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Cost and Outcome of Medical Emergency Teams (COMET) Study. Design and Rationale of a Dutch Multi-Center Study

**Jeroen Ludikhuizen^{1*}, Marcel G. W. Dijkgraaf², Susanne M. Smorenburg¹,
Sophia E. J. A. de Rooij³, Anja H. Brunsveld-Reinders⁶, Peter Tangkau⁴,
Bernard G. Fikkers⁵, Evert de Jonge⁶ and the COMET study group**

¹*Academic Medical Center, Department of Quality Assurance and Process Innovation, PO Box 22660, 1100 DD Amsterdam, The Netherlands.*

²*Academic Medical Center, Clinical Research Unit, PO Box 22660, 1100 DD Amsterdam, The Netherlands.*

³*Academic Medical Center, Department of Geriatrics, PO Box 22660, 1100 DD, Amsterdam, the Netherlands.*

⁴*Reinier de Graaf Hospital, Department of Intensive Care, PO Box 5011, 2600 GA, Delft, The Netherlands.*

⁵*Radboud University Nijmegen Medical Center, Department of Intensive Care, PO Box 9101, 6500 HB Nijmegen, The Netherlands.*

⁶*Leiden University Medical Center, Department of Intensive Care, Albinusdreef 2, PO Box 9600, 2300 RC Leiden, The Netherlands.*

Clinical investigators of the participating clinical centers:

*Academic Medical Center, M.A. van Putten;
BovenIJ hospital, R. D Jong;
Catharina hospital, C. Kerkhoven;
Diaconnessenhuis Leiden, H. de Jong;
Gelre hospital, A. Braber;
Ikazia hospital, M. Middelkoop;
Kennemer Gasthuis, B.M. Kors;
Medical Center Alkmaar, D.P. Sep;
Medical Spectrum Twente, J.W. Vermeijden;
Rijnland Hospital, P.K.C. van der Weijden;
Rivas Beatrix Hospital, S. Koenders;
Sint Lucas Andreas Hospital, M. Meertens;
University Medical Center Leiden, A.H. Brunsveld-Reinders;
Zaans Medical Center. M. Hoeksema.*

*Corresponding author: j.ludikhuizen@amc.nl;

Authors' contributions

This work was carried out in collaboration between all authors. Authors JL, SS, SR and EJ were involved in the design of the study. Authors JL, MD and EJ were primarily involved in the subsequent conceptualization of the study protocol and drafting of this manuscript. Management and logistics were carried out by authors JL and ABR. Author BF and PT participated as individual experts regarding their RRS knowledge. All authors read the final version of the manuscript.

Research Article

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ABSTRACT

Aims: Description of a study protocol to analyze the effectiveness of the sequential implementation of a Rapid Response System (RRS) on the incidence of the composite endpoint of cardiac arrest, unplanned ICU admission, and mortality rates.

Study Design: The COMET trial is a before-after, non-randomized multi-center trial.

Place and Duration of Study: The COMET trial was held in the Netherlands in fourteen Dutch hospitals from April 2009 until November 2011. Each hospital included two surgical and two general medicine nursing wards.

Methodology: Prior to the introduction of the RRS, endpoints were collected for 5 months as part of a baseline assessment. The RRS was introduced in two steps. Initially, two tools were introduced during 7 months for early detection of the deteriorating patient: the Modified Early Warning Score (MEWS) and for structured communication, the Situation-Background-Assessment-Recommendation (SBAR) tool. During the next 15 months the Rapid Response Team (RRT) was operational in addition to both the detection and communication tool. Generalized Estimating Equations (GEE) analysis of trends in outcomes will be performed. The cost description will primarily focus on the program costs associated with training and education sessions and the time invested in all consultations originating from patient care on the study wards.

Conclusion: The COMET study will provide evidence on the clinical outcomes and costs of the implementation of Rapid Response System. This will include an analysis to explore the possible effect of a Rapid Response Team as add-on to the MEWS and SBAR tools for early recognition of the deteriorating patient on the nursing ward.

Keywords: Rapid response systems; modified early warning score; multicenter trial effectiveness; deteriorating patient.

ABBREVIATIONS

COMET: Cost and Outcomes of Medical Emergency Teams; CPR: Cardio Pulmonary Resuscitation; DNAR: Do Not Attempt Resuscitation; GEE: Generalized Estimating Equations; ICC: Intra-class Correlation Coefficient; ICU: Intensive Care Unit; ITS: Interrupted Time Series; LOS: Length of Stay; MET: Medical Emergency Team; MEWS: Modified Early

Warning System; NICE: National Intensive Care Evaluation; RRS: Rapid Response System; RRT: Rapid Response Team; SBAR: Situation-Background-Assessment-Recommendation; TT: Track and Trigger

1. INTRODUCTION

Patient deterioration into critical illness on general nursing wards is generally preceded by alterations in the physiological condition hours before an event occurs. This has been demonstrated for cardiac arrests [1,2], unplanned ICU admissions [3,4] and (unexpected) death [5]. The determinants of these events can potentially be recognized by measurement of readily available vital parameters. Therefore, early recognition and intervention in this patient group could potentially prevent adverse events from occurring. As a direct consequence of these findings, RRS have been developed and were first described in 1995 by [6]. Up to this point, conclusive evidence regarding the effectiveness of the system is absent [7].

Rapid Response Systems are built up from three distinct, but interacting components or limbs [8]. The afferent limb is designed to detect the deteriorating patient by the use of Track and Trigger (TT) systems. These are based on measurement of vital parameters and by deviation of either a single or a combination of parameters (including scores) from a norm which determines if a patient is at risk for deterioration. The efferent limb, the RRT, is subsequently activated. An RRT is a combination of personnel originating from the ICU which responds directly to the patient at the bedside. Finally, an administrative component oversees data registration and analysis together with education of the care takers which are required to operate the system components. These limbs are designed to protect the patient, structure care processes to prevent patient deterioration and serious adverse events including cardiac arrest. Taken together, they form a "chain of prevention" which should ensure adequate response by all care-providers [9].

Despite the unproven nature of RRS, in 2009, a nationwide patient safety initiative has been started in the Netherlands which describes the compulsory implementation of RRS in all Dutch hospitals. This is further acknowledged by the Dutch government and Health Inspectorate. The governmental directive of implementing RRS as soon as possible left no room for the conduct of a randomized trial, but as hospitals needed time to prepare the introduction and implementation of RRS type systems, the opportunity arose to conduct a before-after multicenter trial into the clinical outcomes and costs of RRS type systems in the Netherlands. This manuscript describes the corresponding study protocol.

2. METHODOLOGY

2.1 Objectives

The primary objective of this multicenter study is to evaluate the composite clinical outcome of Rapid Response Systems, defined as the impact on cardiac arrest, unplanned ICU admission, and mortality rate. Also, a secondary analysis will investigate to what extent the impact on clinical outcome may be attributed to the afferent (early detection by a Track and Trigger tool) or efferent (RRT) limb during the phased introduction. Furthermore, the satisfaction of the primary applicants (nurses and doctors) will be assessed and a program cost description (from a hospital perspective) will also be performed.

2.2 Four Steps in a Before-After Design

The COMET study is a pragmatic before-after trial enabling a GEE (Generalized Estimating Equation) analysis of trends in clinical outcome, based on monthly cardiac arrest, ICU admission and mortality data. The study design is depicted in Fig. 1. The before period consisted of 5 months in which baseline data were collected. Most hospitals were able to provide these data prospectively. The implementation of RRS was divided into its two limbs.

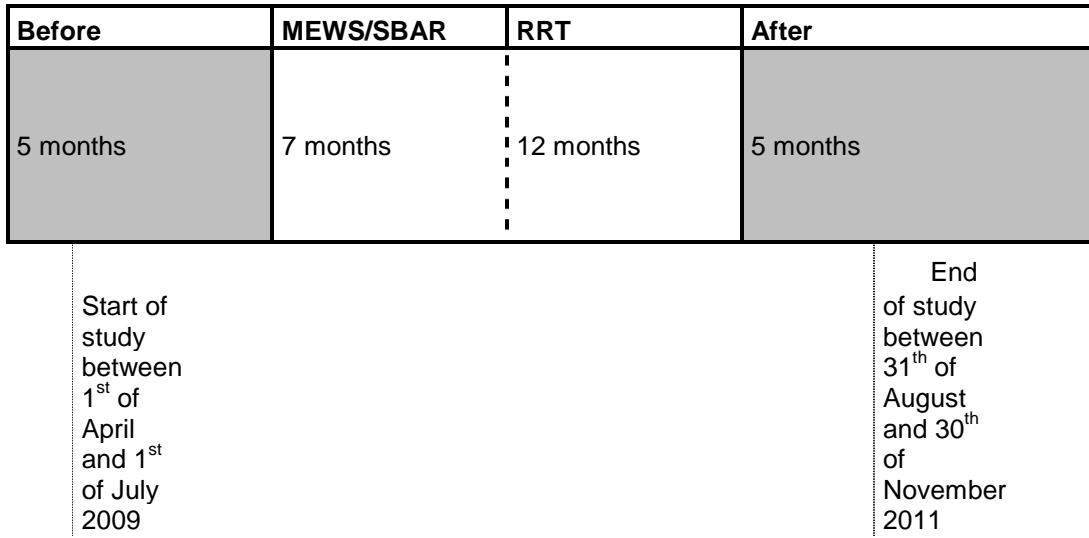


Fig. 1. Design of the COMET study

The COMET study was designed as a before-after study. Hospitals were able to start the study in a three months time span based as logistics within each hospital was different. Following the baseline period of 5 months, the MEWS/SBAR was implemented for 7 months and subsequently followed up by 15 months in which the RRT was available. During this phase and also the after period the entire system was complete. During the entire study, all the endpoints were measured. Besides the before-after comparison, time trend analysis on a monthly basis was also performed.

Initiation of the study was partly left at the discretion of participating hospitals because the time constraints and inter-hospital variation in logistics wouldn't allow a single starting point. Within a restricted three month time frame, starting at the first day of each month between April 2009 and July 2009, the baseline recordings were commenced. Within that same timeframe, a minimum of four participants were trained in the ALERT™ [10] course at the Radboud University Nijmegen Medical Center. In short, this course teaches how to anticipate, recognize, and prevent critical illness at an early stage by providing classroom sessions for theory followed up by multidisciplinary scenario practice. The first intervention phase lasted 7 months during which the MEWS (Modified Early Warning Score) together with the SBAR communication tool (Situation-Background-Assessment-Response instrument) were implemented; Table 1 [11,12]. The MEWS and SBAR tools, and later on the RRT, were introduced using a standardized toolkit in which the system was taught to each care-giver. Applicants were also provided with plasticized handheld cards and implementation was continued throughout the study period with posterson the wards, in patient charts, feed-back session and face-to-face communication with personnel. During the MEWS/SBAR phase, the RRT was not available and awareness of the subsequent introduction of the team was absent since the MEWS/SBAR toolkit didn't mention anything

regarding the next phase. The RRT as add-on to the MEWS/SBAR tools continued for the next 15 months, of which the final 5 months constituted the after measurement period. This design enabled ample time for implementation of the system and would also provide insight in the differential effectiveness of the MEWS/SBAR on the one hand and the RRT on the other.

2.3 Further Details on the Interventions

Throughout the entire study period and therefore irrespective of the phase in the study, the physicians and nurses adhered to the following procedure. Measurement of the vital parameters, including frequency of measurements and MEWS, was not specifically protocolized within the trial. It was defined 'as clinically indicated' in which the nurses and physicians were instructed (using standardized toolkits for each study phase) to determine the full MEWS (Table 1), whenever a patient's vital parameter was outside normal range, for example had a heart rate outside the 51-100 range, or a systolic blood pressure outside the 101-200 range, or a respiration rate outside the 9-14 range, or a temperature outside the 36.6-37.5 range, or whenever a patient was not alert or the nurse was worried about the patient condition. Also the physicians could demand measurement of the MEWS at specific intervals, when required. Whenever the score passed the threshold of 3 or more points, the physician (on call) had to be directly notified and the communication had to be structured using the SBAR tool (Table 2). This physician was a postgraduate resident in charge of all patients at the ward or a (supervising) medical specialist and was at least trained and certified according to the Fundamental Critical Care Support (FCCS) guidelines.

Fig. 2 shows the algorithm used for activation of the RRT during the RRT phase of the study. It entailed that the physician had a maximum of 30 minutes to evaluate and set-up a treatment plan for the patient after the nurse detected a patient with a MEWS of 3 or more. After initiation of treatment (which may also contained direct notification of the RRT), a maximum of 1 hour was available to evaluate the treatment effect. If the patient continued to deteriorate or did not respond to treatment, the physician was instructed to activate the RRT. Within the system, an override option was incorporated. The nurse was able to directly activate the RRT if the physician did not keep to the protocol (e.g. exceeding the prescribed time limits for review and management of the patient) or in case the patient's health status did not improve (according to the nurse) an hour after initial treatment initiation.

In the MEWS/SBAR phase, the staff provided routine patient care. In response to the detection of a patient with a MEWS of 3 or more, the physician would manage the patient "as this would normally be performed" which could include assessment and consultation with other specialties. No protocol or guidelines for initiation of treatment or consultation of the ICU was available. Therefore this phase enabled the analysis of the ability early detection of the deteriorating patient employing the described tools specific tools without the specific protocol for managing the patient after identification (i.e. time lines for treatment options including the RRT).

Table 1. The modified early warning score (MEWS)

MEWS score	3	2	1	0	1	2	3
Heart rate		<40	40-50	51-100	101-110	111-130	>130
Systolic blood pressure	<70	70-80	81-100	101-200		>200	
Respiration rate		<9		9-14	15-20	21-30	>30
Temperature		<35,1	35,1-36,5	36,6-37,5	>37,5		
AVPU score				A (A lert)	V (response to V oice)	P (reacting to P ain)	U (U nresponsive)
Worried about patient's condition:	1 point						
Urine production below 75 milliliter during last 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 score was implemented as the tool for ward staff to identify the patient at risk of deterioration. The described method was adapted from Subbe et al. [11]

Table 2. The SBAR (Situation-Background-Assessment-Recommendation) communication instrument

SBAR communication instrument	
S	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) MMEWS score (score) I'm concerned about (define problem)
B	Background: Admissions diagnosis and admission date If relevant: Medical history and other clinical information
A	Assessment: I think the problem is (describe problem) or I'm unsure what the problem is, but the patient (is deteriorating/unstable)
R	Recommendation: I think that you should (describe exactly what needs to happen at this moment) <ol style="list-style-type: none"> 1. Evaluate the patient now and/or 2. 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

The SBAR method was introduced to facilitate complete and systematic handover over patient data between the nurse and physician (on call) especially whenever a patient reached a MEWS of three or more [12].

Deviation from the MEWS threshold was allowed in specific circumstances. For instance, in case of a patient with chronic obstructive pulmonary disease with altered respiratory status (e.g. maximum peripheral saturation of 85% with supplementary oxygen), a physician was able to adjust the MEWS criteria accordingly because such patient would trigger at any time. This could enclose alteration of thresholds for the MEWS cut off point of three points, but also changes in thresholds for specific vital parameter(s). These adjustments had to be documented in the nursing and medical charts for clear and an undisputable medical policy.

2.4 Setting and Participants

The COMET study is a multicenter study in which 14 Dutch hospitals participated. Two are university hospitals (Academic Medical Center Amsterdam and Leiden University Medical Center), nine are large teaching hospitals (BovenIJ Hospital, Catharina Hospital, Gelre Hospital, Kennemer Gasthuis, Medical Center Alkmaar, Medical Spectrum Twente, Rijnland Hospital, Sint Lucas Andreas Hospital and Zaans Medical Center) and three are smaller regional hospitals (Diaconnessenhuis Leiden, Ikazia Hospital and Rivas Beatrix Hospital). Each hospital included four study wards, 2 surgical and 2 medical based wards. The surgical

type wards include general surgery wards, oncology type surgery, vascular, orthopedics etc. Medical wards include internal medicine, nephrology, infectious diseases, pulmonology and neurology.

All patients (age 18 or above), both electively and acutely admitted from home or from another nursing ward onto the 4 study wards, were eligible for inclusion.

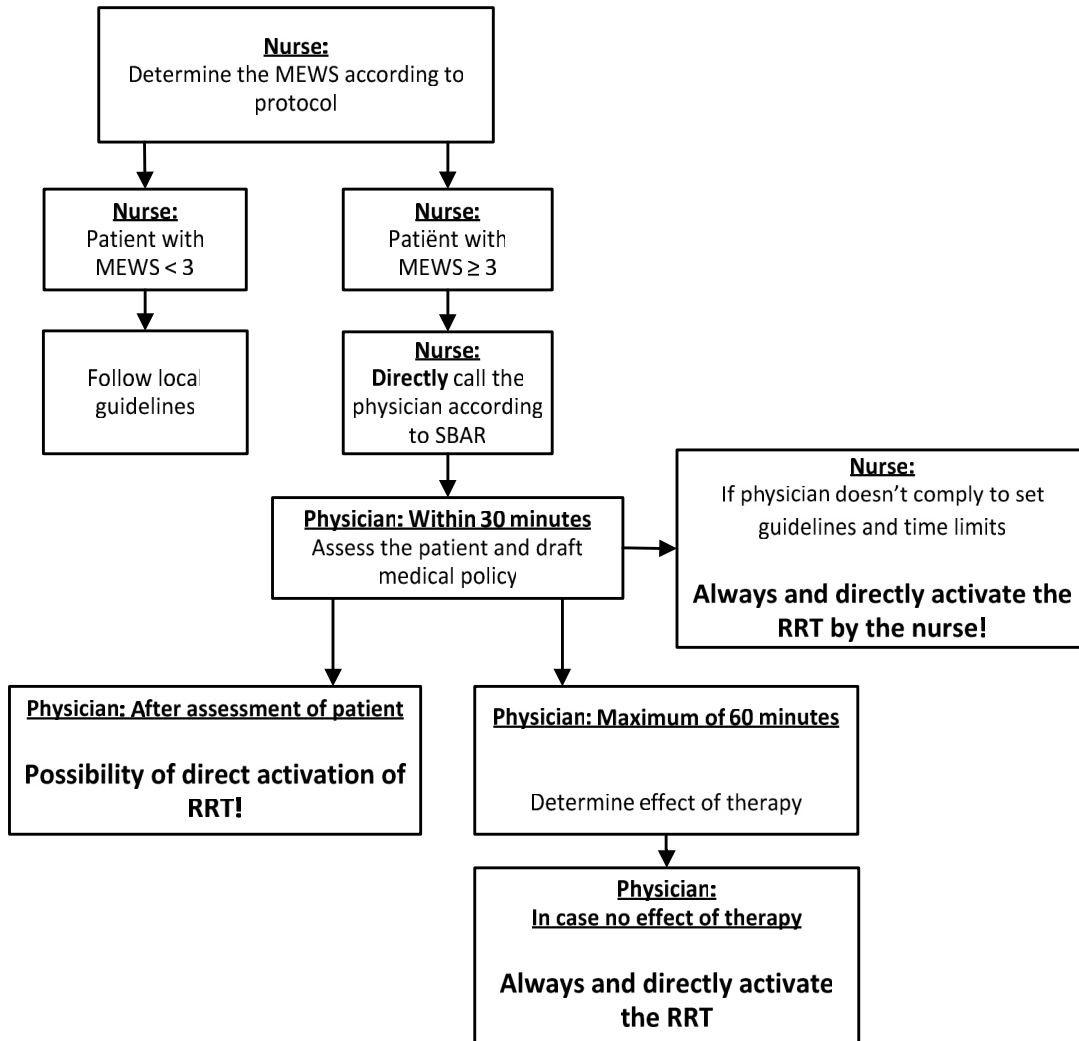


Fig. 2. Algorithm for activation of RRT

Algorithm for RRT activation. The algorithm displays the protocol of handling positive MEWS values and all subsequent actions which either nurse or physician has to undertake together with set time limits.

2.5 Outcome Measures and Definitions

The primary outcome is the composite endpoint of the first occurring cardiac arrest, unplanned ICU admission or death per 1000 admitted patients on the four wards

participating in the COMET study. The same composite endpoint per 1000 inpatient days at these wards is considered a secondary outcome. The components of the composite endpoint will also be assessed separately as secondary endpoints. Cardiac arrest was defined as an event in which a respiratory and/or cardiac activity was absent and for which the cardiac arrest team was called and started Cardio Pulmonary Resuscitation (CPR), either using chemical resuscitation and/or manual chest compressions and/or respiratory ventilation (irrespective of type). An unplanned ICU admission was defined as a situation in which admission could not be delayed for the following 12 hours without risk. This data field is a component of the Dutch national ICU registry (National Intensive Care Evaluation (NICE)), which comprises a continuous and complete registry of all patients admitted to the ICU's of all participating hospitals [13]. Being a member of the NICE registry was mandatory for hospitals to be able to participate in the COMET study.

Analysis of the secondary endpoint includes, according to the MERIT study, the incidence of all cardiac arrests, unplanned ICU admissions, and deaths on the participating wards [14]. Thus, multiple endpoints per patient are possible with the exclusion of a subsequent unplanned ICU admission after successful treatment following a cardiac arrest which is deemed "appropriate care." For these three endpoints, additional information such as APACHE II and IV scores were collected upon admission to ICU and also whether chest compressions and/or artificial ventilation was carried out with patients experiencing a cardiac arrest.

Other secondary outcomes include: (1) Unexpected death defined as death without the presence of any form of a Do Not Attempt Resuscitation (DNAR) order, which primarily includes any form of restriction of active treatment, (2) Hospital Length of Stay (LOS), (3) ICU length of stay, (4) numbers of RRT calls per 1000 admitted patients and per 1000 inpatient days and (5) program costs from a hospital perspective based on team composition and duration of activation during a cardiac arrest, ICU or RRT consultation. Other process parameters will be measured which include a multiple choice written test to be made after each education session in which (based on a case description) the correct action needs to be chosen. Also, at three set time points during the COMET study, a questionnaire will be administered among the nurses and physicians on the included wards regarding their satisfaction with the protocol and its components and perceived benefit of the system. These items were anonymously administered, processed and analyzed. Finally, the number of patients with a primary endpoint without RRT call in the preceding 24 hours per 1000 admitted patients will also be calculated to analyze for possible delay and protocol deviations.

2.6 Sample Size

This study is powered to determine the effectiveness of an RRS. First of all, the incidence of cardiac arrest presumably ranges between 4 and 11 per 1000 admissions [14,15]. The incidence of unplanned ICU admissions in patients on general hospital wards has been estimated at 5/1000 admissions [17].

At the Academic Medical Center (AMC), from 2005 to 2009 (4 years), 100,000 patients were admitted to the hospital. In that same time period, 686 patients (6.9/1000 admissions) were admitted (unplanned) from the general ward to the ICU (re-admissions excluded). Based on the literature and historical AMC data, we anticipate that in the control period 10/1000 admitted patients will reach the primary endpoint (resuscitation, unplanned ICU admission and death) and that this number decreases to 6/1000 during the intervention period, a

reduction by 40%. Fourteen hospitals will participate in this study, each with four wards. In the pre-post study design, these four wards will be clustered by two (surgery versus general wards). The study will thus contain 28 (2×14) clusters. With 28 clusters and a total of 5 time periods in the control (phase 1) and 5 time periods during the RRT intervention (phase 3), 99 patients are needed per cluster per time period to reject the null hypothesis that the difference between the intervention period and the control period is smaller than 0.004 [18] with a power of 80% and a one-sided significance level of 0.05. The total number of eligible patients to be included amounts to 27,720 ($2 \times 28 \times 5 \times 99$). The intra-class correlation coefficient (ICC) used for this calculation is 0.00254. This ICC was derived from the ICC observed (0.00127) in a non-randomised study of three hospitals [19], but it was doubled to account for higher ICCs than one anticipates [14].

The training in MEWS in phase 2 may also exert influence on the primary outcome measure, but probably less than the combined intervention including the RRT [8]. For lack of power to detect a difference between MEWS only and MEWS+RRT phase, the data gathered during the MEWS phase will only be used for exploration and hypothesis generation. To this end, data will be gathered during 7 time periods with a total of 19,404 ($7 \times 28 \times 99$) admitted patients.

2.7 Data Acquisition and Analysis

Data for the COMET study were taken from multiple existing hospital and nationwide (NICE registry) databases. Hospitals were primarily conducting their own data acquisition, registered the data on Case Record Forms (CRF) and entered the source data into an internet database. This enabled data monitoring by the study coordinators while not on site. Most data were prospectively collected, except for baseline data in some hospitals. However, this partial retrospective data gathering did not result in a loss of information, because the procedures and extent of data extraction from the existing databases were identical to procedures during prospective data collection.

The main analysis will focus on the before-after comparison of the primary composite endpoint in which all separate events are presumed to be potentially avoidable. This includes the earlier mentioned exception of an unplanned ICU admission after cardiac arrest.

The total number of 28 clusters over 10 time periods justifies the use of generalized estimating equations (GEE) for statistical analysis of the data. Generalized estimating equations can flexibly handle normal or non-normal endpoints; tend to be more robust to misspecification of the variance structure than (generalized) linear mixed modeling. It is a natural choice for individual-level binary outcomes and may automatically account for variable cluster sizes if they occur [20].

The analysis will account for the segmented pre- and post-intervention phases into the 5 distinct time periods per phase. The generalized model will include terms for the baseline level of occurring events, the pre-intervention trend over time, the impact of the intervention, the post-intervention trend over time, autocorrelation over time within clusters, and error [21]. Additional analyses include a descriptive of the first endpoint encountered by patients by study phase and by time period, as well as GEE-based exploratory analyses contrasting the MEWS/SBAR phase against the RRT phase. Moreover, possible learning curves in the recognition of deteriorating patients will be studied through test and questionnaire, which are part of the toolkits for each phase of the trial. Satisfaction with the RRS and its components is assessed by regular distribution of questionnaires among the users of the system. The

results from these questionnaires will indicate the perceived boundaries in using the system (e.g. ease of use MEWS, activation of RRT).

Dose response analysis according to Chen et al. [22] will be performed to examine possible impact of early review of critically ill ward patients in relation to RRT activation. Taken together, these analyses will portray a clear image of the RRS system within each hospital and by meta-analysis in all COMET hospitals.

2.8 Cost Description

A partial economic evaluation will be performed, restricted to the description of the direct medical costs of the index admission. This provider (hospital) perspective has been chosen because of the high number of patients to be included and the low incidence of the primary outcome measure in the study. For the same reasons no patient outcome analysis concerning quality of life is planned. The time horizon of the study is the index admission.

The cost components include (i) the training of nurses and physicians in recognizing early warning signs, (ii) installation of RRTs, (iii) (intensive) monitoring and treatment of (vitaly threatened) patients, (iv) (ICU) inpatient days and (v) resuscitations. Volume data will be retrieved from hospital information systems and the NICE database. Unit costs of hospital activities will be derived from national guidelines for costing in health care research [23,24] or, if these guidelines seem unsuitable for that purpose, from available local unit costs in participating reference hospitals. Activity based costing of RRT will be applied for all hospitals and based on the detailed monitoring of RRT activities. The costs of MEWS and subsequent RRT training will be based on pre-calculation of the related program costs, including the time investment of trainees. Costs will be estimated for the base year 2011 after price indexing.

Based on the cost description and the difference in event rate between the pre- and post-intervention periods, we will tentatively perform an incremental cost-effectiveness analysis showing the extra provider costs per resuscitation, unplanned ICU-admission and death prevented. Sensitivity analyses will be performed for different levels of economies of scale and capacity utilization which influence the availability costs of rapid response teams. The unit costs of an RRT per admission or per recognized vital threat depend on the total number of admissions for which the team is available. The present study will contribute to determine optimal levels of RRT capacity, relative to its unit costs.

2.9 Ethics and Informed Consent

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.

3. DISCUSSION

The COMET trial is a multicenter, non-randomized before-after trial with the ability to perform GEE analysis to evaluate the effectiveness and costs associated with implementation of an RRS within the fourteen participating Dutch hospitals. The COMET trial consists of the phased implementation of RRS. It starts with the use of MEWS/SBAR tools to detect and communicate about a clinically deteriorating patient. Seven months later the second component of RRS, the physician based RRT which can be warned by ward personnel, is introduced. This phased implementation enables not just the evaluation of the RRS as the combination of MEWS/SBAR and RRT (comparing the after and before measurements); it also allows for exploration of the impact of the RRT as add-on to the use of only the MEWS/SBAR tools (comparing the measurement during the MEWS/SBAR period with the before measurement and with the after measurement).

To our knowledge, this has never been fully attempted on this scale although Priestley et al. have shown reduction in hospital LOS and in-hospital mortality in the training group which had just been trained in the use of the afferent limb [17]. The COMET study is held within the Netherlands where mandatory implementation of an RRS is required by the Health Inspectorate. This enabled a unique opportunity to initiate a multicenter study in which a representative population of Dutch hospitals is present and external validity of the data is perceived to be high. Recently, an editorial by Bellomo et al. has shown that single center trials often show positive results which are not held up in multicenter trials [25]. Much of the scientific knowledge regarding RRS is derived from many mono center or even mono ward trials with less rigorous study designs. Therefore, reticence should be present regarding these data. The COMET study, despite absence of randomization but including an innovative time phased introduction over a substantial timeframe of a RRS, should provide new insight in the effectiveness of the system and, to a lesser extent, each of its components, the MEWS/SBAR and RRT.

The internal validity of research into 'complex interventions', is often at stake and optimal trial design is challenging [26,27]. Randomized controlled trials, in respect to RRS, are merely impossible to conduct. Several reasons for this are present. Prior to the governmental directive on RRS implementation, the COMET study was set up as cluster randomized controlled trial (RCT) following the methodology of a stepped wedge trial. [20] Within this design, not hospitals but the two pairs of wards were randomized for the initiation of the RRS so that there was always a parallel control group from the same hospital present. In the end, all four wards of each hospital would have taken up the intervention. This design or an RCT in which hospitals would be randomized as either placebo or intervention hospital (MERIT study), were too hard to accomplish due to the mandatory nature of RRS in the Netherlands in which every hospital at a certain time point should have an RRS, but also due to problems encountered in the MERIT study including potential contamination in a parallel design [27].

Furthermore, complex interventions are difficult to study because they are built up from components that may act both independently and inter-dependently. Also, they are adaptive to changes in their local environments and behave in a non-linear fashion [26]. Standards of nursing care, education and commitment of all associated health care workers within an RRS are required to be able to correctly assess the program's effectiveness.

The COMET trial is a pragmatic trial in which RRS has to prove itself in the flexible and real-time workspace of general practice. It lacks the sometimes "artificial nature" of more

stringent, protocolized studies, thereby gaining in clinical relevance against, perhaps, a slightly increased risk of a lower internal validity. One manifestation of the pragmatic approach is that the MEWS is determined 'on indication' rather than set at specific intervals and on all patients. This mirrors the clinical practice to a large extent in which no specific guidelines are present regarding measurement of vital signs. On the surface, frequent measurement of complete sets of vital signs should hypothetically increase the chance of identifying a deteriorating patient, but the clinical relevance of our pragmatic approach is supported by two papers showing that fixed measurements of vital signs show low positive predictive power on adverse events [28,29]. Furthermore, the COMET study employs a physician based RRT rather than a nurse led team or a step up procedure in which a physician is called when indicated by the RRT nurse. No evidence exists what composition is more effective; however, it is generally perceived that a physician led team is able to directly initiate therapy which nurses aren't allowed to. The RRT within the COMET study is staffed 24/7 and the minimal competency level of the RRT physician is Fundamental Critical Care Support (FCCS) trained. This ensures, together with the ICU nurse, adequate knowledge and skills levels regarding assessment and treatment options at the bedside of the patient at risk. A final possible limitation of the study lies in the starting point of the study. Because the pressure on hospitals in 2009 to initiate the implementation of the RRS, led to logistical issues for the hospitals which participated in the COMET study. For some hospitals, the organization of also entering the study was minimal. For some it was a bit more challenging. To account for this, hospitals were entitled to initiate the study within a three month time frame, allowing them to start the RRS while being equally well prepared. This minimized the risk of different learning curves early in the study, which would have influenced hospital performance during the MEWS/SBAR phase.

The COMET study is innovative, because it will investigate for the first time, the degree of satisfaction of the care-givers in all participating hospitals and at ward level. This will support the interpretation of possible differences in outcome parameters among hospitals and/or wards, that directly relate to the care givers' opinions regarding (ease) of use of RRS components, perceived effectiveness, but also issues regarding past experiences of RRT members. Finally, because of the sequential introduction of the afferent limb prior the RRT, the additive effect of the RRT on sole, hypothetically earlier recognition of the deteriorating patient, can be studied. Recent evidence suggests that this may indeed be beneficial [30].

An RRS can potentially take up much effort during its implementation in hospital organizations, as suggested by a recent postal survey in the Netherlands [31]. Implementation depends on the willingness among many health care workers to contribute, despite interference with "normal day-to-day" routines. Hence, implementation outcome measures were incorporated in our study design to facilitate the interpretation of the findings. In contrast with the MERIT trial and the trial by Priestley [14,17] accounting for these implementation outcome measures will increase the study duration up to 2.5 years.

4. CONCLUSION

In conclusion, the COMET trial will provide new and important insights into the functioning of an RRS and has incorporated as much insights regarding the analysis of complex interventions.

ETHICAL 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. A receipt from the METC has been uploaded as prove of the above statement.

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COMPETING INTERESTS

The Radboud University Nijmegen Medical Center (B.G. Fikkers, MD, PhD) is a satellite center for the ALERT™ course within the Netherlands.

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