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Johan Olsson

johan.k.olsson@regionstockholm.se

Karolinska University Hospital

Ryan Falck-Jones

Karolinska University Hospital

Anders Holst

RISE Research Institutes of Sweden

Cecilia Åkerlund

Karolinska University Hospital

Logan Froese

Karolinska Institutet

David Nelson

Karolinska University Hospital

Linn Hallqvist

Karolinska University Hospital

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Causal Effects of Helicopter Emergency Medical Services in Interhospital Transfers to Neuro ICUs: A Nationwide Swedish Registry-Based Cohort Study (2019–2024)

Johan Olsson[1,2,✉], Ryan Falck-Jones[3,2], Anders Holst[4,5], Cecilia Åkerlund[3,2], Logan Froese[6], David Nelson[3,2], and Linn Hallqvist[3,2]

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[1] Department of Pediatric Perioperative Medicine and Intensive Care, ECMO Centre Karolinska, Karolinska University Hospital, Stockholm, Sweden

[2] Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden

[3] Department of Perioperative Medicine and Intensive Care, Karolinska University Hospital, Stockholm, Sweden

[4] School of Electrical Engineering and Computer Science, KTH Royal Institute of Technology, Stockholm, Sweden

[5] RISE Research Institutes of Sweden, Stockholm, Sweden

[6] Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden

✉ Correspondence: Johan Olsson <johan.k.olsson@regionstockholm.se>

Abstract

Background: The optimal transfer team setup and transportation modality in transfers of neuro ICU patients are unknown. The purpose of this study was to estimate the effect of helicopter emergency medical services (HEMS) on 30-day mortality in neuro ICU patients transferred to tertiary centers.

Methods: We performed a retrospective cohort study using Swedish healthcare registries and flight movement data. Patients with traumatic brain injury, aneurysmal subarachnoid hemorrhage, intracerebral hemorrhage, or acute ischemic stroke transferred by HEMS were compared to those transferred by other modalities. Weather conditions affecting flight feasibility were used as a natural randomization mechanism in an instrumental variable analysis.

Results: A total of 3451 patients were transferred from 62 Swedish hospitals. There were 584 HEMS transfers (16.9%). The core assumptions for instrumental variable analysis using weather observations appeared to be met. The local average treatment effect (LATE) of HEMS versus non-HEMS transfer on 30-day mortality was estimated at -0.4% (95% credible interval (CrI): -20.3% to 13.2%), with P(LATE > 0) = 0.483. In a post-hoc sensitivity analysis restricted to patients without acute ischemic stroke and with a non-negligible chance of being transferred by HEMS, the LATE of HEMS versus non-HEMS transfer on 30-day mortality was -14.6% (95% CrI: -33.9% to 1.9%), and P(LATE > 0) = 0.046.

Conclusions: The primary instrumental variable analysis showed no evidence of a 30-day mortality benefit with HEMS transfers. A secondary, post-hoc analysis suggested a possible mortality benefit when patients with acute ischemic stroke and those transferred to centers

with negligible HEMS use were excluded. Weather-based instrumental variables could provide a transferable framework for causal inference in transport research, and we provide recommendations for future studies.

Study registration: ClinicalTrials.gov, NCT07052656. Registered 2025-05-28. Retrospectively registered.

Keywords

"Neurocritical care", "Neurointensive care", "Intensive care", "Critical care", "Interfacility transfer", "Interhospital transfer", "Helicopter emergency medical services", "HEMS", "Causal inference", "Instrumental variable analysis"

Background

Interhospital transfer is often necessary for critically ill patients with neurological or neurosurgical emergencies initially managed in community or regional hospitals. In Sweden, as in many other countries, neurosurgical and neurocritical care expertise is centralized in tertiary centers, requiring patients to be transferred for definitive care.

Transporting critically ill patients between hospitals is challenging. These patients require ongoing treatment and monitoring during transit, ideally at a level at least equivalent to that of the referring ICU. Environmental factors such as changes in barometric pressure, temperature, and acceleration can exert physiological stress. Operational challenges, limited access to the patient, low lighting, noise, and a confined workspace further complicate care. The transport team must also, concurrent with patient management,

manage several non-clinical tasks such as planning the logistics with dispatch centers and communicating with ambulance personnel, receiving providers, and flight crews.

Such challenges may explain the high complication rates observed during interhospital transfers, reported in some studies to affect up to 25% of patients [1–9]. Actual rates may be higher due to reliance on self-reporting [8, 10]. Longer transport times are consistently linked to increased complication risk [1, 4, 6].

Some studies suggest that interhospital transfers conducted by specialized retrieval teams may be associated with better care and reduced mortality in adult populations [2, 7, 11, 12]. Similar findings have been reported in pediatric cohorts [13–16]. Only one single-center randomized controlled trial has been conducted to assess the impact of specialized transport teams on patient outcome, which could not establish non-inferiority of nurse-led transports [2]. Despite the limited evidence base, several expert groups and professional societies recommend that interhospital transfers of critically ill patients be conducted by specialized teams [17–21].

However, few studies have specifically examined interhospital transfers of neurocritical care patients [22, 23], and only one, a single-center U.S. study, has evaluated the impact of transport modality on outcomes in this population, finding no difference between air and ground transfers [24].

In Sweden, two similar patients may be transferred by different means and under markedly different standards of care. Broadly, there are two provider configurations for interhospital transfers. Specialized retrieval teams, typically composed of an anesthesiologist-intensivist and a nurse trained in anesthesia and/or intensive care, operate at a regional level,

commonly with neurocritical care experience, and have access to both air and ground transport. In contrast, local solutions are based at the referring hospital. These may consist of a single provider, typically a nurse with anesthetic training or a physician in training, and are sometimes staffed on an ad hoc basis. Local providers or teams rely solely on ground ambulances. All patients transferred between hospitals via HEMS in Sweden are managed by specialized retrieval teams.

The factors influencing the choice of transport modality in interhospital ICU transfers have not been described. It is possible that estimated transport time, clinical urgency, weather, patient characteristics and local practice patterns play a role in the decision-making process. Some of these factors might be confounding variables. Establishing causal relationships from observational transport data is challenging, and most previous studies are limited by residual confounding from unmeasured factors that influence both transport decisions and patient outcomes. Studies using causal inference methodologies such as pseudo-randomization are lacking.

In this study, we describe a national cohort of neurocritically ill patients transferred to tertiary centers. We examine predictors of HEMS use and assess whether HEMS, serving in part as a proxy for specialized teams, has a causal effect on 30-day mortality. To strengthen causal inference and address potential residual confounding, we use weather data as an instrumental variable, acting as a mechanism of pseudo-randomization. The instrumental variable assumptions are systematically assessed before estimating the effect of transport modality.

Methods

The study is part of the EpiNIC project, registered at ClinicalTrials.gov (NCT07052656). The manuscript follows the STROBE reporting guidelines for observational studies [25].

Data Sources

Clinical data were obtained from the Swedish Intensive Care Registry (SIR) and the National Patient Register (NPR). SIR is a national quality registry covering over 80 ICUs, representing most community and regional hospitals in Sweden. The registry includes detailed information on ICU admissions, discharge times, diagnostic categories, interventions, and components of physiological scores such as Simplified Acute Physiology Score 3 (SAPS 3).

The NPR contains administrative records, procedure codes, and ICD-coded discharge diagnoses. The NPR has near-complete national coverage and fair diagnostic validity for several acute neurological conditions [26].

Mortality data were retrieved from the National Cause of Death Register, which includes the date and, when available, the cause of death, with near-complete national coverage.

Since no national registry of ICU transfers exists, transport modality was inferred from flight data. Flight movement data were provided by Flightradar24 AB, Stockholm, Sweden. Historical weather data were sourced from the Swedish Civil Aviation Administration via Ogimet [27]. Geographic coordinates for hospitals, helipads, and airports, as well as road distances between facilities, were obtained from the openrouteservice API (HeiGIT) [28] via its R client [29], based on OpenStreetMap data [30].

Data preprocessing and analyses were performed using SQLite version 3.49.1, R version 4.6.1 (2026-06-24), Python version 3.11, and a set of open-source software packages [31–36].

Patients and Clinical Data

We sought to distill a cohort of patients urgently transferred from non-tertiary hospitals to tertiary hospitals with diagnoses commonly relevant to neurocritical care and in need of intensive care during the transport. The latter was defined as receiving intensive care immediately before or after transfer.

Patients were eligible if they met the following criteria: (1) admission to a tertiary center between November 30, 2019, and November 30, 2024; (2) a preceding non-tertiary ICU stay shorter than 12 hours or a non-tertiary emergency department (ED) discharge less than 10 hours before tertiary ICU admission; (3) patient age ≥18 years; (4) at least one ICU admission during the study period with a diagnosis relevant to neurocritical care; and (5) a diagnosis of aneurysmal subarachnoid hemorrhage (ASAH), acute ischemic stroke (AIS), intracerebral hemorrhage (ICH), or traumatic brain injury (TBI), i.e. the four most common indications for neurocritical care in our data. Finally, only the first such admission per patient was included in the final cohort. The patient identification method is explained at length in Additional file 1.

The start date corresponds to the introduction of a new helicopter at a major transport organization, improving flight tracking accuracy. Follow-up on mortality was available through December 31, 2024, allowing for estimation of 30-day mortality.

Diagnostic data were sourced from the NPR based on ICD-10 and procedural codes (detailed in Additional file 1).

Physiological data were retrieved from the first relevant SIR record. Glasgow Coma Scale (GCS) scores reflected presedation consciousness and were taken from SAPS assessments. In order to specifically examine the contribution of age and consciousness level, we also calculated a modified SAPS excluding the age and GCS components.

Transfer Data

Helicopter flight movements were parsed from Automatic Dependent Surveillance–Broadcast (ADS-B) data. For the latter half of the data (starting June 1, 2022), data on fixed-wing transfers were also available. Details on the flight-matching algorithm and processing steps are provided in Additional file 1.

Transfers were classified as carried out by HEMS or fixed-wing aircraft if a matching flight was identified along the same hospital-to-hospital route, with a departure time within a set time window. The exact size of this window was allowed to vary between subcohorts of patients, depending on data sources for inclusion. The window accounted for potential clerical discrepancies in discharge times and expected patient logistics.

If no matching flight could be found, the transfer modality was set to “other,” meaning ground transfer from June 1, 2022, onward, and ground or fixed-wing transfer before that date. See Additional file 1 for details.

Estimated transit time (time spent in a vehicle) was calculated for all patients; for HEMS and fixed-wing transfers, it was based on actual flight times. In addition to flight times,

assumed times for embarking and disembarking vehicles were included, as well as any ground legs to and from airports. Driving times for ground legs, and for ground-only transfers, were calculated with the Open Source Routing Machine (OSRM) [37] on OpenStreetMap road data [30]. To account for ambulances being allowed to exceed the speed limit, all ground-leg times were reduced by 30% relative to normal driving times. Details can be found in Additional file 1.

Instrumental Variable

Automated weather reports (METeorological Aerodrome Reports, METARs) were used to assess whether meteorological conditions met the minimum requirements for HEMS operations, assuming two-pilot crews operating under performance class 1 or 2, in accordance with European Union Aviation Safety Agency (EASA) regulations [38]. For example, during night operations, a cloud base of at least 1,200 ft and a horizontal visibility of 2,500 m are required to meet HEMS minima. Details on weather data parsing and classification criteria are provided in Additional file 1.

Each hospital was matched to the nearest consistently METAR-reporting airport. Weather conditions were evaluated at both sending and receiving sites at the time of discharge from the referring unit. HEMS was considered technically feasible only if EASA weather minima were met at both locations.

Outcome

The outcome was 30-day mortality following the first ICU admission.

Statistical Methods

In the descriptive part of the study, continuous variables were presented as medians with interquartile ranges (IQRs). No univariate hypothesis testing was performed between HEMS and non-HEMS groups to avoid overinterpreting descriptive differences as causal. Transfer routes were visualized using adapted code from Sadler [39].

All analyses used Bayesian modeling with flat priors, given the limited evidence base for intensive care transfers in Sweden. Regression model estimates were reported as odds ratios with 95% credible intervals (CrI). Convergence was assessed using R-hat (threshold < 1.01) and effective sample sizes; models not meeting these criteria, if any, are noted in the Results.

Predictors of transport modality were assessed using a Bayesian generalized linear model (GLM) with Bernoulli likelihood and a logit link function, implemented in `brms` [34].

We examined the causal effect of HEMS transfers on mortality by estimating the local average treatment effect (LATE). The LATE was estimated using an instrumental variable (IV) approach, leveraging weather-based HEMS operating minima as a pseudo-randomization mechanism [40, 41]. Under its assumptions, IV analysis allows estimation of causal effects in the presence of unmeasured confounding. The LATE describes the effect of treatment in the "complier" subset of patients, i.e. those whose treatment status is influenced by the instrumental variable [41]. The LATE was estimated using a model implemented in `pymc` with flat priors for outcome count and principal strata parameters [36]. Details of the estimand and estimator are provided in Additional file 1. Further, we carried out secondary post-hoc analyses of patients based on diagnosis (acute ischemic

stroke vs other diagnosis), a sensitivity analysis restricted to HEMS-using hospitals, and a fully crossed 3×3 panel of all subgroup LATEs.

For the LATE estimates, we reported the posterior probability of harm, P(LATE > 0), and its complement, the posterior probability of a mortality reduction. These posterior probabilities quantify how likely it is, given the data, model, and priors, that HEMS increased or reduced 30-day mortality among compliers, respectively. They should be interpreted on a continuous scale rather than against a significance threshold.

Identification of the LATE requires four assumptions: (1) instrumental variable relevance, (2) exclusion restriction, (3) exchangeability, and (4) monotonicity [40–45].

Instrumental variable relevance (*assumption 1*) requires that the instrument affect treatment allocation. It was assessed by fitting a multivariable generalized linear model with HEMS minima as one of the predictors of transport modality, adjusting for age, diagnosis, receiving hospital and severity of illness. The exclusion restriction (*assumption 2*) requires that the instrument affect the outcome only through the treatment. Although untestable, it was challenged by assessing the association between the instrumental variable and outcome in subgroups where the instrumental variable is not expected to influence exposure [42, 44], using a multivariable GLM adjusting for diagnosis, month, age, severity of illness and receiving hospital. The exchangeability assumption (*assumption 3*) requires that the instrument and outcome share no unmeasured confounders. It cannot be formally tested, but we used a previously proposed falsification strategy assessing covariate balance across levels of the instrumental variable [44]. The monotonicity assumption (*assumption 4*) requires that the instrumental variable influence exposure in only one

direction, in this case, that weather below HEMS minima never makes HEMS transfer more likely. It cannot be formally tested [44].

Use of Large Language Models (AI)

Language editing, proofreading and revision of text, code review, and code documentation were assisted by Claude Sonnet 4 and Claude Opus 5.5 (Anthropic) and GPT-4o (OpenAI). No AI assistance was used in study planning, conceptualization, data analysis, interpretation, or conclusions. All analytical decisions, interpretations, and conclusions were made by the authors, who take full responsibility for the content.

Results

Patient Selection

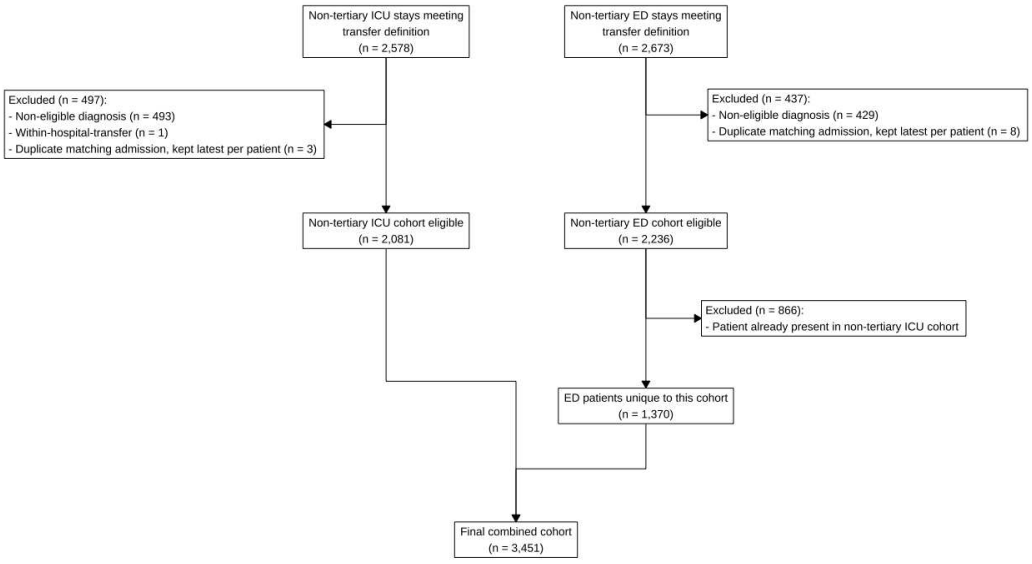


Figure 1. Flowchart of patient inclusion. Patients were eligible if they met the following criteria: (1) admission to a tertiary center between November 30, 2019, and November 30, 2024; (2) a preceding non-tertiary ICU stay shorter than 12 hours or a non-tertiary ED discharge less than 10 hours before tertiary ICU admission; (3) patient age ≥18 years; (4) at least one ICU admission during the study period with a diagnosis relevant to neurocritical care; and (5) a diagnosis of aneurysmal subarachnoid hemorrhage (ASAH), acute ischemic stroke (AIS), intracerebral hemorrhage (ICH), or traumatic brain injury (TBI), i.e. the four most common indications for neurocritical care in our data. Finally, only the first such admission per patient was included in the final cohort.

Patient selection is described in Figure 1. A total of 3451 patients were included in the cohort.

Missing Data

Patients with missing values on relevant variables were excluded prior to statistical modeling (complete-case analysis). The rate of missingness was low. For the Bayesian GLM predicting transfer modality, we excluded 7.6% of patients with missing values. Almost all missingness was attributable to missing SAPS values, and its frequency was similar in the HEMS and non-HEMS groups (Table 1). For the LATE estimation, only 4 of 3451 patients (0.1%) were excluded because of missing weather data.

Travel Routes

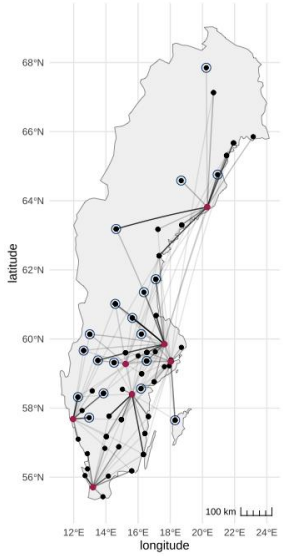


Figure 2. Routes travelled by patients in the cohort by all modes of transport. Only transfers >50 km are plotted for improved visibility. The opacity of the line denotes the relative number of transfers. Receiving tertiary centers are maroon. Sending centers where ≥25% of patients are transferred by HEMS are circled. Note that one of the receiving tertiary centers, Örebro University Hospital, also acts as a sending center.

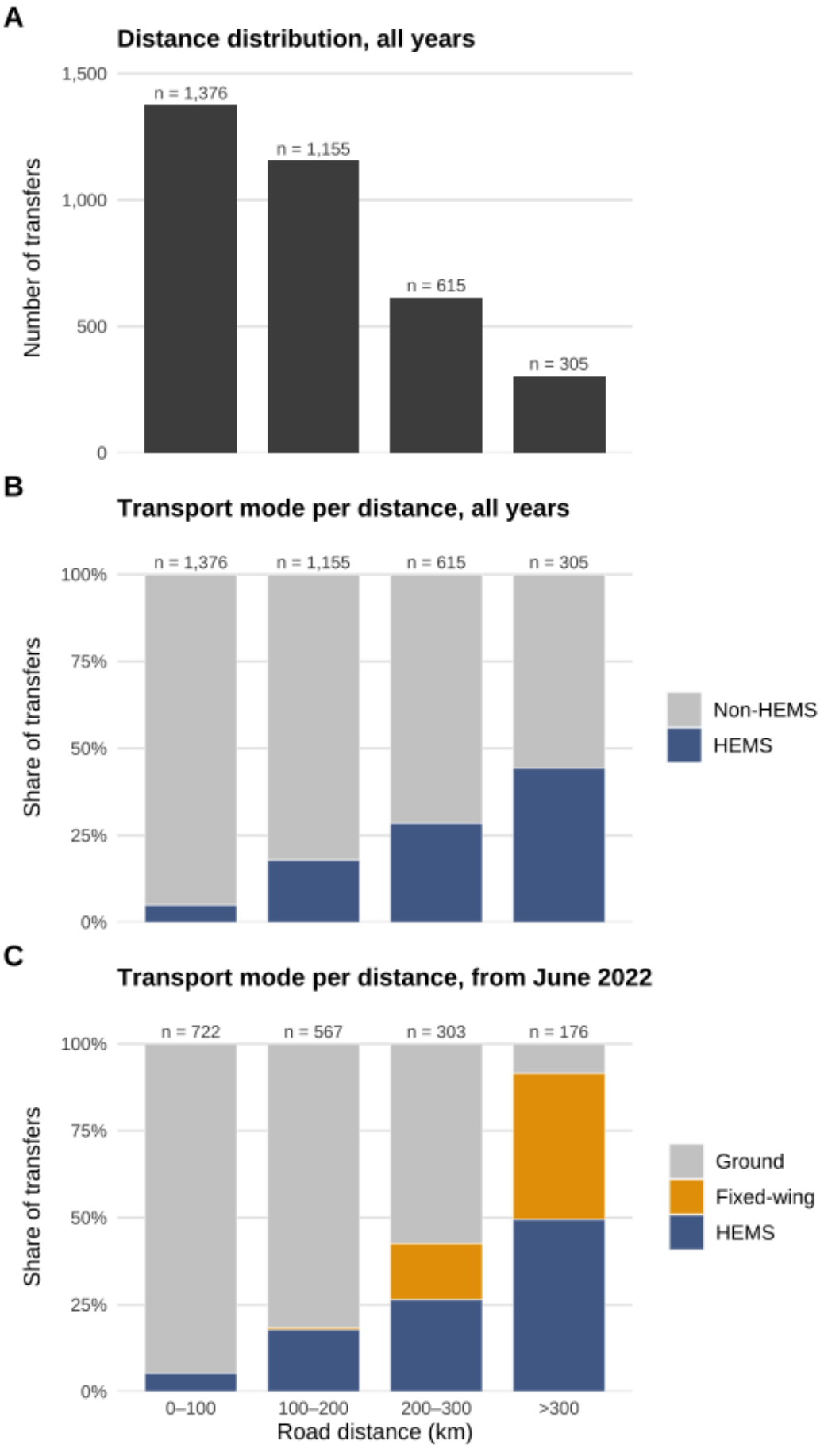

A
Distance distribution, all years
Number of transfers
1,500
1,000
500
0
n = 1,376
n = 1,155
n = 615
n = 305
B
Transport mode per distance, all years
Share of transfers
100%
75%
50%
25%
0%
n = 1,376
n = 1,155
n = 615
n = 305
Non-HEMS
HEMS
C
Transport mode per distance, from June 2022
Share of transfers
100%
75%
50%
25%
0%
n = 722
n = 567
n = 303
n = 176
Ground
Fixed-wing
HEMS
0–100
100–200
200–300
>300
Road distance (km)

Figure 3. Transfers and transport modality by road distance between sending and receiving centers. (A) Number of transfers per distance bin, all years. (B) Share of HEMS and non-HEMS transfers per bin, all years. Non-HEMS includes both ground and fixed-wing transfers, which could not be distinguished before June 2022. (C) Share of HEMS, fixed-wing and ground transfers from June 1, 2022, when fixed-wing transfers could be identified. Numbers above the bars give the number of transfers per bin.

The paths traveled by patients in the cohort are plotted in Figure 2. The distribution of transport distances and transport modality distribution per distance bin are shown in Figure 3. The proportion of HEMS transfers increased with transfer distance. Many long-distance transfers (>300 km) were carried out by fixed-wing.

Description of the Cohort

Table 1. Patient characteristics and logistical details by transfer modality (full dataset).

Characteristic	Transfer modality	
	HEMS transfer N = 584[1]	**Non-HEMS transfer** N = 2,867[1]
Age (years)	61 (47, 72)	63 (51, 72)
Female	236 (40%)	1,252 (44%)
Inferred diagnosis		
AIS	100 (17%)	413 (14%)
ASAH	151 (26%)	954 (33%)
ICH	113 (19%)	565 (20%)
TBI	220 (38%)	935 (33%)
SAPS consciousness level		
I (GCS ≥13)	264 (48%)	1,303 (49%)
II (GCS 7-12)	158 (29%)	721 (27%)
III (GCS 6)	34 (6.1%)	166 (6.3%)
IV (GCS 5)	26 (4.7%)	107 (4.1%)
V (GCS ≤4)	72 (13%)	342 (13%)
Missing	30	228
Mechanical ventilation	335 (57%)	1,725 (60%)
SAPS Score	54 (46, 62)	54 (46, 64)
Missing	16	176
SAPS Score excl. age and GCS components	41 (38, 48)	42 (39, 49)
Missing	30	228
Road distance (km)	212 (136, 283)	108 (46, 195)
Estimated transit time (min)	58 (46, 72)	64 (33, 103)
HEMS weather minima met at discharge	565 (97%)	2,283 (80%)
Missing	1	3
30-day mortality	83 (14%)	507 (18%)

[1]Median (Q1, Q3); n (%)

Table 2. Patient characteristics by transfer modality. Only including transfers where fixed-wing data were available, i.e. from June 1, 2022.

Characteristic	Transfer modality		
	Fixed-wing transfer N = 126[1]	**HEMS transfer** N = 306[1]	**Other (ground) transfer** N = 1,336[1]
Age (years)	66 (56, 74)	62 (48, 74)	63 (51, 73)
Female	40 (32%)	122 (40%)	576 (43%)
Inferred diagnosis			
AIS	23 (18%)	57 (19%)	203 (15%)
ASAH	23 (18%)	77 (25%)	439 (33%)
ICH	24 (19%)	61 (20%)	246 (18%)
TBI	56 (44%)	111 (36%)	448 (34%)
SAPS consciousness level			
I (GCS ≥13)	52 (43%)	134 (47%)	569 (49%)
II (GCS 7-12)	38 (31%)	86 (30%)	312 (27%)
III (GCS 6)	12 (9.8%)	17 (6.0%)	75 (6.5%)
IV (GCS 5)	11 (9.0%)	11 (3.9%)	31 (2.7%)
V (GCS ≤4)	9 (7.4%)	37 (13%)	173 (15%)
Missing	4	21	176
Mechanical ventilation	76 (60%)	177 (58%)	769 (58%)
SAPS Score	55 (46, 65)	53 (46, 62)	54 (46, 64)
Missing	1	12	156
SAPS Score excl. age and GCS components	42 (36, 49)	41 (39, 48)	42 (39, 49)
Missing	4	21	176
Road distance (km)	340 (271, 370)	213 (130, 370)	85 (39, 163)
Estimated transit time (min)	82 (79, 96)	59 (44, 72)	60 (30, 99)
HEMS weather minima met at discharge	89 (71%)	296 (97%)	1,092 (82%)
Missing	0	0	1
30-day mortality	27 (21%)	44 (14%)	227 (17%)

[1]Median (Q1, Q3); n (%)

Minor unadjusted differences between the HEMS and non-HEMS groups were observed: the HEMS group had a slightly lower median age and longer transport distances. Overall, the groups appeared similar across the presented covariates, see Table 1. In the second half of the dataset, data on fixed-wing transfers were available, and the patient cohort could be further subdivided into three categories, see Table 2. In this period, patients transferred by fixed-wing aircraft were slightly older and had worse unadjusted outcomes. Most of them (83%) were transferred to a single tertiary center. While HEMS patients were transferred over longer distances than non-HEMS patients, the calculated transit times were similar.

Factors Associated with HEMS Transfer

Table 3. Multivariable Bayesian logistic regression predicting HEMS transfer.

Predictor	aOR	95% CrI
Inferred diagnosis		
AIS	—	—
ASAH	0.52	0.37, 0.73
ICH	0.69	0.48, 0.99
TBI	0.85	0.62, 1.17
Age (per SD)	0.85	0.77, 0.95
SAPS consciousness level		
I (GCS ≥13)	—	—
II (GCS 7-12)	1.10	0.83, 1.44
III (GCS 6)	0.95	0.59, 1.51
IV (GCS 5)	1.09	0.65, 1.81
V (GCS ≤4)	1.12	0.77, 1.61
SAPS 3 score (excl. age/GCS components, per SD)	1.00	0.89, 1.13
HEMS weather minima met	10.5	6.48, 18.1
Receiving hospital		
Akademiska sjukhuset	—	—
Karolinska universitetssjukhuset, Solna	0.17	0.12, 0.22
Norrlands universitetssjukhus	0.38	0.28, 0.50
Sahlgrenska universitetssjukhuset	0.60	0.45, 0.80
Universitetssjukhuset i Linköping	0.01	0.00, 0.02
Universitetssjukhuset i Lund	0.00	0.00, 0.02
Universitetssjukhuset i Örebro	0.41	0.24, 0.67

Abbreviations: CrI = Credible Interval, aOR = adjusted Odds Ratio

In the multivariable predictive model of transfer modality, HEMS minima being met predicted the choice of HEMS over other transfer modalities. Receiving hospital was also strongly associated with HEMS use. A diagnosis of ASAH and, to a lesser degree, a diagnosis of ICH and increasing age were associated with the choice of other modalities over HEMS, see Table 3. Of note, though not shown in the tables, patients with ASAH more often presented with GCS ≥13 (64%) than patients with other diagnoses (42%).

Instrumental Variable Analysis

Assessment of Instrumental Variable Model Assumptions

In a multivariable GLM with HEMS minima as an adjusted predictor of transport modality, the estimated adjusted odds ratio (aOR) was 10.5 (95% CrI: 6.5 to 18.1), providing evidence for instrumental variable relevance (*assumption 1*).

In a subgroup of patients transferred to receiving hospitals with low HEMS utilization (0.5%), the instrumental variable showed no clear association with outcome: the multivariable GLM, adjusting for diagnosis, month, age, severity of illness and receiving hospital, yielded an aOR of 1.4 (95% CrI: 0.8 to 2.3). This finding is consistent with the exclusion restriction (*assumption 2*) holding, though it does not exclude small violations.

Table 4. Patient characteristics by weather conditions.

	HEMS weather minima met at discharge	
Characteristic	**Weather minima met** N = 2,848[1]	**Weather minima not met** N = 599[1]
Age (years)	62 (50, 72)	63 (52, 72)
Female	1,223 (43%)	263 (44%)
Inferred diagnosis		
AIS	432 (15%)	81 (14%)
ASAH	905 (32%)	200 (33%)
ICH	567 (20%)	110 (18%)
TBI	944 (33%)	208 (35%)
SAPS GCS <15	1,936 (74%)	417 (75%)
Missing	218	40
Pretransfer mechanical ventilation	1,686 (59%)	370 (62%)
SAPS Score	54 (46, 63)	55 (46, 64)
Missing	162	30
SAPS Score excl. age and GCS components	42 (39, 49)	43 (39, 49)
Missing	218	40
30-day mortality	489 (17%)	101 (17%)

[1]Median (Q1, Q3); n (%)

As shown in Table 4, covariates appear balanced across levels of the instrumental variable, suggesting that the exchangeability assumption (*assumption 3*) is plausible. Given regulatory and operational constraints, poor weather cannot increase HEMS transfer

likelihood. Thus, we consider the monotonicity assumption (*assumption 4*) to be met. In summary, the four core assumptions for identifying the local average treatment effect appear to be met.

Estimation of the Local Average Treatment Effect (LATE)

The LATE of HEMS versus non-HEMS transfer on 30-day mortality was estimated at -0.4% (95% CrI: -20.3% to 13.2%), with P(LATE > 0) = 0.483 (the posterior probability of harm), showing no clear effect. As a secondary analysis, we excluded patients with AIS under the hypothesis that intensive care interventions matter less for this subgroup in general. This resulted in an estimated 30-day mortality effect of HEMS of -7.9% (95% CrI: -29.1% to 7.6%), with P(LATE > 0) = 0.201.

In a sensitivity analysis, we limited the above analyses to patients transferred to hospitals with a non-negligible (>1%) chance of HEMS transfer. This excluded patients transferred to two of the receiving centers, which together had a HEMS transfer rate of 0.5% (versus 24.4% in the remaining hospitals). Under this restriction, the LATE of HEMS versus non-HEMS transfer on 30-day mortality was estimated at -8.4% (95% CrI: -26.3% to 7.8%), with P(LATE > 0) = 0.163.

Applying both restrictions, i.e. excluding patients with AIS as well as patients transferred to the two receiving centers with <1% HEMS transfers, the estimated 30-day mortality effect of HEMS was -14.6% (95% CrI: -33.9% to 1.9%), with P(LATE > 0) = 0.046. Although the 95% credible interval included no effect, the posterior probability that HEMS reduced 30-day mortality among compliers was 95%.

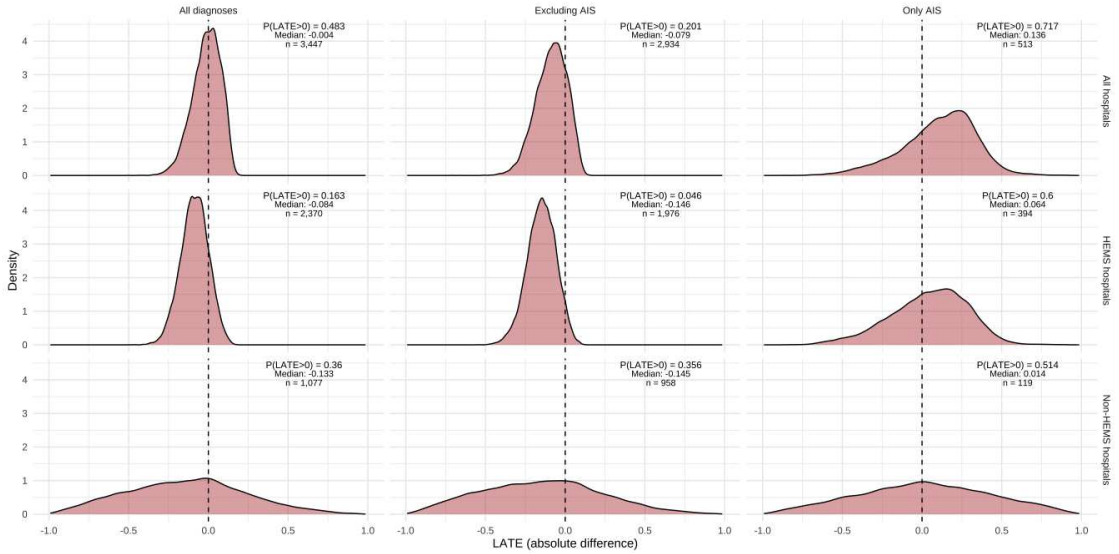


Figure 4. Posterior distributions of the LATE estimates under different restrictions. Columns show estimates for all diagnoses, excluding AIS, and AIS only; rows show estimates by receiving hospital: all hospitals, hospitals with relatively frequent HEMS use (~25%), and hospitals with very rare HEMS use (<1%). The dashed line marks no effect.

Posterior density plots of the full posterior distributions of the LATE estimates under different restrictions are shown in Figure 4. The posterior densities of estimates from the non-HEMS hospitals remained close to the prior implied by the model (a relatively uninformative distribution centered on zero), indicating that these data carry little information about the LATE.

Discussion

Key Findings

We aimed to evaluate the effect of HEMS transfer on 30-day mortality in a Swedish cohort of neuro ICU patients requiring urgent transfer to a higher level of care. Weather minima

emerged as a strong predictor of whether HEMS was utilized. Given the random nature of weather, this was recognized as a candidate for IV analysis and thus a means to more closely research causal effects. A diagnosis of ASAH was associated with a lower likelihood of HEMS transfer. The reason for this is not clear, but ASAH patients tended to have higher GCS scores, which could have shifted the transfer modality decision toward ground transfer without a specialized transfer team. Further, receiving hospital was associated with HEMS use.

The main instrumental variable analysis did not show a reduction in 30-day mortality with HEMS transfers. In a post-hoc analysis, excluding patients transferred to two of the seven receiving hospitals with a practically negligible chance of being transferred by HEMS, we observed a result suggesting a 30-day mortality benefit in patients without AIS.

Further, this study describes a national cohort of neurocritically ill patients transferred to tertiary centers, including their clinical characteristics, travel distances, and transfer modalities.

Findings in Relation to Previous Research

Previous studies examining the association between HEMS interhospital transfers and outcomes have reported mixed findings, with some suggesting benefits and others showing no clear effect [2, 7, 11, 12]. Our primary estimate was inconclusive, whereas the post hoc restricted analyses are consistent with a mortality benefit.

While previous studies provide valuable evidence, most face methodological challenges in establishing causal relationships. Several rely on unadjusted comparisons [12, 15] or use

statistical significance to guide variable selection [11, 14], which may not adequately control for confounding. Other studies do not specify the selection process for covariates in multivariable regression [13, 24] or propensity score methods [16], which decreases transparency and may limit inferences due to lingering unmeasured confounders.

Instrumental variable methods remain relatively uncommon in intensive care research. A few notable exceptions have applied parametric two-stage regression models to estimate treatment effects using IVs [46–48]. These models rely on assumptions about the functional form of the model and the distribution of error terms, which, if violated, can compromise estimates.

The instrumental variables used in those studies include prior regional HEMS usage (as an instrument for prehospital HEMS versus ground transfer selection), ICU bed availability (as a proxy for ICU admission promptness), and provider preference (as an instrument for prophylactic magnesium use to prevent atrial fibrillation). All of these IVs are, in effect, variants of region-, hospital-, or provider-level preferences. However, such instruments risk violating the exchangeability assumption, since unmeasured factors, such as differences in case mix or quality of care across regions, hospitals, or providers, may affect both the instrument and patient outcomes and thus open backdoor paths between the two.

While we commend these studies for advancing causal inference in intensive care research, they also underscore the challenge of identifying valid instrumental variables. In contrast, weather conditions may provide a defensible instrumental variable for studying the effectiveness of HEMS. To our knowledge, this is the first study to use weather minima as an instrumental variable to examine the effect of HEMS interhospital transfers.

Heterogeneous Treatment Effects

In a post-hoc analysis stratifying by AIS versus non-AIS, the LATE estimates differed in direction between the two subgroups, which would be consistent with heterogeneous treatment effects. If this is a true effect, it could be understood in terms of priorities in different diagnostic groups. Shorter time to endovascular treatment in AIS has been repeatedly shown to be associated with large benefits in functional outcome and mortality [49–51]. Assuming that the effect and its magnitude are causal, decreasing time to endovascular treatment could, in general, dominate the potential benefit of intensive care interventions provided before endovascular treatment.

Our clinical experience suggests that in the Swedish context, ground transfers over distances up to 250 km may often achieve comparable or shorter times to the tertiary center than HEMS, due to cumulative HEMS lead times. Hence, our findings motivate the hypothesis that faster transfers by non-specialized teams could outperform slower transfers by specialized teams, at least for a highly time-sensitive condition like AIS.

By contrast, the benefit of reducing time to arrival at a tertiary center or to definitive treatment is less well established for patients with TBI, ASAH, and ICH [24]. While rapid transfer time is likely to be critical in selected cases, the indications for transfer and intended interventions vary substantially across these patient groups, making the overall time-dependent benefit less clear. The capacity of HEMS to provide high-quality neuroprotective care by a specialized team may outweigh differences in total transfer time.

First-stage Heterogeneity in Instrumental Variable Analysis

The weather instrument did not influence transport modality equally across receiving hospitals, which has implications for how the LATE is best estimated. The strength of an instrumental variable, i.e., the proportion of compliers, can differ across subsets of a cohort, a phenomenon known as first-stage heterogeneity that has recently received attention in methodological research. A nonzero effect of the instrument on treatment (the IV relevance assumption) is necessary for identification of the LATE overall, but it need not hold in every subgroup. Including subgroups with low compliance can increase noise, whereas excluding subgroups using arbitrary cutoffs can bias estimates [52]. This raises the question of whether excluding the two receiving centers with <1% HEMS transfers, as in our sensitivity analysis, was justified.

We believe the exclusion was reasonable. When these two centers were excluded, the uncertainty around the LATE estimates decreased. Although not formally shown, this is in line with our expectation that low-complier subcohorts mainly add variance. Consistent with this, when the LATE was estimated using only transfers to these two centers, the posterior densities remained close to the prior, suggesting that these patients carry little information about the effect. Including low-complier subcohorts also exposes the estimates to bias if any of the IV assumptions are violated, for example through a chance difference in mortality across levels of the instrument. However, this was not a preplanned analysis, and its results carry a substantial risk of bias. Our cutoff of <1% probability of HEMS transfer is arbitrary, but it is defensible from a mechanistic viewpoint: patients transferred to these two centers will practically never be transferred by HEMS because of the long distances to

the nearest HEMS bases. In conclusion, excluding subgroups in which the instrument cannot plausibly affect treatment may improve LATE estimation, but the approach to such exclusions should ideally be prespecified in future studies.

Limitations

Patients who die during transfer are expected to be underrepresented in our analysis, as such patients will not be admitted to the receiving center. Nevertheless, in-transfer deaths are rare in ICU interhospital transfers [1, 9], making substantial bias from this source unlikely. Patients dying before an intended transfer are also unaccounted for. While we believe, based on clinical experience, that such events are rare, an ideal study should track all potential transfers.

Another limitation concerns the studied exposure. Our hypothesis was that the composition and experience of the transfer team, rather than the choice of vehicle, was the key factor influencing patient outcomes. While HEMS transfers serve as a proxy for specialized team involvement, this is an imperfect surrogate. Ground-based transfers may also involve specialized teams, though more commonly they are conducted by local providers. Fixed-wing transfers are performed either by specialized teams or by a single retrieval nurse with anesthetic training. Importantly, transport modality reflects not only team composition but also unmeasured factors such as transfer time. We chose not to group HEMS and fixed-wing transfers together for the instrumental variable analysis. Since fixed-wing transfers are rarely affected by inclement weather, adding them would dilute the instrument and not add any valuable information. Hence, we are limited to comparing the effect of transfer modality

in the complier subgroup, rather than the ideal analysis that would disentangle the effect of transfer modality and team composition on patient outcome.

The primary outcome used in this study, 30-day mortality, is coarse. For patients with brain injury, functional outcomes are more informative. It is possible that HEMS transfers affect functional outcome more than mortality rates. Future studies should preferably include functional outcomes as an endpoint.

In the IV analysis, the estimand, the LATE, reflected the causal effect among compliers, i.e., patients whose transport modality would vary based on weather minima. The generalizability of this estimate depends on how representative this group is of the broader population and whether effect sizes are consistent across subgroups.

While the sample size of the total cohort is relatively large at 3451, there are, in expectation, approximately 710 compliers, who are only partially identified and have a skewed distribution of treatment regimes, with the subset of compliers under control treatment being few (160). LATE estimation would benefit from a larger sample size and a higher compliance rate.

The suggested heterogeneous treatment effect when patients were stratified by AIS status in the post-hoc analysis would be more convincing if there were supporting evidence for a possible mechanistic explanation. We speculate that differences in total transfer time, defined as the time from the decision to transfer to the patient's arrival at the tertiary center, could be an explanation. Our data were not granular enough to capture this interval.

Finally, the exposure was inferred from flight records rather than systematically collected clinical data, meaning that there is measurement error in the exposure. This is discussed in more detail in Additional file 1.

Strengths

A key strength of this study is the use of a transparent and reproducible causal inference framework. By leveraging observed weather data to approximate random assignment of transport modality, we strengthen causal inference beyond what is typically achievable with conventional regression methods. Although tailored to our setting, this approach may be applicable in other countries and healthcare systems where HEMS operations are subject to well-defined weather criteria or similar external constraints. In such contexts, comparable methods could support causal inference using observational data to evaluate the effectiveness of HEMS in both interhospital and prehospital care.

Our study integrates high-quality national registry data, which supports the generalizability of findings to ICU settings across Sweden. The relatively large cohort size supports the reliability of the descriptive findings for patients transferred to neurocritical care.

Implications

Our findings may modestly shift prior beliefs for future studies of interhospital ICU transfer modalities, suggesting a possible beneficial effect of HEMS transfer on patient outcomes in subsets of patients.

If the LATE estimates reflect a real mortality benefit, practical implications include prioritizing HEMS availability for patients most likely to benefit. This could involve

ensuring adequate funding and implementing point-in-space (PinS) procedures to expand HEMS operational capacity in poor weather conditions.

We propose that weather minima can serve as a valid instrumental variable for causal inference regarding the effect of HEMS transfers. Where testable, the core IV assumptions appear to be met. Ideally, future studies should limit the dataset to patients with a reasonable chance of being transferred by HEMS, for example by excluding centers with no HEMS utilization, to improve LATE estimation. Given our post-hoc findings of potential heterogeneous treatment effects in AIS vs. non-AIS patients, we suggest prespecified subgroup analyses with this distinction.

Future steps to strengthen inferences about the choice of transfer modality in ICU patients include expanding the cohort to encompass all ICU diagnoses, which, using Swedish registries, could increase the sample to approximately 10,000 patients from 2019 to 2025. Ideally, prospective collection of data on transfer team composition and operational metrics is needed to better characterize the ICU transfer process.

A central principle of neurocritical care is the prevention and management of "secondary insults," i.e. physiological disturbances that exacerbate primary brain injury [53]. Hypotension and hypoxia are examples of such insults and are also commonly reported complications [3–6]. Future studies should, in addition to examining transport planning, logistics and team composition, ideally incorporate detailed records of interventions and physiological parameters during transfer. This would enable a better understanding of how care delivery during transport affects patient outcomes and help identify subgroups of patients who might benefit from transfers by specialized teams. Expanding the Swedish

Intensive Care Registry to include data on the transfer process could be an impactful way to collect a large, generalizable dataset. Since the infrastructure for entering data into the registry is already broadly available, such data gathering could be implemented relatively quickly.

Beyond this specific clinical context, the study illustrates how natural experiments can be leveraged to strengthen causal inference in observational healthcare research. Valid instruments can be identified even in complex clinical settings, which may inspire similar approaches across intensive care research.

Conclusions

In this national Swedish cohort of emergency interhospital neuro ICU transfers, we demonstrate a rigorous approach to causal inference using a weather-based instrumental variable. The primary statistical analysis showed no evidence of a mortality benefit with HEMS transfers. Secondary findings suggest a potential mortality benefit with HEMS in non-AIS patients with a non-negligible chance of HEMS transfer, but should be interpreted with great caution given the post-hoc nature of the analysis. We present a transferable methodological framework that addresses fundamental challenges in observational transport research. In addition, we provide concrete advice for future studies. The systematic assessment of IV assumptions and the transparent analytical approach provide a foundation for future causal inference studies in the field.

List of Abbreviations

ADS-B Automatic Dependent Surveillance–Broadcast

AIS Acute Ischemic Stroke

ASAH Aneurysmal Subarachnoid Hemorrhage

CrI Credible Interval

EASA European Union Aviation Safety Agency

ED Emergency Department

GCS Glasgow Coma Scale

GLM Generalized Linear Model

HEMS Helicopter Emergency Medical Services

ICH Intracerebral Hemorrhage

IV Instrumental Variable

LATE Local Average Treatment Effect

METAR Meteorological Aerodrome Report

NPR National Patient Register

SAPS 3 Simplified Acute Physiology Score 3

SIR Swedish Intensive Care Registry

TBI Traumatic Brain Injury

Declarations

Ethics approval and consent to participate

This study was performed in accordance with the Declaration of Helsinki and was approved by the Swedish Ethical Review Authority (Dnr 2022-03054-01 and 2024-00776-02). The study used pseudonymized registry data, and the Swedish Ethical Review Authority waived the requirement for individual informed consent to participate.

Consent for publication

Not applicable.

Availability of data and materials

Data are available from the authors upon reasonable request. Weather data are publicly available from Ogimet [27]. The analysis code is available from the corresponding author on request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

J.O., R.F-J., A.H., C.Å., D.N. and L.H. conceived the study. J.O. and R.F-J. preprocessed and analysed the data and wrote the analysis code, which L.F. reviewed. J.O. drafted and wrote the manuscript, and R.F-J., A.H., C.Å., L.F., D.N., and L.H. critically revised it for important intellectual content. All authors read and approved the final manuscript.

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Additional files

Additional file 1 (.docx). Methodological supplement: patient identification, flight matching, weather classification and the instrumental variable estimator.

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