



## UvA-DARE (Digital Academic Repository)

### Mobile Intensive Care Unit: Technical and clinical aspects of interhospital critical care transport

van Lieshout, E.J.

**Publication date**

2016

**Document Version**

Final published version

[Link to publication](#)

**Citation for published version (APA):**

van Lieshout, E. J. (2016). *Mobile Intensive Care Unit: Technical and clinical aspects of interhospital critical care transport*. [Thesis, fully internal, Universiteit van Amsterdam].

**General rights**

It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

**Disclaimer/Complaints regulations**

If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: <https://uba.uva.nl/en/contact>, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.

# Chapter 5

## Nurses versus physician-led interhospital critical care transport: a randomized non-inferiority trial

Erik Jan van Lieshout  
Jan Binnekade  
Elmer Reusien  
Dave Dongelmans  
Nicole Juffermans  
Rob de Haan  
Marcus Schultz  
Margreeth Vroom

## ABSTRACT

### Purpose

Regionalization and concentration of critical care increases the need for interhospital transport. However, optimal staffing of ground critical care transport has not been evaluated.

### Methods

In this prospective, randomized, open-label, blinded-endpoint non-inferiority trial, critically ill patients on mechanical ventilation transported by interhospital ground critical care transport were randomized between transport staffed by a dedicated team of critical care nurse and paramedic (nurses group) or a dedicated team including a critical care physician (nurses+physician group).

The primary outcome was the number of patients with critical events, both clinical and technical, during transport. Clinical events included decrease in blood pressure, oxygen saturation or temperature, blood loss, new cardiac arrhythmias or death. Non-inferiority was assumed if the upper limit of the two-sided 90% confidence interval (CI) for the between-group difference lies below the non-inferiority margin of 3%.

### Results

Of 618 eligible transported critically ill patients, 298 could be analyzed after randomization and allocation to the nurses group (n = 147) or nurses+physician group (n = 151).

The percentages of patients with critical events were 16.3% (24 incidents in 147 transports) in the nurses group and 15.2 % (23 incidents in 151 transports) in the nurses+physician group (difference 1.1 %, two sided 90% CI [-5.9 to 8.1]). Critical events occurred in both groups at a higher than the expected (0-1%) rate. In the nurses group consultations for physician assistance were asked in 8.2% (12 in 147 transports), of which all were performed prior to transport.

### Conclusions

The number of patients with critical events did not markedly differ between critical care transports staffed by a critical care nurse and paramedic compared to a team including a critical care physician. However, due to an unexpected higher rate of critical events in both groups recorded by an electronic health record, non-inferiority of nurse-led interhospital critical transport could not be established (<http://www.controlled-trials.com/ISRCTN39701540>).

## INTRODUCTION

The need for interhospital critical care transport of adults is likely to increase by the continual regionalization of care<sup>1-3</sup>. Regionalization is supported by the association between volume and improved outcome in specialties such as trauma and critical care<sup>4,5</sup>. Transport of a critically ill patient between hospitals bears risks of clinical and technical events which should be outweighed against the individual benefit<sup>6,7</sup>. A combination of a registered critical care nurse and a paramedic as team in critical care transports is more common in the United States than in Europe where a critical care physician as a team member is a generally adopted practice<sup>8-10</sup>. However, the added value of a critical care physician as part of the transport team has not been demonstrated<sup>11-15</sup>. We conducted a randomized non-inferior trial which compared ground critical care transports staffed by a team of paramedic and critical care nurse or a team including a critical care physician. The hypothesis of the study was that interhospital ground critical care transports staffed by a team of critical care nurse and paramedic is non-inferior compared to a team including a critical care physician, as expressed in the number of patients with critical events during transport.

## METHODS

### Design and randomization

The design of the study was a prospective, randomized, open-label, blinded-endpoint trial (PROBE-design) to demonstrate non-inferiority of a critical care transport team staffed by a dedicated team of critical care nurse and paramedic (nurses group) or a dedicated team including a critical care physician (nurses+physician group). Patients were randomized between these two transport strategies. The randomization procedure was web-based using permuted blocks with a variable block size and stratified by interhospital distance ( $\leq$  or  $>$  40 km). Randomization was done immediately after the transport request by phone by the referring hospital. Referring hospitals were not informed about the result of randomization to prevent study induced bias in the pre-transport stabilization period.

The critical care nurse, registered in the Dutch Intensive Care nurse registry, had at least two years of additional clinical experience in an critical care unit of an academic medical center after registration. The paramedic was licensed in Advanced Cardiac Life Support including rescue endotracheal intubation according to federal regulations with at least five years of pre hospital experience and an active professional at the municipal Emergency Medical Service of Amsterdam. The critical care physician was a European board-certified intensivist, an anesthesiologist or a senior resident in anesthesiology with at least a half year of full-time critical care training in an academic medical center. Both

nurses and physicians completed the extended critical care transport training of the Academic Medical Center including certification for the use of the trolley of the Mobile Intensive Care Unit.

In the nurses group, the critical care nurse, assisted by the paramedic was allowed to adjust ventilator settings and titrate active medication dosage at their professional discretion excluding new drugs or other emergency therapy. In the nurses group, a critical care physician accompanied every transport for safety reasons but was not physically present in the patient compartment of the ambulance to avoid unsolicited medical advice or intervention. As the physician stayed in the driver compartment, the critical care nurses were able to request for physician's assistance at any time. After a request the transport was executed and completed by both physician and nurses.

In the nurses+physician group the physician was in charge and supervising patient care. The equipment used in both transport strategies was identical and included a mobile intensive care trolley with an IC-ventilator (model Raphael color, Hamilton Medical, Switzerland), six channel vital signs monitor (model MP50, Philips Medical Systems, the Netherlands), eight syringe-pumps, suction unit, defibrillator, medication and disposables transported in a dedicated intensive care ambulance <sup>8</sup>.

### Study setting

In this single-center trial the ground critical care transports were executed using a Mobile Intensive Care Unit based at the Academic Medical Center, University of Amsterdam, Netherlands. The interhospital transports were executed between all hospitals nationwide and not only those to and from the Academic Medical Center. The annual transport rate is approximately 350. Outside the setting of this trial a team of a critical care nurse and physician is used. All critical care nurses and physicians were members of the ICU staff in the Academic Medical Center.

### Patients

All consecutive critically ill patients (> 18 years of age), to be transported by the Mobile Critical Care Unit between January 2006 and March 2008, were eligible.

Patients were excluded if they met one of the following criteria:

- i.  $\text{PaO}_2$  (mmHg) /  $\text{FiO}_2$  (P/F ratio) < 100 with positive end expiratory pressure (PEEP) > 15 cmH<sub>2</sub>O, or mean arterial pressure < 60 mmHg despite adequate fluid therapy and vasoactive medication (noradrenalin > 0,35 µg/kg/min, dopamine > 15 µg/kg/min) or after cardiopulmonary resuscitation (chest compression or cardiac defibrillation) within 24 hours prior to transport;
- ii. in need of immediate transport by local emergency medical services within 30 minutes, mandatory for emergency therapy in another facility according to federal rules and precluding study needs.

## Ethical approval and informed consent

Approval was obtained from the local Medical Ethics Committee that waived the need for informed consent according to Dutch Act on Research Involving Human Subjects.

## Data collection

Patient characteristics were collected by the transport coordinator over the phone at time of the transport request including date and reason of admission, indication of transport, Acute Physiology and Chronic Health (APACHE) II score, actual intravenous medication, hemodynamic (invasive arterial blood pressures), and pulmonary status (e.g., ventilation mode, PEEP, (P/F ratio)) to evaluate eligibility for randomization by the transport coordinator.

Transport was defined as the time frame between the departure of the Intensive Care unit of the sending unit and arrival in the unit of the receiving hospital including intra-hospital transport in corridors, elevators and ambulance garage. At the start of transport an electronic health record (MetaVision<sup>®</sup>, iMDsoft, Israel) was initiated on a laptop connected to both patient monitor and IC-ventilator storing their parameters every minute for off-line analysis. The APACHE II scores of admissions in both sending and receiving hospital were calculated.

## Study outcomes

The primary outcome was the number of patients with critical events, both clinical and technical during transport. Clinical events included decrease in transcutaneous arterial oxygen saturation of > 10% for > 10 minutes, rise or fall in arterial blood pressure (systolic, diastolic or mean, defined as > 20 mm Hg from baseline for > 10 minutes), temperature fall below 36 °C, hemorrhage or blood loss estimated to be > 250 ml, new cardiac arrhythmias with associated hemodynamic deterioration (occasional premature cardiac complexes were not considered significant), or death. Technical events (defined as related to technical aspects of critical care transport) included EKG lead disconnections, loss of battery power or any other technical equipment failure, airway loss requiring airway manipulation or reintubation, loss of any intravascular device, dislodgment of any chest tube, Foley catheter, or surgical drain<sup>16</sup>.

The a priori defined secondary outcome parameters were the separate numbers of clinical events and technical events, number and type of adjustments in ventilator settings, number and type of adjustments in rate of infusion and bolus medication (vasoactive medication and sedative medication) and amount of fluid therapy during transport. All outcome parameters were assessed offline blinded for their allocation group by use of the anonymized electronic medical records. In the nurses group, the incidence of consults for physician assistance was registered as a process variable.

## Statistical analysis

### *Sample size*

The incidence of critical events in ground critical care transport under supervision of both nurses and physician is around 0-1%<sup>11, 17, 18</sup>. Hence, it was expected that in 1% of the patients, critical events would occur in the nurses+physician group (control). The same incidence rate of critical events was expected in the nurses group (intervention) and a non-inferiority margin of 3% was considered as clinically acceptable. A sample size of 137 patients in each group (274 in total) achieves 80% power to detect a non-inferiority margin difference between the group proportions of 0.03. The nurses-physician (control) group proportion was assumed to be 0.01 and the nurses (intervention) group proportion 0.04 under the null hypothesis of inferiority. The power was computed for the case when the actual nurses (intervention) group proportion is 0.01. The test statistic used is the one-sided Z test (pooled) with a significance level targeted at 0.05. To anticipate for possible dropouts a total of 307 patients were randomized.

### *Data analysis*

Baseline characteristics of the transported patients were summarized using descriptive statistics. Continuous variables were expressed in medians with their 25<sup>th</sup> and 75<sup>th</sup> percentiles, whereas categorical variables were expressed as number and percentage of case. Incidence of critical events (primary outcome) and the components of the critical events (clinical events and technical events: secondary outcome parameters) were statistically tested for non-inferiority.

Groups were compared on the other secondary outcomes under a common superiority hypothesis. All analyses were based on the intention-to-treat principle, whereas the primary outcome was additionally analysed on both as-treated and per-protocol basis. The as-treated analysis included the transported patients who initially were randomized to the nurses group but were switched to the nurses+physician group after a formal request for assistance by the nurses. Hence, in the as-treated analysis the switched patients were analysed according to the treatment they received whereas in the per-protocol approach they were omitted from the analysis (figure 1). Multiple critical events per patient were analyzed as a single event as the patient was considered the unit of measurement in the sample size calculation. An additional sensitivity analysis was performed pooling all events as they occurred in each group to analyse the effects of multiple events per patient.

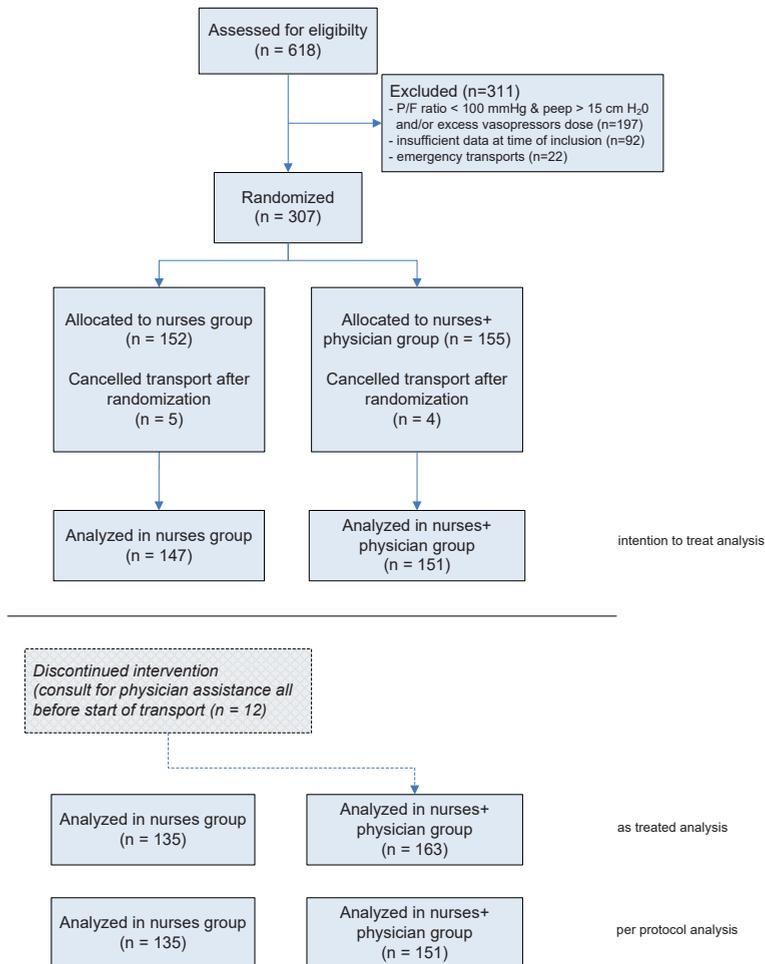


Figure 1. Flow diagram of randomization and analysis (according to CONSORT 2010)

Statistical uncertainty of the between-group difference between the primary (critical events) and secondary outcome (clinical and technical events) proportions were expressed in two-sided 90% confidence intervals (CIs). If the upper-limit of the CI crosses the 3% margin, non-inferiority of the nurse group is not established. We also applied one-sided significance testing using a method based on a Chi-square analysis<sup>19</sup>. A one-sided p value < 0.05 indicates non-inferiority of the nurses group. With regard to the remaining secondary outcomes, between-group difference of the proportions were expressed in two-sided 95% CIs and analysed using the  $\chi^2$  test (two-sided p value < 0.05 was considered statistically significant). Analyses were performed in SPSS (version 22.0) and R (version 3.2.1).

## RESULTS

Patient assignment is shown in figure 1. Of a total of 618 eligible patients, 311 were excluded based on exclusion criteria (n=197), insufficient data at time of inclusion (n=92, i.e. missing P/F ratio) or emergency transport (n=22). Finally, 307 patients were randomized, 152 were allocated to the nurses group and 155 to the nurses+physician group. In the nurses group 147 patients could be analyzed versus 151 in the nurses+physician group due to 9 transports cancelled after randomization.

The baseline characteristics of the randomized patients are summarized in table 1. The groups were well matched. The median [25<sup>th</sup>-75<sup>th</sup>] APACHE II score in the sending hospital was 19 [14-24] in the nurses group versus 18 [14-23] in the nurses+physician group. Lack of an ICU bed as indication for transport occurred in 78 patients in both groups (53% vs. 52%). Median [25<sup>th</sup>-75<sup>th</sup>] transport distance was 30 km [17-53 vs. 16-53] and median [25<sup>th</sup>-75<sup>th</sup>] transport time was 66 minutes [55-81] vs. 65 minutes [50-85].

**Table 1.** Baseline characteristics of the transported patients

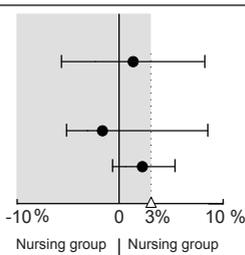
	Nurses group (n=147)	Nurses+physician group (n=151)
Age - years [median & 25 <sup>th</sup> -75 <sup>th</sup> percentile]	60 [46-74]	65 [52-74]
Women - no. (%)	62 (42%)	66 (45%)
APACHE II score in sending hospital [median & 25 <sup>th</sup> -75 <sup>th</sup> percentile]	19 [14-24]	18 [14-23]
Length of stay in ICU before transport - days [median & 25 <sup>th</sup> -75 <sup>th</sup> percentile]	3 [1-66]	3 [1-41]
Patients		
< 24 hours in sending ICU - no. (%)	86 (59%)	81 (54%)
> 24 hours in sending ICU - no. (%)	61 (41%)	70 (46%)
Reason for admission – no (%)		
medical	81 (55%)	90 (60%)
surgical	45 (31%)	42 (28%)
neurological / neurosurgical	21 (14%)	19 (12%)
Indication for transport		
lack of ICU beds - no (%)	78 (53%)	78 (52%)
expertise in referral center - no (%)	56 (38%)	61 (40%)
return to primary hospital - no (%)	13 (9%)	12 (8%)
Interhospital transport distance - km [median & 25 <sup>th</sup> -75 <sup>th</sup> percentile]	30 [17-53]	30 [16-53]
Transport time - minutes [median & 25 <sup>th</sup> -75 <sup>th</sup> percentile]	66 [55-81]	65 [50-85]
Transports ≤ 40 km - no	90	97
> 40 km - no	57	54
PaO <sub>2</sub> / FiO <sub>2</sub> ratio at inclusion - mmHg [median & 25 <sup>th</sup> -75 <sup>th</sup> percentile]	211 [150 - 286]	233 [158 - 301]
Inotropic / vasoactive medication - no		
dopamine	32	37
noradrenalin	78	70
dobutamine	16	11
nitroglycerine	12	11
phosphodiesterase inhibitors	11	9

**Table 1.** Baseline characteristics of the transported patients (continued)

	Nurses group	Nurses+physician group
	(n=147)	(n=151)
others (i.e., alpha-adrenergic agonist, calcium channel blocker)	12	9
Mechanical ventilation modes - no		
pressure controlled	99	102
volume controlled	7	13
assisted spontaneous breathing	41	36

5

The primary outcome parameter is depicted in figure 2, indicating that non-inferiority of the nurses group was not established. The percentages of patients with critical events were 16.3% (24 incidents in 147 patients) in the nurses group and 15.2% (23 incidents in 151 patients) in the nurses+physician group (difference 1.1%, 90% CI [-5.9 to 8.1],  $p=0.38$ ).

	Nurses n=147	Nurses + Physician n=151	Difference	90% CI for the difference between two proportions	P value*
<i>Primary outcome parameter</i>					
Number of patients with <b>critical</b> events <sup>1</sup>	24 (16.3%)	23 (15.2%)	1.1%		0.38
<i>Secondary outcome parameters</i>					
Number of patients with <b>clinical</b> events <sup>2</sup>	20 (13.6%)	22 (14.6%)	-1.8%		0.44
Number of patients with <b>technical</b> events	4 (2.7%)	1 (0.7%)	2.1%		0.35

The dashed line at  $\Delta$  3% indicates the non-inferiority margin. The grey tinted region to the left of the non-inferiority margin indicates the zone of non-inferiority: if the upper limit of the two-sided 90% CI lies left of the non-inferiority margin of 3%, non-inferiority of the nurses group is demonstrated. If the upper-limit of the CI crosses the margin of 3%, the trial has failed to establish non-inferiority of the nurses group.

\* one-sided significance testing;  $p$  value < 0.05 indicates non-inferiority.

1) Multiple events per patient were analyzed as single event. In the nurses+physician group, five transports were identified with two critical events per patient.

2) Clinical events included decrease in arterial saturation of > 10% for > 10 minutes, rise or fall in arterial blood pressure (systolic, diastolic or mean, defined as > 20 mm Hg from baseline for > 10 minutes), temperature fall below 36°C, hemorrhage or blood loss estimated to be > 250 ml, new cardiac arrhythmias with associated hemodynamic deterioration or death.

**Figure 2.** Comparisons of primary (critical events) and secondary outcome parameters (clinical and technical events) by non-inferiority between nurses (intervention) and nurses+physician (control) group

The percentages of patients with *clinical* events as secondary outcome parameter, were 13.6% (20/147 patients) in the nurses group and 14.6% (22/151 patients) in the nurses+physician group (difference -1.0%, 90% CI [-5.2 to 8.7],  $p=0.44$ ). Of note, there were no hemorrhages, arrhythmias or deaths in both groups. The percentages of

patients with *technical* events were 2.7% (4/147 patients) in the nurses group and 0.7% (1/151 patients) in the physician group (difference 2.1%, 90% CI [-0.7 to 5.3],  $p=0.35$ ). In the nurses+physician group, five transports were identified with two critical events per patient.

In the nurse group 8.2% (12 in 147 patients) consultations for physician's assistance were asked and all occurred before the start of the transports in the unit of the sending hospital without any involvement of the sending ICU-staff. All 12 consults were related to hemodynamic and/or respiratory instability beyond the perceived skills of the nurse in charge. Analyzing these switched patients according to their actual received treatment revealed an incidence of critical events of 17.8% (24 events in 135 patients) in the nurses group vs. 14.1% (23 events in 163 patients) in the nurses+physician group (difference 3.7%, 90%CI [-3.3 to 10.9],  $p=0.49$ ), also indicating absence of non-inferiority of the nurses group. This absence was also demonstrated in the per-protocol analysis, where the switchovers were omitted from the nurses group: 17.8% (24 events in 135 patients) in the nurses group vs. 15.2% (23 events in 151 patients) in the nurses+physician group (difference 2.6%, 90%CI [-4.7 to 9.9],  $p=0.48$ ).

No between-group differences were observed concerning the other secondary outcomes parameter, although the nurses-physician group tended to give more fluid therapy > 1000 ml during transport (table 2). The sensitivity analysis of the primary outcome with pooled events per group, resulting in 28 critical events in the nurses+physician group, confirmed the absence of non-inferiority: percentages of critical events were 16.3% (24 events in 147 patients) in the nurses group and 18.5% (28 events in 151 patients) in the nurses+physician group (difference -2.2%, 90% CI [-9.5 to 5.1],  $p=0.15$ ). The same applies to the as-treated (difference 0.6%, 90% CI [-6.6 to 8.04],  $p=0.35$ ) and per protocol analysis (difference -0.7%, 90% CI [-8.3 to 6.9],  $p=0.25$ ).

**Table 2.** Comparisons of secondary outcome parameters between nurses (intervention) group and nurses+physician (control) group

	Nurses group (n=147)	Nurses+physician group (n=151)	% difference* [95% CI]	p*
Adjustments in ventilator settings				0.92
zero adjustments	90 (61.2%)	95 (62.9%)	-1.7 [-12.6 to 9.3]	
1 adjustment	29 (19.7%)	27 (17.9%)	1.8 [-7.1 to 10.8]	
>1 adjustments	28 (19.0%)	29 (19.2%)	-0.2 [-9.2 to 8.9]	
Type of ventilator adjustments				
PEEP	14 (9.5%)	15 (9.9%)	-0.4 [-7.4 to 6.6]	1.00
fiO <sub>2</sub>	18 (12.2%)	24 (15.9%)	-3.7 [-11.7 to 4/4]	0.46
pressure (Pmax or Psupport)	29 (19.7%)	29 (19.2%)	0.5 [-8.5 to 9.6]	1.00
respiratory rate	30 (20.4%)	22 (14.6%)	5.8 [-2.8 to 14.6]	0.24
Adjustments in vasoactive medication				0.86
zero adjustments	113 (76.9%)	120 (79.5%)	-2.6 [-12.1 to 6.8]	
1 adjustment	23 (15.6%)	21 (13.9%)	1.7 [-6.4 to 10.0]	
>1 adjustments	11 (7.5%)	10 (6.6%)	0.9 [-5.3 to 7.1]	
Adjustments in sedative medication				0.92
zero adjustments	111 (75.5%)	125 (82.8%)	1.6 [-7.0 to 10.1]	
1 adjustment	19 (12.9%)	21 (13.9%)	-1.0 [-8.9 to 6.9]	
>1 adjustments	4 (2.7%)	5 (3.3%)	-0.6 [-5.2 to 3.9]	
Use of bolus medication	13 (8.8%)	7 (4.6%)	4.2 [-1.6 to 10.5]	0.22
Fluid therapy during transport				0.06
< 500 ml	72 (49%)	82 (54.3%)	-5.3 [-16.5 to 6.0]	
500-1000 ml	67 (45.6%)	52 (34.4%)	11.2 [0.0 to 22.0]	
> 1000 ml	8 (5.4%)	17 (11.3%)	-5.9 [-12.5 to 0.5]	

\* Between-group difference of the proportions were expressed in two-sided 95% CIs and using the  $\chi^2$  test, two-sided p value < 0.05 was considered statistically significant.

## DISCUSSION

The present trial failed to establish non-inferiority in interhospital ground critical care transports staffed by a dedicated team of critical care nurse and paramedic compared to a dedicated team including a critical care physician as expressed in number of critical events during transport.

Results of the intention-to treat analysis were confirmed in the per-protocol, as-treated and in our sensitivity analyses. The risks associated with critical care transport, either between or within hospitals, have been widely recognized<sup>15, 20-22</sup>. In previous studies of

interhospital transports with comparable cohorts of critical care patients, rates of critical events were high as 40-50% if a regular ambulance transport system was used and were thought to be as low as 0-10% with a dedicated critical care transport system<sup>15, 16, 23-25</sup>.

Here, we found an overall critical events rate of about 16-17%. In previous studies event rates were either based on self-reported events or on pre- and post-transport cardiovascular and respiratory point measurements from the written chart. The use of an electronic health record instead of self-report critical events is conceivably more accurate compared to self-reporting events by the staff or pre- and post-transport point measurements only. Those undetected or unreported deteriorations during transport are not taking into account in previous studies which might explain our higher than expected critical event rate<sup>11, 16, 17, 26, 27</sup>. Our composite primary endpoint was the combination of both clinical (14% in the nurses vs 17% in the nurses+physician group) and technical events (3% vs 2%). The latter is self-reported and is indeed comparable to previous studies. An alternative explanation for the high event rates in the transported patients might be the absence of a validated checklist for the pre-transport stabilization period<sup>10, 28</sup>. However, no studies have evaluated the effect of a pre-transport checklist on safety in interhospital transports, either nurses or physician-led<sup>15, 28, 29</sup>. In our study the staff in both groups was trained and experienced in interhospital transport including pre-transport stabilization. In line with this, there were 12 requests for physician's assistance in the nurses group prior to transport. These requests were based on the nurses' opinion that the complexity and/or instability of these patients exceeded the professional limits of critical care nursing and indicative for their careful pre-transport evaluation<sup>30-32</sup>.

Undoubtedly our trial turned out to be too small to unequivocally establish non-inferiority of nurses staffed transport due to this higher than expected critical events rates in the transported patients. . At the same time, in order to tailor-made staffing to individual patient needs while avoiding overstaffing, future research should focus on definitions and factors influencing hemodynamic and respiratory stability prior to transport and subsequent transport-related observed outcome<sup>10, 15, 29, 33</sup>. The additional role of telemedicine or validated pre-transport scoring systems to indicate physician attendance in limited cases of transport should be part of this research<sup>34, 35</sup>.

In the PROBE design of our trial the electronic medical record during IC-transport enabled blinded assessment of outcome parameters and is indubitable more accurate in documenting clinical deteriorations otherwise undetected or unreported. The applicability of our results might depend on regional differences in critical transport programs including the level of critical care nursing. The level of their education, additional transport programs and professional performance including self-reliance guided by nurse-driven protocols undoubtedly influence their critical events rates. Nevertheless, our trail suffers from several limitations. Firstly, the surrogate endpoint critical events in this study might not necessarily reflect clinical relevant outcome<sup>27</sup>. The relationship between critical event

rates during transport and multi-factorial determined morbidity or mortality in critical care medicine has not been established yet. Definitions of critical events used in this trial reflect expert opinion on what might be harmful for a transported critically ill patient.

The resolution of a critical event during transport might better reflect competence of the escorting team rather than the incidence of events. But to our knowledge there is no validated and standardized way to score the quality of the team's response to an event. It is conceivable that this competence is already partially measured by the absence of critical events for many events are either preventable (i.e. technical by proper use of device's checklist ) or treatable (i.e. clinical by anticipating on a fall in blood pressure before it exceeds the clinical event definition's limit of 10 minutes).

Secondly, for safety reasons the most severe critically ill patients were excluded and the critical care physician, although not participating actively, was present and might have impacted on nurses' behavior. Nevertheless, scores of severity of illness in our trial were still high in both groups and comparable to other studies<sup>7,11, 20, 23</sup>. Thirdly, the study was limited to patients admitted to the ICU and excluded emergency transports for immediate advanced care (e.g. from peripheral hospital emergency rooms to a tertiary cardiac cath. lab). The response time of a regional specialized retrieval team is usually longer compared to emergency medical services, which excludes its availability in emergency transports if immediate advanced treatment is warranted. In conclusion, the number of patients with critical events during ground critical care transport staffed by a critical care nurse and paramedic does not markedly differ from a team including a critical care physician. However, non-inferiority of nurse-led interhospital critical care transport could not be established. A definitive answer on the appropriate patient selection and team composition might arise from larger multi-center trials or meta-analysis. Until then, the results might not change the present policy of physicians escorting critical care transports in Western Europe and could fuel the discussion on critical care paramedics in the US<sup>36</sup>.

## AUTHORS DISCLOSURE

All authors have no potential conflicts of interest to disclose.

## SUPPLEMENTARY MATERIAL

Interhospital critical care transport in the Amsterdam region captured in a video clip (<https://youtu.be/HEX-HeniXIY>)

## AUTHORS CONTRIBUTIONS

All authors had substantial contributions to the conception, design of the work, the acquisition, analysis, interpretation of data for the work, drafting the work and revising it critically for important intellectual content. They all had final approval of the version to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conception and design: EjlL, RdH, MS, MV; analysis and interpretation: EjlL, JB, ER, DD, NJ; drafting the manuscript for important intellectual content: EjlL, JB, NJ, RdH, MS, MV.

## ACKNOWLEDGEMENTS

We would like to thank all patients, critical care nurses, physicians and paramedics who participated in this trial for their support and both M.M. Levi and H.R. Büller for their fruitful comments on the manuscript.

## REFERENCES

1. Zimmermann M, Bein T, Philipp A, Ittner K, Foltan M, Drescher J, et al. (2006) Interhospital transportation of patients with severe lung failure on pumpless extracorporeal lung assist. *Br J Anaesth* 96(1):63-6
2. Ramnarayan P, Thiru K, Parslow RC, Harrison DA, Draper ES, Rowan KM (2010) Effect of specialist retrieval teams on outcomes in children admitted to paediatric intensive care units in England and Wales: a retrospective cohort study. *Lancet* 376:698-704
3. Iwashyna TJ (2012) The incomplete infrastructure for interhospital patient transfer. *Crit Care Med* (40):2470-8
4. Kahn JM, Goss CH, Heagerty PJ, Kramer AA, O'Brien CR, Rubenfeld GD (2006) Hospital volume and the outcomes of mechanical ventilation. *N Eng J Med* 355:41-50
5. MacKenzie EJ, Rivara FP, Jurkovich GJ, Nathens AB, Frey KP, Egleston BL, et al (2006) A national evaluation of the effect of trauma-center care on mortality. *N Eng J Med* 354:366-78
6. Arthur KR, Kelz RR, Mills AM, Reinke CE, Robertson MP, Sims CA, et al (2013) Interhospital transfer: an independent risk factor for mortality in the surgical intensive care unit. *Am Surg* 79:909-13
7. Strauch U, Bergmans DC, Winkens B, Roekaerts PM (2015) Short-term outcomes and mortality after interhospital intensive care transportation: an observational prospective cohort study of 368 consecutive transports with a mobile intensive care unit. *BMJ open* 5:e006801-2014
8. van Lieshout EJ, de VR, Binnekade JM, de HR, Schultz MJ, Vroom MB (2008) Decision making in interhospital transport of critically ill patients: national questionnaire survey among critical care physicians. *Intensive Care Med* 34:1269-73
9. Australian, New Zealand College of Anesthetists (2015) Guidelines for Transport of Critically Ill Patients. <http://www.anzca.edu.au/resources/professional-documents/pdfs/ps52-2015-guidelines-for-transport-of-critically-ill-patients.pdf> Accessed 26 January 2016
10. Droogh JM, Smit M, Absalom AR, Ligtenberg JJ, Zijlstra JG (2015) Transferring the critically ill patient: are we there yet? *Crit Care* 19:749-015-0749-4
11. Hill AD, Vingilis E, Martin CM, Hartford K, Speechley KN (2007) Interhospital transfer of critically ill patients: Demographic and outcomes comparison with nontransferred intensive care unit patients. *J Crit Care* 22:290-5
12. Duke GJ, Green JV (2001) Outcome of critically ill patients undergoing interhospital transfer. *Med J Australia* 174:122-5
13. Harrison TH, Thomas SH, Wedel SK (2004) Success rates of pediatric intubation by a non-physician-staffed critical care transport service. *Pediatr Emerg Care* 20:101-7
14. Hallas P, Folkestad L, Brabrand M (2009) Level of training and experience in physicians performing interhospital transfers of adult patients in the internal medicine department. *Emerg Med J* 26:743-4
15. Belway D, Henderson W, Keenan SP, Levy AR, Dodek PM (2006) Do specialist transport personnel improve hospital outcome in critically ill patients transferred to higher centers? A systematic review. *Journal of critical care* 21:8-17
16. Gebremichael M, Borg U, Habashi NM, Cottingham C, Cunsolo L, McCunn M, et al. (2000) Interhospital transport of the extremely ill patient: the mobile intensive care unit. *Critical Care Medicine* 28:79-85
17. Kreeftenberg HG, Jr., Ligtenberg JJ, Arnold LG, van dW, Tulleken JE, Zijlstra JG (2000) Condition on arrival of transferred critically ill patients. *Neth J Med* 57:180-4
18. Selevan JS, Fields WW, Chen W, Petitti DB, Wolde-Tsadiq G. (1999) Critical care transport: outcome evaluation after interfacility transfer and hospitalization. *Ann Emerg Med.* 33:33-43
19. Dunnett CW, Gent M (1977) Significance testing to establish equivalence between treatments, with special reference to data in the form of 2X2 tables. *Biometrics* 33:593-602

20. Flabouris A, Runciman WB, Levings B (2006) Incidents during out-of-hospital patient transportation. *Anaesth Intensive Care* 34:228-36
21. Beckmann U, Gillies DM, Berenholtz SM, Wu AW, Pronovost P (2004) Incidents relating to the intra-hospital transfer of critically ill patients. An analysis of the reports submitted to the Australian Incident Monitoring Study in Intensive Care. *Intensive Care Med* 30:1579-85
22. Kue R, Brown P, Ness C, Scheulen J (2011) Adverse Clinical Events During Intrahospital Transport by a Specialized Team: A Preliminary Report. *Am J Crit Care* 20:153-62
23. Wiegersma JS, Droogh JM, Zijlstra JG, Fokkema J, Ligtenberg JJ (2011) Quality of interhospital transport of the critically ill: impact of a Mobile Intensive Care Unit with a specialized retrieval team. *Crit Care* 15:R75
24. Etxebarria MJ, Serrano S, Ruiz RD, Cia MT, Olaz F, Lopez J (1998) Prospective application of risk scores in the interhospital transport of patients. *Eur J Emerg Med* 5:13-7
25. Uusaro A, Parviainen I, Takala J, Ruokonen E (2002) Safe long-distance interhospital ground transfer of critically ill patients with acute severe unstable respiratory and circulatory failure. *Intensive Care Med* 28:1122-5
26. Durairaj L, Will JG, Torner JC, Doebbeling BN (2003) Prognostic factors for mortality following interhospital transfers to the medical intensive care unit of a tertiary referral center. *Critical Care Med.* 31:1981-6
27. Frey B (2009) Is the number of reported critical incidents relevant? *Critical Care Med* 37:334-5
28. Handy JM (2011) Critical care transfers: the lack of information and systemic shortcomings continue. *Anaesthesia* 66:337-40.
29. Lampariello S, Clement M, Aralihond AP, Lutman D, Montgomery MA, Petros A, et al. (2009) Stabilisation of critically ill children at the district general hospital prior to intensive care retrieval: a snapshot of current practice. *Arch Dis Child* 95:681-5
30. Kupas DF, Wang HE (2014) Critical care paramedics -a missing component for safe interfacility transport in the United States. *Ann Emerg Med* 64:17-8
31. King BR, King TM, Foster RL, McCans KM (2007) Pediatric and neonatal transport teams with and without a physician: a comparison of outcomes and interventions. *Pediatr Emerg Care* 23:77-82.
32. Raynovich W, Hums J, Stuhlmiller DF, Bramble JD, Kasha T, Galt K (2013) Critical Care Transportation by Paramedics: A Cross-sectional Survey. *Air Med J* 32:280-8.
33. Schwebel, C., Clec'h, Magne, S, Minet, C, Garrouste-Orgeas, M, Bonadona, A et al. (2013) Safety of Intrahospital Transport in Ventilated Critically Ill Patients: A Multicenter Cohort Study. *Crit Care Med* 41(8): 1919-1928
34. Nangalia V, Prytherch D, Smith G (2010) Health technology assessment review: Remote monitoring of vital signs - current status and future challenges. *Crit Care* 14:233.
35. Lee LL, Yeung KL, Lo WY, Lau YS, Tang SY, Chan JT (2008) Evaluation of a simplified therapeutic intervention scoring system (TISS-28) and the modified early warning score (MEWS) in predicting physiological deterioration during inter-facility transport. *Resuscitation* 76:47-51.
36. Critical Care Paramedic. PennWell Corporation. <http://connect.jems.com/forum/topics/critical-care-paramedic>. Accessed March 11, 2016