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UTILITY OF THE MODIFIED EARLY WARNING SCORE FOR INTERFACILITY TRANSFER OF PATIENTS WITH TRAUMATIC INJURY

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3 **UTILITY OF THE MODIFIED EARLY WARNING SCORE FOR INTERFACILITY**
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5 **TRANSFER OF PATIENTS WITH TRAUMATIC INJURY**
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ABSTRACT

Objective: The modified early warning score (MEWS) is a “track and trigger” score utilizing routine physiologic vital signs. The objective is to determine if the pre-transfer MEWS can be used for predicting outcomes in patients with traumatic injury requiring interfacility transfer to higher levels of care.

Design, setting, participants: Retrospective study of consecutively transferred patients with traumatic injury into a level II trauma center from 2013-2014.

Interventions: None.

Outcome measures: Mortality, ICU admission, operative procedure, MEWS deterioration in-transit, air transport interfacility, and secondary overtriage (low injury severity, LOS < 1 day, discharged home). The association between the pre-transfer MEWS and outcomes were analyzed with Cochran-Armitage trend tests, ROC curves, and univariate logistic regression.

Results: There were 587 transferred patients; outcomes were reported in 339 patients with complete data on all 5 vital signs used to calculate the MEWS. The MEWS ranged from 0-9 (median of 1). There was a significant linear relationship between MEWS and study outcomes, especially mortality, ICU admission, and air medical transport ($p < 0.001$ for all). A threshold score ≥ 4 was identified by ROC analysis; 11.2% of patients had MEWS ≥ 4 . Outcomes were significantly worse in patients with MEWS ≥ 4 vs. < 4 : mortality (26.2% vs. 3.0%, OR = 11.59, $p < 0.001$); ICU admission (73.7% vs. 47.2%, OR = 3.14, $p=0.003$); air transfer (42.1% vs. 15.6%, OR=3.93, $p < 0.001$). The MEWS was not associated with surgery, in-transit MEWS deterioration, or secondary overtriage.

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3 **Conclusion:** While MEW scores were low for patients transferred interfacility, a pre-transfer
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5 MEWS ≥ 4 may be utilized by the receiving facility for predicting mortality, air transport, and
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8 ICU resource utilization. In the interfacility transport setting, the MEWS may be useful for
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10 identifying patients with less obvious need for transfer or requiring more expeditious transfer.
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3 **Article Summary:** Strengths and limitations of this study
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6 • **Strength:** The utility of the modified early warning score (MEWS), a “track and trigger”
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8 score comprised of common physiologic vital signs, has been previously described for
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10 risk deterioration in ED settings, but its utility has not been examined during interfacility
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12 transfer.
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- 14 • **Limitation:** Emergency physicians and EMS personnel did not prospectively utilize the
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16 MEWS during the study period so our findings need to be considered in combination
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18 with clinical judgment.
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- 20 • **Limitation:** There was a considerable amount of missing vital signs at the transferring
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22 facility, resulting in nearly half of patients being removed from our outcomes analysis,
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24 although there were no demographic or outcome differences in patients with missing
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26 versus complete vital signs.
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- 29 • **Limitation:** The acuity of the patients was low, which may have prevented more robust
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31 analyses between MEWS and outcomes.
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INTRODUCTION

Traumatic injury is the leading cause of death in persons under 45 years of age.¹ Emergency medical service (EMS) personnel transported nearly 5 million patients with traumatic injury in 2008 alone.² The pre-hospital care, triage and transport of patients with traumatic injury to a trauma center are determined by protocols and guidelines published by the American College of Surgeons (ACS) Committee on Trauma³ and the Centers for Disease Control and Prevention.² However, not all injuries are immediately obvious, and patients are occasionally undertriaged to a lower-level or non-trauma center that requires interfacility EMS transport to a higher-level trauma center for care.

The mode of EMS transport interfacility is determined and requested by the transferring emergency physician. Communication between the transferring physician and the receiving trauma surgeon includes a review of physiologic status, initial management, and discussion on the optimal timing of transfer, such as stabilizing patients prior to transfer. EMS agencies are staffed with providers having a range of training and experience dictating the scope of tasks they can perform, from administration of medications, use of medical devices, performing cardiopulmonary resuscitation, initiating ventilation and intubation, and other monitoring techniques. While there are some criteria to help the transferring physician determine if the trauma patient should be transferred, for example patients with carotid or vertebral injuries, cardiac rupture, and grade IV or V liver injuries,³ there are no solid guidelines on if, when, and how a patient should be transferred.

The modified early warning score (MEWS) is a “track and trigger” score used for recognizing patients who are at risk for deterioration and determines degree of illness of the patient.⁴ The initial validation of the MEWS was performed in 709 emergency department

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3 patients and identified MEWS ≥ 5 was associated with mortality and admission to the intensive
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5 care unit (ICU).⁵
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8 Our objectives were to determine whether the MEWS can be used in the interfacility
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10 transport setting for patients with traumatic injury to detect patients potentially requiring higher
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12 levels of care. Specifically, we examined whether the pre-transfer MEWS was associated with
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14 poor clinical outcomes, transport mode, and secondary overtriage.
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18 19 20 **METHODS**

21 22 **Design, setting and participants**

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24 This was a retrospective cohort study that included all consecutively admitted trauma patients
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26 transferred into an ACS verified level II trauma center from another healthcare facility between
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28 January 1, 2013 and December 31, 2014. The patient populations were identified from the
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30 trauma registry called TraumaBase® (CDM, Conifer, CO), which is a registry used by the
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32 hospital and the State of Texas to track patients with traumatic injury for epidemiology and
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34 prevention studies as well as for quality assurance and quality improvement. Patients less than 18
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36 years of age were excluded. We also excluded patients missing all five vital signs used to
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38 calculate the MEWS (n=65, 10.0% of patients). This study received institutional review board
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40 approval with waiver of informed consent.
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45 46 **Modified Early Warning Score**

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48 The MEWS is derived from 5 common physiologic vital signs of systolic blood pressure (SBP,
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50 mm Hg), heart rate (HR, beats per minute), respiratory rate (RR, breaths per minute),
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52 temperature (T, Celcius), and AVPU score ("alert, voice, pain, unresponsive"), **Figure 1**. The
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54 Glasgow coma scale is favored to the AVPU in traumatic injury, and the AVPU was derived
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3 from the GCS as follows: A=14-15, V=9-13, P = 4-8, U = 3. The MEWS was calculated as the
4 total of the five subcomponent scores (**figure 1**). Scores range from 0 to a maximum of 14.
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8 The pre-transfer MEWS was calculated using vital signs from the transferring facility
9 (obtained from the transfer facility record), before interfacility transport. The post-transfer
10 MEWS was calculated from vital signs collected on arrival to the receiving facility.
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13 **Covariates and outcomes**

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15 Clinical outcomes included in-hospital mortality, intensive care unit (ICU) admission, surgical
16 procedure, EMS transport mode (air medical vs. ground transport), MEWS deterioration (an
17 increase in MEWS during transit, calculated as the difference between pre-transfer MEWS and
18 post-transfer MEWS), and secondary overtriage (injury severity score (ISS) < 10, hospital LOS <
19 1 day, and discharged home).
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29 The following demographic and clinical information was abstracted from the registry:
30 vital sign information (vital sign location, timing, and values before interfacility transport and on
31 arrival at the receiving facility); demographics (age, gender, race); injury severity measures
32 (abbreviated injury scale score, injury severity score (ISS), anatomic location of injury), and
33 cause of injury. We also examined the occurrence of in-transit events, defined as a significant
34 change in vital signs during transport (any normal to abnormal change in SBP, HR, RR, T, and
35 GCS) or procedures performed in transit (e.g. fluid bolus, new or significant change in
36 medication, sedation, or paralytics, placement of chest tube or central line, needle
37 decompression). Information on in-transit events were abstracted from detailed, scanned EMS
38 run reports, which were only available in 149 charts.
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52 **Analysis**

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3 The association between pre-transfer MEWS and outcomes were examined with Cochran-
4 Armitage trend tests. Receiver operator characteristic (ROC) curves were used to identify an
5 optimal threshold score; we examined ROC curves for mortality and ICU admission, which were
6 the outcomes used in the initial validation of the MEWS.⁵ This threshold score was examined in
7 separate logistic regression models for each of our study outcomes to estimate the unadjusted
8 odds of the threshold score for the outcome. The threshold score was also used to examine the
9 proportion of patients who did not meet the physiologic criteria outlined in the Guidelines for
10 triage to a trauma center of GCS ≤ 13 , SBP ≤ 90 mm Hg, and respirations < 10 or > 29
11 breaths/min signaling potential, impending deterioration.^{1 3}

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SAS version 9.4 (SAS Institute, Cary, NC) was used for all analyses, and $p \leq 0.05$ was considered statistically significant.

RESULTS

Patient characteristics and outcomes

There were 587 transferred patients in our study. The population had a median (IQR) age of 56 years (37-74), 60% were male, and the most common cause of injury was due to fall (57%), followed by a vehicular accident (28%). Nearly half of patients suffered a head injury (46%), although the acuity of injuries was not severe: the median GCS was 15 (15-15) and the ISS was 10 (5-17). Overall, 18% were transported interfacility by air medical services. The average distance traveled was 23 miles (range: 7 – 79 miles).

The rates of our study outcomes are shown in **table 1**. There was low mortality of less than 6% among our transferred trauma population, although half of patients were admitted to the ICU and 35% required surgery. Additionally, 17.4% experienced an in-transit event. The most

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3 common in-transit events were development of tachycardia or an abnormal RR (n=6 each),
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5 followed by development of hypotension (< 90mm Hg, n=4), administration of fluid bolus (n=4),
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7 and GCS decline of two or more points (n=3).
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10 **Modified early warning score**

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12 The majority of patients (90%) were not missing any vital signs post-transfer. However, 42%
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14 (n=248) were missing at least one vital sign pre-transfer (83% of those patients were missing
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16 only 1 vital sign). Thus, only 58% of patients (n=339) had complete data for all 5 vital signs.
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20 We examined whether there were differences in demographics, clinical characteristics,
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22 and outcomes in patients with complete vital sign data (n=339) vs. missing vital sign(s) (n=248),
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24 **table 1**. There were no differences in any covariate or in any study outcome. Still, to be
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26 conservative we analyzed the association between pre-transfer MEWS and outcomes in those
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28 with complete vital sign data only (n=339), rather than using multiple imputation to calculate an
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30 imputed MEWS in patients with missing vital sign(s).
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33 **MEWS relationship to outcomes**

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35 The median (IQR) MEWS score was 1 (1-2). As shown in **table 2**, the pre-transfer MEWS
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37 showed a significant, linear relationship with study outcomes of mortality, ICU admission, and
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39 air transport. The pre-transfer MEWS was borderline significant for predicting a surgical
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41 procedure.
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46 Threshold scores were determined with ROC curves (**figure 2**). The ROC curve for
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48 mortality was clinically and statistically significant (AUROC: 0.79 (95% CI: 0.74-0.83, p <
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50 0.001), identifying a threshold MEWS ≥ 4 for predicting mortality with a high specificity of 91.3
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52 (92% of survivors were correctly identified by a pre-transfer MEWS < 4) and good sensitivity of
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54 52.6 (53% of patients who expired were correctly identified by a MEWS ≥ 4), figure 2a. The
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3 ROC curve for ICU admission was weaker but still statistically significant (AUROC: 0.56 (95%
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5 CI: 0.51-0.62, p=0.02), demonstrating specificity of 94.1 and sensitivity of 16.5 with a threshold
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7 MEWS \geq 4 on ROC analysis, figure 2b.
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11 When the threshold score \geq 4 was modeled for our outcomes, the pre-transfer MEWS
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13 continued to show a significant association with study outcomes of mortality, ICU admission,
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15 and air transport (**table 3**).
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18 In patients with MEWS \geq 4, 45% (17/38) did not have abnormal physiologic vital signs
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20 signaling triage to a trauma center by the ACS COT and CDC decision guidelines; further, 63%
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22 (12/19) of patients with a MEWS=4 would not have met the physiologic criteria outlined in the
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24 Guidelines. Outcomes in these twelve patients include one death, seven admissions to the ICU,
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26 five patients requiring surgery, but only three patients transferred by air. Ninety-five percent
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28 (286/301) of patients with MEWS $<$ 4 did not have abnormal vital signs per the guidelines.
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34 DISCUSSION

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36 Our study examined patients with traumatic injury requiring interfacility transfer, demonstrating
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38 that a MEWS \geq 4 calculated prior to interfacility transport is associated with mortality, ICU
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40 admission, and air medical transport. In the interfacility transport setting, the MEWS may act as
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42 a more holistic measure that may lessen the chance of underestimating a poor clinical outcome
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44 and delaying or not transferring a patient appropriately. While it may seem obvious that out-of-
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46 range vital signs would increase the odds of an unfavorable outcome, only 21 of 38 patients with
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48 MEWS \geq 4 would have met abnormal physiologic criteria by the ACS COT and CDC decision
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50 guidelines.^{1 3} In this setting, the MEWS may be useful for identifying patients with less obvious
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52 need for transfer.
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3 The main limitation of the study is that emergency physicians and EMS personnel did not
4 prospectively utilize the MEWS during the study period so our findings need to be considered in
5 combination with clinical judgment. Fullerton et al. observed that the MEWS in combination
6 with clinical judgment increases the utility of the MEWS in a pre-hospital setting.⁴ At least one
7 study reported that implementing the MEWS in a trauma setting did not result in a statistically
8 significant reduction in mortality ($p=0.09$).⁶ A prospective study that factors in clinical judgment
9 will need to validate this threshold of ≥ 4 to determine if it leads to more appropriate transfer and
10 improved outcomes.
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22 Additional limitations are as follows: There was a considerable amount of missing vital
23 sign data at the transferring facility, resulting in 47% of patients being removed from our
24 outcomes analysis. While there were no differences in the characteristics or outcomes of patients
25 with complete data and patients with incomplete data, there may be some residual bias in
26 excluding patients with one or more missing vital signs. This limitation also suggests a need for
27 more efficient, routine collection of pre-transport vital signs and EMS reports to receiving
28 facilities. Next, the acuity of the patients was low, which may have prevented more robust
29 analyses between MEWS and outcomes. The median pre-transfer MEWS was only 1. This might
30 not be a limitation as much as it suggests that guidelines for the pre-hospital triage and transport
31 of patients minimizes over- and under-triage of trauma patients. Further study is needed to
32 examine the MEWS for inter-hospital transport to level I trauma centers. Patients transferred into
33 level I trauma centers theoretically have higher acuity injuries and more severe MEWS pre-
34 hospital, which may help with the robustness of these analyses. Finally, the AVPU component of
35 the MEWS score was estimated from the GCS. There are no standard criteria for estimating GCS
36 from AVPU;⁷⁻¹¹ using a different cut-off might result in different MEWS scores.
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3 Literature published within the past few years have identified a range of MEWS values
4 associated with poor outcomes. Such studies include a pre-hospital MEWS ≥ 3 for requiring a
5 life-saving intervention,¹² MEWS ≥ 5 with early mortality in the ED,¹³ MEWS ≥ 6 for mortality
6 in the ICU,¹⁴ MEWS ≥ 7 for rapid response team and cardiac arrest in the ED.¹⁵ Still others have
7 used the MEWS ≥ 5 identified by Subbe et al. and examined this threshold in other settings, such
8 as in developing countries.¹⁶ A MEWS threshold ≥ 4 was associated with poor outcomes in
9 patients requiring interfacility transfer in our study. Higher scores may lead to more efficient
10 secondary triage and transfer of patients to a higher-level trauma center who are at risk for
11 deterioration and poor outcomes. Using an integrated score such as the MEWS might help avoid
12 situations where a clinician might dismiss a potentially problematic clinical presentation as not
13 requiring an interfacility transfer. Additional applications of the MEWS include determining
14 when to transfer a patient: a MEWS ≥ 4 suggests expeditious transfer, rather than a thorough
15 work-up until the discovery of an injury that is not admissible at the transferring facility. Another
16 example is from a bed capacity sense: the house supervisor may be able to determine if a patient
17 may need a bed, and if the ICU is full at the transferring or receiving facility.

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39 The EAST practice management guidelines on the triage of the trauma patient describe
40 77 articles of pre-hospital triage of adult patients, 9 articles of pre-hospital triage of pediatric
41 patients, and 16 articles of in-hospital triage of trauma patients.¹⁷ There are no guidelines or
42 referenced articles on the *interfacility* triage and transport of patients. Our findings contribute to
43 the literature in that we identify a simple score utilizing common vital signs that can aid in early
44 recognition of patients at risk for poor clinical outcomes for triage and transport in the inter-
45 facility setting. Our findings suggest the pre-transfer MEWS can aid in interfacility triage and
46 transport, to be utilized for predicting in-hospital mortality, allotment of ICU resources, and for
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3 identifying patients requiring interfacility transport by air, particularly with scores ≥ 4 . The pre-
4 transfer MEWS appeared to be less useful in identifying secondary overtriage and risk for
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6 deterioration during interfacility transfer, although the utility of the pre-transfer MEWS for these
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8 outcomes requires further study in populations with higher acuity injuries.
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Tables

Table 1. Descriptive statistics by study population, defined by vital sign missingness

% (n)	All 5 vital signs available (n=339)	Missing vital sign(s) (n=248)	P value
Demographics			
Age, years*	54 (35-74)	57 (40.5-78)	0.05
Male Gender	62.2 (211)	56.9 (141)	0.19
White race	73.5 (249)	78.2 (194)	0.18
Cause of injury			0.89
Vehicular	29.2 (99)	26.2 (65)	
Fall	55.5 (188)	58.1 (144)	
Recreational	2.7 (9)	2.4 (6)	
GSW / Homicide	7.1 (24)	6.5 (16)	
Other	5.6 (19)	6.9 (17)	
Injury severity score*	10 (5-17)	10 (5-17)	0.71
Head injury	44.0 (149)	48.9 (121)	0.25
Neck or spine injury	14.5 (49)	16.5 (41)	0.49
Chest injury	9.7 (33)	9.7 (24)	0.98
Limb injury	27.7 (94)	25.4 (63)	0.53
Outcomes			
In-hospital mortality	5.6 (19)	8.1 (20)	0.24
ICU admission	50.2 (170)	51.2 (127)	0.80
Surgical procedure	35.4 (120)	29.4 (73)	0.13
Air transport, interfacility	18.6 (63)	18.2 (45)	0.91
MEWS deterioration	21.9 (72)	21.2 (52)	0.99
Secondary overtriage	21.5 (73)	22.2 (55)	0.85

*Data are presented as median (IQR).

ICU, intensive care unit; GSW, gunshot wound. Secondary overtriage: injury severity score < 10, hospital LOS < 1 day, and discharged home.

Table 2. Clinical and transit outcomes by pre-transfer modified early warning score (MEWS)

MEWS	MEWS % (n)	Mortality	ICU admission	Surgical procedure	Air transport	MEWS deteriora tion	Secondary over-triage
0 or 1	69.6 (236)	2.1%	45.8%	31.8 %	14.0%	19.3%	22.5%
2	13.6 (46)	4.4%	52.2%	45.7%	23.9%	34.9%	23.9%
3	5.6 (19)	10.5%	52.6%	36.8%	15.8%	5.9%	10.5%
4	5.6 (19)	15.8%	63.2%	42.1%	15.6%	22.2%	26.3%
5	3.5 (12)	16.7%	75.0%	41.7%	66.7%	8.3%	16.7%
≥ 6	2.1 (7)	71.4%	100%	57.1%	71.4%	20.0%	0%
p value		< 0.001	< 0.001	0.07	< 0.001	0.65	0.27

Analyzed with Cochran-Armitage trend test

ICU, intensive care unit. Secondary overtriage: injury severity score < 10, hospital LOS < 1 day, and discharged home

Table 3. Association between clinical outcomes with pre-transfer modified early warning score (MEWS) threshold of ≥ 4

Outcomes, % (n)	MEWS < 4, n=301	MEWS ≥ 4, n=38	OR* (95% CI)	P value
In-hospital mortality	3.0 (9)	26.2 (10)	11.6 (4.4, 30.9)	< 0.001
ICU admission	47.2 (142)	73.7 (28)	3.1 (1.5, 6.7)	0.003
Surgical procedure	34.2 (103)	44.7 (17)	1.6 (0.8, 3.1)	0.20
Air transport, interfacility	15.6 (47)	42.1 (16)	3.9 (1.9, 8.0)	< 0.001
MEWS deterioration	21.0 (57)	17.1 (6)	0.7 (0.3, 1.7)	0.43
Secondary overtriage	21.9 (66)	18.4 (7)	0.8 (0.3, 1.9)	0.62

*OR, Odds ratio for MEWS ≥ 4 vs. MEWS < 4, analyzed with univariate logistic regression

ICU, intensive care unit. Secondary overtriage: injury severity score < 10, hospital LOS < 1 day, and discharged home

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3 **Figure Legends**
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5 **Figure 1.** Modified early warning score (MEWS)
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8 **Figure 2.** Receiver operator characteristic (ROC) curves for mortality (a) and ICU admission (b).
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4

5 **Author contributions:** MG and JJ conceived the study. KS and JJ designed the study. KS
6 performed the statistical analysis and drafted the manuscript. JJ was involved in data selection
7 and data collection. MG, MC and DBO contributed substantially to its revision. DBO takes
8 responsibility for the manuscript as a whole.
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13 **Competing interests:** None.
14

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16 public, commercial or not-for-profit sectors.
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29 **Data sharing:** Data are available from corresponding author DBO.
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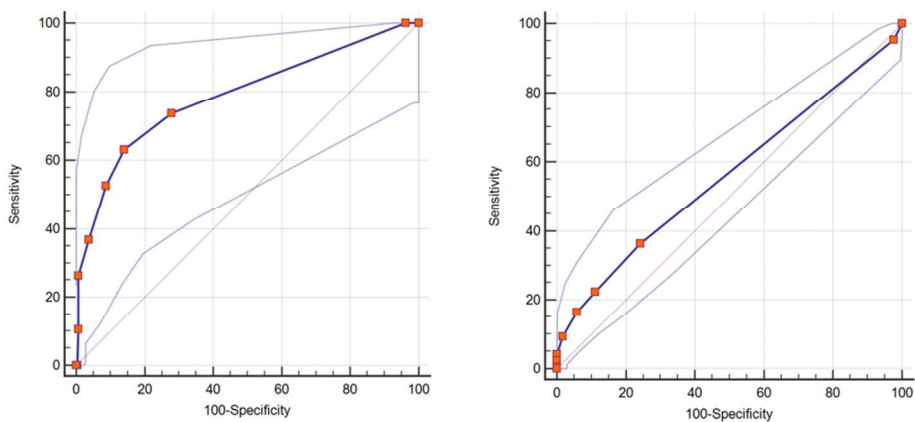
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Modified Early Warning Score							
Vital sign	3	2	1	0	1	2	3
Systolic blood pressure (mmHg)	< 70	71-80	81-100	101-199		≥ 200	
Heart rate (bpm)		< 40	41-50	51-100	101-110	111-129	≥ 130
Respiratory rate (bpm)		< 9		9-14	15-20	21-29	≥ 30
Temperature (C)		< 35		35-38.4		≥ 38.5	
AVPU				Alert	React to Voice	React to Pain	Unresponsive
Glasgow Coma Scale				14-15	10-13	4-9	3

Figure 1. Modified early warning score (MEWS)

361x270mm (72 x 72 DPI)



A Mortality

B ICU admission

Figure 2. Receiver operator characteristic (ROC) curves for mortality (a) and ICU admission (b)

361x270mm (72 x 72 DPI)

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BMJ Open

A RETROSPECTIVE COHORT STUDY OF THE UTILITY OF THE MODIFIED EARLY WARNING SCORE FOR INTERFACILITY TRANSFER OF PATIENTS WITH TRAUMATIC INJURY

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Manuscripts

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3 **A RETROSPECTIVE COHORT STUDY OF THE UTILITY OF THE MODIFIED**
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5 **EARLY WARNING SCORE FOR INTERFACILITY TRANSFER OF PATIENTS WITH**
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8 **TRAUMATIC INJURY**
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ABSTRACT

Objective: The modified early warning score (MEWS) is a “track and trigger” score utilizing routine physiologic vital signs. The objective is to determine if the pre-transfer MEWS can be used for predicting outcomes in trauma patients requiring interfacility transfer to higher levels of care.

Design, setting, participants: Retrospective study of consecutively transferred trauma patients into a level II trauma center from 2013-2014.

Interventions: None.

Outcome measures: Mortality, ICU admission, operative procedure, MEWS deterioration in-transit, air transport interfacility, secondary overtriage (low injury severity score < 10, LOS < 1 day, discharged home), and severe injury (injury severity score \geq 16). The association between the pre-transfer MEWS and outcomes were analyzed with Cochran-Armitage trend tests, ROC curves, and univariate logistic regression.

Results: There were 587 transferred patients; outcomes were reported in 339 patients with complete data on all 5 vital signs used to calculate the MEWS. The MEWS ranged from 0-9 (median of 1). There was a significant linear relationship between MEWS and study outcomes, especially mortality, ICU admission, air medical transport, and severe injury ($p < 0.001$ for all). A threshold score ≥ 4 was identified by ROC analysis; 11.2% of patients had MEWS ≥ 4 . Outcomes were significantly worse in patients with MEWS ≥ 4 vs. < 4 : mortality (26.2% vs. 3.0%, OR = 11.59, $p < 0.001$); ICU admission (73.7% vs. 47.2%, OR = 3.14, $p = 0.003$); air transfer (42.1% vs. 15.6%, OR=3.93, $p < 0.001$); severe injury (59.5% vs. 27.2%, OR=3.9, $p < 0.001$). The MEWS was not associated with surgery, in-transit MEWS deterioration, or secondary overtriage.

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3 **Conclusion:** Pre-transfer MEWS ≥ 4 may be utilized by the receiving facility for predicting
4 injury severity, mortality, air transport, and ICU resource utilization. In the interfacility transport
5 setting, the MEWS may be useful for identifying patients with less obvious need for transfer or
6 requiring more expeditious transfer.
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For peer review only

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3 **Article Summary:** Strengths and limitations of this study
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- 6 • Strength: The utility of the modified early warning score (MEWS), a “track and trigger”
7 score comprised of common physiologic vital signs, has been previously described for
8 risk deterioration in ED settings, but its utility has not been examined during interfacility
9 transfer.
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 - 11 • Limitation: Emergency physicians and EMS personnel did not prospectively utilize the
12 MEWS during the study period so our findings need to be considered in combination
13 with clinical judgment.
14
 - 15 • Limitation: There was a considerable amount of missing vital signs at the transferring
16 facility, resulting in nearly half of patients being removed from our outcomes analysis,
17 although there were no differences in demographics, vital signs, or outcomes in patients
18 with missing versus complete vital signs.
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 - 20 • Limitation: The acuity of the patients was low, which may have prevented more robust
21 analyses between MEWS and outcomes.
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INTRODUCTION

Traumatic injury is the leading cause of death in persons under 45 years of age.¹ Emergency medical service (EMS) personnel transported nearly 5 million patients with traumatic injury in 2008 alone.² The pre-hospital care, triage and transport of patients with traumatic injury to a trauma center are determined by protocols and guidelines published by the American College of Surgeons (ACS) Committee on Trauma³ and the Centers for Disease Control and Prevention.² However, not all injuries are immediately obvious, and patients are occasionally undertriaged to a lower-level or non-trauma center that requires interfacility EMS transport to a higher-level trauma center for care.

The mode of EMS transport interfacility is determined and requested by the transferring emergency physician. Communication between the transferring physician and the receiving trauma surgeon includes a review of physiologic status, initial management, and discussion on the optimal timing of transfer, such as stabilizing patients prior to transfer. EMS agencies are staffed with providers having a range of training and experience dictating the scope of tasks they can perform, from administration of medications, use of medical devices, performing cardiopulmonary resuscitation, initiating ventilation and intubation, and other monitoring techniques. While there are some criteria to help the transferring physician determine if the trauma patient should be transferred, for example patients with carotid or vertebral injuries, cardiac rupture, and grade IV or V liver injuries,³ there are no solid guidelines on if, when, and how a patient should be transferred. Field triage guidelines^{2,3}, although not explicitly intended for the interfacility transport or ED setting, could be used to aid in interfacility transfer of patients. These available guidelines, however, may not be as useful as a composite score in the interfacility transport setting.

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3 The modified early warning score (MEWS) is a “track and trigger” score used for
4 recognizing patients who are at risk for deterioration and determines degree of illness of the
5 patient.⁴ The initial validation of the MEWS was performed in 709 emergency department
6 patients and identified MEWS ≥ 5 was associated with mortality and admission to the intensive
7 care unit (ICU).⁵

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10 Our objectives were to determine whether the MEWS can be used in the interfacility
11 transport setting for patients with traumatic injury to detect patients potentially requiring higher
12 levels of care. Specifically, we examined whether the pre-transfer MEWS was associated with
13 poor clinical outcomes, transport mode, injury severity, and secondary overtriage.
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15 16 17 18 19 20 21 22 23 24 25 26 27 **METHODS**

28 29 30 **Design, setting and participants**

31 This was a retrospective cohort study that included all consecutively admitted trauma patients
32 transferred into an ACS verified level II trauma center from another healthcare facility between
33 January 1, 2013 and December 31, 2014 and followed through discharge of the index
34 hospitalization. The patient populations were identified from the trauma registry called
35 TraumaBase® (CDM, Conifer, CO), which is a registry used by the hospital and the State of
36 Texas to track patients with traumatic injury for epidemiology and prevention studies as well as
37 for quality assurance and quality improvement. Patients less than 18 years of age were excluded.
38 We also excluded patients with no vital sign data (n=65, 10.0% of patients). This study received
39 institutional review board approval with waiver of informed consent from The Medical Center of
40 Plano Institutional Review Board (study #163).
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55 56 57 58 59 60 **Modified Early Warning Score**

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3 The MEWS is derived from 5 common physiologic vital signs of systolic blood pressure (SBP,
4 mm Hg), heart rate (HR, beats per minute), respiratory rate (RR, breaths per minute),
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6 temperature (T, Celcius), and AVPU score ("alert, voice, pain, unresponsive"), **Figure 1**. The
7
8 Glasgow coma scale is favored to the AVPU in traumatic injury, and the AVPU was derived
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10 from the GCS as follows: A=14-15, V=9-13, P = 4-8, U = 3. This substitution is common
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12 although there is no standard method for estimating GCS from AVPU⁶⁻¹⁰. The MEWS was
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14 calculated as the total of the five subcomponent scores (**figure 1**). Scores range from 0 to a
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16 maximum of 14.
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22 The pre-transfer MEWS was calculated using vital signs from the transferring facility
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24 (obtained from the transfer facility record), before interfacility transport. The post-transfer
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26 MEWS was calculated from vital signs collected on arrival to the receiving facility.
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29 **Covariates and outcomes**

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31 Clinical outcomes included in-hospital mortality, intensive care unit (ICU) admission, surgical
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33 procedure, EMS transport mode (air medical vs. ground transport), MEWS deterioration (an
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35 increase in MEWS during transit, calculated as the difference between pre-transfer MEWS and
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37 post-transfer MEWS), secondary overtriage (injury severity score (ISS) < 10, hospital LOS < 1
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39 day, and discharged home), and severe injury (injury severity score (ISS) ≥ 16).
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43 The following demographic and clinical information was abstracted from the registry:
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45 vital sign information (vital sign location, timing, and values before interfacility transport and on
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47 arrival at the receiving facility); demographics (age, gender, race); injury severity measures
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49 (abbreviated injury scale score, ISS, anatomic location of injury), and cause of injury. We also
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51 examined the occurrence of in-transit events, defined as a significant change in vital signs during
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53 transport (any normal to abnormal change in SBP, HR, RR, T, and GCS) or procedures
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3 performed in transit (e.g. fluid bolus, new or significant change in medication, sedation, or
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6 paralytics, placement of chest tube or central line, needle decompression). Information on in-
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9 transit events were abstracted from detailed, scanned EMS run reports, which were only
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11 available in 149 charts.

12 **Analysis**

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15 The association between pre-transfer MEWS and outcomes were examined with Cochran-
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18 Armitage trend tests. Receiver operator characteristic (ROC) curves were used to identify an
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21 optimal threshold score; we examined ROC curves for mortality and ICU admission, which were
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24 the outcomes used in the initial validation of the MEWS.⁵ This threshold score was examined in
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27 separate logistic regression models for each of our study outcomes to estimate the unadjusted
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30 odds of the threshold score for the outcome. The threshold score was also used to examine the
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33 proportion of patients who did not meet the physiologic criteria outlined in the Guidelines for
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36 triage to a trauma center of $GCS \leq 13$, $SBP \leq 90$ mm Hg, and respirations < 10 or > 29
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39 breaths/min signaling potential, impending deterioration.¹³

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SAS version 9.4 (SAS Institute, Cary, NC) was used for all analyses, and $p \leq 0.05$ was
considered statistically significant.

43 **RESULTS**

46 **Patient characteristics and outcomes**

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There were 587 transferred patients in our study. The population had a median (IQR) age of 56
years (37-74), 60% were male, and the most common cause of injury was due to fall (57%),
followed by a vehicular crash (28%). Nearly half of patients suffered a head injury (46%),
although the acuity of neurologic deficit was low with a median GCS was 15 (15-15). Overall,

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3 18% were transported interfacility by air medical services. The average distance traveled was 23
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5 miles (range: 7 – 79 miles).
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8 The rates of our study outcomes are shown in **table 1**. There was low mortality of less
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10 than 6% among our transferred trauma population, although half of patients were admitted to the
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12 ICU, 35% required surgery, and 31% had a severe injury with ISS \geq 16.
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15 Additionally, 17.4% (26/149) experienced an in-transit event. The most common in-
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17 transit events were development of tachycardia or an abnormal RR (n=6 each), followed by
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19 development of hypotension (< 90mm Hg, n=4), administration of fluid bolus (n=4), and GCS
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21 decline of two or more points (n=3).
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24 **Modified early warning score**

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26 The majority of patients (90%) were not missing any vital signs post-transfer. However, 42%
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28 (n=248) were missing between one and four vital signs pre-transfer (83% of those patients were
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30 missing only 1 vital sign). Thus, only 58% of patients (n=339) had complete data for all 5 vital
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32 signs.
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36 We examined whether there were differences in demographics, clinical characteristics,
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38 and outcomes in patients with complete vital sign data (n=339) vs. missing vital sign(s) (n=248),
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40 **table 1**. There were no differences in any covariate or in any study outcome. We also examined
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42 whether there were differences in deterioration of the MEWS vital sign subscores between
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44 patients with complete vital sign data vs. those with missing vital signs; no differences existed
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46 (**table 1**). Still, to be conservative we analyzed the association between pre-transfer MEWS and
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48 outcomes in those with complete vital sign data only (n=339), rather than using multiple
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50 imputation to calculate an imputed MEWS in patients with missing vital sign(s).
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55 **MEWS relationship to outcomes**

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3 The median (IQR) MEWS was 1 (1-2). As shown in **table 2**, the pre-transfer MEWS showed a
4 significant, linear relationship with study outcomes of mortality, ICU admission, air transport,
5 and severe injury. The pre-transfer MEWS was borderline significant for predicting a surgical
6 procedure.
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12 Threshold scores were determined with ROC curves (**figure 2**). The ROC curve for
13 mortality was clinically and statistically significant (AUROC: 0.79 (95% CI: 0.74-0.83, $p <$
14 0.001), identifying a threshold MEWS ≥ 4 for predicting mortality with a high specificity of 91.3
15 (91% of survivors were correctly identified by a pre-transfer MEWS < 4) and good sensitivity of
16 52.6 (53% of patients who expired were correctly identified by a MEWS ≥ 4), figure 2a. The
17 ROC curve for ICU admission was weaker but still statistically significant (AUROC: 0.56 (95%
18 CI: 0.51-0.62, $p=0.02$), demonstrating specificity of 94.1 and sensitivity of 16.5 with a threshold
19 MEWS ≥ 4 on ROC analysis, figure 2b.
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31 When the threshold score ≥ 4 was modeled for our outcomes, the pre-transfer MEWS
32 continued to show a significant association with study outcomes of mortality, ICU admission, air
33 transport, and severe injury (**table 3**).
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38 In patients with MEWS ≥ 4 , 45% (17/38) did not have abnormal physiologic vital signs
39 signaling triage to a trauma center by the ACS COT and CDC decision guidelines; further, 63%
40 (12/19) of patients with a MEWS=4 would not have met the physiologic criteria outlined in the
41 Guidelines. Outcomes in these twelve patients include one death, seven admissions to the ICU,
42 five patients requiring surgery, but only three patients transferred by air. Ninety-five percent
43 (286/301) of patients with MEWS < 4 did not have abnormal vital signs per the guidelines.
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55 DISCUSSION

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3 Our study examined patients with traumatic injury requiring interfacility transfer, demonstrating
4 that a MEWS ≥ 4 calculated prior to interfacility transport is associated with mortality, ICU
5 admission, air medical transport, and severe injury. In the interfacility transport setting, the
6 MEWS may act as a more holistic measure that may lessen the chance of underestimating a poor
7 clinical outcome and delaying or not transferring a patient appropriately. While it may seem
8 obvious that out-of-range vital signs would increase the odds of an unfavorable outcome, only 21
9 of 38 patients with MEWS ≥ 4 would have met abnormal physiologic criteria by the ACS COT
10 and CDC decision guidelines.¹³ In this setting, the MEWS may be useful for identifying patients
11 with less obvious need for transfer.
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24 The main limitation of the study is that emergency physicians and EMS personnel did not
25 prospectively utilize the MEWS during the study period so our findings need to be considered in
26 combination with clinical judgment. Fullerton et al. observed that the MEWS in combination
27 with clinical judgment increases the utility of the MEWS in a pre-hospital setting.⁴ At least one
28 study reported that implementing the MEWS in a trauma setting did not result in a statistically
29 significant reduction in mortality ($p=0.09$).¹¹ A prospective study that factors in clinical
30 judgment will need to validate this threshold of ≥ 4 to determine if it leads to more appropriate
31 transfer and improved outcomes.
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43 Additional limitations are as follows: There was a considerable amount of missing vital
44 sign data at the transferring facility, resulting in 47% of patients being removed from our
45 outcomes analysis. While there were no differences in the characteristics or outcomes of patients
46 with complete data and patients with incomplete data, there may be some residual bias in
47 excluding patients with one or more missing vital signs. This limitation also suggests a need for
48 more efficient, routine collection of pre-transport vital signs and EMS reports to receiving
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3 facilities. Next, the acuity of the patients was low, which may have prevented more robust
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5 analyses between MEWS and outcomes. The median pre-transfer MEWS was only 1. This might
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7 not be a limitation as much as it suggests that guidelines for the pre-hospital triage and transport
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9 of patients attempts to minimize under-triage of trauma patients at the expense of over-triage.
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11 Further study is needed to examine the MEWS for inter-hospital transport to level I trauma
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13 centers. Patients transferred into level I trauma centers theoretically have higher acuity injuries
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15 and more severe MEWS pre-hospital, which may help with the robustness of these analyses.
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17 Finally, the AVPU component of the MEWS score was estimated from the GCS. There are no
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19 standard criteria for estimating GCS from AVPU;⁶⁻¹⁰ using a different cut-off might result in
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21 different MEWS scores.
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27 Literature published within the past few years have identified a range of MEWS values
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29 associated with poor outcomes. Such studies include a pre-hospital MEWS ≥ 3 for requiring a
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31 life-saving intervention,¹² MEWS ≥ 5 with early mortality in the ED,¹³ MEWS ≥ 6 for mortality
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33 in the ICU,¹⁴ MEWS ≥ 7 for rapid response team and cardiac arrest in the ED.¹⁵ Still others have
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35 used the MEWS ≥ 5 identified by Subbe et al. and examined this threshold in other settings, such
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37 as in developing countries.¹⁶ A MEWS threshold ≥ 4 was associated with poor outcomes in
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39 patients requiring interfacility transfer in our study. Higher scores may lead to more efficient
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41 secondary triage and transfer of patients to a higher-level trauma center who are at risk for
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43 deterioration and poor outcomes. Using an integrated score such as the MEWS might help avoid
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45 situations where a clinician might dismiss a potentially problematic clinical presentation as not
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47 requiring an interfacility transfer. Additional applications of the MEWS include determining
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49 when to transfer a patient: a MEWS ≥ 4 suggests expeditious transfer, rather than a thorough
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51 work-up until the discovery of an injury that is not admissible at the transferring facility. Another
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3 example is from a bed capacity sense: the house supervisor may be able to determine if a patient
4 may need a bed, and if the ICU is full at the transferring or receiving facility.
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8 The EAST practice management guidelines on the triage of the trauma patient describe
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10 77 articles of pre-hospital triage of adult patients, 9 articles of pre-hospital triage of pediatric
11 patients, and 16 articles of in-hospital triage of trauma patients.¹⁷ There are no guidelines or
12 referenced articles on the *interfacility* triage and transport of patients. Our findings contribute to
13 the literature in that we identify a simple score utilizing common vital signs that can aid in early
14 recognition of patients at risk for poor clinical outcomes for triage and transport in the inter-
15 facility setting. Our findings suggest the pre-transfer MEWS can aid in interfacility triage and
16 transport, to be utilized for predicting in-hospital mortality, allotment of ICU resources, for
17 identifying patients requiring interfacility transport by air, and for recognizing severe injuries,
18 particularly with scores ≥ 4 . The pre-transfer MEWS appeared to be less useful in identifying
19 secondary overtriage and risk for deterioration during interfacility transfer, although the utility of
20 the pre-transfer MEWS for these outcomes requires further study in populations with higher
21 acuity injuries.
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Tables

Table 1. Descriptive statistics by study population, defined by vital sign missingness

% (n)	All 5 vital signs available (n=339)	Missing vital sign(s) (n=248)	P value
Demographics			
Age, years*	54 (35-74)	57 (40.5-78)	0.05
Male Gender	62.2 (211)	56.9 (141)	0.19
White race	73.5 (249)	78.2 (194)	0.18
Fall cause of injury	55.5 (188)	58.1 (144)	0.89
Head injury	44.0 (149)	48.9 (121)	0.25
Neck or spine injury	14.5 (49)	16.5 (41)	0.49
Chest injury	9.7 (33)	9.7 (24)	0.98
Limb injury	27.7 (94)	25.4 (63)	0.53
MEWS subscore change from transferring to receiving facility			
Deterioration in SBP	3.83 (13)	3.23 (8)	0.76
Deterioration in HR	11.80 (40)	14.11 (35)	0.34
Deterioration in RR	9.44 (32)	8.87 (22)	1.0
Deterioration in Temp	0.29 (1)	0 (0)	1.0
Deterioration in GCS	6.49 (22)	2.02 (5)	0.07
Outcomes			
In-hospital mortality	5.6 (19)	8.1 (20)	0.24
ICU admission	50.2 (170)	51.2 (127)	0.80
Surgical procedure	35.4 (120)	29.4 (73)	0.13
Air transport, interfacility	18.6 (63)	18.2 (45)	0.91
MEWS deterioration	21.9 (72)	21.2 (52)	0.99
Secondary overtriage	21.5 (73)	22.2 (55)	0.85
Severe injury (ISS \geq 16)	30.75 (103)	32.39 (80)	0.67

*Data are presented as median (IQR).

ICU, intensive care unit; GSW, gunshot wound; ISS, injury severity score. Secondary overtriage:

ISS < 10, hospital LOS < 1 day, and discharged home.

Table 2. Clinical and transit outcomes by pre-transfer modified early warning score (MEWS)

MEWS	MEWS % (n)	Mortality	ICU admission	Surgical procedure	Air transport	MEWS deteriora tion	Secondary over-triage	Severe injury (ISS \geq 16)
0 or 1	69.6 (236)	2.1%	45.8%	31.8 %	14.0%	19.3%	22.5%	24.0%
2	13.6 (46)	4.4%	52.2%	45.7%	23.9%	34.9%	23.9%	32.6%
3	5.6 (19)	10.5%	52.6%	36.8%	15.8%	5.9%	10.5%	52.6%
4	5.6 (19)	15.8%	63.2%	42.1%	15.6%	22.2%	26.3%	61.1%
5	3.5 (12)	16.7%	75.0%	41.7%	66.7%	8.3%	16.7%	41.7%
\geq 6	2.1 (7)	71.4%	100%	57.1%	71.4%	20.0%	0%	100%
p value		< 0.001	< 0.001	0.07	< 0.001	0.65	0.27	< 0.001

Analyzed with Cochran-Armitage trend test

ICU, intensive care unit; ISS, injury severity score. Secondary overtriage: ISS < 10, hospital LOS < 1 day, and discharged home.

Table 3. Association between clinical outcomes with pre-transfer modified early warning score (MEWS) threshold of \geq 4

Outcomes, % (n)	MEWS < 4, n=301	MEWS \geq 4, n=38	OR* (95% CI)	P value
In-hospital mortality	3.0 (9)	26.2 (10)	11.6 (4.4, 30.9)	< 0.001
ICU admission	47.2 (142)	73.7 (28)	3.1 (1.5, 6.7)	0.003
Surgical procedure	34.2 (103)	44.7 (17)	1.6 (0.8, 3.1)	0.20
Air transport, interfacility	15.6 (47)	42.1 (16)	3.9 (1.9, 8.0)	< 0.001
MEWS deterioration	21.0 (57)	17.1 (6)	0.7 (0.3, 1.7)	0.43
Secondary overtriage	21.9 (66)	18.4 (7)	0.8 (0.3, 1.9)	0.62
Severe injury (ISS \geq 16)	27.2 (81)	59.5 (22)	3.9 (1.9, 8.0)	< 0.001

*OR, Odds ratio for MEWS \geq 4 vs. MEWS < 4, analyzed with univariate logistic regression

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3 ICU, intensive care unit; ISS, injury severity score. Secondary overtriage: ISS < 10, hospital LOS
4 < 1 day, and discharged home.
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3 **Figure Legends**
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5 **Figure 1.** Modified early warning score (MEWS)
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8 **Figure 2.** Receiver operator characteristic (ROC) curves for mortality (a) and ICU admission (b)
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4

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8
9 and data collection. MG, MC and DBO contributed substantially to its revision. DBO takes
10
11 responsibility for the manuscript as a whole.
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18
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24 for the Surgery of Trauma in September 2016 in Haikoloa, HI.
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27 **Permissions:** None.
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29 **Data sharing:** Data are available from corresponding author DBO.
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32 **Research reporting checklist:** STROBE statement checklist complete.
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Modified Early Warning Score							
Vital sign	3	2	1	0	1	2	3
Systolic blood pressure (mmHg)	< 70	71-80	81-100	101-199		≥ 200	
Heart rate (bpm)		< 40	41-50	51-100	101-110	111-129	≥ 130
Respiratory rate (bpm)		< 9		9-14	15-20	21-29	≥ 30
Temperature (C)		< 35		35-38.4		≥ 38.5	
AVPU				Alert	React to Voice	React to Pain	Unresponsive
Glasgow Coma Scale				14-15	10-13	4-9	3

Figure 1. Modified early warning score (MEWS)

149x62mm (300 x 300 DPI)

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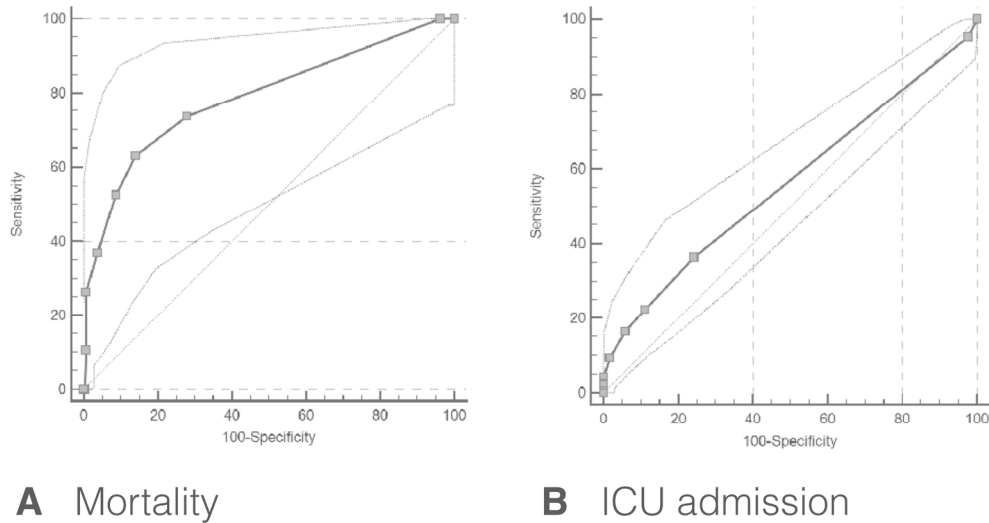


Figure 2. Receiver operator characteristic (ROC) curves for mortality (a) and ICU admission (b)

176x93mm (300 x 300 DPI)

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Page	Recommendation
Title and abstract	1	2	(a) Indicate the study's design with a commonly used term in the title or the abstract
		2	(b) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction			
Background/rationale	2	5	Explain the scientific background and rationale for the investigation being reported
Objectives	3	6	State specific objectives, including any prespecified hypotheses
Methods			
Study design	4	6	Present key elements of study design early in the paper
Setting	5	6	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants
		NA	(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case
Variables	7	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	7	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	8-9	Describe any efforts to address potential sources of bias
Study size	10	6	Explain how the study size was arrived at
Quantitative variables	11	8-9	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	8	(a) Describe all statistical methods, including those used to control for confounding
		8-9	(b) Describe any methods used to examine subgroups and interactions
		8-9	(c) Explain how missing data were addressed
		NA	(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy
		NA	(e) Describe any sensitivity analyses

Continued on next page

Results	Page	
Participants	13*	8-9 (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		8-9 (b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	8 (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		8-9 (b) Indicate number of participants with missing data for each variable of interest
		NA (c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)
Outcome data	15*	10-12 <i>Cohort study</i> —Report numbers of outcome events or summary measures over time
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures
Main results	16	11-12 (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		11 (b) Report category boundaries when continuous variables were categorized
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	NA Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	12 Summarise key results with reference to study objectives
Limitations	19	14 Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	13 Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	14-15 Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	17 Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.