Rapid response systems. Recognition and management of the deteriorating patient

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Chapter 9

Nationwide introduction of Rapid Response Systems in the Netherlands. Analysis of the Cost and Outcomes of Medical Emergency Teams (COMET) study

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Submitted
ABSTRACT

Importance: Clinical deterioration of patients on nursing wards resulting in cardiopulmonary arrest, unplanned Intensive Care Unit (ICU) admission and even death is potentially preventable. Rapid Response Systems (RRS) have been developed almost twenty years ago but there is limited evidence that RRSs lower the incidence of life threatening adverse events.

Objective: To determine the effectiveness of RRS on the clinical outcome of patients.

Design, setting and participants: Pragmatic Dutch multi-center before-after trial including 12 hospitals (2 surgical and 2 non-surgical wards) with patients 18 years or older between April 2009 and November 2011.

Interventions: The Modified Early Warning Score (MEWS) and Situation-Background-Assessment-Recommendation (SBAR) instruments were implemented during seven months. The Rapid Response Team (RRT) was then implemented during the following 17 months to complete the Rapid Response System (RRS).

Main outcomes and measures: The primary outcome was the incidence of the composite endpoint of either cardiopulmonary arrest, unplanned ICU admission, and death. Secondary outcomes were the individual components of the primary endpoint. Primary comparison were between the before (5 months) phase and the last 5 months of the RRT phase.

Results: In total 166,569 patients were included in the study representing 1,031,172 hospital admission days. The primary endpoint was significantly reduced in the RRT versus the before phase, adjusted odds ratio (OR) 0.847 (95% CI 0.725-0.989, p=0.036). Cardiopulmonary arrests and in hospital mortality were also significantly reduced, OR 0.607 (95 CI 0.393-0.937, p=0.018) and OR 0.802 (95% CI 0.644-1.0, p=0.05) respectively. Unplanned ICU admission showed a declining trend, OR 0.878 (95% CI 0.755-1.021, p=0.092). Specific characteristics of these endpoints, including patient demographics but also markers for disease severity (APACHE scores, survival to ICU/hospital discharge) remained similar.

Conclusions and relevance: In this study, RRSs were shown to lower the composite endpoint including cardiopulmonary arrest, unplanned ICU admission and mortality in patients on general hospital wards. These findings support the implementation of RRSs in hospitals to reduce severe adverse events.

TRAIL REGISTRATION: This trial is registered at the Dutch trial registry (www.trialregister.nl) with trial number NTR2706.
Introduction

Patients who experience adverse events during their hospital stay, including cardiopulmonary arrest, unplanned ICU admissions and unexpected death, show clear signs of deterioration in the hours preceding the event. Rapid Response Systems (RRS) have been developed for timely identification and treatment of patients on general wards at risk for clinical deterioration. To note, in the literature, RRSs and Medical Emergency Systems are used interchangeably. The first report describing a system that aims at preventing these events was described in 1995 by Lee et al. RRSs are designed as a three component system. The two primary components are the afferent and efferent limbs. The afferent limb aims at the early detection of the deteriorating condition by systematic measurement of vital signs using a track and trigger system. After reaching a predefined threshold, the efferent limb is activated and the Medical Emergency Team (MET) or Rapid Response Team (RRT) is called and responds to the patient’s bedside. These teams are most often composed of Intensive Care Unit (ICU) physicians together with ICU nurses. The final component is the education, data collection and analysis limb which directs its focus on the maintenance of the system within an institution. Up to this moment, only two randomised studies have been performed investigating the effectiveness of RRSs. The single largest randomized trial, the Medical Early Response Intervention and Therapy (MERIT) study, failed to demonstrate a benefit. One study from the United Kingdom demonstrated a reduction in hospital mortality after introduction of an RRT. Besides these two studies, many smaller and less well designed studies have been performed and recently reviewed. A general trend in reduction of cardiorespiratory arrests was found. Results regarding hospital mortality varied widely and only a small trend in reduction was found.

In 2008, a nationwide directive by the Dutch government stated that implementation of RRS was mandatory for all Dutch hospitals. We took the opportunity to study the effects of this nationwide implementation of an RRS on outcome of patients admitted to general hospital wards. Primary endpoint was the incidence of the composite endpoint of either cardiopulmonary arrest, unplanned ICU admission, or death.

Methods

Trial design

The study protocol has been described previously. In short, the COMET study was designed as a prospective, pragmatic before-after multi-center trial enabling the analysis of clinical outcomes after sequential introduction of the RRS components. Twelve Dutch hospitals participated in this study. Originally, 14 hospitals started the study but two were excluded after the first phase introducing the afferent limb of the RRS. This was
due to substantial reorganizations at the participating wards including major changes in case mix. Two large university hospitals, eight large teaching hospitals and two smaller regional hospitals completed the study. Each hospital included four study wards, 2 surgical and 2 medical wards. The surgical wards included general surgery, oncology type surgery, vascular surgery and orthopaedics. Medical wards included internal medicine, nephrology, infectious diseases, pulmonology and neurology. All patients 18 years or above, admitted to one of the COMET wards during their hospital stay, were included.

The trial design is shown in figure 1. The before period consisted of 5 months in which baseline data were collected. The implementation of RRS was divided into two phases. The first phase lasted 7 months in which the MEWS (Modified Early Warning Score) together with the SBAR communication tool (Situation-Background-Assessment-Response instrument) were implemented. Both instruments are shown in the supplementary materials. In the second phase, a RRT was introduced in addition to the MEWS and SBAR instruments. This phase lasted 17 months of which the first 12 months were used to fully implement this intervention and the last 5 months to measure the effects on outcome of patients. Implementation of the interventions was supported by the use of standardized toolkits including pocket cards, posters and multiple face-to-face briefings.

<table>
<thead>
<tr>
<th>Before</th>
<th>MEWS/SBAR</th>
<th>RRT implementation</th>
<th>RRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 months</td>
<td>7 months</td>
<td>12 months</td>
<td>5 months</td>
</tr>
</tbody>
</table>

← Start of study between 1st of April and 1st of July 2009

End of study between 31st of August and 30th of November 2011

**Fig. 1.** Design of the COMET study

Following the baseline period of 5 months, the MEWS/SBAR was implemented for 7 months and subsequently followed up by 17 months in which the RRT was available. Effects of the RRT on outcomes were measured during the last 5 months and compared with the 5 months baseline period. During the entire length of the study, data was collected on all the endpoints.

**Outcomes**

The primary outcome is the composite endpoint of either cardiopulmonary arrest, unplanned ICU admission or death while being admitted on a COMET ward per 1,000 admitted patients. Other endpoints were the components of the composite
endpoint and also the composite endpoint per 1,000 admission days on a COMET ward. Cardiopulmonary arrest was defined as an event for which the cardiopulmonary arrest team was called starting Cardio Pulmonary Resuscitation (CPR), either using chemical resuscitation and/or manual chest compressions and/or respiratory ventilation (irrespective of type). Unplanned ICU-admissions were registered according to the definitions of the Dutch National Intensive Care Evaluation (NICE) registry as admissions that were unscheduled and could not be delayed for at least 12 hours without risk. All hospitals had followed training in data collection and data definitions as used in the NICE registry.  

**Details of the interventions**

In the first implementation phase, all nurses and physicians on the study wards were trained in using the MEWS and SBAR communication tool. Nurses and physicians were instructed to determine the full MEWS whenever any vital parameter was outside

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**Figure 2. Algorithm for activation of RRT.**

- **Nurse:** Determine the MEWS according to protocol
- **Nurse:** Patient with MEWS \(< 3\)
  - Follow local guidelines
- **Nurse:** Patient with MEWS \(\geq 3\)
  - Directly call the physician according to SBAR
- **Physician:** Within 30 minutes
  - Assess the patient and draft medical policy
- **Physician:** After assessment of patient
  - Possibility of direct activation of RRT
- **Physician:** Maximum of 60 minutes
  - Determine effect of therapy
- **Physician:** In case no effect of therapy
  - Always and directly activate RRT
- **Nurse:** If physician doesn’t comply to set guidelines and time limits
  - Always and direct activation of RRT by the nurse
the normal range. In addition, physicians could also demand measurement of the MEWS at specific time intervals, when considered appropriate. Upon reaching the threshold of 3 or more points, the responsible physician on that ward was directly notified with communication structured using the SBAR tool. Deviation from the MEWS threshold was allowed in specific circumstances. For instance, in case of a patient with chronic obstructive pulmonary disease with chronic hypoxemia, a physician was allowed to adjust the MEWS criteria accordingly because such patient could have a MEWS higher than 3 points at all times. Any adjustments of the threshold(s) had to be documented in the nursing and medical charts.

In the second implementation phase, a RRT was implemented and available 24 hours per day. The use of the MEWS and SBAR was continued. The RRT included both an ICU nurse and a physician who was at least Fundamental Critical Care Support (FCCS) trained. RRTs were called according to the algorithm presented in figure 2.

Algorithm for RRT activation. The algorithm displays the protocol of handling positive MEWS values and all subsequent actions which either nurse or physician had to undertake together with set time limits. During the MEWS/SBAR phase, the RRT was not available and after notification of the physician by the nurse, no specified actions were protocolized. An action could include consultations to other specialties or the ICU in general and no time frames were specified as well. See for full description of the protocol, Ludikhuize et al. 15

Sample size
The calculation of the sample size has been described in detail previously.15 In deviation from the original protocol, about twice the planned number of 27,720 admissions was available for analysis. The actual analysis to detect, if the RRT period would show a lower incidence of patients experiencing a reanimation, unplanned ICU admission or death by at least 4 per 1,000, was based on 54,479 admissions, 26,659 stemming from the before period and 27,820 from the RRT period.

Data acquisition and statistical analysis
Admission data of patients who had spent time on a COMET ward at any time during the study observation period were provided by the information departments of participating hospitals. Data on cardiopulmonary arrest, unplanned ICU admission and death on COMET wards were collected with clinical report forms. Clinical report forms were also used to gather information on RRT calls and consultations.
Incidence of cardiopulmonary arrest, unplanned ICU admission and death, both as composite endpoint and each separately, are presented graphically over time for the before, MEWS, RRT implementation and RRT period respectively. Incidences per 1,000 admissions as well as per 1,000 COMET inpatient days are shown. Admissions were counted when a
patient had spent at least 1 day of his admission on a COMET ward. Inpatient days were counted when a patient had spent some part of the day on a COMET ward. A generalized linear mixed model (GLMM) was applied to assess the differences in outcomes per 1,000 admissions between the before and RRT periods. In deviation from the published study protocol it was decided to simplify the original analysis. It was first nested admissions within hospitals rather than within the wards as clusters, because during the introduction, implementation and maintenance of the rapid response systems at the local level, hospitals seemed more distinct than ward types. Secondly, it was decided to compare the before and RRT periods as whole periods and to refrain from the analysis of data by successive months, because the latter approach introduced complex dependencies over time, in case admissions included two or more months.

Potential confounders were included in GLMM as fixed or random parameters. Potential confounders were identified following (i) cross-tabulation with the before-RRT period in case of categorical variables (sex, emergency admission, hospital) or after t-testing for the difference between the before and RRT periods regarding patients’ age as a continuous variable, and following (ii) simple univariable logistic regression analyses on the composite outcome with the same confounders. Seasonality - reflecting differences in risk of cardiopulmonary arrests, unplanned ICD-admission or death by calendar month - could be ignored, because in each hospital the months of the year included were identical for the before and RRT periods.

In the GLMM, a binomial distribution was assumed for the composite primary endpoint and for deaths. For unplanned ICU admission days, a binomial distribution was assumed after recoding the original count variable into a dichotomous one, expressing whether patients were at least once admitted to the ICU or not during their stay. For cardiopulmonary arrests a Poisson distribution was assumed because of its observed (extremely) low incidence. Hospitals were modelled as a random parameter, accounting for differences in background incidence (level) and varying impact of the intervention (slope), while simultaneously controlling for the differentially distributed numbers of admissions by hospital during the before and RRT periods. Age of patients was modelled as a random component, whereas patients’ sex and admission type (planned versus unplanned/emergency) were modelled as fixed parameters. No off-set variable was taken into account. The mean numbers of cardiopulmonary arrests, ICU admissions, and deaths - as well as their composite - were reported per 1000 admissions. Additionally, the uncorrected odds ratio and odds ratio after correction for confounding were reported along with their confidence intervals and corresponding p-values.

All analyses were performed in SPSS version 20.0.0.1. In deviation of the original protocol, the level of significance was set at a two-sided alpha of 0.05.
Ethics approval
The medical ethics committee (METC) of the Academic Medical Center in Amsterdam waived the need for formal evaluation of the study due to the obligatory nature of the intervention and the observational nature of the study. Consequently, the need for informed consent was not applicable. The trial was registered at the Dutch Trial Register under number TC2706. All authors hereby declare that all experiments have been examined performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

Results
Characteristics of the study population from the twelve hospitals are presented in Table 1. Because patients could be transferred during their hospital admission from non-COMET wards to COMET wards and vice versa, the ratio of COMET admission days to the total length of hospital admissions was calculated, ranging from 0.97 to 0.98 in the different study periods.

Table 1. Characteristics of study population

<table>
<thead>
<tr>
<th></th>
<th>Before</th>
<th>MEWS</th>
<th>RRT implementation</th>
<th>RRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>N of months</td>
<td>5</td>
<td>7</td>
<td>12</td>
<td>5</td>
</tr>
<tr>
<td>N of hospitals</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>N of hospital admissions</td>
<td>28,298</td>
<td>40,499</td>
<td>68,212</td>
<td>29,560</td>
</tr>
<tr>
<td>Percentage emergency</td>
<td>47.2*</td>
<td>47.1**</td>
<td>47.4</td>
<td>49.7</td>
</tr>
<tr>
<td>Mean overall LOS</td>
<td>6.42</td>
<td>6.57</td>
<td>6.34</td>
<td>5.81</td>
</tr>
<tr>
<td>COMET part of admissions</td>
<td>0.981</td>
<td>0.972</td>
<td>0.984</td>
<td>0.983</td>
</tr>
<tr>
<td>N of COMET admission days</td>
<td>178,156</td>
<td>258,710</td>
<td>425,558</td>
<td>168,748</td>
</tr>
<tr>
<td>Male patients</td>
<td>49.2</td>
<td>50.1</td>
<td>49.9</td>
<td>50.1</td>
</tr>
<tr>
<td>Mean age of patients (SD)</td>
<td>62.2 (18)</td>
<td>62.3 (18)</td>
<td>62.4 (18)</td>
<td>62.3 (18)</td>
</tr>
</tbody>
</table>

^ = Number; *Based on 26,659 admissions, excluding one hospital without provided information on emergency. **Based on 37,883 admissions, excluding one hospital without provided information on emergency.

Figure 3 shows the primary endpoint, i.e. the number of patients per 1,000 admissions with either a cardiopulmonary arrest, unplanned admission to the ICU, or death while being admitted to a COMET ward. The number of patients who reached the primary outcome decreased from 37.14 (95% CI 34.94 to 39.34) per 1,000 admissions in the before period to 32.92 (95% CI 30.88 – 34.95) in the RRT period. The unadjusted odds ratio of reaching the primary endpoint was 0.88 for the RRT phase relative to the before phase. The number of patients reaching the primary endpoint in the MEWS and the RRT implementation period were 39.14 ([95% CI 37.24 – 41.03) and 37.28 (95% CI 35.86 – 38.70) respectively. Per 1,000 COMET inpatient days the number of affected patients
The results for the individual components of the primary outcome are presented in Table 2. The table shows that, per 1,000 admissions, the number of cardiopulmonary arrests remained stable in the before and MEWS periods and gradually declined in the RRT implementation and RRT periods. The number of unplanned ICU admissions only slightly decreased in the before, MEWS and RRT implementation periods, but dropped in the RRT period. Mortality increased from the before to the MEWS period, fell back again to the baseline level in the RRT implementation period, before it further decreased in the RRT period.

The unadjusted odds ratios of having a cardiopulmonary arrest in the RRT period relative to the before period was 0.626, of being at least admitted once unexpectedly to the ICU admission 0.881 and of dying 0.865. (Data not shown)

Table 2 shows that the composite endpoint was mostly made up of unplanned ICU admissions and deaths; cardiopulmonary arrest was a less frequent event.

**Table 2. Secondary outcomes per 1,000 admissions**

<table>
<thead>
<tr>
<th></th>
<th>Before</th>
<th>MEWS</th>
<th>RRT implementation</th>
<th>RRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiopulmonary Arrest, n/1,000 (95%CI)</td>
<td>1.94 (1.43-2.46)</td>
<td>1.93 (1.50-2.35)</td>
<td>1.54 (1.25-1.83)</td>
<td>1.22 (0.82-1.61)</td>
</tr>
<tr>
<td>ICU admission*, n/1,000 (95%CI)</td>
<td>19.8 (18.1-21.6)</td>
<td>19.6 (18.1-21.0)</td>
<td>19.5 (18.3-20.6)</td>
<td>17.1 (15.5-18.6)</td>
</tr>
<tr>
<td>Death, n/1,000 (95%CI)</td>
<td>20.4 (18.7-22.0)</td>
<td>22.5 (21.0-23.9)</td>
<td>20.5 (19.5-21.6)</td>
<td>17.7 (16.2-19.2)</td>
</tr>
</tbody>
</table>

*Including multiple unplanned ICU admissions per patient.
Table 3. Odds ratios (OR) of composite endpoint and its individual components for the RRT versus the before period, corrected for sex, age, hospital and emergency of admission. (N admissions in before period = 26,659; N admissions in RRT period 27,820)

<table>
<thead>
<tr>
<th></th>
<th>Uncorrected odds ratio</th>
<th>Corrected odds ratio</th>
<th>95% CI of corrected OR</th>
<th>P-value corrected OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite endpoint</td>
<td>0.882</td>
<td>0.847</td>
<td>0.725-0.989</td>
<td>0.036</td>
</tr>
<tr>
<td>Cardiopulmonary Arrest, n/1,000 (95%CI)</td>
<td>0.626</td>
<td>0.607</td>
<td>0.393-0.937</td>
<td>0.018*</td>
</tr>
<tr>
<td>ICU admission**, n/1,000 (95%CI)</td>
<td>0.881</td>
<td>0.878</td>
<td>0.755-1.021</td>
<td>0.092</td>
</tr>
<tr>
<td>Death, n/1,000 (95%CI)</td>
<td>0.865</td>
<td>0.802</td>
<td>0.644-1.0</td>
<td>0.05</td>
</tr>
</tbody>
</table>

*A GLM model based on Poisson distributed cardiopulmonary arrest with identity link converged during its iteration and showed a p-value of 0.018; the corrected odds ratio reported stems from a non-converging Poisson based GLM model with a log link which is slightly more conservative (p=0.024). **Odds ratio presented for being unexpectedly admitted at least once to the ICU.

Per 1,000 COMET inpatient days the point estimates for the before, MEWS, RRT implementation and RRT periods are 0.31, 0.30, 0.25, and 0.21 for cardiopulmonary arrests, 3.15, 3.06, 3.12, and 2.99 for unplanned ICU admissions, and 3.23, 3.52, 3.29, and 3.09 for deaths respectively.

Table 3 shows the odds ratios for the primary and secondary endpoints after correction for the potential confounders gender, age, individual hospital, and urgency of admission, while simultaneously accounting for clustering of admissions within hospitals. Preparatory analyses revealed associations of these variables with the composite endpoint, whereas sex, hospital and emergence level were also differentially distributed over the before and after periods (data not shown). The corrected odds ratios were calculated after exclusion of the single hospital without provided information on the emergency level of admissions in the before period. The point-estimated, uncorrected odds ratios are listed as well. The benefits of the RRS turned out slightly better after correcting for confounding, while taking clustering of admissions within hospitals into account.

Table 4 shows the characteristics of patients reaching the individual components of the primary endpoint for all study phases. Statistical comparisons were restricted to the before and RRT periods of the study only. During the before period more patients were transferred to the coronary care unit and less patients to other hospitals or other destinations after a cardiopulmonary arrest (p=0.013), when compared to the RRT period. Patients who deceased were younger in the RRT phase (75.0, SD 14) compared to the before phase (76.8, SD 12) (p=(0.021).
Table 4. Distributions of characteristics for secondary outcomes.

<table>
<thead>
<tr>
<th></th>
<th>Before</th>
<th>MEWS</th>
<th>RRT implementation</th>
<th>RRT</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N(^*) of cardiopulmonary arrests</strong></td>
<td>55</td>
<td>78</td>
<td>105</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>Male patients</td>
<td>62</td>
<td>68</td>
<td>68</td>
<td>58</td>
<td>0.18</td>
</tr>
<tr>
<td>Mean age of patients (SD)</td>
<td>70.6 (13)</td>
<td>68.6 (17)</td>
<td>72.2 (12)</td>
<td>70.7 (12)</td>
<td>0.95</td>
</tr>
<tr>
<td>Chest compression</td>
<td>89</td>
<td>86</td>
<td>80</td>
<td>89</td>
<td>0.54</td>
</tr>
<tr>
<td>Defibrillation</td>
<td>29</td>
<td>23</td>
<td>22</td>
<td>22</td>
<td>0.38</td>
</tr>
<tr>
<td>Tracheal intubation</td>
<td>73</td>
<td>82</td>
<td>74</td>
<td>83</td>
<td>0.074</td>
</tr>
<tr>
<td>Direct outcome</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.015</td>
</tr>
<tr>
<td>Death during CPR</td>
<td>53</td>
<td>33</td>
<td>33</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>Transfer to ICU</td>
<td>35</td>
<td>55</td>
<td>44</td>
<td>44</td>
<td></td>
</tr>
<tr>
<td>Transfer to CCU</td>
<td>11</td>
<td>10</td>
<td>9</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>To other hospital</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>1</td>
<td>13</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Survival to hospital discharge</td>
<td>13</td>
<td>30</td>
<td>31</td>
<td>28</td>
<td>0.075</td>
</tr>
<tr>
<td><strong>N(^*) of ICU admissions</strong></td>
<td>561</td>
<td>792</td>
<td>1,328</td>
<td>504</td>
<td></td>
</tr>
<tr>
<td>Male patients</td>
<td>61</td>
<td>57</td>
<td>58</td>
<td>57</td>
<td>0.47</td>
</tr>
<tr>
<td>Mean age of patients (SD)</td>
<td>67.0 (14)</td>
<td>67.5 (14)</td>
<td>67.8 (14)</td>
<td>65.7 (14)</td>
<td>0.13</td>
</tr>
<tr>
<td>Mean SAPS II (SD)</td>
<td>41.2 (19)</td>
<td>42.7 (18)</td>
<td>41.4 (18)</td>
<td>41.4 (18)</td>
<td>0.87</td>
</tr>
<tr>
<td>Mean APACHE II (SD)</td>
<td>19.1 (9)</td>
<td>19.8 (8)</td>
<td>19.5 (9)</td>
<td>19.5 (8)</td>
<td>0.44</td>
</tr>
<tr>
<td>Mean APACHE IV (SD)</td>
<td>66.8 (34)</td>
<td>69.9 (34)</td>
<td>68.1 (34)</td>
<td>68.0 (32)</td>
<td>0.59</td>
</tr>
<tr>
<td>Median ICU LOS (IQR)</td>
<td>19 (10 - 37)</td>
<td>19 (10 - 39)</td>
<td>19 (10 - 37)</td>
<td>18 (9 - 32)</td>
<td>0.30</td>
</tr>
<tr>
<td>ICU survival</td>
<td>85</td>
<td>84</td>
<td>85</td>
<td>84</td>
<td>0.63</td>
</tr>
<tr>
<td>Survival to hospital discharge</td>
<td>75</td>
<td>74</td>
<td>76</td>
<td>76</td>
<td>0.14</td>
</tr>
<tr>
<td><strong>N(^*) of deaths</strong></td>
<td>576</td>
<td>910</td>
<td>1,400</td>
<td>522</td>
<td></td>
</tr>
<tr>
<td>Male patients</td>
<td>55</td>
<td>53</td>
<td>55</td>
<td>52</td>
<td>0.36</td>
</tr>
<tr>
<td>Mean age of patients (SD)</td>
<td>76.8 (12)</td>
<td>77.1 (13)</td>
<td>77.6 (12)</td>
<td>75.0 (14)</td>
<td>0.021</td>
</tr>
<tr>
<td>Median LOHS (IQR)</td>
<td>6 (2 - 15)</td>
<td>7 (3 - 14)</td>
<td>7 (3 - 14)</td>
<td>7 (2 - 12)</td>
<td>0.25</td>
</tr>
</tbody>
</table>

\(^*\) = Number, ICU: Intensive Care Unit, CCU: Coronary Care Unit, LOS: Length of stay in days, LOHS: Length Of Hospital Stay in days. Unless stated otherwise, numbers represent percentages. Statistical comparisons were performed between the before and RRT phase. The Chi-square test, Fisher’s exact test, T-tests were performed as appropriate.

Only in the RRT implementation and RRT phase, the RRT was available for the care providers. The call rate in the RRT implementation phase was 6.8/1,000 admitted patients and increased to 7.3/1,000, see table 5. In this study, the RRT was called by the responsible physicians and not directly after a patient triggered with a MEWS of 3 or more. The nurse was able to call the RRT only if the physicians did not comply with the protocol as shown in figure 2. In the RRT implementation phase, 15% of the RRT calls was initiated by a nurse which decreased to 9% in the RRT phase with a
seemingly corresponding increase of activations by the resident. Rarely, Do Not Attempt Resuscitation (DNAR) orders were instituted after an RRT was called.

**Discussion**

The Cost and Outcomes analysis of Medical Emergency Teams multi-center trial is the second largest trial which has been performed investigating the effectiveness of RRSs. Eventually, twelve Dutch hospitals participated in this trial in which an approximately 15% risk adjusted reduction in severe adverse events, including cardiac arrests, unplanned ICU admissions and deaths was found.

As recently reviewed, 42 studies have been published describing the effectiveness of RRSs. Many of these studies were relatively small and underpowered to find effects on clinically relevant endpoints. Methodological quality was suboptimal in most studies. Interpretation of this reduction is difficult however, as no adjustment was made for DNAR policies. It cannot be ruled out that institution of RRTs lead to an increase of DBAR orders and consequently to less registered cardiopulmonary resuscitation attempts. Two large, randomized, well designed studies have been published on the effects of RRSs on outcome of in-hospital patients. The first study by Priestley and coworkers used a stepped wedge design, was performed in England and included 7450 patients. Introduction of a RRT lowered in-hospital mortality with an odds ratio of 0.52. In contrast, the MERIT trial, randomizing 23 Australian hospitals to introduce a RRS or to continue usual care, didn’t show an improvement on a composite endpoint consisting of unexpected death, unplanned ICU admission or cardiac arrest after introduction of a RRS. Several possible explanations for these negative results have been suggested. First, there may have been contamination of the control group. Unintended, cardiac arrest teams also functioned as RRT with more than half of calls not being due to cardiac arrest. Also, this cluster randomized trial may have been underpowered to detect the anticipated decrease in mortality. Lastly, the time taken for implementation of RRSs may have been too short for optimal functioning. The COMET study was initiated at the time that the Dutch government demanded that RRSs should be instituted in all hospitals in the Netherlands. Due to this mandatory nature of RRS in the Netherlands, any form of a randomized trial, including a stepped wedge design, was not feasible. The COMET study was therefore designed with a before-after methodology. Correction for simultaneous interventions - which may include the SURPASS checklist - or general background trends during the study, could not be quantified adequately. Such developments, if applicable, may have impacted our findings and caution should be taken in this respect when interpreting the study results. To maximally
adjust for other confounders, we performed a multivariate analysis with gender, age, individual hospital, and urgency of admissions, while simultaneously accounting for clustering of admissions within hospitals as covariates. After correction for these variables, the effect of the RRS on the composite endpoint even increased with ORs being 0.85 (95% CI 0.72-0.99) and 0.88 with and without adjustment for confounders.

Participating hospitals included four nursing wards in the study. Consequently, patient transfers between COMET and non-COMET wards could take place during the study. During the before period patients in this study spent on average 98.1% and during the RRT period on average 98.3% of their admission days on the COMET ward(s), indicating that transfers between COMET and non-COMET wards were highly limited making it unlikely that this could have had important influence on our findings.

Strengths of this study include the prospective data collection, the large number of participating hospitals and patients, and the long period taken to fully implement the intervention. The twelve participating hospitals (out of a total of 92 hospitals in the Netherlands) included larger and smaller, teaching and non-teaching hospitals. The implementation of the RRS was coordinated by the COMET study group, but locally performed by regular hospital staff, making this study highly representative for real-life implementation in any hospital, at least in the Netherlands. Before measuring the effects of having an RRS, we took ample time for full implementation of the system. Introducing the MEWS and SBAR communication tool took five months, and the effects of the subsequent introduction of a RRT were evaluated after an implementation phase of 12 additional months.

This study is the first looking into the effectiveness of the individual components of the RRS, the rapid identification of patients at risk using the MEWS and the SBAR communication tool, and the additional value of the RRT. From our data, it appears that instituting only the afferent limb of the RRS, that is the MEWS/SBAR, is not effective in decreasing the number of cardiac arrests, unplanned ICU admissions or deaths. However, this finding should be interpreted as hypothesis generating only and more research on this subject is necessary. In our study, the effects of the afferent limb were measured in other months of the year than the before period and the RRT period. Seasonal influences may have major impact on the study results when comparing these periods. Consequently, we decided not to provide p-values or confidence intervals for the measurements of outcomes in the MEWS/SBAR phase. It should be emphasized that for the primary analyses of the RRT compared with the before period, no seasonal influence is present because the months of the year are identical for these two periods.

In this study, clear instructions were provided how vital signs should be collected, how communication should be structured and when RRTs should be called. However, due to the pragmatic approach, we were unable to detect whether nurses and physicians
adhered to these instructions in all circumstances. It may well be possible that adherence to the RRS was not always perfect, potentially decreasing the effect on outcomes of patients. At the same time, this is also representative of the real-life situation when RRS are introduced in regular hospital care.

Finally, from post-hoc analyses of the MERIT study, we know that the number of RRT calls per 1,000 admissions correlates with the degree of implementation and also with patient outcome. 46 RRT activations were measured in the COMET study, and appear to be relatively infrequent. Approximately half of calls are followed by transfer of the patient to an ICU or CCU, suggesting that RRT activations are mostly in severely ill patients. Possibly, the effects of an RRS would be more pronounced if RRTs were activated more often. It is, however, also possible that the number of RRT calls may be underestimated if ICU physicians and nurses are frequently called directly without being a formal RRT activation. Future research will focus on the relation between the number of RRT calls and the effects of an RRS on outcome of patients.

Based on the results of this study, implementation of an RRS with the MEWS and SBAR for early identification and a RRT for early management of patients at risk for deterioration decreases the incidence of severe adverse events including death, unplanned ICU admission and cardiac arrest. As part of the COMET study, a budget impact analysis will be performed in further analyses. We recommend instituting RRSs in all hospitals caring for patients that may suffer severe life threatening adverse events following hospital admission.

COMPETING INTERESTS
The Radboud University Nijmegen Medical Center (Dr. B.G. Fikkers) is a satellite center for the ALERT™ course within the Netherlands.

AUTHORS CONTRIBUTIONS AND ACKNOWLEDGEMENTS
JL and ABR are both primary authors and shared responsibility for the logistical process together with data entry, validation and analysis. Principle design of the study was performed by JL, EdJ and MD. Data analysis was performed primarily by MD and writing of the manuscript by JL and ABR with supervision of EdJ and MD. All co-authors read and acknowledge the content of this manuscript.

JL and ABR had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Reference List


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Supplementary materials

The Modified Early Warning Score (MEWS)

The MEWS system was introduced as the major instrument to recognize a deteriorating patient and was based upon the original instrument of Subbe et al. 17

Figure 1. The Modified Early Warning Score (MEWS).

MEWS system:

<table>
<thead>
<tr>
<th>MEWS score</th>
<th>3</th>
<th>2</th>
<th>1</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate</td>
<td>&lt;40</td>
<td>40-50</td>
<td>51-100</td>
<td>101-110</td>
<td>111-130</td>
<td>&gt;130</td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>&lt;70</td>
<td>70-80</td>
<td>81-100</td>
<td>101-200</td>
<td>&gt;200</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiration rate</td>
<td>&lt;9</td>
<td>9-14</td>
<td>15-20</td>
<td>21-30</td>
<td>&gt;30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temperature</td>
<td>&lt;35,1</td>
<td>35,1-36,5</td>
<td>36,6-37,5</td>
<td>&gt;37,5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AVPU score</td>
<td>A (Alert)</td>
<td>V (response to Voice)</td>
<td>P (reacting to Pain)</td>
<td>U (Unresponsive)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Worried about patient’s condition: 1 point
Urine production below 75 milliliter during previous 4 hours: 1 point
Saturation below 90% despite adequate oxygen therapy: 3 points
Upon reaching 3 or more points → call resident in charge

The MEWS instrument was implemented as a tool that ward staff can use to identify the patient at risk of deterioration. The described method was adapted from Subbe et al. 17
The Situation-Background-Assessment-Recommendation communication instrument

This instrument was introduced during the MEWS/SBAR phase to primarily aid in the communication between nurses and physicians whenever a patient was clinically deteriorating with a MEWS of 3 or more.\textsuperscript{18}

\textbf{Figure 2.} The SBAR (Situation-Background-Assessment-Recommendation) communication instrument. The SBAR method was introduced to facilitate complete and systematic handover of patient data between the nurse and physician (on call) especially whenever a patient reached a MEWS of three or more.\textsuperscript{18}

\begin{table}[h]
\centering
\begin{tabular}{|p{2cm}|p{10cm}|}
\hline
\textbf{SBAR communication instrument} & \\
\hline
\textbf{Situation:} & I’m calling about (name of patient, ward and room number)  
The problem I’m calling about is (problem)  
The vital parameters are (Heart rate, Blood pressure, Breathing rate, Saturation with/without suppl. Oxygen, Temperature, AVPU scale, Urine production, other non-specified parameters)  
MEWS score (score)  
I’m concerned about (define problem)  \\
\hline
\textbf{Background:} & Admissions diagnosis and admission date  
If relevant: Medical history and other clinical information  \\
\hline
\textbf{Assessment:} & I think the problem is (describe problem) or  
I’m unsure what the problem is, but the patient (is deteriorating/unstable)  \\
\hline
\textbf{Recommendation:} & I think that you should (describe exactly what needs to happen at this moment)  
1. You should evaluate the patient now and/or  
2. You should evaluate the patient [set specific time interval] and/or  
3. Determines medical policy  
What should I do now?  
How often do you want the vital parameters checked and at which thresholds do you want to be called again?  
Repeat-back:  
We have agreed on the following (repeat the medical policy systematically and who does what and when)  
Write the determined policy up into the patients records  \\
\hline
\end{tabular}
\end{table}