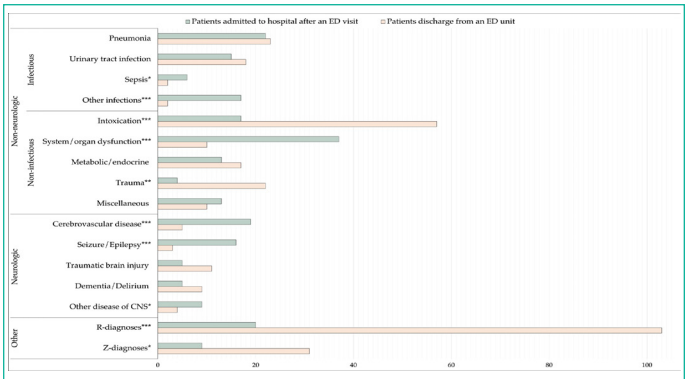

Figure 3: *Aetiologies of AMS cases in the ED stratified against hospital admission.*

Note: X-axis shows the number of patients, *n*. Patients admitted to short-stay ED units only were included under 'patients discharged from an ED unit'. 'Admission to hospital' refers to patients who were transferred to specialised wards after the initial ED visit. *Other infections* comprise various infectious diseases, including skin infections, endocarditis, and bacterial infections without further specification. *$p < 0.05$, **$p \leq 0.01$, ***$p \leq 0.001$.

Mortality

The overall30-day mortality rate in the study population was 10.8% (*n*=60), of which 50%of deaths occurred within the first 7 days after presentation to the ED. As depicted in Figure4, mortality was found to be significantly higher in the elderly (≥60 years) than in younger adults (14.8% vs. 3.2%, *p-value*<0.001).

The distribution of deaths across all aetiologies is shown in (Table 2). Among the patients who died, the most frequent diagnoses were *system/organ dysfunction* (*n*=18), *infection* (*n*=17), and *neurological disorders* (*n*=11). The most common infectious cause of death was pneumonia, accounting for 70.6% of all infection-related deaths. After adjusting for age and gender, only patients with *system/organ dysfunction* had significantly higher odds of dying within 30 days compared to the rest of the study population (OR: 6.2, 95% CI: 3.0-12.6). See supplemental digital content figure 2for the cumulative incidence proportions for the top five diagnoses.

Discussion

This study presents data on the aetiologies and mortality rates among patients presenting to the ED with AMS. It was found that AMS occurred in patients of all ages and that patients had various discharge diagnoses across the ICD-10 chapters. Non-neurological disorders were found to be the most common causes of AMS, and the causative composition differed significantly between age groups. *Infection* was the most frequent cause of AMS among the elderly, while *intoxication* dominated among younger adults. In the present study, two-thirds of the included patients were 60 years of age or older. Previous studies have described mean ages ranging from 49 to 69 years [1,7,9,10,18]. These discrepancies might be due to diverse inclusion criteria and demographic differences between regions. A bimodal age distribution has been described by some authors [1,7], including young adults and the elderly, respectively. In this study, a similar bi-peaked pattern could not be demonstrated. However, two clusters of patients on each side of around 60 years occurs, in similarity to the findings reported by Xiao *et al* [7].

Among all the patients included, 41.7% were found to have a Glasgow Coma Scale (GSC) score of 15, which normally indicates that a person is fully conscious. This might be explained by fluctuations in the patient's clinical state or by the fact that the GCS score was assessed later than the time of triage, when some patients might have improved spontaneously or due to initial therapy. Moreover, some patients may have been admitted due to qualitative impairments (e.g., impairment in social interaction), which are not measured by the GCS scale.

The composition of aetiologies in this study was found to differ significantly between age groups, which is in accordance with the findings of previous studies [1,7,10]. The most common discharge diagnosis was *unspecific R-diagnoses*. *R-diagnoses* were mostly used in the ED, as 83.7% of all *R-diagnoses* were given upon discharge from one of the ED units. This underlines that unspecific complaints such as AMS can be difficult to diagnose, and that an underlying cause is often not determined. *R-diagnoses* had a 30-day mortality rate of 4.9% and an adjusted OR of 0.4 (95% CI: 0.2-1.1). Thus, patients discharged with unspecific *R-diagnoses* seem to have a lower risk of dying compared to other AMS patients. Presumably, these patients represent milder or transient cases of AMS. However, a recent Danish study by Sørensen *et al*. including all ED patients found an overall 30-day mortality rate of 3% [19]. Therefore, a 30-day mortality rate of 4.9% cannot be ignored, and AMS patients with *R-diagnoses* might still be at increased risk of adverse outcomes. Thorough diagnostic workups should be prioritised in unclear cases to assure correct treatment and follow-up. *Infection* was the major cause of AMS among the elderly ≥60years of age. Pneumonia and Urinary Tract Infections (UTI) accounted for 42.9% and 31.4% of all infections, respectively. Before adjustment, the odds ratio of dying from an *infection* within 30 days were 1.8 (95% CI: 1.0-3.3). However, after adjusting for age and gender, the odds were 1.0 (95% CI: 0.6-2.0), and thus not statistically significant compared to the remaining study population. The high prevalence of pneumonia in the elderly group might explain the high rate of chest x-rays performed within this group (43.6% of patients). A similar pattern of infectious diseases has been reported by other authors [9,10].

Intoxication was associated with a low mortality rate (1.4%) compared with other aetiologies. This might be due to the young age composition and because intoxication is a transient condition. A noticeable smell on the breath or a known substance use disorder could guide physicians, thus leading to rapid diagnostics and treatment. However, a recent study found that a presumptive diagnosis of ethanol intoxication in patients with AMS was erroneous in 5% of cases [20]. Thorough, examination for differential diagnoses should always be considered in unclear cases. Neurological disorders were found to be less prevalent (15.5%), with *cerebrovascular diseases* accounting for only 4.3% of all cases. These findings are in line with those of previous studies [1,7-10,18]. However, some authors have described primary neurological conditions as one of the major causes of AMS, accounting for 27% to 44% of all cases [1,7,9]. In particular, *cerebrovascular diseases* and *epilepsy* have been frequently reported [7,9]. The lower prevalence of neurological conditions in this study might be explained by the fact that patients suspected of stroke are referred directly to the department of neurology at this particular hospital.

The overall 30-day mortality rate in this study was 10.8%, with the highest mortality rate among adult's ≥60 years (14.8%). *System/organ dysfunction* was associated with the highest mortality rate (30% of all deaths), and an adjusted odds ratio of 6.2 (95% CI: 3.0-12.6). Our findings on overall mortality are in line with previous studies revealing mortality rates ranging from 8.1% to 11.5% in patients presenting with AMS [1,7-10]. Sørensen *et al*. compared 30-day mortality in all ED patients regardless of chief complaint, and found that patients with AMS stood out with the highest 30-day mortality rate of 8.4% [19].

Previous studies including AMS ED patients have mainly focused on in-hospital deaths, and stroke in particular has been associated with a high mortality rate [7,9,10]. Völk *et al*. found an in-hospital mortality rate of 11% in AMS patients. They also found that patients with primary neurological disorders had a higher mortality rate than those with non-neurological disorders (13% vs. 9%) [9]. the in-hospital mortality rate in the present study was 5.4%, which is remarkably lower than the rates described by other authors. One explanation could be that in this particular hospital, patients suspected of stroke are referred directly to specialised wards from the pre-hospital area, thus bypassing the ED. Moreover, patients admitted through a pre-hospital emergency call are not triaged, as they are seen immediately after admission. Additionally, some studies have only included patients with GCS-scores below 15 [1,7], while others have only included patients with no obvious underlying aetiology, and thus such patients have a potentially increased risk of adverse outcomes due to diagnostic delay [9].

Clinical Value

Based on this study, it seems beneficial to adapt the initial diagnostics of AMS and clinical care to the patient's age. A standard approach to managing young adults with no obvious cause of AMS may include a urine and blood test to check blood alcohol levels, blood glucose, ketone bodies, and traces of selected drugs. Besides the normal clinical examination, initial diagnostic workups on elderly patients may includes urine dipstick test, a chest x-ray, an ultrasound scan, and blood tests to check liver and kidney function, blood oxygen level, fluid balance, level of electrolytes, and inflammation markers to rule out organ dysfunction and commonplace infections (i.e., pneumonia and UTI). In the case of specific signs of infection, a blood culture and lumbar puncture should always be considered. Neurological causes of AMS are relatively rare in the ED. If the patient shows no signs of head trauma, headache, or neurological deficits, abstention from a cranial CT scan may be considered. However, a CT scan should always be considered in patients with undetermined or descending levels of consciousness.

Limitations

This is a single-centre study, and caution should be taken regarding generaliz ability outside this region due to socio-demographic distinctions and differences in ED workflows, in-hospital resources, and triage systems. However, the results were somewhat in line with those of previous studies, thus suggesting that the results might be generalisable to other settings. All deaths within 30 days after the initial ED contact were assumed to be related to the cause of the ED visit. However, it is conceivable that some deaths were non-AMS related, which is why this study might overestimate the mortality in AMS patients. Lastly, the impact of comorbidities and therapeutic management were not examined in this study. Future studies should therefore take comorbidities and initial treatments into account.

Conclusion

The data presented in this study reveal that AMS is caused by a wide range of different conditions. However, non-neurological disorders appear dominant at all ages. Intoxication was primarily seen among younger adults (18–59 years), while infection was a more common cause among the elderly (>60 years). AMS is associated with a high 30-day mortality rate, and patients with *system/organ dysfunction* had significantly higher odds of dying within 30 days compared to the rest of the study population.

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