Making Healthcare Safer IV

Failure To Rescue – Rapid Response Systems

Rapid Review

Structured Abstract

Objectives. Rapid response systems address unexpected and unrecognized clinical deterioration on general hospital wards and aim to prevent cardiorespiratory arrests. These systems have an afferent limb (recognition and activation) and an efferent limb (response). Our main objectives were to determine the effectiveness of rapid response systems on patient safety and clinical outcomes and how rapid response systems can be implemented effectively.

Methods. We searched PubMed and the Cochrane library for eligible systematic reviews and primary studies published from January 2018 through June 2023, supplemented by targeted gray literature searches. We included reviews and primary studies of rapid response systems reporting the incidence of cardiorespiratory arrest, hospital mortality, transition to higher level of care, serious adverse events related to clinical deterioration, or unintended consequences.

Findings. We retrieved 867 citations, of which 23 articles were eligible for review (4 systematic reviews and 19 primary studies). Three categories of interventions were identified: implementation of a new system, modifications to the afferent limb, and modifications to the efferent limb. Based on systematic reviews and primary studies, rapid response systems may have a large impact in reducing in-hospital mortality (low strength of evidence for adult and pediatric populations) and an even greater impact in reducing the incidence of cardiorespiratory arrest on hospital general wards in adult populations (low strength of evidence), but the effect is unclear in pediatric populations (insufficient strength of evidence). Their impact on unanticipated intensive care unit (ICU) admission is unclear (insufficient strength of evidence for both populations). Modifications to the afferent and/or efferent limb were associated with a reduction in mortality and the incidence of cardiorespiratory arrest for adults (low strength of evidence) but the evidence was insufficient in pediatric populations. Serious adverse events (e.g., arrest soon after ICU arrival) were infrequently reported (insufficient strength of evidence for both adult and pediatric populations). One included systematic review of the unintended consequences of staffing models

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examined risks for ICU patients, but the strength of evidence was insufficient for both children and adults.

Conclusions. Overall, rapid response systems may have a large beneficial effect on the outcomes of hospital mortality and the incidence of in-hospital cardiorespiratory arrest but the strength of the evidence is low due to methodological weaknesses of the studies. Innovations in afferent and efferent limb structures show promise for increased benefit.

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1. Background and Purpose

The Agency for Healthcare Research and Quality (AHRQ) Making Healthcare Safer (MHS) reports consolidate information for healthcare providers, health system administrators, researchers, and government agencies about practices that can improve patient safety across the healthcare system—from hospitals to primary care practices, long-term care facilities, and other healthcare settings. In spring 2023, AHRQ launched its fourth iteration of the MHS Report (MHS IV).[1] Rapid response systems as a patient safety practice (PSP) were identified as high priority for inclusion in the MHS IV reports using a modified Delphi technique by a Technical Expert Panel (TEP) that met in December 2022. The TEP included 15 experts in patient safety with representatives of governmental agencies, healthcare stakeholders, clinical specialists, experts in patient safety issues, and a patient/consumer perspective. See the MHS IV Prioritization Report for additional details.[2]

Failure to rescue is the term commonly used to describe failure or delay in recognizing and responding to a hospitalized patient experiencing unexpected deterioration. In patients on general hospital wards, unexpected deterioration, complicated by failure to rescue, may result in cardiorespiratory arrest, which can cause additional morbidity and mortality.[3] These events may be heralded by clear premonitory signs and symptoms that create opportunities to recognize the deterioration in a timely manner, intervene to stabilize the patient, and halt the clinical deterioration.[4-13] Rapid response systems were developed to respond to early warnings of unexpected deterioration,[14-20] but their effectiveness may be limited by a variety of factors impacting rapid response system activation (i.e., partial or complete afferent limb failure) or response (i.e., partial or complete efferent limb failure).[14,21-23]

1.1 Overview of the Patient Safety Practice

Rapid response systems (RRS) were implemented in the mid-1990s to address the problem of unexpected and unrecognized clinical deterioration on general hospital wards with the goal of preventing cardiorespiratory arrests. Activation criteria were generated using data gathered from studies that defined the premonitory signs and symptoms of cardiorespiratory arrest.[4-13] General ward staff were educated on the importance of early recognition of the signs and symptoms of clinical deterioration, and how to activate the response team if and when patients met activation criteria (i.e., the afferent limb of rapid response). The response team (i.e., the efferent limb) would then rapidly come to the patient's bedside to assess, intervene if necessary, and potentially triage patients to a higher level of care. In 2009, The Joint Commission made response to general ward clinical deterioration a patient safety goal leading to widespread implementation of rapid response systems in the United States.[24] However, despite decades of dissemination and implementation of rapid response systems, patients still experience unrecognized deterioration on general hospital wards, and activation of the rapid response system is often delayed or does not occur due to

failure of monitoring and recognition of clinical deterioration. The previous MHS III report found moderate evidence that rapid response systems are effective in reducing cardiorespiratory arrest, but the evidence was inconclusive as to how they reduce hospital mortality and intensive care unit (ICU) transfers.[3] Any benefit from rapid response systems may take time to be realized. A study published in 2009 showed that rapid response systems need to reach a threshold of utilization (i.e., a "dose" defined as the number of activations per 1,000 admissions) to have measurable impact.[25] The MHS III report also found that afferent and efferent limb partial or complete failures impact the effectiveness of rapid response systems.

In the prioritization process, the MHS IV TEP advised that rapid response systems be defined more broadly as "systems" to allow for a focus on newer work on identification of at-risk individuals and implementation through "systems" such as automated alerts for vital signs or daily huddles. In this review, we adopt this broader view and focus on both afferent and efferent limbs of a rapid response system. While patient monitoring has become a focus of rapid response system afferent limb improvement efforts, we will not include patient monitoring as a component of this Rapid Review. Patient monitoring merits a separate PSP review since patient monitoring is relevant to additional areas of care not commonly serviced by rapid response systems such as emergency departments, and patient monitoring has intersections with other patient safety concerns such as alarm and alert fatigue. Studies included here need to include efferent limb information and not focus solely on patient monitoring and the afferent limb. We expect that a separate review of patient monitoring will capture broad aspects of patient monitoring including its role and impacts in all areas including the afferent limb, alarm and alert fatigue, predictive analytics for deterioration, etc.

1.2 Purpose of the Rapid Review

The overall purpose of this rapid review is to describe the current literature on the effectiveness of efforts to optimize the afferent and efferent limbs of rapid response systems, which aim to mitigate failure to rescue and decrease the incidence of in-hospital cardiorespiratory arrest, hospital mortality, and unanticipated transfer to a higher level of care, such as the ICU. The intent is to consolidate information for healthcare providers, health system administrators, researchers, and government agencies about how rapid response systems can improve patient safety.

1.3 Review Questions

1. What are the frequency and severity of harms associated with the failure to rescue?
2. What patient safety measures or indicators have been used to examine the harms associated with failure to rescue?
3. What rapid response system practices have been used to prevent or mitigate the harms and in what settings have they been used?

4. What is the rationale for rapid response system practices that have been used to prevent or mitigate the harms associated with failure to rescue?
5. What are the effectiveness and unintended effects of rapid response systems and what new evidence has been published since the search was done for the MHS III report in 2019?
6. What are common barriers, limitations, and facilitators to successfully implementing a rapid response system?
7. What resources (e.g., cost, staff, time) are required for implementation of rapid response systems?
8. What toolkits are available to support implementation of rapid response systems?

2. Methods

We followed rapid review processes proposed by the Agency for Healthcare Research and Quality (AHRQ) Evidence-based Practice Center (EPC) Program.[26] The final protocol for this rapid review is posted on the AHRQ website.[27] We registered the protocol for this rapid review in PROSPERO (registration number CRD42023444807).

For this rapid review, strategic adjustments were made to streamline traditional systematic review processes and deliver an evidence product in the allotted time. Adjustments included being as specific as possible about the questions, limiting the number of databases searched, modifying search strategies to focus on finding the most valuable studies (i.e., being flexible on sensitivity to increase the specificity of the search), and restricting the search to studies published in English and performed in the United States. For this report, we used the artificial intelligence (AI) feature of DistillerSR (AI Classifier Manager) as a second reviewer at the title and abstract screening stage.

We asked our content experts to answer Review Questions 1 and 2 by citing selected references that best answer the questions without conducting a systematic search for all evidence on the targeted harms and related patient safety measures or indicators. For Review Question 2, we focused on identifying relevant measures that are included in the Centers for Medicare & Medicaid Services (CMS) patient safety measures, AHRQ's Patient Safety Indicators, or the National Committee for Quality Assurance (NCQA) patient safety–related measures. We asked content experts to answer Review Questions 3 and 4 by citing selected references, including patient safety practices (PSPs) used and explanations of the rationale presented in the studies we found for Review Question 5. For Review Questions 6 and 7, we focused on the barriers, facilitators, and required resources reported in the studies we found for Review Question 5. For Review Question 8, we identified publicly available patient safety toolkits developed by AHRQ or other organizations that could help to support implementation of the PSPs. To accomplish that task, we reviewed AHRQ's Patient Safety Network (PSNet) and AHRQ's listing of patient safety related toolkits and we included any toolkits mentioned in the studies we found for Review Question 5.[28,29] We identified toolkits without assessing or endorsing them.

2.1 Eligibility Criteria for Studies of Effectiveness

We searched for original studies and systematic reviews on Review Question 5 (the question addressing effectiveness studies) according to the inclusion and exclusion criteria presented in Table 1.

Table 1. Inclusion and exclusion criteria

Study Parameter	Inclusion Criteria	Exclusion Criteria
Population	Hospitalized patients on general hospital wards (non-ICU patients)	• ICU patients, ED patients, hospital staff, and hospital visitors (who are not the target of rapid response systems) •
Intervention*	Implementation or maintenance of a rapid response system regardless of afferent or efferent limb structure	• Intervention does not include an in-hospital team of responders • Disease-specific rapid response systems
Comparator	Defined time periods (such as historically controlled "before-after" trials) or cohort group(s) of patients without a rapid response system implemented	No defined historical or contemporaneous cohort comparison group
Outcome	• Incidence of cardiorespiratory arrest • Hospital mortality • Transition to higher level of care (ICU, procedural area [e.g., operating room, interventional radiology]) • Serious adverse events related to clinical deterioration such as unanticipated ICU admission • Unintended consequences of the efferent limb team members leaving their primary responsibilities to respond to an activation	No outcome of interest
Timing	Original studies and systematic reviews published from January 2018 through June 2023	Published before 2018
Study Time Period	Defined study periods with and without a rapid response system for trials with historical or other comparison groups. For cohort studies and trials, the study time frame also needs to be specified	Study time periods are not defined
Setting	Any hospital general ward that is not an ICU	• Inclusion of non-general–ward patients such as ED or ICU patients • No site in the United States
Type of Studies	RCTs, nonrandomized trials, "before-after" trials, and observational studies with a comparison group	• Study design not specified or no control described • Comparator group is not appropriate (would not have equivalent exposure to the intervention)

*In the prioritization of topics for the MHS IV reports, we included early warning system validity, automated alerts, artificial intelligence algorithms, and machine learning approaches to monitoring vital sign data and deterioration under the topic of "patient monitoring systems."

ED = emergency department; MHS = Making Healthcare Safer; ICU = intensive care unit; RCT = randomized controlled trial

2.2 Literature Searches for Studies of Effectiveness

We searched PubMed and Cochrane, supplemented by a narrowly focused search for unpublished reports from January 2018 to June 2023 that are publicly available

from governmental agencies or professional societies having a strong interest in the topic. For details of the search strategy, see Appendix A.

2.3 Data Extraction (Selecting and Coding)

We used the AI feature of DistillerSR (AI Classifier Manager) as a semi-automated screening tool to conduct this review efficiently at the title and abstract screening stage. The title and abstract of each citation were screened by a team member based on predefined eligibility criteria (Table 1), and then the AI Classifier Manager served as a second reviewer of each citation. The threshold for the AI Classifier to include citations was set at a ranking score of 0.5 or above. The ranking score is generated by the AI algorithm to determine the likelihood of inclusion based on a training set of titles and abstracts screened by team members first. Citations were included for full text review if both a team member and the AI Classifier Manager agreed to include. Conflicts between team members and the AI Classifier Manager were resolved by team members. The full text of each remaining potentially eligible article was reviewed by a single team member to confirm eligibility. A second team member checked a 10 percent sample of the full-text reviews to verify that important studies were not excluded.

Reviewers extracted available information and organized it according to the review questions and included author, year, study design, frequency and severity of the harms, measures of harm, characteristics of the rapid response system, rationale for the rapid response system, outcomes, implementation barriers and facilitators, resources needed for implementation, and description of toolkits. One reviewer completed the data abstraction, and a second reviewer checked the first reviewer's abstraction for completeness and accuracy.

2.4 Risk of Bias (Quality) Assessment

We did not identify any eligible randomized controlled trials (RCTs) for Review Question 5. For nonrandomized studies that addressed Review Question 5 about the effectiveness of rapid response systems, we used the ROBINS-I tool for assessing the Risk Of Bias In Non-randomized Studies – of Interventions. We used specific items in the ROBINS-I tool that assess bias due to confounding, bias in selection of participants into the study, bias in classification of interventions, bias due to deviations from intended interventions, bias due to missing data, bias in measurement of outcomes, and bias in selection of the reported results. The risk of bias assessments focused on the main outcome of interest in each study.[30]

For a recent eligible systematic review, the primary reviewer used the criteria developed by the United States Preventive Services Task Force Methods Workgroup for assessing the quality of systematic reviews.[31]

- Good – Recent relevant review with comprehensive sources and search strategies; explicit and relevant selection criteria; standard appraisal of included studies; and valid conclusions.

- Fair – Recent relevant review that is not clearly biased but lacks comprehensive sources and search strategies.
- Poor – Outdated, irrelevant, or biased review without systematic search for studies, explicit selection criteria, or standard appraisal of studies.

2.5 Strategy for Data Synthesis

Selected data was compiled into evidence tables. We narratively summarized findings across systematic reviews and across primary studies. We did not conduct a meta-analysis. For Review Question 5 about the effectiveness of rapid response systems, we recorded information about the context of each primary study and whether the effectiveness of rapid response systems differed across patient subgroups. We graded the strength of evidence for rapid response systems with more than one recent primary study of effectiveness using the methods outlined in the AHRQ Effective Health Care Program Methods Guide for Effectiveness and Comparative Effectiveness Reviews.[32] We also noted whatever the included systematic reviews reported about the strength of evidence.

We relied on our clinical assessment of the severity of the outcome and the size of the risk reduction to estimate whether the magnitude of differences in outcomes was large or small. Specifically, an absolute reduction in mortality of 5 percent or more was considered clinically important, and an absolute reduction in mortality of 10 percent or more was considered a large difference. Given a 70 percent mortality rate associated with cardiorespiratory arrest,[4] we also considered an absolute reduction of 10 percent or more in the incidence of cardiorespiratory arrest as being a large clinically important difference.

3. Evidence Summary

3.1 Benefits and Harms

- Based on systematic reviews and primary studies included in this review, rapid response systems may have a large beneficial effect on the outcomes of hospital mortality and the incidence of in-hospital cardiorespiratory arrest (defined as arrests outside of the intensive care unit (ICU) and/or emergency department) but the strength of the evidence for that benefit is low for adults due to methodological weaknesses in the studies. For pediatrics, rapid response systems may have a large impact on hospital mortality, but like adults, the strength of the evidence is low due to methodological weaknesses. The effect on in-hospital cardiorespiratory arrest is unclear in pediatric populations (insufficient strength of evidence)
- The impact of rapid response systems on unanticipated intensive care unit (ICU) admission is unclear (insufficient strength of evidence for adult and pediatric populations).
- Modifications to the afferent and/or efferent limb were associated with a reduction in mortality and the incidence of cardiorespiratory arrest for adults (low strength of evidence) but the evidence was insufficient in pediatric populations in the primary studies reporting on these outcomes.
- Serious adverse events (e.g., intubation and need for mechanical ventilation, arrest soon after ICU arrival, ICU mortality, and severity scores on arrival to a higher level of care) were infrequently reported (insufficient strength of evidence for both populations).
- One included systematic review examined unintended consequences of rapid response system staffing models requiring ICU staff to respond to activations, but the evidence from that review was insufficient to support a conclusion about the risk for ICU patients while ICU staff were away.
- The quality of the rapid response system literature is limited by significant heterogeneity and risk of bias, and studies often draw conclusions with limited or no statistical analysis.

3.2 Future Research Needs

- Modifications to both the afferent limb and efferent limbs have improved the outcomes of incidence of cardiorespiratory arrest and hospital mortality. Future research should seek to develop sensitive and specific strategies for earlier recognition of clinical deterioration since many studies have shown that failure to rescue is a persistent problem despite the wide implementation of rapid response systems.[21] Additionally, future research needs to examine the unintended consequences as well as the benefits of efferent limb staffing

models because of concerning data about how current rapid response efferent limb staffing models that use dual responsibilities with critically ill ICU patients may put those ICU patients at risk.

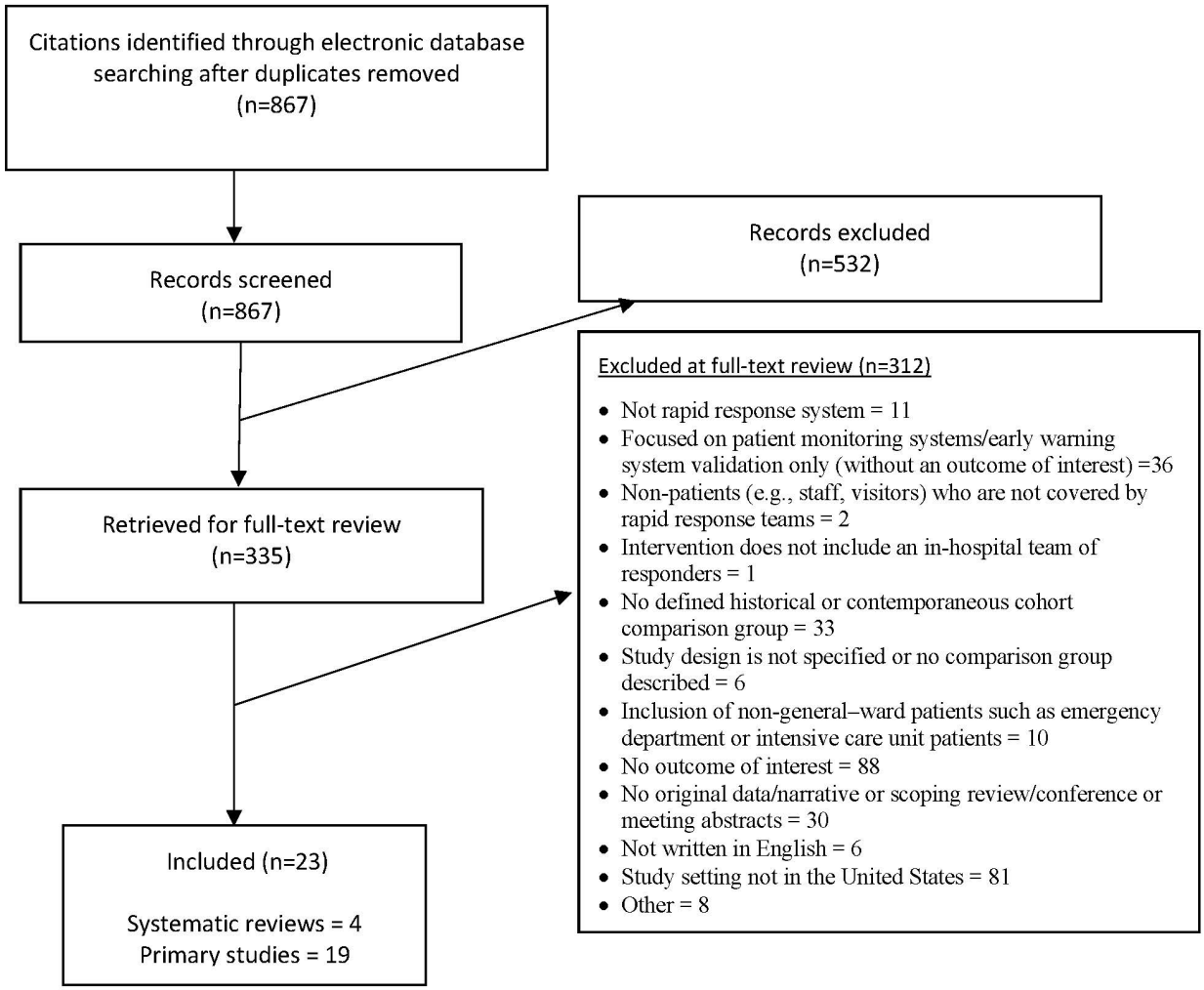
- Family activation of rapid response systems is a promising development, but future research should compare different methods of engaging family members in activation in addition to comparing clinician-initiated activation to family-initiated activations. Family-initiated rapid response activations have very different drivers behind the activation and the need for transfer to a higher level of care after family-initiated activation is much less common than with clinician-initiated activation.[33] Further studies are needed to improve understanding of the differences between family-initiated and clinician-initiated activations so that rapid responses systems can be appropriately tailored to address the concerns identified by families or clinicians.

4. Evidence Base

4.1 Number of Studies

We found 23 studies (4 systematic reviews and 19 primary studies) that met our eligibility criteria (Figure 1). A listing of studies excluded during full-text review is included in Appendix B, List of Excluded Studies. Information abstracted from each included study is provided in Appendix C, Evidence Tables.

Figure 1. Results of the search and screening



4.2 Findings for Review Questions

Summaries of the included systematic reviews and primary studies are presented in Tables 2a and 2b. In-hospital cardiorespiratory arrest is defined as an arrest outside of the intensive care unit (ICU) or emergency department.

Table 2a. Summary of the included reviews

Author, Year Type of Review	Objective*	Literature Search Dates	Number of Included Studies	Quality Assessment Tool*	Authors' Conclusions*
Rocha, 2018[34] Systematic review and meta-analysis	To evaluate the effectiveness of rapid response teams using early identification of clinical deterioration in reducing the occurrence of in-hospital mortality and cardiorespiratory arrest.	2000 to 2016	15 2 clinical trials 10 observational studies 3 meta-analyses	Newcastle-Ottawa Scale for cohort studies, the modified Jadad scale for clinical trials, and the Assessment of Multiple Systematic Reviews for systematic reviews. GRADE system for quality of evidence	Authors concluded that rapid response teams may reduce in-hospital mortality and cardiac arrests, although the quality of evidence for both outcomes is low. Evidence was assessed as low quality due to the high heterogeneity and risk of bias in primary studies.
Teuma, 2020[35] Literature review	To evaluate the evidence on whether rapid response systems decrease in-hospital mortality and non-intensive care unit cardiac arrests.	January 2014 to October 2017	15 1 stepped wedge cluster RCT 1 concurrent cohort controlled study 13 historical controlled studies	The Critical Appraisal Skills Programme (2010) Eligible studies were categorized according to Harbour and Miller's (2001) grading system[36]	Evidence suggests that when the process of introducing/maintaining a RRS is successful and under certain favorable conditions, RRSs significantly decrease mortality and cardiac arrests. This review indicates that the best evidence about RRS effectiveness at reducing mortality and cardiac arrests is at Level 2 based on the framework of Harbour and Miller, 2001.
McGaughey, 2021[37] Cochrane review	To determine the effect of EWS and RRS implementation on adults who deteriorate on acute hospital wards compared to people receiving hospital care without EWS and RRS in place.	March 2019	11 4 RCTs 7 non-randomized studies	Cochrane risk of bias tool GRADE system for quality of evidence	Given the low-to-very low certainty evidence for all outcomes from non-randomized studies, conclusions were drawn from the randomized evidence. This review provides low-certainty evidence that EWS and RRS may lead to little or no difference in hospital mortality, unplanned ICU admissions, length of hospital stay or adverse events; and moderate-certainty evidence of little to no difference on composite outcome.

Author, Year Type of Review	Objective*	Literature Search Dates	Number of Included Studies	Quality Assessment Tool*	Authors' Conclusions*
					The evidence highlights the diversity in outcome selection and poor methodological quality of most studies investigating EWS and RRS. As a result, no strong recommendations can be made regarding the effectiveness of EWS and RRS based on the evidence currently available. There is a need for a patient-informed core outcome set comprising clear and consistent definitions and recommendations for measurement as well as EWS and RRS interventions conforming to a standard to facilitate meaningful comparison and future meta-analyses.
Fildes, 2022[38] Systematic review	To synthesize the available evidence on the consequences of ICU nurses' absence due to attending rapid response calls away from the ICU on service delivery and resourcing in the ICU.	March 2020	9 6 quantitative 2 qualitative 1 mixed methods	The flexible appraisal tool of Law et al for quantitative studies, the Critical Appraisal Skills Program checklist for qualitative studies, and a tool introduced by Pluye et al for mixed study.[39]	The staffing of both the ICU and the rapid response team should be examined carefully with an eye toward sustainability, cost-effectiveness, and clear outcome measures.

*As reported in the review
EWS = Early Warning Score; ICU = intensive care unit; RCT = randomized controlled trial; RRS = Rapid Response System

Table 2b. Summary of the included primary studies

Comparison	Author, Year, Design	Study Period	Hospital Type Patient Population, N	Outcome of Interest	Risk of Bias
No RRS vs RRS	Girotra, 2022[40] Pre-post	2000-2014 data	Hospital type: Teaching, n=32; Non-teaching, n=24 Population: Adult N: NR	• Hospital mortality	Moderate
	Kolovos, 2018[41] Pre-post	2005 to 2011	Hospital type: Academic Population: Pediatric N: 2152	• Incidence of cardiorespiratory arrest • Serious adverse events • Total hospital mortality	Critical

Comparison	Author, Year, Design	Study Period	Hospital Type Patient Population, N	Outcome of Interest	Risk of Bias
				• Transition to higher levels of care	
	Kutty, 2018[42] Pre-post	2000 to 2015	Hospital type: Not for profit (97.4% academic) Population: Pediatric N: 6,051,451 hospitalizations	• Hospital mortality	Moderate
	McKeta, 2021[43] Pre-post	2015 to 2018	Hospital type: Academic Population: Pediatric N: NR	• Hospital mortality • Incidence of cardiorespiratory arrest • Transition to higher levels of care	Critical
	Winterbottom, 2021[44] Pre-post	2017 to 2020	Hospital type: NR Population: NR N: NR	• Hospital mortality • Incidence of cardiorespiratory arrest • Transition to higher levels of care	Critical
	Young, 2023[45] Pre-post	1994 to 2018	Hospital type: NR Population: NR N: 11218	• Hospital mortality • Incidence of cardiorespiratory arrest • Serious adverse events • Transition to higher levels of care	Moderate
Afferent limb change	Danesh, 2019[46] Pre-post	2010 to 2012	Hospital type: Community Population: Adult N: 12148	• Transition to higher levels of care	Moderate
	Escobar, 2020[47] Pre-post	2015 to 2019	Hospital type: Kaiser Permanent Northern California system Population: Adult N: 43949	• Hospital mortality • Transition to higher levels of care	Moderate
	Stellpflug, 2021[48] Observational study with a comparison group	2016 to 2018	Hospital type: Academic Population: Adult N: 112	• Transition to higher levels of care	Critical
	Bavare, 2018[33] Observational study with a comparison group	2011 to 2014	Hospital type: Academic Population: Pediatric N: 1442	• Hospital mortality • Incidence of cardiorespiratory arrest • Transition to higher levels of care	Critical
	Dean, 2020[49] Pre-post	2014 to 2018	Hospital type: Not reported Population: Pediatric N: NR	• Hospital mortality • Incidence of cardiorespiratory arrest • Transition to higher level of care	Critical

Comparison	Author, Year, Design	Study Period	Hospital Type Patient Population, N	Outcome of Interest	Risk of Bias
	Penney, 2021[50] Pre-post	2015 to 2018	Hospital type: Academic Population: Pediatric N: NR	• Transition to higher levels of care • Serious adverse events	Critical
	Weller, 2018[51] Pre-post	10 months	Hospital type: Academic Population: NR N: 1958 discharges	• Unexpected mortality • Transition to higher levels of care	Serious
Efferent limb change	Hatlem, 2018[52] Observational study with a comparison group	2005 to 2008	Hospital type: Not for profit Population: Adult N: 701	• Hospital mortality • Transition to higher levels of care • Serious adverse events	Critical
	Mankidy, 2020[53] Observational study with a comparison group	2013 to 2017	Hospital type: Academic Population: Adult N: 122541	• Incidence of cardiorespiratory arrest	Moderate
	Sawicki, 2021[54] Pre-post	2017 to 2020	Hospital type: Not reported Population: Pediatric N: 892	• Incidence of cardiorespiratory arrest • Transition to higher levels of care • Serious adverse events	Moderate
Multiple comparisons: No RRS vs RRS Efferent limb change	Factora, 2022[55] Pre-post	2005 to 2018	Hospital type: Academic Population: Adult N: 628538	• Hospital mortality	Serious
Multiple comparisons: Afferent limb change Efferent limb change	Sebat, 2018[56] Pre-post	2008 to 2013	Hospital type: Community Population: Adult N: 68716	• Hospital mortality • Incidence of cardiorespiratory arrest	Critical
	Vandegrift, 2021[57] Pre-post	240 months	Hospital type: Community Population: NR N: 69358	• Hospital mortality	Critical

N = number of patients; NR = not reported; RRS = Rapid Response System; vs = versus

4.2.1 Question 1. What Are the Frequency and Severity of Harms Associated With Failure To Rescue?

Rapid response systems were designed to address unrecognized patient deterioration with the goal of preventing cardiorespiratory arrests. Between 2008 and 2017 an estimated 292,000 adult in-hospital cardiac arrests occurred annually, representing 9.7 cardiac arrests per 1,000 patients admitted to a hospital (based on a report that did not explicitly state whether that included patients in an ICU or

emergency department).[4,58] Outcomes for patients experiencing an in-hospital cardiac arrest are poor, with only 25 percent of patients surviving to discharge in the most recently available data from the American Heart Association's Get With the Guidelines Registry.[59] However, there is significant variation in the prevalence and outcomes of in-hospital cardiac arrests regionally and institutionally.[60] The broader phenomenon of clinical deterioration, defined as a patient's transition to a worse clinical state, thereby increasing their risk of morbidity or death, impacts between 3 and 9 percent of hospitalized patients.[61]

4.2.2 Question 2. What Patient Safety Measures or Indicators Have Been Used To Examine the Harms Associated With Failure To Rescue?

The original Institute for Healthcare Improvement (IHI) guide for deploying rapid response systems included key utilization metrics for implementation evaluation:[62]

- The number of calls to the rapid response system;
- Cardiorespiratory arrests outside of the ICU or emergency department per 1,000 discharges; and
- Percentage of cardiorespiratory arrests occurring outside of the ICU.

Studies included in this review also used:

- Hospital mortality;
- The overall incidence of in hospital cardiorespiratory arrest outside of the ICU or emergency department;
- Transitions to higher levels of care;
- Serious adverse events related to clinical deterioration; and
- Unintended consequences resulting from the efferent limb team members leaving their primary responsibilities to respond to an activation.

Outcomes that we did not find in this review but that have been addressed in other publications include the number and timing of delayed and missed activations and their impact on mortality and morbidity.

4.2.3 Question 3. What Rapid Response System Practices Have Been Used To Prevent or Mitigate the Harms and in What Settings Have They Been Used?

Rapid response systems are typically implemented in acute care hospitals in both adult and pediatric populations though some outpatient centers may implement very similar systems to respond to patients who develop serious illness while receiving care in those environments. This includes academic, nonacademic, for-

profit, not-for-profit, small and large hospitals, and rural, suburban, and urban hospitals.

All rapid response systems identified in our review used the same overall model, which was first outlined by Devita et al. 2006 and has been widely adopted.[63] It includes an afferent limb for detection/recognition of deterioration; an efferent limb of clinical responders; an administrative component for oversight, quality improvement, data collection; and an education component.

In the studies that reported details regarding their afferent limb, variations were present in the afferent limb. Most studies that provided this information reported using an early warning scoring system as the tool for determining when an activation should occur.[33,43,44,46,48-50] Several studies reported using vital sign thresholds[41,45,51,56] and a few made comparisons between the different afferent limb strategies.[47,-57] One study specifically described their family-initiated rapid response (FIRR) data in comparison to clinician-initiated activation.[33]

Most studies described their efferent limb in detail[41,44-47,49,50,52-56] and several made comparisons between efferent limb models.[46,52,53,55,56] Many efferent limbs were based on nurse-led teams (known as Rapid Response Teams)[44-47,49,56] while others were based on physician-led teams (known as Medical Emergency Teams).[41,47,49,50,54] Some studies compared these two models.[52,53,55] Others used a proactive critical care outreach approach to evaluate patients for whom there was concern but had not yet reached physiological vital sign or early warning score activation thresholds (Table 3).[46,52]

Table 3. Overview of rapid response system practices and settings reported in the included recent primary studies

Author, Year	Hospital Information	Rapid Response Afferent Limb	Rapid Response Efferent Limb	Rapid Response Implementation Period
Girotra, 2022[40]	Type: Teaching, n=32, Non-teaching, n=24 n: 56 Number of beds: 200 beds: 9 (16.4%) 200–499 beds: 29 (52.7%) >500 beds: 17 (30.9%)	Used the American Heart Association Get with the Guidelines database which includes many different afferent limb models	Used the American Heart Association Get with the Guidelines database which includes many different efferent limb models	Pre-implementation period: Median 7.6 years (range, 3.5 to 12.0) Post-implementation period: Median 7.2 years (range, 3.0 to 11.5)
Factora, 2022[55]	Type: Academic n: 1 Number of beds: NR	NS	2005 to 2008: Pre-implementation 2009-2012: Nurse led, team included a nurse practitioner or physician's assistant 2013-2018: Anesthesiology led, team included a registered nurse with critical care background and a respiratory therapist.	108 months
Winterbottom, 2021[44]	Type: NR n: 1 Number of beds: NR	EWS	24/7 rapid response nurse model of care, nurse led.	36 months
Escobar, 2020[47]	Type: Kaiser Permanent Northern California system n: 19 Number of beds: NR	Intervention: Automated EWS system. Comparison: Involved patients whose conditions would have triggered alerts had the system been operational.	Physician initiates a clinical rescue protocol, an urgent palliative care consultation, or both, coordinating with rapid response nurses.	Pre-implementation observed: 12 months Post-implementation observed: 36 months
Kutty, 218[42]	Type: Not for profit (97.4% academic) n: 38 Number of beds: 126–249 beds: 9 hospitals 250–592 beds: 29 hospitals	NR	Medical emergency team implementation. Unknown lead and team compositions.	Implementation: between 2005-2013, mean duration of pre-implementation and post-implementation periods was 3 years

Author, Year	Hospital Information	Rapid Response Afferent Limb	Rapid Response Efferent Limb	Rapid Response Implementation Period
Kolovos, 2018[41]	Type: Academic n: 1 Number of beds: 258 beds	An acute change In a patient's physiologic condition or caregiver concern for instability.	Pediatric Critical Care Medicine fellow, PICU charge nurse, respiratory therapist, and the hospital-wide nursing administrative supervisor.	Pre-implementation observed: 36 months Post-implementation observed: 36 months
Dean, 2020[49]	Type: NR n: 1 Number of beds: NR	EWS system	Led by a critical care physician, and includes an acute care inpatient nursing director, and a performance improvement specialist.	48 months
Bavare, 2018[33]	Type: Academic n: 1 Number of beds: 570 beds	FIRR: Family member personally called the number available on the FIRR flier to activate a response. Pediatric Acute Warning Score and Clinical Respiratory Score. C-RR: Afferent limb not specified. Pediatric Acute Warning Score and Clinical Respiratory Score.	Efferent limb not specified for either FIRR or C-RR arm.	FIRR implemented since 2009
Penney, 2021[50]	Type: Academic n: 1 Number of beds: 16 bed pediatric in-patient; 6 beds in PICU	EWS system	Pre-implementation: NR PEWS system implementation period: • PICU resident • PICU charge nurse • Respiratory therapist • Patient's primary team • Team lead not specified Modified PEWS implemented: • Same as PEWS implementation period	Pre-implementation: 2015 to 2016 data PEWS system implementation: 2016 to 2017 Modified PEWS: 2017 to 2018
McKeta, 2021[43]	Type: Academic n: 1 Number of beds: 14 bed pediatric cardiac stepdown unit, 14 bed PICU	EWS system	Cardiac patient specific team (composition and lead not specified).	Data collected over 48 months

Author, Year	Hospital Information	Rapid Response Afferent Limb	Rapid Response Efferent Limb	Rapid Response Implementation Period
Sebat, 2018[56]	Type: Community n: 1 Number of beds: 500 beds	Vital sign threshold	Control period: registered nurse, rapid response team with additional resources summoned as needed. Intervention period: registered nurse, lab, radiology, pharmacy, EKG with additional resources summoned as needed.	Control period: 24 months Intervention period: 33 months
Danesh, 2019[46]	Type: Community n: 1 Number of beds: 237 beds	EWS system	Traditional RRT: Nurse role was staffed by a pool of ICU nurses cross-trained to respond to patient deteriorations in non-ICU areas of the hospital and provided 24-hour coverage. EWS with proactive RRT: Implementation included installation and activation of the Rothman Index application, revision of role expectations and workflows for the rapid response team nurse.	12-month intervention period
Mankidy, 2020[53]	Type: Academic n: 1 Number of beds: 850 beds	NR	RRT: Nurse led: three critical care nurses. MET: Intensivist led: physician intensivist, an advanced nurse practitioner, and a critical care fellow.	RRT period: 24 months RRT-MET: 36 months

Author, Year	Hospital Information	Rapid Response Afferent Limb	Rapid Response Efferent Limb	Rapid Response Implementation Period
Vandegrift, 2021[57]	Type: Community n: 4 Number of beds: Only reported for one hospital: 450-bed regional medical center	First iteration, 1999: implemented in 3 out of 4 hospitals. Empiric focused early warning score, focused on five classic forms of shock. Second iteration, 2007: implemented in 3 out of 4 hospitals. Modified the EWS to address respiratory failure and early sepsis better. Final iteration, 2011: Only implemented in 1 out of 4 hospitals. 10-SOV recorded at the beginning of each shift. Repeated any time new routine vital sign abnormality occurs.	First iteration, 1999: implemented in 3 out of 4 hospitals. Shock team and VIPPS. Second iteration, 2007: implemented in 3 out of 4 hospitals. VIPPS protocol divided into two parts. (1) AOV, (2) IPPS implemented if patient did not improve Final iteration, 2011: Implemented in 1 out of 3 hospitals). Nurse initiates AOV resuscitation while awaiting arrival of the team.	Implementation over 20 years
Young, 2023[45]	Type: NR n: 1 Number of beds: NR	Includes vital sign threshold and allows any individual involved in a patient's care to activate a response.	ICU or emergency department-trained nurses with critical care experience.	Implementation began in 2009. Data collected through 2018.
Weller, 2018[51]	Type: Academic n: 1 Number of beds: 26 beds	Vital sign threshold	Team not specified.	5-month implementation

Author, Year	Hospital Information	Rapid Response Afferent Limb	Rapid Response Efferent Limb	Rapid Response Implementation Period
Sawicki, 2021[54]	Type: NR n: 1 Number of beds: 289 beds	Any staff with any clinical concern.	Team made up of three clinicians: (1) A pediatric critical care medicine fellow, attending physician, or a pediatric critical care nurse practitioner, (2) A pediatric critical care charge nurse, and (3) A respiratory therapist. Implementation: developed and implemented clinical pathways (rapid response algorithms), to help guide the ME"s and floor teams' management steps when evaluating patient deterioration.	Implementation from 2019 to 2020
Stellpflug, 2021[48]	Type: Academic n: 1 Number of beds: 27 beds	Modified EWS and digital continuous vital sign monitoring.	NR	Original EWS in 2016. EWS with digital vital sign monitoring, 2017.
Hatlem, 2018[52]	Type: Not for profit n: 1 Number of beds: 870 beds	NR	Original MET (2005-2007): • Critical care nurse • Hospitalist • Respiratory therapist, • Registered nurse • Clinical administrator Revised RRT (2007-2008): No hospitalist	Original RRT: 2005-2007 Revised RRT: 2007-2008

AOV = Airway maintenance, the provision of supplemental Oxygen and noninvasive or invasive Ventilation; C-RR = clinician-activated rapid response; CRT = capillary refill time; EWA = early warning bedside assessment; EWS = early warning score; FIRR = family-initiated rapid response; ICU = intensive care unit; IPPS = Infusion of volume and assessing need for Pressors and/or pump support, other Pharmacologic interventions and/or Specific interventions; LA/BD = lactic acid/base deficit; n = number of hospitals; NR = not reported; NS = not specified; PEWS = pediatric early warning score; PICU = pediatric intensive care unit; RRT = rapid response team; RRT -MET = rapid response team-medical emergency team; SOV = signs of vitality; VIPPS = Ventilation and Infusion of volume, and then the need for Pressors and pump support, Pharmacologic interventions and/or Specific interventions

4.2.4 Question 4. What Is the Rationale for the Rapid Response System Practices That Have Been Used To Prevent or Mitigate the Harms Associated With Failure To Rescue?

Abnormal vital signs often precede critical deterioration for hours before events such as cardiac arrests occur.[64] These leading indicators create the potential for windows wherein severe adverse clinical events can be avoided with appropriate intervention. Clinical deterioration outside of an ICU setting creates a mismatch between patient care needs and the resources available (i.e., staff, equipment).[63,65] Rapid response systems are designed to capitalize on these windows through early detection of clinical deterioration and responding to potential events by moving critical resources to the patient.

4.2.5 Question 5. What Are the Effectiveness and Unintended Effects of Rapid Response Systems and What New Evidence Has Been Published Since the Search Was Done for the Making Healthcare Safer (MHS) III Report in 2019?

The limited search in the MHS III report included 14 studies of rapid response systems. Of these, three presented a meta-analysis and two were systematic reviews. Thirteen of the studies focused on rapid response system outcomes including the incidence of cardiorespiratory arrest, hospital mortality and unplanned transfer to a higher level of care (usually an ICU). One study specifically compared two different efferent limb models (an ICU physician led team versus a senior resident led team). No studies were presented that examined how modifications to the afferent limb component of rapid response systems might influence the above outcomes.

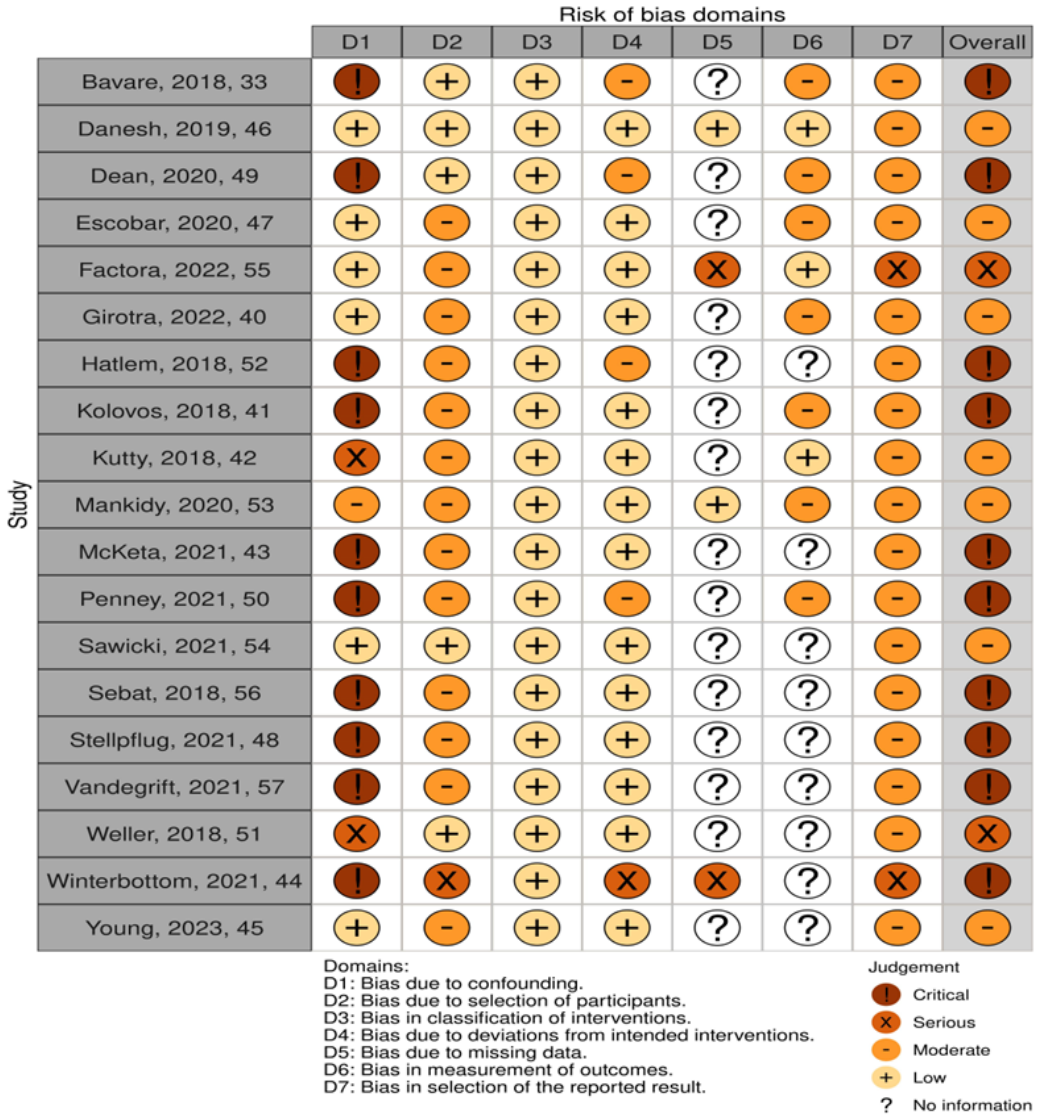
We identified four good-quality reviews [34,35,37,38] and 19 primary studies published since the time frame examined in the 2019 MHS III report.[33,40-57] Eleven studies compared outcomes with and without a rapid response system. One study specifically examined the unintended consequences of the most common rapid response system model that relies on critical care providers being the efferent limb. Ten studies compared outcomes after implementing changes in the afferent limb component of the rapid response system. Six studies examined outcomes using different efferent limb models. Two studies implemented changes to both the afferent and efferent component of their rapid response system program.

Several types of risk of bias were present in the included nonrandomized studies based on our assessments using the ROBINS-I tool (Risk Of Bias In Non-randomized Studies – of Interventions).[30] Our assessments revealed concerns for bias in confounding, patient selection, missing data, measurement of outcomes, and

selection of reported results. Ten of the 19 nonrandomized studies had critical risk of bias (Figure 2).

We present the findings by comparison (tables 4a and 4b). We first discuss the evidence from systematic reviews, followed by evidence from primary studies.

Figure 2. Risk of bias assessments for nonrandomized studies included in this review*



*The figure was created using the robvis visualization tool[66]

Table 4a. Overview of strength of evidence from systematic reviews and recent primary studies by outcome and comparison type for studies of adult populations

Outcome	Comparing Outcomes With and Without a Rapid Response System	Comparing Outcomes Associated With an Afferent Limb Model Change	Comparing Outcomes Associated With an Efferent Limb Model Change
Hospital mortality	SR = 3 Primary studies = 4  Low SOE	SR = 0 Primary studies = 4  Low SOE	SR = 0 Primary studies = 4  Low SOE
Incidence of cardiorespiratory arrest	SR =3 Primary studies = 2  Low SOE	0 studies	SR =0 Primary studies = 3  Low SOE
Transition to higher level of care	SR =1 Primary study = 1  Insufficient SOE	SR =0 Primary studies = 4  Low SOE	SR =0 Primary study = 1  Insufficient SOE
Other serious adverse events related to clinical deterioration	SR =1 Primary study = 1  Low to moderate SOE depending on the adverse outcome and whether the studies were randomized or not	0 studies	0 studies
Unintended consequences of the efferent limb team members leaving their primary responsibilities to respond to an activation	SR =1 Primary studies = 0 Insufficient SOE	0 studies	0 studies

Note: Each circle represents a primary study and the symbol inside the circle indicates the risk of bias judgment.
SR = systematic review
SOE = Strength of Evidence taking into consideration our assessment of primary studies and what previous systematic reviews reported about the strength or certainty of evidence.
Risk of bias judgment:

Table 4b. Overview of strength of evidence from systematic reviews and recent primary studies by outcome and comparison type for studies of pediatric populations

Outcome	Comparing Outcomes With and Without a Rapid Response System	Comparing Outcomes Associated With an Afferent Limb Model Change	Comparing Outcomes Associated With an Efferent Limb Model Change
Hospital mortality	SR = 0 Primary studies = 3 (!) (!) (-) Low SOE	SR = 0 Primary studies = 2 (!) (!) Insufficient SOE	0 studies
Incidence of Cardiorespiratory Arrest	SR = 0 Primary studies = 1 (!) Insufficient SOE	SR = 0 Primary studies = 2 (!) (!) Insufficient SOE	0 studies
Transition to Higher Level of Care	SR = 0 Primary studies = 1 (!) Insufficient SOE	SR = 0 Primary studies = 3 (!) (!) (!) Insufficient SOE	SR = 0 Primary studies = 1 (-) Insufficient SOE
Other Serious Adverse Events Related to Clinical Deterioration	SR = 0 Primary studies = 1 (!) Insufficient SOE	SR = 0 Primary studies = 1 (!) Insufficient SOE	SR = 0 Primary studies = 1 (-) Insufficient SOE
Unintended consequences resulting from team members leaving their primary responsibilities to respond to an activation	0 studies	0 studies	0 studies

Each circle represents a primary study and the symbol inside the circle indicates the risk of bias judgment.
SR = Systematic Review
SOE = Strength of Evidence taking into consideration our assessment of primary studies and what previous systematic reviews reported about the strength or certainty of evidence

Risk of bias judgement:

(!) Critical
(X) Serious
(-) Moderate

4.2.5.1 Comparing Outcomes With and Without a Rapid Response System

We identified four systematic reviews[34,35,37,38] and seven recent primary studies[40-45,55] comparing outcomes with and without a rapid response system in place. All primary studies used a pre-post historical control design.

For unpublished grey literature, we reviewed the websites of relevant organizations including the Society of Critical Care Medicine, Society of

Hospital Medicine, IHI, AHRQ, National Quality Forum, and the Joint Commission. We did not find any materials meeting our eligibility criteria, most commonly because materials were posted before 2018, not relevant, or was excluded at the full text review phase.

4.2.5.1.1 Hospital Mortality

Three of the included reviews examined hospital mortality. Only one included systematic review also performed a meta-analysis of the available data. This meta-analysis pooled 15 studies published between 2000 and 2016 and found that rapid response systems reduced the risk of hospital mortality by 15 percent (relative risk (RR) 0.85; 95% confidence interval (CI), 0.76 to 0.94).[34]

A second review was published in 2020 and included 15 studies. The authors of the review did not perform a pooled meta-analysis but reported that 7 of the 13 studies that examined the outcome of hospital mortality found statistically significant reductions in mortality in association with rapid response system implementation.[35]

A third review was performed by the Cochrane collaborative and defined the intervention to include early warning system (EWS) scores and a rapid response system though they were agnostic as to what type of EWS was part of the intervention. All rapid response systems include some type of EWS designed to activate the efferent limb. This may be single abnormal vital sign thresholds or calculated severity scores based on vital signs and other data such as altered mental status and laboratory data such as a lactate level. Single vital sign thresholds are not usually described as EWSs since they are not aggregated into a single numerical score, while calculated severity scores are described as EWSs since they represent an aggregated value. Studies published up to March 2019 were eligible in this Cochrane review. The authors found four randomized studies and three non-randomized trials meeting the inclusion criteria and concluded that the intervention made little to no difference in hospital mortality (low certainty).[37]

All three reviews rated the quality of the included studies as low due to heterogeneity and high risk of bias.

We also identified seven primary studies addressing overall hospital mortality.[40-45,55] One study focused exclusively on pediatric post-cardiac surgery patients.[43] Two additional studies were in pediatric patients,[41,42] one of which was a multisite study across 38 pediatric hospitals.[42]

Of the adult patient primary studies, one primary study[40] found no improvement in overall mortality after implementation of a rapid response system. Another study changed their part-time rapid response system to a full 24/7 rapid response system with a proactive rounding process and reported a 27 percent reduction in the hospital risk adjusted mortality index, but provided no data on whether this was statistically significant.[44]

Another primary study[55] initially found a small statistically significant increase in overall hospital mortality in the first three years after rapid response system implementation. They did not offer an explanation for this initial increase but noted that when applying risk adjustment, they found that co-morbidities were often not documented. This may have influenced the results. However, over time, and with modifications to their rapid response system (this was a time-interrupted series study design), they reported a statistically significant downward mortality trend of an average of 4 percent per year.

One study reported a statistically significant reduction (nearly 50%, $p<0.001$) in unexpected mortality in post-cardiac surgery patients after implementing a rapid response system.[45]

Of the pediatric rapid response system studies, two primary studies reported statistically significant reductions across all hospitals that participated.[41,42] Of note, the 38-hospital study found benefit based on sub-group analysis, regardless of hospital size or geographic region, but the point estimates for mortality reduction were small (4–9%).[42]

The third pediatric primary study focused on pediatric cardiac patients and showed a reduction in mortality from four deaths to one death but did not provide statistics.[43]

We graded the strength of evidence (SOE) as low for hospital mortality in both adult and pediatric populations, considering what previous systematic reviews reported about the quality of evidence and our assessment of the risk of bias in recent primary studies.

4.2.5.1.2 Incidence of Cardiorespiratory Arrest

Three reviews examined the incidence of cardiorespiratory arrest outcome.[34,35,37]

One review pooled 15 studies published between 2000 and 2016. Their meta-analysis found that rapid response systems significantly reduced the risk of cardiorespiratory arrest on the general hospital ward (RR 0.65; 95% CI, 0.49 to 0.87).[34]

Another review was published in 2020 and included 15 studies. The authors of the review did not perform a pooled meta-analysis but reported that 8 of the 13 studies that investigated cardiorespiratory arrest found statistically significant reductions in this outcome in association with rapid response system implementation.[35]

A Cochrane review published in 2021 reported the incidence of cardiorespiratory arrest under the heading of "adverse outcomes." They found that in both included randomized and non-randomized studies that the EWS and rapid response system intervention had little to no impact on the incidence of cardiorespiratory arrest with a low degree of certainty.[37]

We also identified three primary studies[41,44,45] that reported on the incidence of cardiorespiratory arrest, one of which was in a pediatric population.[41]

One primary study found a 65 percent reduction but provided no statistical analysis of its data.[44] The other study[45] found that implementation of a rapid response system for post-cardiac surgery patients did not change the incidence of cardiorespiratory arrest in that population.

In the pediatric study,[41] only arrest once the patient was in the pediatric intensive care unit (PICU) was used as an outcome measure as opposed to arrest on the general ward which is the more standard metric used for rapid response system studies. This metric using arrest after arrival to the ICU implies that the rapid response system improves that patient's condition prior to transfer to the ICU such that subsequent in-ICU arrest is less frequent. This study found a significant drop in these events.

We graded the SOE as low for incidence of cardiorespiratory arrest outcome in adult and insufficient in pediatric populations, considering what previous systematic reviews reported about the quality of evidence and our assessment of the risk of bias in recent primary studies.

4.2.5.1.3 Transition to Higher Level of Care

Transition to a higher level of care is most often defined as transfer to an ICU. It may also include transfer to an intermediate care unit or an unplanned transfer to the operating room or another procedural area such as interventional radiology.

Of the included reviews, only one addressed this outcome. This was a Cochrane review[37] which found that an EWS and rapid response system did not have a measurable impact on transition to a higher level of care in either the randomized or the nonrandomized studies though the certainty of the data was low to very low.

We also identified two primary studies[43,44] that reported on this outcome. One in pediatric cardiac surgery patients found a statistically significant reduction ($p<0.001$) in unanticipated ICU readmission (all patients had been admitted to the ICU post-operatively due to the nature of their surgery)[43] and the other, in an adult population, reported a reduction of 4.7 percent but provided no statistical analysis.[44]

We graded the SOE for the outcome of transition to higher level of care in both adult and pediatric populations as insufficient, considering what previous systematic reviews reported about the quality of evidence and our assessment of the risk of bias in recent primary studies.

4.2.5.1.4 Other Serious Adverse Events Related to Clinical Deterioration

A variety of other adverse events and outcomes are addressed in the reviews and primary studies identified in our review.[37,41,45]

We identified one review that examined additional outcomes including a composite outcome that combined unanticipated ICU admission, death, and the incidence of cardiorespiratory arrest, and length of stay.[37] For the composite outcome, randomized trials demonstrated no impact with a certainty level that was moderate. Non-randomized studies had the same result with a low level of certainty. Length of stay was, likewise, found to be unaffected by the implementation of an EWS and rapid response system.

We also identified two primary studies that addressed other serious adverse events.[41,45] One study in pediatric patients reported a number of other adverse events for patients who were cared for by the rapid response system prior to their arrival in the PICU (all of the evaluated patients had unanticipated admission to the ICU). This study found that endotracheal intubation and mechanical ventilation within an hour of arrival in the PICU nearly doubled after rapid response system implementation but that the need for mechanical ventilation while in the PICU was unchanged. This study also reported a statistically significant reduction in ICU mortality and in PICU length of stay ($p<0.001$).[41] A pre-post design study in adult cardiac surgical patients[45] also looked at a number of other adverse events such as need for dialysis, re-operation and others, and found no statistical difference after the implementation of the rapid response system for any of the adverse events they measured.

We graded the SOE as low to moderate depending on the adverse outcome and whether the studies were randomized or not in adult and insufficient in pediatric populations, considering what previous systematic reviews reported about the quality of evidence and our assessment of the risk of bias in recent primary studies.

4.2.5.1.5 Unintended Consequences of the Efferent Limb Team Members Leaving Their Primary Responsibilities To Respond to an Activation

We identified one review, which included nine studies, that examined the adverse unintended consequences of a rapid response system, specifically how ICU patients were affected when their nurses stepped away to respond to an activated rapid response system on non-ICU units.[38] Four key themes were identified that were thought to increase the risk of adverse events in ICU patients whose nurses were called away to a rapid response system activation. These were: workforce, staffing processes, and resource allocation; alterations to workload and resource allocation; adverse events or incidents; and funding

variability of rapid response team models. The included studies suggested that dual ICU and rapid response team roles (the most common staffing model) had negative effects on nurses' workload and increased risk of adverse events in ICU patients. The unintended consequences for physicians, advanced practice providers and other clinicians were not examined.

The review did not report on the overall SOE so we graded the SOE as insufficient to support a conclusion about this outcome.

4.2.5.2 Comparing Outcomes Associated With an Afferent Limb Model Change

As rapid response system implementation has become widespread in the United States in response to the Joint Commission's 2009 Patient Safety Goal requiring hospitals to improve their responsiveness to patients on general hospital wards who are experiencing clinical deterioration, many hospitals have sought to improve their rapid response systems through modifications of the afferent limb.[67] A substantial body of evidence shows that the rapid response system activation is often delayed or does not occur at all even though activation thresholds have been met, and that these delays are associated with poorer outcomes.[68-70]

We identified eight primary studies published since the 2019 MHS III report, that examined specific rapid response system afferent limb modifications and their impact on relevant outcomes. Afferent limb modifications most often included changes in rapid response system activation criteria. The modifications included implementation of EWS where weighted scores are given to the severity of various signs and symptoms resulting in a calculated deterioration or risk score in lieu of single vital sign thresholds, implementation of electronic risk scoring using electronic health record data, addition of critical care outreach review of higher risk general ward patients prior to rapid response system activation, and/or changes in policy to support these efforts. Several studies implemented multiple modifications to their afferent limb and are described below.

4.2.5.2.1 Hospital Mortality

No reviews on afferent limb model change met our inclusion criteria for addressing hospital mortality.

We identified six primary studies addressing mortality in association with one or more afferent limb modifications. Two were performed in a pediatric populations[33,49] while the rest were carried out in adults.[47,51,56,57]

One primary study[57] implemented, over the course of several years, a number of changes to their afferent limb including overlaying an early warning assessment on their initial focus of addressing shock states in order to improve the early recognition of problems such as respiratory compromise

that did not fit into classic shock states. This study demonstrated statistically significant reductions in total hospital mortality across several hospitals ($p<0.001$). Since this study also included modifications to the efferent limb, attribution of the outcome improvements solely to the afferent limb modification is not possible.

One pre-post study examined wearable continuous vital sign sensors to enhance recognition of deterioration and improve earlier activation of the rapid response system. The rationale for this approach is that studies have shown that manually collected vital sign data (the usual standard on general hospital wards) has poor accuracy and fidelity.[21] The study found a nearly 40 percent and 30 percent reduction in mortality on the two populations studied (neurosurgical and neurological patients), though this was not statistically significant.[51]

Another study, in pediatric patients, assessed implementation of several afferent limb changes including EWSs, automation of EWS scoring, huddles to identify high risk patients, learning collaboratives, workgroups, and policy changes to support these efforts. This study found that the number of deaths after an arrest on the general wards fell from four during the pre-implementation period to zero over the last 3 years of the time series study.[49] No statistical analysis was given.

Another primary study used a multipronged intervention (pre-post design) that included enhanced nurse education in recognizing deteriorating patients and adopting systems changes to encourage prompt activation found a statistical improvement ($p<0.001$) in both overall hospital mortality as well as observed to expected mortality ratios.[56] This study, however, also made modifications to the efferent limb so attribution of the outcome improvements to the afferent limb modifications alone is not possible.

Another primary study[47] assessed the addition to their rapid response system, in a stepwise fashion, of real-time deterioration risk scoring with remote nurse-led monitoring of those scores. The study, which was across nineteen hospitals, found that the risk of mortality at 30 days after meeting rapid response system activation thresholds was statistically lower ($p<0.001$). Total hospital mortality for the target population also dropped (14.4 to 9.8%) but no statistical analysis was given for this metric.

Patient/family activation of the rapid response system or family initiated rapid response system (FIRRS) is a not uncommon afferent limb modification that has been strongly advocated for and is not typically based on traditional vital signs abnormality thresholds or EWS scores but rather family or patient concern about the patient's condition. One study found that FIRRS activations, when an available option, often makes up a small fraction of the total number of rapid response system activations.[33] This same primary study compared FIRRS and clinician (nurse or other healthcare professional)-initiated activation. They found that approximately half of the FIRRS

activations met clinical trigger thresholds, though the reasons given for FIRRS activations were very different from those of clinician-initiated activation. No deaths occurred in the FIRRS subgroup, but the authors did not provide any data on mortality in the clinician activated events for comparison. Clinician-initiated events were much more likely to be for respiratory compromise (65%) and the patients had much higher acuity scores, while FIRRS activations were most often for uncontrolled pain (37%) and concern regarding the plan of care (31%).

We graded the SOE as low for hospital mortality associated with an afferent limb model change in adults and insufficient in pediatric populations.

4.2.5.2.2 Incidence of Cardiorespiratory Arrest

No reviews met our inclusion criteria for this outcome.

We identified two primary studies that reported this outcome in association with modifications of the afferent limb; both were in pediatric patients.[33,49] One study,[49] in a time series evaluation of a multipronged afferent limb improvement project, found that the incidence of cardiorespiratory arrest fell from 0.31 per 1,000 patient days to 0.11 but provided no statistical analysis. The other pediatric study,[33] in comparing FIRRS to clinician-initiated rapid response system activation, found that clinician-initiated rapid response system events were statistically more likely to progress to arrest during the activation event, but the underlying reasons for activation between the clinician-initiated and the FIRRS were substantially different. Clinician-initiated events were much more likely to be for respiratory compromise (65%) and the patients had much higher acuity scores, while FIRRS activations were most often for uncontrolled pain (37%) and concern regarding the plan of care (31%). The impact on the overall incidence of cardiac arrest for the hospital was not reported.

We graded the SOE as insufficient for incidence of cardiorespiratory arrest associated with an afferent limb model change in pediatric population.

4.2.5.2.3 Transition to Higher Level of Care

No reviews met our inclusion criteria for this outcome.

We identified seven primary studies that examined this outcome after modifications to the afferent limb of the rapid response system. One primary study,[48] implemented a sequential series of modifications to their rapid response system including introducing a calculated EWS, engaging respiratory therapy, adding specific evening rounds, adding protocols for communication, and finally implementing continuous wireless vital sign monitoring. The study reported that the number of rapid response system activations dropped in half, but there was no significant change in transfers to the ICU. Similarly, another study[51] found nonsignificant decreases in transfer

to higher levels of care after implementing a wireless continuous monitoring system to enhance the afferent limb in a neurosurgical/neurological patient population.

A third primary study added real-time deterioration risk scoring with remote nurse-led monitoring of the scores to their rapid response system in a stepwise fashion across nineteen hospitals. This study found, in both the unadjusted and adjusted analysis, that the incidence of admissions to the ICU (transfer to a higher level of care) was statistically reduced.[47]

Another study, in pediatric patients, also found no significant change in the incidence of transfer to the ICU. They implemented a pediatric EWS and then modified it further with the intent of reducing "unnecessary" rapid response system activations which were defined as erroneous activations that would have been triggered by their original single vital sign threshold system. The study was successful in reducing these "unnecessary" activations while at the same time avoiding changes in ICU transfer since that might constitute a missed triage putting patients at risk.[50] A second study in pediatrics[49] also found no change in the incidence of transfer to ICU with several afferent limb modifications, but did not provide statistics.

Another study reported a statistically significant drop in transfer to ICU care in the post-implementation period after instituting a combination of EWS and a proactive critical care outreach model that sought early detection and intervention.[46]

Finally, one study found that clinician-initiated rapid response system activations were more likely to result in transfer to the ICU as compared to FIRRS but direct comparisons are difficult because of the different reasons for activation between the two afferent limb processes, as noted above in Sections 4.2.5.2.1 and 4.2.5.2.2.[45]

We graded the SOE as low for transition to higher level of care associated with an afferent limb model change in adults and insufficient in pediatric populations.

4.2.5.2.4 Other Serious Adverse Events Related to Clinical Deterioration

We identified only one primary study performed in a pediatric population[50] reporting other serious adverse events in relationship to afferent limb modifications. This study reported a statistically significant reduction in the incidence of missed/delayed rapid response system activations with the afferent limb changes implemented. These modifications included plan-do-study-act cycles focused on an EWS implementation process.

We graded the SOE as insufficient for other serious adverse events associated with an afferent limb model change in pediatric populations.

4.2.5.2.5 Unintended Consequences of the Efferent Limb Team Members Leaving Their Primary Responsibilities to Respond to an Activation

No studies met our inclusion criteria for this outcome.

4.2.5.3 Comparing Outcomes Associated With an Efferent Limb Model Change

4.2.5.3.1 Hospital Mortality

No reviews met our inclusion criteria for this outcome.

We identified four primary studies in adults addressing hospital mortality after modifications to the efferent limb.[52,55-57] One of the studies,[56] used a pre-post design and a multi-pronged intervention that included developing and implementing rapid response system treatment protocols and enhancing data collection and analysis for performance improvement. The study found a statistically significant improvement ($p<0.001$) in both overall hospital mortality as well as observed to expected mortality ratios. Since this study also included modifications to the afferent limb, attribution of the outcome improvements to the efferent limb solely is not possible.

A second study[52] changed the composition of their rapid response system efferent limb, removing a hospitalist physician and adding a critical care nurse for initial peer to peer consult prior to escalating to the whole rapid response system efferent team. This study found that the Hospital Standardized Mortality Ratio, which compares observed mortality to expected mortality, decreased by 31.2 percent. This ratio takes the actual number of inpatients who die and compares it to the number of patients that would be expected to die during their hospital stay. This expected mortality number is based on their admitting diagnosis, comorbidities and other factors. This finding suggested that the efferent limb changes improved care while overall percent mortality remained flat over the entire study period. However, the study provided no analysis of statistical significance.

Another study made changes to their efferent limb primarily through implementation of a series of deteriorating patient management protocols. The study found that these changes along with afferent limb changes yielded statistically significant mortality reductions.[57] Since this study also included modifications to the afferent limb, attribution of the outcome improvements solely to the efferent limb is not possible.

A fourth study made two substantial efferent limb modifications when the mortality trend slope increased after their initial rapid response system implementation. The first change was adding a critical care educated anesthesiologist to the efferent team and having the anesthesiology department assume leadership and management of the entire program. This

first change in the efferent limb resulted in no significant change in the mortality trend slope reported. A second modification that involved unspecified policy changes (some of these may have also affected the afferent limb) two years after the leadership and team member change also resulted in no statistical change in the reported mortality trend slope. However, combining the data over the course of all of the efferent limb changes (anesthesiology leadership, anesthesiologist membership on the rapid response system team, and policy changes did lead to a statistically significant downward slope trend in mortality ($p<0.001$) and improved odds of hospital mortality ($p=0.0014$).[55]

We graded the SOE as low for hospital mortality associated with an efferent limb model change in adult populations.

4.2.5.3.2 Incidence of Cardiorespiratory Arrest

No reviews met our inclusion criteria for this outcome.

We identified three primary studies that reported on how efferent limb modification may affect the incidence of cardiorespiratory arrest.[53,54,56]

Using a pre-post design that implemented a multi-pronged intervention that included developing and implementing rapid response system treatment protocols and enhancing data collection and analysis for performance improvement, one study found a statistically significant improvement in the incidence of cardiorespiratory arrest ($p=0.04$).[56] Since this study also made modifications to the afferent limb, attribution of the outcome improvements to the efferent limb modifications alone is not possible.

The second study by modified their nurse led efferent limb rapid response system to a physician-led efferent limb and identified a statistically significant drop for the incidence of arrest from 2.2 to 0.8 events per 1000 patient days. These improvements applied to both pulseless electrical activity arrests as well as shockable rhythm arrests (ventricular tachycardia and ventricular fibrillation).[53]

The third study[54] examined the introduction of care algorithms into their existing rapid response system program and found no change in the incidence of cardiorespiratory arrest on the general pediatric ward after these modifications were made.

We graded the SOE as low for incidence of cardiorespiratory arrest associated with an efferent limb model change in adult populations.

4.2.5.3.3 Transition to Higher Level of Care

No reviews met our inclusion criteria for this outcome.

We identified two primary studies that reported on modifications to the efferent limb and their impact on transfer to a higher level of care as well as other outcomes.[52,54]

One study in adults[52] found that, after changing the composition of their rapid response system efferent limb from a physician-led team to a nurse-led team, that unanticipated ICU transfers dropped by 35.9 percent over time while the adjusted length of stay in the ICU increased by 0.44 days. No statistical analysis was given as to whether these were significant changes. The other study performed in a pediatric population[54] found no statistically significant change in unplanned transfer to a higher level of care.

We graded the SOE as insufficient for transition to higher level of care associated with an efferent limb model change in both adult and pediatric populations.

4.2.5.3.4 Other Serious Adverse Events Related to Clinical Deterioration

We identified one primary study[54] that examined whether the introduction of specific care algorithms into an existing pediatric rapid response system would change their primary outcome of a "critical deterioration event" which was defined as an event that required intubation, noninvasive positive pressure ventilation or the need to use vasopressors within 12 hours of arriving in the PICU. Secondary outcomes included transfer to the PICU, PICU length of stay, intubation within 1 and 12 hours of PICU admission, and mortality prior to PICU discharge. For overall unplanned transfer to the PICU from the general ward, the post-implementation period showed a small drop from 8.08 to 7.62 per 1,000 patient days (no p-value or other statistic given), though there was substantial month to month variation. The number of transfers after rapid response system activation went up significantly ($p<0.001$). Clinical deterioration events did not change immediately after implementation of the algorithms, but the authors reported a statistically significant beneficial change ($p<0.001$) in the trajectories for all of the outcomes over the post-modification period as compared to the trajectories of the pre-modification period.

We graded the SOE as insufficient for other serious adverse events associated with an efferent limb model change in pediatric populations.

4.2.5.3.5 Unintended Consequences of the Efferent Limb Team Members Leaving Their Primary Responsibilities to Respond to An Activation

No studies met our inclusion criteria for this outcome.

4.2.6 Question 6. What Are Common Barriers, Limitations, and Facilitators to Successfully Implementing a Rapid Response System?

One primary study included in this review provided information about facilitators. Winterbottom et al. reported that implementation of the rapid response system restructuring intervention was facilitated by staff support, standardized practices, and enhanced rapid penetration of clinical changes into routine patient care as well as a financial return on investment demonstrated for staffing salary support.[44]

Two studies included in this review reported on implementation barriers. Both studies reported barriers with afferent limb recognition (which may include knowledge deficits, miscommunications, and poorly acquired or low fidelity data) and rapid response system activation. The barriers included variable frequency of nursing vital sign checks (particularly at night),[48] and poor multidisciplinary collaboration, including communication of change in patient condition,[48] and lack of nurse comfort in nurses consulting with a physician-led team.[48,52]

The barriers and facilitators reported above are consistent with a review of qualitative evaluations of rapid response system implementation from 22 studies which found barriers and facilitators in three areas: the administrative and quality improvement aspects of rapid response system implementation, the afferent limb, and connections between the afferent and efferent limbs.[71] Leadership support, shared mission, involvement of healthcare professionals, continuous quality improvement, and interprofessional training were facilitators in the administrative aspects of rapid response system implementation and lack of commitment, unclear protocols, lack of staff and equipment, and poorly designed monitoring and documentation systems were recurring barriers. In the afferent limb, knowledge of the patient, clear protocols, and empowered nurses and physicians were common facilitators, whereas high staff workload, breakdowns between vital sign measurement and interpretation, hierarchy, and poor usability of the monitoring and documentation systems were barriers. For connections between the afferent and efferent limbs, expertise of staff members and patient-centered teamwork were documented facilitators, and reprimanding staff across the hierarchy (which reduces psychological safety and speaking up) and hesitancy to activate for patients before a critical event when deterioration was still uncertain were barriers.

4.2.7 Question 7. What Resources (e.g., Cost, Staff, Time) Are Required for Implementation of Rapid Response Systems?

None of the included studies provided information about resources required to implement the rapid response system. The first consensus conference on rapid response systems[63] identified four core components of an effective RRS. These included the afferent limb focused on detection and recognition of deterioration; an

efferent limb of qualified clinical responders, an administrative component, and a data collection and quality improvement component for self-analysis. The resources for establishing these may vary depending on local availability.

A dedicated, and ideally funded, individual or individuals should be established for data collection and analysis. Depending on the size of the hospital and the volume of activations, this position and role may require a full-time employee. Additionally, an administrator(s) will need a portion of dedicated time to oversee the program. This may be an individual, team or committee.

A core resource necessary for implementing a rapid response program is the efferent limb of clinical responders. The most common efferent limb staffing model is based on dual role staffing, where responding to an RRS activation is secondary to the primary clinical responsibility. These staff are usually critical care clinicians (nurses and/or physicians) whose primary duty is patient care in an ICU but who leave that role, temporarily, to respond to a rapid response system activation. Some hospitals, due to staffing limitations (for example, no critical care physicians), rely on other models such as deploying emergency medicine clinicians as their efferent limb. While dual roles may not increase staffing costs, this model may come at other costs, such as the potential for adverse events in unattended ICU patients, work stress, and staff burnout. The adverse events in ICU patients may occur due to the ICU providers stepping away from the ICU to go to the rapid response system activation. This may leave the ICU under-resourced, especially if the activation consumes considerable time. Finally, educational resources are necessary for the afferent limb. The afferent limb and its shortcomings were specifically addressed by the second consensus conference on rapid response systems; "Identifying the hospitalized patient in crisis"—A consensus conference on the afferent limb of Rapid Response Systems."[72] This conference identified several resources necessary for an effective afferent limb. These include educational resources such as simulation exercises to train and educate general ward staff on the purpose of the rapid response system, how to recognize signs of deterioration, and how to activate the team. They also include resources to improve the quality and fidelity of vital sign acquisition, including development of early warning scores and potentially implementing better monitoring hardware and software. The latter would likely incur significant financial costs.

While we did not identify any studies on cost-effectiveness or financial costs, one systematic review on the unintended consequences of using ICU staff to respond to rapid response system calls noted that ameliorating risks to ICU patients caused by the absence of ICU staff would require a different efferent limb staffing approach. For example, a standalone rapid response system could rely on one clinician whose sole responsibility would be the rapid response system.[38] Such an approach would cost hospitals additional full-time employee salaries to staff the rapid response system as a single-role clinical activity. One included primary study evaluated a dedicated Rapid Response Nurse role[44] and while no formal financial data was included, the study did report a financial return on investment for this staffing model.

4.2.8 Question 8. What Toolkits Are Available To Support Implementation of Rapid Response Systems?

No original studies or systematic reviews included in this rapid review provided information about toolkits for implementing a rapid response system. The toolkit used in the initial national implementation campaign for rapid response systems is still available:

- *IHI's How-to Guide for Deploying Rapid Response Systems* which was initially developed as a part of the 5 Million Lives Campaign.[73] This resource has not been updated since 2008.

5. Discussion

5.1 Summary and Interpretation of Findings

Since the Making Healthcare Safer (MHS) III report was completed in 2019, the number and type of studies examining the impact of rapid response systems in the United States has shifted to include a substantial number of studies examining how either the afferent limb or efferent limb or both components of rapid response systems might be improved to achieve better outcomes. Specifically, the number of publications has increased from one identified in MHS III that compared a resident led rapid response system to an attending physician led rapid response system, to fourteen in this review.

Only one systematic review with a meta-analysis has been published since the MHS III report and most of the studies included in that systematic review were not done in United States hospitals. The meta-analysis presented in that systematic review found overall benefit from rapid response systems for both hospital mortality and the incidence of cardiorespiratory arrest though there was heterogeneity in these outcomes across hospitals. Most hospitals achieved substantial reductions while a few others did not experience any reduction in these outcomes. This is consistent with the previously published systematic reviews,[16-20] but stands in contrast to a Cochrane systematic review included here,[37] which showed no beneficial effect from implementation of a rapid response system for any of the outcomes examined. This Cochrane review excluded many studies that were included in the other systematic reviews due to extremely stringent inclusion criteria which may explain their divergent conclusions. The other systematic reviews with meta-analyses, including the one identified in our review, found that rapid response systems are associated with a statistically significant 10–15 percent risk reduction in hospital mortality and a 35–40 percent risk reduction in the incidence of cardiorespiratory arrest. The impact of the rapid response systems on transition to a higher level of care (unanticipated ICU admission typically) is much less clear. However, these reviews are in agreement with the Cochrane study regarding the low or very low quality and high risk of bias of their included primary studies.

In our review of primary studies examining the impact of rapid response systems on mortality, one study in adults found no benefit while all of the others, including the pediatric studies, found benefit. For the incidence of cardiorespiratory arrest, only two studies used a definition that is consistent with previous studies and the MHS III report. One study found benefit while the other study, which was in a restricted patient population, (and therefore possibly not generally applicable), found no benefit. The impact on transition to a higher level of care was highly variable.

We conclude that rapid response systems may have a large impact on hospital mortality and an even greater impact on the incidence of cardiorespiratory arrest. We base these conclusions on the clinical impact that the measured reductions would have. A ten percent reduction in mortality is clinically important. It means that 1 out of every 15 patients who would otherwise die will survive. Given that overall ICU

mortality in the United States for adult patients is between 10 percent and 29 percent, and the overall mortality rate for pediatric ICU patients ranges from 2 percent to 6 percent[74] and mortality from cardiorespiratory arrest is approximately 70 percent,[4] these reductions are clinically important and large. Unfortunately, the quality of the data supporting all of these conclusions and the certainty of the conclusions is low due to methodological weaknesses.

We can draw no conclusion regarding the impact on unanticipated transfer to a higher level of care. If a rapid response system can effectively respond and stabilize patients on the general ward, unanticipated ICU admission may go down. Alternatively, the need for transfer to an ICU may increase due to better response to life threatening deterioration that might otherwise progress to arrest and death.

As rapid response systems mature, many institutions are implementing modifications to their programs to achieve success where they previously failed or for achieving greater success in hospitals that still see room for further improvement. We conclude that implementing modifications to rapid response systems, both in the afferent and efferent limbs, is warranted and yields positive results. The afferent limb has been the focus of most of the research on how to improve rapid response systems and deterioration recognition/response, in general. Studies focused on monitoring and early warning system strategies are numerous, but a more limited set of studies have directly linked implementation of any one or more strategies to clinical outcomes prospectively. Studies that did do this, either alone or in combination with other modifications to the afferent limb, resulted in mortality improvements in all primary studies we identified, with several reaching statistical significance. The data was more limited for cardiorespiratory arrest but also found a large benefit. Modifications to the efferent limb also resulted in reductions in the risk of mortality and the incidence of cardiorespiratory arrest in all of the primary studies reporting these two outcomes. These results were statistically significant in all studies reporting statistical analysis. Transfer to higher level of care was not consistently affected by afferent or efferent limb modifications.

Family-initiated rapid response system (FIRRS) activation is an afferent limb modification that deserves more attention. While FIRRS should be analyzed in comparison to clinician activation so both can learn from each other to improve care and outcomes, we suggest that FIRRS programs should also be examined through a different perspective as well, since the underlying reasons described for FIRRS activations are often quite different. Clinician activation is usually driven by physiological instability. While physiological instability may also be present during a FIRRS activation, family activation occurs primarily because of poor pain management and lack of communication regarding the plan of care. It may be appropriate to compare family activations across hospitals to each other, in addition to comparisons to clinician activations, to learn how to better engage family members in the afferent limb. Family activation is likely a marker for poor communication with clinical staff and may even be influenced by social determinants of health. Family activation may give families a tool when they believe the health system is failing them

and more in-depth analysis is required. However, it is also essential to compare family-initiated and clinician-initiated activations when there is physiological instability to understand if and how families recognize subtle signs, such as mental status change, better than clinicians, how they translate this into a FIRRS activation, and how to best use this to the patient's benefit.

Rapid response systems may have unintended consequences, most notably, a risk to ICU patients when an efferent limb staffing model is implemented that pulls critical care nurses from their primary responsibility of caring for ICU patients. This was a common model described in the publications we identified, but it may not be the most common model nationally. Whether this unintended consequence applies to other ICU providers (physicians, respiratory therapists, etc.) is unknown. While we did not identify any studies in our review on cost-effectiveness or financial costs, the authors reporting on these unintended consequences noted that ameliorating some of these risks to ICU patients would require different efferent limb staffing approaches that may engender additional full-time employee salaries.

Overall, rapid response systems appear to be effective in reducing mortality and the incidence of cardiorespiratory arrest. However, not every hospital or patient population benefits equally. This may result from differences between hospitals in the culture of safety and teamwork or resources (human, monitoring, data collection and analysis, financial) available. Heterogeneity in outcomes may also be secondary to local deficiencies and limitations in the afferent and efferent limbs. Some patient populations may have an inherently lower risk of deterioration limiting impact. Unfortunately, these issues are only recently being evaluated in the literature. Ongoing research on developing improvements in the afferent and efferent limb should help to enhance the benefit of rapid response systems and, hopefully, ensure that all hospitals and patient populations experience improved outcomes. Other areas that deserve more attention include barriers and facilitators encountered, resources required, and updated toolkits to support the implementation process.

5.2 Limitations

The quality of the rapid response systems literature is generally low and limited by significant heterogeneity and risk of bias, with no studies presenting a low risk of bias. For example, while the Danesh et al. (2019) study had a low risk of bias assessment in 6 of the 7 domains, this study had an overall moderate risk of bias due to concern for bias in the selection of reported results.[46] Many other studies had a critical risk of bias because of concerns due to confounding factors, such as Bavare et al. (2018) where this information was lacking.[33] Primary studies often draw conclusions with limited or no statistical analysis. All primary studies are observational though some apply cluster randomization designs. Because of these reasons we can only report associations not causality and these are reported with low certainty.

Some of the studies included older data that may not reflect the current state of the systems. However, this review still helps to provide insight about how rapid response

systems have matured in recent years because we focused on studies that assessed afferent and efferent limb modifications in existing rapid response systems.

Another limitation to consider is that this analysis deconstructed systems that have integrated and possibly interdependent components between the afferent and efferent limbs. While that distinction is important and informative, it may also have limited the ability to determine the effectiveness of the intervention as a unified whole.

Our review is also limited in that we restricted eligible publications to recent primary studies performed in the United States or reviews that included primary studies in the United States. We realize that studies of rapid response systems have been done in other countries over the last 5 years. While many of these health systems bear close resemblance to ours, this limitation is also a strength for those who seek a focused perspective on the effectiveness of rapid response systems in the United States.

5.3 Implications for Clinical Practice and Future Research

Future efforts should focus on improving the quality of research in this area by addressing better study design, reporting both numerator and denominator data in a standardized and consistent manner and improving statistical analysis to justify conclusions made by investigators. In general, including comprehensive data elements and providing better statistical analysis could improve the quality of studies of rapid response systems. While the inherent difficulties of using randomization methods in rapid response system study design may limit the types of data that can be collected, there is much room for improvement in the science on rapid response systems.

Despite the limitations, low quality of many studies, and the heterogeneity in results, rapid response system appear to be effective. Given the limited number of studies examining the implementation of a rapid response system where one did not previously exist, we conclude that there are few hospitals in the United States without some type of rapid response system. However, there appears to be much opportunity for improvement in outcomes and processes. The measured effect that rapid response systems have on outcomes has not changed over the course of time as calculated by the several published meta-analyses; achieving greater effectiveness will require further research into modifications in both the afferent and efferent limbs. Hospitals should consider carefully how they staff the efferent limb given the risk that staffing the rapid response team with dual role ICU providers may have for patients already in the ICU. While there are no direct comparisons of an afferent limb modification against an efferent limb modification, based on our review, we suggest afferent limb modifications should be considered first, especially the application of early warning system scoring.

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Disclaimers

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The information in this report is intended to help healthcare decision makers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of healthcare services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any

medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

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Afterword

Recognized for excellence in conducting comprehensive systematic reviews, the Agency for Healthcare Research and Quality (AHRQ) Evidence-based Practice Center (EPC) Program is developing a range of rapid evidence products to assist end-users in making specific decisions in a limited timeframe. AHRQ recognizes that people are struggling with urgent questions on how to make healthcare safer. AHRQ is using this rapid format for the fourth edition of its Making Healthcare Safer series of reports, produced by the EPC Program and the General Patient Safety Program. To shorten timelines, reviewers make strategic choices about which processes to abridge. However, the adaptations made for expediency may limit the certainty and generalizability of the findings from the review, particularly in areas with a large literature base. Transparent reporting of the methods used and the resulting limitations of the evidence synthesis are extremely important.

AHRQ expects that these rapid evidence products will be helpful to health plans, providers, purchasers, government programs, and the healthcare system as a whole. Transparency and stakeholder input are essential to AHRQ. If you have comments related to this report, they may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to MHS@ahrq.hhs.gov.

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Appendixes

Appendix A. Methods

Search Strategies for Published Literature

Table A-1. PubMed search strategy

#	Concept	Search Terms
1	Rapid Response Systems	"Hospital Rapid Response Team"[Mesh] OR "rapid response team" [tiab] OR "rapid response teams"[tiab] OR "rapid response system" [tiab] OR "rapid response systems" [tiab] OR "medical emergency team" [tiab] OR "medical emergency teams" [tiab] OR "emergency medical team" [tiab] OR "emergency medical teams" [tiab] OR "patient at-risk team" [tiab] OR "patient at risk team" [tiab] OR "critical care outreach"[tiab]
2	Standard Patient safety/harm search string for all PSPs topics	"patient safety"[mh] OR "patient safety" [tiab] OR "Patient Harm"[mh] OR "Patient Harm*"[tiab] OR "patient risk*"[tiab] OR "quality care" [tiab] OR "adverse event*"[tiab] OR "undesired event*"[tiab] OR "medical errors"[mh] OR "medical error*"[tiab] OR "Diagnostic Errors" [mh] OR "diagnostic error*"[tiab] OR "diagnostic mistake*"[tiab] OR "health care error*"[tiab] OR "healthcare error*"[tiab] OR "medical fault*"[tiab] OR "medical mistake*"[tiab] OR "erroneous diagnos*"[tiab] OR "failure to diagnose"[tiab] OR "false diagnos*"[tiab] OR "faulty diagnos*"[tiab] OR misdiagnos*[tiab] OR "mistaken diagnos*"[tiab] OR "wrong diagnos*"[tiab] OR "Clinical Deterioration" [mh] OR Deterioration [tiab] OR Deteriorations [tiab] OR Decompensation [tiab] OR deteriorating [tiab] OR resuscitation [mh] OR resuscitation [tiab] OR resuscitations [tiab] OR resuscitate [tiab] OR resuscitating [tiab] OR cardiopulmonary [tiab] OR "cardiac arrest" [tiab] OR "cardiac arrests" [tiab] OR "Failure to Rescue, Health Care" [mh] OR "Failure-to-Rescue" [tiab] OR "Failure to Rescue" [tiab] OR implement* [tiab] OR mortality [tiab] OR "Hospital Mortality" [mh]
3	#1 AND #2	
4	Limit to January 1, 2018 -June 2023	

Table A-2. Cochrane search strategy

#	Concept	Search Terms
1	Rapid Response Systems	("rapid response team" OR "rapid response teams" OR "rapid response system" OR "rapid response systems" OR "medical emergency team" OR "medical emergency teams" OR "emergency medical team" OR "emergency medical teams" OR "patient at-risk team" OR "patient at-risk team" OR "critical care outreach"):ti OR ("rapid response team" OR "rapid response teams" OR "rapid response system" OR "rapid response systems" OR "medical emergency team" OR "medical emergency teams" OR "emergency medical team" OR "emergency medical teams" OR "patient at-risk team" OR "patient at-risk team" OR "critical care outreach"):ab OR MeSH descriptor: [Hospital Rapid Response Team] explode all trees

#	Concept	Search Terms
2	Standard Patient safety/harm search string for all PSPs topics	("patient safety" OR "Patient Harm*" OR "patient risk*" OR "quality care" OR “adverse event" OR “adverse events” OR "undesired event" OR "undesired events" OR "medical error" OR “medical errors” OR "diagnostic error" OR "diagnostic errors” OR "diagnostic mistake" OR "diagnostic mistakes" OR "health care error" OR "health care errors" OR "healthcare error" OR "medical fault" OR "medical mistake" OR "erroneous diagnoses" OR "failure to diagnose" OR "false diagnoses" OR "faulty diagnoses" OR misdiagnose OR misdiagnoses OR "mistaken diagnoses" OR "wrong diagnoses" OR Deterioration OR Deteriorations OR Decompensation OR deteriorating OR resuscitation OR resuscitations OR resuscitate OR resuscitating OR cardiopulmonary OR "cardiac arrest" OR "cardiac arrests" OR “Failure-to-Rescue” OR “Failure to Rescue” OR implement* OR mortality):ti OR ("patient safety" OR "Patient Harm*" OR "patient risk*" OR "quality care" OR “adverse event" OR “adverse events” OR "undesired event" OR "undesired events" OR "medical error" OR “medical errors” OR "diagnostic error" OR "diagnostic errors” OR "diagnostic mistake" OR "diagnostic mistakes" OR "health care error" OR "health care errors" OR "healthcare error" OR "medical fault" OR "medical mistake" OR "erroneous diagnoses" OR "failure to diagnose" OR "false diagnoses" OR "faulty diagnoses" OR misdiagnose OR misdiagnoses OR "mistaken diagnoses" OR "wrong diagnoses" OR Deterioration OR Deteriorations OR Decompensation OR deteriorating OR resuscitation OR resuscitations OR resuscitate OR resuscitating OR cardiopulmonary OR "cardiac arrest" OR "cardiac arrests" OR “Failure-to-Rescue” OR “Failure to Rescue” OR implement* OR mortality):ab OR MeSH descriptor: [patient safety] explode all trees OR MeSH descriptor: [Patient Harm] explode all trees OR MeSH descriptor: [medical errors] explode all trees OR MeSH descriptor: [Diagnostic Errors] explode all trees OR MeSH descriptor: [Clinical Deterioration] explode all trees OR MeSH descriptor: [resuscitation] explode all trees OR MeSH descriptor: [Failure to Rescue, Health Care] explode all trees OR MeSH descriptor: [Hospital Mortality] explode all trees
3	#1 AND #2	
4.	Limit to January 1, 2018 -June 2023	

Appendix B. List of Excluded Studies Upon Full-Text Review

1. Acorda DE, Bracken J, Abela K, et al. Longitudinal Evaluation of a Pediatric Rapid Response System with Realist Evaluation Framework. Jt Comm J Qual Patient Saf. 2022 Apr;48(4):196-204. doi: 10.1016/j.jcjq.2022.01.004. PMID: 35181251. **- Study design is not specified or no comparison group described**
2. Acworth J, Dodson L, Acworth E, et al. Changing patterns in paediatric medical emergency team (MET) activations over 20 years in a single specialist paediatric hospital. Resusc Plus. 2020 Sep;3:100025. doi: 10.1016/j.resplu.2020.100025. PMID: 34223308. **- Study design is not specified or no comparison group described**
3. Ahmed M, Sarwer F, Gunjan, et al. Evaluation of Automated Alert and Activation of Medical Emergency Team in Head and Neck Cancer Patients Using Early Warning Score at Tertiary Level Hospital in North India. Cureus. 2022 Nov;14(11):e31428. doi: 10.7759/cureus.31428. PMID: 36524959. **- Study setting not in the United States**
4. Ahn JH, Jung YK, Lee JR, et al. Predictive powers of the Modified Early Warning Score and the National Early Warning Score in general ward patients who activated the medical emergency team. PLoS One. 2020;15(5):e0233078. doi: 10.1371/journal.pone.0233078. PMID: 32407344. **- No defined historical or contemporaneous cohort comparison group**
5. Almeida MC, Portela MC, Paiva EP, et al. Implementation of a rapid response team in a large nonprofit Brazilian hospital: improving the quality of emergency care through Plan-Do-Study-Act. Rev Bras Ter Intensiva. 2019 Jun 10;31(2):217-26. doi: 10.5935/0103-507x.20190036. PMID: 31215601. - **Study setting not in the United States**
6. Al-Omari A, Al Mutair A, Aljamaan F. Outcomes of rapid response team implementation in tertiary private hospitals: a prospective cohort study. Int J Emerg Med. 2019 Oct 30;12(1):31. doi: 10.1186/s12245-019-0248-5. PMID: 31666005. - **Study setting not in the United States**
7. Alves Silva LM, Moroço DM, Pintya JP, et al. Clinical impact of implementing a rapid-response team based on the Modified Early Warning Score in wards that offer emergency department support. PLoS One. 2021;16(11):e0259577. doi: 10.1371/journal.pone.0259577. PMID: 34762677. - **Study setting not in the United States**
8. Anantharam P, Hoffman A, Noonan M, et al. Addressing Operational Challenges Faced by COVID-19 Public Health Rapid Response Teams

in Non-United States Settings. Disaster Med Public Health Prep. 2022 Aug;16(4):1599-603. doi: 10.1017/dmp.2020.487. PMID: 33719992. **- Not rapid response system**

9. Anstey MH, Bhasale A, Dunbar NJ, et al. Recognising and responding to deteriorating patients: what difference do national standards make? BMC Health Serv Res. 2019 Sep 5;19(1):639. doi: 10.1186/s12913-019-4339-z. PMID: 31488141. **- No outcome of interest**
10. Areia C, Biggs C, Santos M, et al. The impact of wearable continuous vital sign monitoring on deterioration detection and clinical outcomes in hospitalised patients: a systematic review and meta-analysis. Crit Care. 2021 Sep 28;25(1):351. doi: 10.1186/s13054-021-03766-4. PMID: 34583742. **- Focused on patient monitoring systems/early warning system validation only**
11. Arora V, Juneja D, Singh O, et al. The epidemiology and outcomes of adult rapid response team patients in a tertiary care hospital in India. Med Intensiva (Engl Ed). 2022 Oct;46(10):577-80. doi: 10.1016/j.medine.2021.11.022. PMID: 36155680. **- No original data**
12. Ashbeck R, Stellpflug C, Ihrke E, et al. Development of a Standardized System to Detect and Treat Early Patient Deterioration. J Nurs Care Qual. 2021 Jan-Mar 01;36(1):32-7. doi: 10.1097/ncq.0000000000000484. PMID: 32282504. **- No defined historical or contemporaneous cohort comparison group**
13. Azimirad M, Magnusson C, Wiseman A, et al. A clinical competence approach to examine British and Finnish nurses' attitudes towards the rapid response system model: A study in two acute hospitals. Aust Crit Care. 2022 Jan;35(1):72-80. doi: 10.1016/j.aucc.2021.02.011. PMID: 34088574. **- No outcome of interest**
14. Azimirad M, Magnusson C, Wiseman A, et al. British and Finnish nurses' attitudes, practice, and knowledge on deteriorating patient in-service education: A study in two acute hospitals. Nurse Educ Pract. 2021 Jul;54:103093. doi: 10.1016/j.nepr.2021.103093. PMID: 34052539. **- No outcome of interest**
15. Azimirad M, Magnusson C, Wiseman A, et al. Identifying teamwork-related needs of the medical emergency team: Nurses' perspectives. Nurs Crit Care. 2022 Nov;27(6):804-14. doi: 10.1111/nicc.12676. PMID: 34216412. - **Study setting not in the United States**
16. Azimirad M, Magnusson C, Wiseman A, et al. Nurses' ability to timely activate rapid response systems for deteriorating patients: A comparative case scenario study between Finnish and British nurses. Intensive Crit Care Nurs. 2020 Oct;60:102871. doi: 10.1016/j.iccn.2020.102871. PMID: 32651053. **- No outcome of interest**
17. Baig MM, GholamHosseini H, Afifi S, et al. A systematic review of rapid response applications based on early warning score for early detection of inpatient deterioration. Inform Health Soc Care. 2021 Jun 2;46(2):148-57. doi:

10.1080/17538157.2021.1873349. PMID: 33472485. **- No outcome of interest**

18. Balshi AN, Al-Odat MA, Alharthy AM, et al. Tele-Rapid Response Team (Tele-RRT): The effect of implementing patient safety network system on outcomes of medical patients-A before and after cohort study. PLoS One. 2022;17(11):e0277992. doi: 10.1371/journal.pone.0277992. PMID: 36413553. - **Study setting not in the United States**
19. Bassin L, Raubenheimer J, Bell D. The implementation of a real time early warning system using machine learning in an Australian hospital to improve patient outcomes. Resuscitation. 2023 May 5;188:109821. doi: 10.1016/j.resuscitation.2023.109821. PMID: 37150397. - **Study setting not in the United States**
20. Batterbury A, Douglas C, Coyer F. The illness severity of ward remaining patients reviewed by the medical emergency team: A retrospective cohort study. J Clin Nurs. 2023 Mar 9doi: 10.1111/jocn.16678. PMID: 36894523. **- No defined historical or contemporaneous cohort comparison group**
21. Bavare AC, Afonso NS, Sembera KA, et al. Paediatric cardiac rapid response systems: a survey of multicentre practices. Cardiol Young. 2022 Jun;32(6):944-51. doi: 10.1017/s1047951121003322. PMID: 34407898. **- No defined historical or contemporaneous cohort comparison group**
22. Bavare AC, Bracken JA, Guffey D, et al. Comparison of Rapid-Response Systems Across Multisite Locations of a Pediatric Hospital System. Hosp Pediatr. 2020 Jul;10(7):563-9. doi: 10.1542/hpeds.2019-0280. PMID: 32601053. **- No defined historical or contemporaneous cohort comparison group**
23. Bellomo R, Chan M, Guy C, et al. Laboratory alerts to guide early intensive care team review in surgical patients: A feasibility, safety, and efficacy pilot randomized controlled trial. Resuscitation. 2018 Dec;133:167-72. doi: 10.1016/j.resuscitation.2018.10.012. PMID: 30316952. - **Study setting not in the United States**
24. Berrens ZJ, Gosdin CH, Brady PW, et al. Efficacy and Safety of Pediatric Critical Care Physician Telemedicine Involvement in Rapid Response Team and Code Response in a Satellite Facility. Pediatr Crit Care Med. 2019 Feb;20(2):172-7. doi: 10.1097/pcc.0000000000001796. PMID: 30395026. **- No defined historical or contemporaneous cohort comparison group**
25. Berry D, Street M, Hall K, et al. Recognizing and responding to clinical deterioration in adult patients in isolation precautions for infection control: a retrospective cohort study. Int J Qual Health Care. 2022 Apr 12;34(2)doi: 10.1093/intqhc/mzac020. PMID: 35323935. **- No outcome of interest**

26. Bhonagiri D, Lander H, Green M, et al. Reduction of in-hospital cardiac arrest rates in intensive care-equipped New South Wales hospitals in association with implementation of Between the Flags rapid response system. Intern Med J. 2021 Mar;51(3):375-84. doi: 10.1111/imj.14812. PMID: 32133760. - **Study setting not in the United States**

27. Bingham G, Fossum M, Hughes L, et al. The pre-Medical Emergency Team response: Nurses' decision-making escalating deterioration to treating teams using urgent review criteria. J Adv Nurs. 2020 May 20doi: 10.1111/jan.14433. PMID: 32432363. **- No original data**

28. Bittle M, O'Rourke K, Srinivas SK. Interdisciplinary Skills Review Program to Improve Team Responses During Postpartum Hemorrhage. J Obstet Gynecol Neonatal Nurs. 2018 Mar;47(2):254-63. doi: 10.1016/j.jogn.2017.09.002. PMID: 29080398. **- Not rapid response system**

29. Blans MJ, Bousie E, van der Hoeven JG, et al. A point-of-care thoracic ultrasound protocol for hospital medical emergency teams (METUS) improves diagnostic accuracy. Ultrasound J. 2021 Jun 4;13(1):29. doi: 10.1186/s13089-021-00229-3. PMID: 34089087. - **Study setting not in the United States**

30. Bloos F. The importance of a hospital-dedicated sepsis response team. Expert Rev Anti Infect Ther. 2020 Dec;18(12):1235-43. doi: 10.1080/14787210.2020.1794813. PMID: 32662689. **- Inclusion of non-general ward patients**

31. Breen D, O'Brien S, McCarthy N, et al. Effect of a proficiency-based progression simulation programme on clinical communication for the deteriorating patient: a randomised controlled trial. BMJ Open. 2019 Jul 9;9(7):e025992. doi: 10.1136/bmjopen-2018-025992. PMID: 31289064. **- Non-patients (staff, visitors) who are not covered by rapid response teams**

32. Bucknall TK, Considine J, Harvey G, et al. Prioritising Responses Of Nurses To deteriorating patient Observations (PRONTO): a pragmatic cluster randomised controlled trial evaluating the effectiveness of a facilitation intervention on recognition and response to clinical deterioration. BMJ Qual Saf. 2022 Apr 21;31(11):818-30. doi: 10.1136/bmjqs-2021-013785. PMID: 35450936. - **Study setting not in the United States**

33. Bunch JL, Groves PS, Perkhounkova Y. Realistic Evaluation of a Rapid Response System: Context, Mechanisms, and Outcomes. West J Nurs Res. 2019 Apr;41(4):519-36. doi: 10.1177/0193945918776310. PMID: 29768987. **- No defined historical or contemporaneous cohort comparison group**

34. Bunkenborg G, Barfod O'Connell M, Jensen HI, et al. Balancing responsibilities, rewards and challenges: A qualitative study illuminating the complexity of being a rapid response team nurse. J Clin

Nurs. 2022 Dec;31(23-24):3560-72. doi: 10.1111/jocn.16183. PMID: 34985170. **- No outcome of interest**

35. Burke J, Wood S, Hermon A, et al. Improving outcome of sepsis on the ward: introducing the 'Sepsis Six' bundle. Nurs Crit Care. 2019 Jan;24(1):33-9. doi: 10.1111/nicc.12358. PMID: 30039637. **- Inclusion of non-general ward patients**

36. Campbell V, Conway R, Carey K, et al. Predicting clinical deterioration with Q-ADDS compared to NEWS, Between the Flags, and eCART track and trigger tools. Resuscitation. 2020 Aug;153:28-34. doi: 10.1016/j.resuscitation.2020.05.027. PMID: 32504769. **- Focused on patient monitoring systems/early warning system validation only**

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Appendix C. Evidence Tables

Note: References are located in the reference list in the body of the report.

Evidence Table C-1. Included systematic reviews addressing harms, effectiveness and unintended effects of rapid response systems

Author, Year Quality of Review	Objective*	Literature Search Date	Number of Included Studies	Quality Assessment Tool Used in the Review*	Outcome of Interest*	Authors' Conclusions*
Fildes, 2022 [38] Good	To synthesize the available evidence on the consequences of ICU nurses' absence due to attending rapid response calls away from the ICU on service delivery and resourcing in the ICU.	March 2020	9 6= quantitative 2 =qualitative 1=mixed	The flexible appraisal tool of Law et al for quantitative studies, the Critical Appraisal Skills Program checklist for qualitative studies, and a tool introduced by Pluye et al for mixed study.[39, 75, 76]	Four key themes were identified: (1) workforce, staffing processes, and resource allocation; (2) alterations to workload and resource allocation; (3) adverse events or incidents; and (4) funding variability of rapid response team models. Review of the studies indicated that dual intensive care unit and rapid response team nursing roles have negative effects on nurses' workload, increase the risk of adverse events, and may compromise patient safety.	The staffing of both the intensive care unit and the rapid response team should be examined carefully with an eye toward sustainability, cost-effectiveness, and clear outcome measures.
McGaughey, 2021[37] Good	To determine the effect of EWS and RRS implementation on adults who deteriorate on acute hospital wards compared to people receiving hospital care without EWS and RRS in place.	March 2019	11 4= randomized trials 7= non-randomized studies	Cochrane risk of bias tool The GRADE system for quality of evidence	**Hospital mortality:** Randomized trials provided low-certainty evidence that an EWS and RRS intervention may result in little or no difference in hospital mortality (4 studies, 455,226 participants; results not pooled). The evidence on hospital mortality from 3 non-randomized studies was of very low certainty (210,905 participants)." **Unplanned ICU admissions:** Randomized trials provided low-certainty evidence that an EWS and RRS intervention may result in little or no difference in unplanned ICU admissions (3 studies, 452,434 participants; results	Given the low-to-very low certainty evidence for all outcomes from non-randomized studies, we have drawn our conclusions from the randomized evidence. This evidence provides low-certainty evidence that EWS and RRS may lead to little or no difference in hospital mortality, unplanned ICU admissions, length of hospital stay or adverse events; and moderate-certainty evidence of little to no difference on composite outcome. The evidence from this review update highlights the diversity in

Author, Year Quality of Review	Objective*	Literature Search Date	Number of Included Studies	Quality Assessment Tool Used in the Review*	Outcome of Interest*	Authors' Conclusions*
					not pooled). The evidence from 1 non-randomized study is of very low certainty (aOR 0.88, 95% CI 0.75 to 1.02; 57,858 participants). **Composite outcome (unexpected cardiac arrests, unplanned ICU admissions and death):** One randomized study showed that an EWS and RRS intervention probably results in no difference in this composite outcome (adjusted odds ratio (aOR) 0.98, 95% CI 0.83 to 1.16; 364,094 participants; moderate-certainty evidence). One non-randomized study suggests that implementation of an EWS and RRS intervention may slightly reduce this composite outcome (aOR 0.85, 95% CI 0.72 to 0.99; 57,858 participants; low-certainty evidence).	outcome selection and poor methodological quality of most studies investigating EWS and RRS. As a result, no strong recommendations can be made regarding the effectiveness of EWS and RRS based on the evidence currently available. There is a need for development of a patient-informed core outcome set comprising clear and consistent definitions and recommendations for measurement as well as EWS and RRS interventions conforming to a standard to facilitate meaningful comparison and future meta-analyses.
Rocha, 2018[34] Good	To evaluate the effectiveness of rapid response teams using early identification of clinical deterioration in reducing the occurrence of in-hospital mortality and cardiorespiratory arrest.	2000 to 2016	15 2 clinical trials 10 observational studies 3 meta-analyses	Newcastle-Ottawa Scale for cohort studies, the modified Jadad scale for clinical trials, and the Assessment of Multiple Systematic Reviews for systematic reviews. The GRADE system for quality of evidence	**Mortality**: A total of 12 studies evaluated mortality. 9 of these studies yielded results indicating that RRTs are associated with a significant reduction in mortality, with estimates varying from 10 - 48%. The three remaining studies did not find RRTs to be effective in achieving reduced mortality. Of the three meta-analyses included, two reported no significant reduction in mortality. However, the most recent meta-analysis conducted in 2015 indicated a statistically significant reduction. The results of the meta-analysis of studies reporting mortality suggested that RRTs	We conclude that rapid response teams may reduce in hospital mortality and cardiac arrests, although the quality of evidence for both outcomes is low. Evidence was assessed as low quality due to the high heterogeneity and risk of bias in primary studies.

Author, Year Quality of Review	Objective*	Literature Search Date	Number of Included Studies	Quality Assessment Tool Used in the Review*	Outcome of Interest*	Authors' Conclusions*
					demonstrated a protective effect, with a risk ratio of 0.85 (95% CI 0.76 - 0.94). **Cardiopulmonary arrests**: 11 studies considered the occurrence of cardiopulmonary arrests. 9 of these studies, including two meta-analyses, presented results indicating that RRTs are associated with a significant reduction in cardiopulmonary arrest occurrence, with ORs ranging between 0.47 and 0.74. The remaining two studies did not find RRTs to be effective in reducing cardiopulmonary arrest. The results of the meta-analysis of studies: similar results were identified for the occurrence of cardiac arrest (RR 0.65; 95% CI 0.49 - 0.87).	
Teuma, 2020 [35] Good	To evaluate the evidence on whether rapid response systems decrease in-hospital mortality and non-intensive care unit cardiac arrests.	1st January 2014 to 31st October 2017	15 1 =stepped wedge cluster RCT 1 =concurrent cohort controlled study 13 =historically controlled studies	The Critical Appraisal Skills Programme (2010) The eligible studies were categorized according to Harbour and Miller's (2001) grading system[36]	**Mortality**: 13 studies investigated mortality of which 7 reported statistically significant findings in favor of rapid response systems. **Cardiac arrests**: 13 studies investigated cardiac arrests, of which 8 reported statistically significant findings in favor of rapid response systems. **Other outcomes**: 11 studies investigated both mortality and CAs, of which 8 reported a similar effect of the RRS on both outcomes while 3 reported that the RRS favored one outcome but not the other	Evidence suggests that when the process of introducing/maintaining a RRS is successful and under certain favorable conditions, RRSs significantly decrease mortality and cardiac arrests. This review indicates that the best evidence about RRS effectiveness at reducing mortality and cardiac arrests is at Level 2.

* as reported in the systematic review

aOR=adjusted odds ratio; CI=confidence interval; EWS=early warning system; GRADE=Grading of Recommendations, Assessment, Development, and Evaluations; ICU=intensive care unit; OR=odds ratio; RCT=randomized controlled trial; RR=relative risk; RRS=rapid response system; RRT=rapid response team

Evidence Table C-2. Study characteristics of included studies addressing harms, effectiveness and unintended effects of rapid response systems

Author, Year	Study Period	Study Design	Country	Hospital Information	Patient Population	Funding
Bavare, 2018[33]	2011 to 2014	Observational study with a comparison group	US	Type: Academic n: 1 Number of beds: 570 beds	Pediatric	Not reported
Danesh, 2019[46]	2010 to 2012	Pre-post	US	Type: Community n: 1 Number of beds: 237 beds	Adult	No external funding
Dean, 2020[49]	2014 to 2018	Pre-post	US	Type: Not reported n: 1 Number of beds: Not reported	Pediatric	Not reported
Escobar, 2020[47]	2015 to 2019	Pre-post	US	Type: Kaiser Permanent Northern California system n: 19 Number of beds: Not reported	Adult	Gordon and Betty Moore Foundation, the Sidney Garfield Memorial Fund, the Agency for Healthcare Research and Quality, the Permanente Medical Group, Kaiser Foundation Hospitals, and the National Institutes of Health
Factora, 2022[55]	2005 to 2018	Pre-post	US	Type: Academic n: 1 Number of beds: Not reported	Adult	Institutional and/or departmental sources
Girotra, 2022[40]	2000-2014 data	Pre-post	US	Type: Teaching, n=32, Non-teaching, n=24 n: 56 Number of beds: 200 beds: 9 (16.4%) 200 to 499 beds: 29 (52.7%) >500 beds: 17 (30.9%)	Adult	Individual investigators received contributions from the National Institutes of Health

Author, Year	Study Period	Study Design	Country	Hospital Information	Patient Population	Funding
Hatlem, 2018[52]	2005 to 2008	Observational study with a comparison group	US	Type: Not for profit n: 1 Number of beds: 870 beds	Adult	Not reported
Kolovos, 2018[41]	2005 to 2011	Pre-post	US	Type: Academic n: 1 Number of beds: 258 beds	Pediatric	The author institution received funding from the National Institutes of Health, the Department of Defense, and the Children's Discovery Institute
Kutty, 218[42]	2000 to 2015	Pre-post	US	Type: Not for profit (97.4% academic) n: 38 Number of beds: 126–249 beds: 9 hospitals 250–592 beds: 29 hospitals	Pediatric	Individual investigators received contributions from the National Institute of Child Health and Development, and the National Heart, Lung and Blood Institute
Mankidy, 2020[53]	2013 to 2017	Observational study with a comparison group	US	Type: Academic n: 1 Number of beds: 850 beds	Adult	Not reported
McKeta, 2021[43]	2015 to 2018	Pre-post	US	Type: Academic n: 1 Number of beds: 14 bed pediatric cardiac stepdown unit, 14 bed PICU	Pediatric	Not reported

Author, Year	Study Period	Study Design	Country	Hospital Information	Patient Population	Funding
Penney, 2021[50]	2015 to 2018	Pre-post	US	Type: Academic n: 1 Number of beds: 16 bed pediatric in-patient; 6 beds in PICU	Pediatric	No external funding
Sawicki, 2021[54]	2017 to 2020	Pre-post	US	Type: Not reported n: 1 Number of beds: 289 beds	Pediatric	National Center for Advancing Translational Sciences, National Institutes of Health
Sebat, 2018[56]	2008 to 2013	Pre-post	US	Type: Community n: 1 Number of beds: 500 beds	Adult	Medline Industries, Kaweah Delta Foundation
Stellpflug, 2021[48]	2016 to 2018	Observational study with a comparison group	US	Type: Academic n: 1 Number of beds: 27 beds	Adult	Not reported
Vandegrift, 2021[57]	240 months	Pre-post	US	Type: Community n: 4 Number of beds: Only reported for one hospital: 450 bed regional medical center	Not reported	Not reported

Author, Year	Study Period	Study Design	Country	Hospital Information	Patient Population	Funding
Weller, 2018[51]	10 months	Pre-post	US	Type: Academic n: 1 Number of beds: 26 beds	Not reported	Not reported
Winterbottom, 2021[44]	2017 to 2020	Pre-post	US	Type: Not reported n: 1 Number of beds: Not reported	Not reported	Not reported
Young, 2023[45]	1994 to 2018	Pre-post	US	Type: Not reported n: 1 Number of beds: Not reported	Not reported	National Heart, Lung, and Blood Institute, National Institutes of Health

n=number of hospitals; PICU=pediatric intensive care unit; US=United States

Evidence Table C-3. Incidence of cardiorespiratory arrest outcome (categorical data) of included studies comparing rapid response systems to no rapid response systems

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Kolovos, 2018[41]	Arm 1	Pre-RRT	Patients receiving CPR during PICU admission	NR	1097	NR (29)	NR	Ref	NR
Kolovos, 2018[41]	Arm 2	Post-RRT	Patients receiving CPR during PICU admission	NR	1055	NR (8)	NR	Comparison: Arm 1-Pre-RRT p-value only: p=0.001	NR
Kolovos, 2018[41]	Arm 1	Pre-RRT	CPR within first hour of ICU admission	NR	1097	NR (4)	NR	Ref	NR
Kolovos, 2018[41]	Arm 2	Post-RRT	CPR within first hour of ICU admission	NR	1055	NR (0)	NR	Comparison: Arm 1-Pre-RRT p-value only: p=NS	NR
Winterbottom, 2021[44]	Arm 1	Start of implementation	Cardiac arrests outside of ICU	2017	NR	NR	NR	Ref	NR
Winterbottom, 2021[44]	Arm 2	Post-implementation period	Cardiac arrests outside of ICU	End of 2019	NR	NR	NR	Comparison: Arm 1 - Start of implementation % difference from baseline: -0.65, p=NR	NR
Winterbottom, 2021[44]	Arm 1	Start of implementation	Cardiac arrests inside of ICU	2017	NR	NR	NR	Ref	NR
Winterbottom, 2021[44]	Arm 2	Post-implementation period	Cardiac arrests inside of ICU	End of 2019	NR	NR	NR	Comparison: Arm 1 - Start of implementation % difference from baseline: -0.27, p=NR	NR
Young, 2023[45]	Arm 1	Pre-MET	Postoperative cardiac arrest	2004-2009	7690	172 (2.2)	NR	Ref	NR
Young, 2023[45]	Arm 2	MET	Postoperative cardiac arrest	2009-2018	3528	54 (1.5)	NR	Comparison: Arm 1-Pre-MET p-value only: p=0.16	NR

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Young, 2023[45]	Arm 1	Pre-MET	Postoperative atrial fibrillation	2004-2009	7690	1680 (21.8)	NR	Ref	NR
Young, 2023[45]	Arm 2	MET	Postoperative atrial fibrillation	2009-2018	3528	860 (24.4)	NR	Comparison: Arm 1-Pre-MET p-value only: p=0.003	NR

CPR=; ICU=intensive care unit; MET=medical emergency team; N=sample size; NR=not reported; p=p-value; PICU=pediatric intensive care unit; Ref=reference arm; RRT=rapid response team

Evidence Table C-4. Incidence of cardiorespiratory arrest outcome (continuous data) of included studies comparing rapid response systems to no rapid response systems

Author, Year	Arm	Arm Name	Outcome Definition	Followup Timepoint	N at Analysis	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
McKeta, 2021[43]	Arm 1	Pre-implementation	Cardiac stepdown unit cardiac arrest rate	NR	NR	Per 1,000 patient days: 1.2	NR	Ref	NR
McKeta, 2021[43]	Arm 2	Post-implementation	Cardiac stepdown unit cardiac arrest rate	NR	NR	Per 1,000 patient days: 0	NR	Comparison: Arm 1-Pre-implementation p-value only: p=0.02	NR
McKeta, 2021[43]	Arm 1	Pre-implementation	Overall cardiac arrest rate in the cardiac ICU	NR	NR	Per 1,000 patient days: 5.6	NR	Ref	NR
McKeta, 2021[43]	Arm 2	Post-implementation	Overall cardiac arrest rate in the cardiac ICU	NR	NR	Per 1,000 patient days: 2.4	NR	Comparison: Arm 1-Pre-implementation p-value only: p=0.1	NR

ICU=intensive care unit; N=sample size; NR=not reported; p=p-value; Ref=reference arm

Evidence Table C-5. Serious adverse events related to clinical deterioration outcome (categorical data) of included studies comparing rapid response systems to no rapid response systems

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Kolovos, 2018[41]	Arm 1	Pre-RRT	Intubation within first hour of ICU admission	NR	1097	NR (49) Number of events: 4.5	NR	Ref	NR
Kolovos, 2018[41]	Arm 2	Post-RRT	Intubation within first hour of ICU admission	NR	1055	NR (88) Number of events: 8.3	NR	Comparison: Arm 1-Pre-RRT p-value only: p<0.001	NR
Young, 2023[45]	Arm 1	Pre-MET	Prolonged ventilation	2004-2009	7690	615 (8)	NR	Ref	Multivariable, risk-adjusted logistic regression, but factors not specified
Young, 2023[45]	Arm 2	MET	Prolonged ventilation	2009-2018	3528	289 (8.2)	NR	Comparison: Arm 1-Pre-MET Odds ratio: 0.92 (95% CI: 0.79 to 1.07), p=0.285	Multivariable, risk-adjusted logistic regression, but factors not specified
Young, 2023[45]	Arm 1	Pre-MET	Postoperative bleeding requiring reoperation	2004-2009	7690	201 (2.6)	NR	Ref	NR
Young, 2023[45]	Arm 2	MET	Postoperative bleeding requiring reoperation	2009-2018	3528	92 (2.6)	NR	Comparison: Arm 1-Pre-MET p-value only: p=1	NR
Young, 2023[45]	Arm 1	Pre-MET	Reoperation for any reason	2004-2009	7690	271 (3.5)	NR	Ref	Multivariable, risk-adjusted logistic regression, but factors not specified

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Young, 2023[45]	Arm 2	MET	Reoperation for any reason	2009-2018	3528	98 (2.8)	NR	Comparison: Arm 1-Pre-MET Odds ratio: 0.75 (95% CI: 0.59 to 0.95), p=0.017	Multivariable, risk-adjusted logistic regression, but factors not specified
Young, 2023[45]	Arm 1	Pre-MET	Deep sternal wound infection	2004-2009	7690	38 (0.5)	NR	Ref	Multivariable, risk-adjusted logistic regression, but factors not specified
Young, 2023[45]	Arm 2	MET	Deep sternal wound infection	2009-2018	3528	3 (0.1)	NR	Comparison: Arm 1-Pre-MET Odds ratio: 0.16 (95% CI: 0.04 to 0.45), p=0.002	Multivariable, risk-adjusted logistic regression, but factors not specified
Young, 2023[45]	Arm 1	Pre-MET	Postoperative stroke	2004-2009	7690	0 (0)	NR	Ref	NR
Young, 2023[45]	Arm 2	MET	Postoperative stroke	2009-2018	3528	8 (0.2)	NR	Comparison: Arm 1-Pre-MET p-value only: p<0.001	NR
Young, 2023[45]	Arm 1	Pre-MET	Postoperative dialysis	2004-2009	7690	93 (1.2)	NR	Ref	NR
Young, 2023[45]	Arm 2	MET	Postoperative dialysis	2009-2018	3528	73 (2.1)	NR	Comparison: Arm 1-Pre-MET p-value only: p=0.001	NR
Young, 2023[45]	Arm 1	Pre-MET	Postoperative renal failure	2004-2009	7690	395 (5.2)	NR	Ref	Multivariable, risk-adjusted logistic regression, but factors not specified

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Young, 2023[45]	Arm 2	MET	Postoperative renal failure	2009-2018	3528	118 (3.3)	NR	Comparison: Arm 1-Pre-MET Odds ratio: 0.57 (95% CI: 0.46 to 0.70), p<0.001	Multivariable, risk-adjusted logistic regression, but factors not specified
Young, 2023[45]	Arm 1	Pre-MET	Postoperative sepsis	2004-2009	7690	136 (1.8)	NR	Ref	NR
Young, 2023[45]	Arm 2	MET	Postoperative sepsis	2009-2018	3528	22 (0.6)	NR	Comparison: Arm 1-Pre-MET p-value only: p<0.001	NR

CI=confidence interval; ICU=intensive care unit; MET=medical emergency team; N=sample size; NR=not reported; p=p-value; Ref=reference arm; RRT=rapid response team

Evidence Table C-6. Serious adverse events related to clinical deterioration outcome (continuous data) of included studies comparing rapid response systems to no rapid response systems

Author, Year	Arm	Arm Name	Outcome Definition	Followup Timepoint	N at Analysis	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Kolovos, 2018[41]	Arm 1	Pre-RRT	Code rate inpatient ward (per 1,000 patient-days)	NR	1097	Per 1,000 patient days: 0.52	NR	Ref	NR
Kolovos, 2018[41]	Arm 2	Post-RRT	Code rate inpatient ward (per 1,000 patient-days)	NR	1055	Per 1,000 patient days: 0.51	NR	Comparison: Arm 1-Pre-RRT p-value only: p=NS	NR

N=sample size; NR=not reported; NS=not significant; p=p-value; Ref=reference arm; RRT=rapid response team

Evidence Table C-7. Mortality outcome (categorical data) of included studies comparing rapid response systems to no rapid response systems

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Girotra, 2022[40]	Arm 1	Initial year of implementation	Hospital mortality trend	NR	NR	NR	Relative risk: 0.98 (95% CI: 0.94 to 1.02), p=0.3	Ref	Risk adjusted (not specified)
Girotra, 2022[40]	Arm 2	Post-implementation period	Hospital mortality trend	NR	NR	NR	Relative risk: 1.01 (95% CI: 0.99 to 1.02), p=0.3	Comparison: Arm 1-Initial year of implementation p-value only: p=0.36	Risk adjusted (not specified)
Kolovos, 2018[41]	Arm 1	Pre-RRT	In-patient ward mortality	NR	1097	NR (0.04)	NR	Ref	NR
Kolovos, 2018[41]	Arm 2	Post-RRT	In-patient ward mortality	NR	1055	NR (0.07)	NR	Comparison: Arm 1-Pre-RRT p-value only: p=NS	NR
Kolovos, 2018[41]	Arm 1	Pre-RRT	ICU mortality	NR	1097	NR (4.9)	NR	Ref	NR
Kolovos, 2018[41]	Arm 2	Post-RRT	ICU mortality	NR	1055	NR (3.8)	NR	Comparison: Arm 1-Pre-RRT p-value only: p=0.001	NR
Kolovos, 2018[41]	Arm 1	Pre-RRT	ICU mortality	NR	1097	NR (4.9)	NR	Ref	NR
Kolovos, 2018[41]	Arm 2	Post-RRT	ICU mortality	NR	1055	NR (3.8)	NR	Comparison: Arm 1-Pre-RRT p-value only: p=0.001	NR
Kutty, 2018[42]	Arm 1	Before MET Intervention	Hospital mortality trend	Mean implementation duration: 3 years	Hospitalizations: 1,659,059	NR	Odds ratio: 0.94 (95% CI: 0.92 to 0.96), p=NR	Ref	Risk adjusted (not specified)

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Kutty, 2018[42]	Arm 2	After MET Intervention	Hospital mortality trend	Mean implementation duration: 7 years	Hospitalizations: 4,392,392	NR	Odds ratio: 0.94 (95% CI: 0.93 to 0.95), p=NR	Comparison: Arm 1 -After MET p-value only: p=0.98	Risk adjusted (not specified)
Kutty, 2018[42]	Arm 1	Before MET Intervention	Hospital mortality trend	Mean implementation duration: 3 years	Hospitalizations: 1,659,059	NR	Odds ratio: 0.91 (95% CI: 0.86 to 0.97), p=NR	Ref	Risk adjusted (not specified)
Kutty, 2018[42]	Arm 2	After MET Intervention	Hospital mortality trend	Mean implementation duration: 7 years	Hospitalizations: 4,392,392	NR	Odds ratio: 0.96 (95% CI: 0.93 to 0.98), p=NR	Comparison: Arm 1 -After MET Overall P value for interaction between hospital characteristic and MET implementation: p=0.69	Risk adjusted (not specified)
Kutty, 2018[42]	Arm 1	Before MET Intervention	Hospital mortality trend	Mean implementation duration: 3 years	Hospitalizations: 1,659,059	NR	Odds ratio: 0.94 (95% CI: 0.92 to 0.97), p=NR	Ref	Risk adjusted (not specified)
Kutty, 2018[42]	Arm 2	After MET Intervention	Hospital mortality trend	Mean implementation duration: 7 years	Hospitalizations: 4,392,392	NR	Odds ratio: 0.94 (95% CI: 0.93 to 0.95), p=NR	Comparison: Arm 1 -After MET Overall P value for interaction between hospital characteristic and MET implementation: p=0.69	Risk adjusted (not specified)

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Kutty, 2018[42]	Arm 1	Before MET Intervention	Hospital mortality trend	Mean implementation duration: 3 years	Hospitalizations: 1,659,059	NR	Odds ratio: 0.96 (95% CI: 0.85 to 1.07), p=NR	Ref	Risk adjusted (not specified)
Kutty, 2018[42]	Arm 2	After MET Intervention	Hospital mortality trend	Mean implementation duration: 7 years	Hospitalizations: 4,392,392	NR	Odds ratio: 0.95 (95% CI: 0.93 to 0.97), p=NR	Comparison: Arm 1 -After MET Overall P value for interaction between hospital characteristic and MET implementation: p=0.85	Risk adjusted (not specified)
Kutty, 2018[42]	Arm 1	Before MET Intervention	Hospital mortality trend	Mean implementation duration: 3 years	Hospitalizations: 1,659,059	NR	Odds ratio: 0.94 (95% CI: 0.89 to 0.99), p=NR	Ref	Risk adjusted (not specified)
Kutty, 2018[42]	Arm 2	After MET Intervention	Hospital mortality trend	Mean implementation duration: 7 years	Hospitalizations: 4,392,392	NR	Odds ratio: 0.94 (95% CI: 0.93 to 0.96), p=NR	Comparison: Arm 1 -After MET Overall P value for interaction between hospital characteristic and MET implementation: p=0.85	Risk adjusted (not specified)
Kutty, 2018[42]	Arm 1	Before MET Intervention	Hospital mortality trend	Mean implementation duration: 3 years	Hospitalizations: 1,659,059	NR	Odds ratio: 0.94 (95% CI: 0.91 to 0.97), p=NR	Ref	Risk adjusted (not specified)

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Kutty, 2018[42]	Arm 2	After MET Intervention	Hospital mortality trend	Mean implementation duration: 7 years	Hospitalizations: 4,392,392	NR	Odds ratio: 0.94 (95% CI: 0.91 to 0.96), p=NR	Comparison: Arm 1 -After MET Overall P value for interaction between hospital characteristic and MET implementation: p=0.85	Risk adjusted (not specified)
Kutty, 2018[42]	Arm 1	Before MET Intervention	Hospital mortality trend	Mean implementation duration: 3 years	Hospitalizations: 1,659,059	NR	Odds ratio: 0.96 (95% CI: 0.92 to 0.99), p=NR	Ref	Risk adjusted (not specified)
Kutty, 2018[42]	Arm 2	After MET Intervention	Hospital mortality trend	Mean implementation duration: 7 years	Hospitalizations: 4,392,392	NR	Odds ratio: 0.93 (95% CI: 0.91 to 0.95), p=NR	Comparison: Arm 1 -After MET Overall P value for interaction between hospital characteristic and MET implementation: p=0.85	Risk adjusted (not specified)
McKeta, 2021[43]	Arm 1	Pre-implementation	Mortality	NR	NR	4 (NR)	NR	NR	NR
McKeta, 2021[43]	Arm 2	Post-implementation	Mortality	NR	NR	1 (NR)	NR	NR	NR
Winterbottom, 2021[44]	Arm 1	Start of implementation	Risk-adjusted mortality index	2017	NR	NR	NR	Ref	Not specified

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Winterbottom, 2021[44]	Arm 2	Post-implementation period	Risk-adjusted mortality index	End of 2019	NR	NR	NR	Comparison: Arm 1 - Start of implementation % difference from baseline: -0.27, p=NR	Not specified
Young, 2023[45]	Arm 1	Pre-MET	Operative mortality	2004-2009	7690	251 (3.3)	NR	Ref	Multivariable, risk-adjusted logistic regression, but factors not specified
Young, 2023[45]	Arm 2	MET	Operative mortality	2009-2018	3528	69 (2)	NR	Comparison: Arm 1-Pre-MET Odds ratio: 0.51 (95% CI: 0.38 to 0.67), p<0.001	Multivariable, risk-adjusted logistic regression, but factors not specified
Young, 2023[45]	Arm 1	Pre-MET	Failure to rescue	2004-2009	7690	NR	NR	Ref	Multivariable, risk-adjusted logistic regression, but factors not specified
Young, 2023[45]	Arm 2	MET	Failure to rescue	2009-2018	3528	NR	NR	Comparison: Arm 1-Pre-MET Odds ratio: 0.46 (95% CI: 0.33 to 0.64), p<0.001	Multivariable, risk-adjusted logistic regression, but factors not specified

CI=confidence interval; ICU=intensive care unit; MET=medical emergency team; N=sample size; NR=not reported; NS=not significant; p=p-value; Ref=reference arm; RRT=rapid response team

Evidence Table C-8. Mortality outcome (continuous data) of included studies comparing rapid response systems to no rapid response systems

Author, Year	Arm	Arm Name	Outcome Definition	Followup Timepoint	N at Analysis	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Factora, 2022[55]	Arm 1	Pre-RRT implementation	In-hospital mortality, trend slope	2005 to 2008	177760	Slope: 0.001 (SE 0.001)	Odds ratio: 1.01 (95% CI: 0.98 to 1.04), p=NR	Ref	Demographic factors and surgical procedures
Factora, 2022[55]	Arm 2	Post-implementation period	In-hospital mortality, trend slope	2009 to 2018	450778	Slope: –0.003 (SE 0)	Odds ratio: 0.961 (95% CI: 0.955 to 0.968), p=NR	Comparison: Arm 1-Postimplementation Slope change: –0.004 (SE 0.001), p=0.001	Demographic factors and surgical procedures
Factora, 2022[55]	Arm 1	Pre-RRT implementation	In-hospital mortality, intercept change	2005 to 2008	NR	NR	Odds ratio: 1.01 (95% CI: 0.98 to 1.04), p=NR	Ref	Demographic factors and surgical procedures
Factora, 2022[55]	Arm 2	Post-implementation period	In-hospital mortality, intercept change	2009 to 2018	NR	NR	Odds ratio: 1.17 (95% CI: 1.09 to1.25), p=NR	Comparison: Arm 1-Postimplementation Intercept change: 0.154 (SE 0.036), p<0.001	Demographic factors and surgical procedures
Factora, 2022[55]	Arm 1	Pre-RRT implementation	In-hospital mortality, intercept	2005 to 2008	177760	Intercept: –6.122 (SE 0.072)	Odds ratio: 0.002 (95% CI: 0.002 to 0.003), p=NR	Ref	Demographic factors and surgical procedures
Factora, 2022[55]	Arm 2	Post-implementation period	In-hospital mortality, intercept	2009-2011	NR	NR	NR	Comparison: Arm 1-Postimplementation Intercept change: 0.087 (SE 0.045) Odds Ratio: 1.091 (95% CI: 0.999 to 1.192) p=0.054	Demographic factors and surgical procedures

Author, Year	Arm	Arm Name	Outcome Definition	Followup Timepoint	N at Analysis	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Factora, 2022[55]	Arm 2	Post-implementation period	In-hospital mortality, intercept	2012-2013	NR	NR	NR	Comparison: Arm 1-Postimplementation Intercept change: –0.209 (SE 0.05) Odds Ratio: 0.812 (95% CI: 0.736 to 0.896) p<0.001	Demographic factors and surgical procedures
Factora, 2022[55]	Arm 2	Post-implementation period	In-hospital mortality, intercept	2014-2018	NR	NR	NR	Comparison: Arm 1-Postimplementation Intercept change: –0.136 (SE 0.048) Odds Ratio: 0.872 (95% CI: 0.794 to 0.958) p=0.004	Demographic factors and surgical procedures
Factora, 2022[55]	Arm 1	Pre-RRT implementation	In-hospital mortality, trend slope	2005 to 2008	177760	Slope: 0 (SE 0.001)	Odds ratio: 0.996 (95% CI: 0.002 to 0.003), p=0.782	Ref	Demographic factors and surgical procedures
Factora, 2022[55]	Arm 2	Post-implementation period	In-hospital mortality, trend slope	2009-2011	NR	Slope: 0.003 (0.002)	NR	Comparison: Arm 1-Postimplementation Intercept change: 0.003 (SE 0.002) Odds Ratio: 1.038 (95% CI: 0.992 to 1.088) p=0.111	Demographic factors and surgical procedures
Factora, 2022[55]	Arm 2	Post-implementation period	In-hospital mortality, trend slope	2012-2013	NR	Slope: 0.002 (0.002)	NR	Comparison: Arm 1-Postimplementation Intercept change: –0.001 (SE 0.003) Odds Ratio: 0.812 (95% CI: 0.736 to 0.896) p=0.71	Demographic factors and surgical procedures

Author, Year	Arm	Arm Name	Outcome Definition	Followup Timepoint	N at Analysis	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Factora, 2022[55]	Arm 2	Post-implementation period	In-hospital mortality, trend slope	2014-2018	NR	Slope: -0.001 (0.001)	NR	Comparison: Arm 1-Postimplementation Intercept change: –0.003 (SE 0.002) Odds Ratio: 0.872 (95% CI: 0.794 to 0.958) p=0.26	Demographic factors and surgical procedures
Factora, 2022[55]	Arm 1	Pre-RRT implementation	In-hospital mortality, fully adjusted	2005 to 2008	177760	NR	Odds ratio: 1.16 (95% CI: 1.09 to1.25), p<0.001	Ref	Demographic factors, surgical procedures, patient medical history
Factora, 2022[55]	Arm 2	Post-implementation period	In-hospital mortality, fully adjusted	2009 to 2018	450778	NR	Odds ratio: 0.74 (95% CI: 0.63 to 0.85), p<0.001	Comparison: Arm 1-Postimplementation Odds ratio: 0.96 (95% CI: 0.96 to 0.97), p=<0.001	Demographic factors, surgical procedures, patient medical history
Kolovos, 2018[41]	Arm 1	Pre-RRT	PICU standardized mortality ratio	NR	1097	Standardized mortality ratio: 1.4	NR	Ref	NR
Kolovos, 2018[41]	Arm 2	Post-RRT	PICU standardized mortality ratio	NR	1055	Standardized mortality ratio: 1.2	NR	Comparison: Arm 1-Pre-RRT p-value only: p=NS	NR
Kolovos, 2018[41]	Arm 1	Pre-RRT	RRT cohort standardized mortality ratio	NR	1097	Standardized mortality ratio: 2	NR	Ref	NR
Kolovos, 2018[41]	Arm 2	Post-RRT	RRT cohort standardized mortality ratio	NR	1055	Standardized mortality ratio: 2	NR	Comparison: Arm 1-Pre-RRT p-value only: p=NS	NR

Author, Year	Arm	Arm Name	Outcome Definition	Followup Timepoint	N at Analysis	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Kutty, 2018[42]	Arm 1	Before MET Intervention	Hospital mortality trend, deaths per 1000 admissions (risk adjusted)	Mean implementation duration: 3 years	Hospitalizations: 1,659,059	Mean: 8.4 (95% CI: 7.8 to 9.0)	NR	Ref	NR
Kutty, 2018[42]	Arm 2	After MET Intervention	Hospital mortality trend, deaths per 1000 admissions (risk adjusted)	Mean implementation duration: 7 years	Hospitalizations: 4,392,392	Mean: 8.8 (95% CI: 8.3 to 9.3)	NR	Comparison: Arm 1 -After MET p-value only: p=0.11	NR
Kutty, 2018[42]	Arm 1	Before MET Intervention	Hospital mortality trend, deaths per 1000 admissions (risk adjusted)	Mean implementation duration: 3 years	Hospitalizations: 1,659,059	Mean: 7.6 (95% CI: 6.4 to 9.0)	NR	Ref	NR
Kutty, 2018[42]	Arm 2	After MET Intervention	Hospital mortality trend, deaths per 1000 admissions (risk adjusted)	Mean implementation duration: 7 years	Hospitalizations: 4,392,392	Mean: 8.1 (95% CI: 7.2 to 9.1)	NR	Comparison: Arm 1 -After MET Overall P value for interaction between hospital characteristic and MET implementation: p=0.69	NR
Kutty, 2018[42]	Arm 1	Before MET Intervention	Hospital mortality trend, deaths per 1000 admissions (risk adjusted)	Mean implementation duration: 3 years	Hospitalizations: 1,659,059	Mean: 8.6 (95% CI: 8.0 to 9.3)	NR	Ref	NR

Author, Year	Arm	Arm Name	Outcome Definition	Followup Timepoint	N at Analysis	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Kutty, 2018[42]	Arm 2	After MET Intervention	Hospital mortality trend, deaths per 1000 admissions (risk adjusted)	Mean implementation duration: 7 years	Hospitalizations: 4,392,392	Mean: 9 (95% CI: 8.4 to 9.6)	NR	Comparison: Arm 1 -After MET Overall P value for interaction between hospital characteristic and MET implementation: p=0.69	NR
Kutty, 2018[42]	Arm 1	Before MET Intervention	Hospital mortality trend, deaths per 1000 admissions (risk adjusted)	Mean implementation duration: 3 years	Hospitalizations: 1,659,059	Mean: 7.3 (95% CI: 5.3 to 10.2)	NR	Ref	NR
Kutty, 2018[42]	Arm 2	After MET Intervention	Hospital mortality trend, deaths per 1000 admissions (risk adjusted)	Mean implementation duration: 7 years	Hospitalizations: 4,392,392	Mean: 8.1 (95% CI: 6.7 to 9.9)	NR	Comparison: Arm 1 -After MET Overall P value for interaction between hospital characteristic and MET implementation: p=0.85	NR
Kutty, 2018[42]	Arm 1	Before MET Intervention	Hospital mortality trend, deaths per 1000 admissions (risk adjusted)	Mean implementation duration: 3 years	Hospitalizations: 1,659,059	Mean: 8.4 (95% CI: 7.3 to 9.6)	NR	Ref	NR

Author, Year	Arm	Arm Name	Outcome Definition	Followup Timepoint	N at Analysis	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Kutty, 2018[42]	Arm 2	After MET Intervention	Hospital mortality trend, deaths per 1000 admissions (risk adjusted)	Mean implementation duration: 7 years	Hospitalizations: 4,392,392	Mean: 8.6 (95% CI: 7.8 to 9.6)	NR	Comparison: Arm 1 -After MET Overall P value for interaction between hospital characteristic and MET implementation: p=0.85	NR
Kutty, 2018[42]	Arm 1	Before MET Intervention	Hospital mortality trend, deaths per 1000 admissions (risk adjusted)	Mean implementation duration: 3 years	Hospitalizations: 1,659,059	Mean: 8.6 (95% CI: 7.8 to 9.6)	NR	Ref	NR
Kutty, 2018[42]	Arm 2	After MET Intervention	Hospital mortality trend, deaths per 1000 admissions (risk adjusted)	Mean implementation duration: 7 years	Hospitalizations: 4,392,392	Mean: 9.4 (95% CI: 8.4 to 10.4)	NR	Comparison: Arm 1 -After MET Overall P value for interaction between hospital characteristic and MET implementation: p=0.85	NR
Kutty, 2018[42]	Arm 1	Before MET Intervention	Hospital mortality trend, deaths per 1000 admissions (risk adjusted)	Mean implementation duration: 3 years	Hospitalizations: 1,659,059	Mean: 8.8 (95% CI: 7.8 to 9.9)	NR	Ref	NR

Author, Year	Arm	Arm Name	Outcome Definition	Followup Timepoint	N at Analysis	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Kutty, 2018[42]	Arm 2	After MET Intervention	Hospital mortality trend, deaths per 1000 admissions (risk adjusted)	Mean implementation duration: 7 years	Hospitalizations: 4,392,392	Mean: 8.6 (95% CI: 7.8 to 9.5)	NR	Comparison: Arm 1 -After MET Overall P value for interaction between hospital characteristic and MET implementation: p=0.85	NR

CI=confidence interval; ICU=intensive care unit; MET=medical emergency team; N=sample size; NR=not reported; NS=not significant; p=p-value; PICU=pediatric intensive care unit; Ref=reference arm; RRT=rapid response team; SE=standard error

Evidence Table C-9. Transition to higher level of care outcome (categorical data) of included studies comparing rapid response systems to no rapid response systems

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Kolovos, 2018[41]	Arm 1	Pre-RRT	Mechanical ventilation admitted to PICU	NR	1097	NR (285) Events: 26	NR	Ref	NR
Kolovos, 2018[41]	Arm 2	Post-RRT	Mechanical ventilation admitted to PICU	NR	1055	NR (233) Events: 22.1	NR	Comparison: Arm 1-Pre-RRT p-value only: p=NS	NR
Winterbottom, 2021[44]	Arm 1	Start of implementation	Patients admitted to ICU from inpatient beds	2017	NR	NR	NR	Ref	NR
Winterbottom, 2021[44]	Arm 2	Post-implementation period	Patients admitted to ICU from inpatient beds	End of 2019	NR	NR	NR	Comparison: Arm 1 - Start of implementation % difference from baseline: -0.047, p=NR	NR
Young, 2023[45]	Arm 1	Pre-MET	Readmitted to the ICU during their admission	2004-2009	7690	NR	NR	Ref	Multivariable, risk-adjusted logistic regression, but factors not specified
Young, 2023[45]	Arm 2	MET	Readmitted to the ICU during their admission	2009-2018	3528	NR	NR	Comparison: Arm 1-Pre-MET Odds ratio: 0.25 (95% CI: 0.11 to 0.58), p=0.002	Multivariable, risk-adjusted logistic regression, but factors not specified

CI=confidence interval; ICU=intensive care unit; MET=medical emergency team; N=sample size; NR=not reported; NS=not significant; p=p-value; PICU=pediatric intensive care unit; Ref=reference arm; RRT=rapid response team

Evidence Table C-10. Transition to higher level of care outcome (continuous data) of included studies comparing rapid response systems to no rapid response systems

Author, Year	Arm	Arm Name	Outcome Definition	Followup Timepoint	N at Analysis	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Kolovos, 2018[41]	Arm 1	Pre-RRT	Code rate, ICU (per 1,000 patient-days)	NR	1097	Per 1,000 patient days: 9.1	NR	Ref	NR
Kolovos, 2018[41]	Arm 2	Post-RRT	Code rate, ICU (per 1,000 patient-days)	NR	1055	Per 1,000 patient days: 6.4	NR	Comparison: Arm 1-Pre-RRT p-value only: p=0.001	NR
McKeta, 2021[43]	Arm 1	Pre-implementation	Unplanned transfers to the cardiac ICU	NR	NR	Per 1,000 patient days: 16.8	NR	Ref	NR
McKeta, 2021[43]	Arm 2	Post-implementation	Unplanned transfers to the cardiac ICU	NR	NR	Per 1,000 patient days: 7.1	NR	Comparison: Arm 1-Pre-implementation p-value only: p<0.01	NR

ICU=intensive care unit; N=sample size; NR=not reported; p=p-value; Ref=reference arm; RRT=rapid response team

Evidence Table C-11. Incidence of cardiorespiratory arrest outcome (categorical data) of included studies comparing afferent limb changes

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bavare, 2018[33]	Arm 1	C-RR (clinician initiated)	Escalation to cardiopulmonary arrest	NR	1396	NR (4.5)	NR	Ref	NR
Bavare, 2018[33]	Arm 2	FIRR (family initiated)	Escalation to cardiopulmonary arrest	NR	46	NR (2)	NR	Comparison: Arm 1-C-RR p-value only: p<0.01	NR

C-RR=clinician initiated rapid response; FIRR=family initiated rapid response; ICU=intensive care unit; N=sample size; NR=not reported; p=p-value; Ref=reference arm

Evidence Table C-12. Incidence of cardiorespiratory arrest outcome (continuous data) of included studies comparing afferent limb changes

Author, Year	Arm	Arm Name	Outcome Definition	Followup Timepoint	N at Analysis	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Dean, 2020[49]	Overall	Whole cohort	Non-ICU arrest rates	NR	NR	per 1, 000 non-ICU patient days: 0.11	NR	NR	NR
Sebat, 2018[56]	Arm 1	Control period	Cardiac arrests, per 1000 discharges	NR	28914	Per 1,000 discharges: 3.1	NR	Ref	NR
Sebat, 2018[56]	Arm 2	Intervention period	Cardiac arrests, per 1000 discharges	NR	39802	Per 1,000 discharges: 2.4	NR	Comparison: Arm 1-Control period p-value only: p=0.04	NR

ICU=intensive care unit; N=sample size; NR=not reported; p=p-value; Ref=reference arm

Evidence Table C-13. Serious adverse events related to clinical deterioration outcome (continuous data) of included studies comparing afferent limb changes

Author, Year	Arm	Arm Name	Outcome Definition	Followup Timepoint	N at Analysis	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Penney, 2021[50]	Arm 1	Vital Sign–Based System	Percentage of unnecessary RRT activations	2015 to 2016	NR	Mean: 33 (SE 9)	NR	Ref	NR
Penney, 2021[50]	Arm 2	PEWS	Percentage of unnecessary RRT activations	2016 to 2017	NR	Mean: 15 (SE 5)	NR	Comparison: Arm 1-Vital sign-based p-value only: p=NS	NR
Penney, 2021[50]	Arm 3	m-PEWS	Percentage of unnecessary RRT activations	2017 to 2018	NR	Mean: 3.5 (SE 2)	NR	Comparison: Arm 1-Vital sign-based p-value only: p<0.05	NR
Penney, 2021[50]	Arm 1	Vital Sign–Based System	Rate of missed RRT activations per 1000 patient care days	2015 to 2016	NR	Mean: 16.5 (SE 5.7)	NR	Ref	NR
Penney, 2021[50]	Arm 2	PEWS	Rate of missed RRT activations per 1000 patient care days	2016 to 2017	NR	Mean: 2.2 (SE 1.7)	NR	Comparison: Arm 1-Vital sign-based p-value only: p<0.05	NR
Penney, 2021[50]	Arm 3	m-PEWS	Rate of missed RRT activations per 1000 patient care days	2017 to 2018	NR	Mean: 0.3 (SE 0.2)	NR	Comparison: Arm 1-Vital sign-based p-value only: p<0.05	NR

m-PEWS=modified pediatric early warning system; N=sample size; NR=not reported; NS=not significant; p=p-value; PEWS= pediatric early warning system; Ref=reference arm; RRT=rapid response team; SE=standard error

Evidence Table C-14. Mortality outcome (categorical data) of included studies comparing afferent limb changes

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bavare, 2018[33]	Arm 1	C-RR (clinician initiated)	Within 30 days after RR events	NR	1396	NR (4.5)	NR	NR	NR
Bavare, 2018[33]	Arm 2	FIRR (family initiated)	Within 30 days after RR events	NR	46	NR (0)	NR	NR	NR
Dean, 2020[49]	Overall	Whole cohort	Mortality	2014-2015	NR	4 (NR)	NR	NR	NR
Dean, 2020[49]	Overall	Whole cohort	Mortality	2016-2018	NR	0 (NR)	NR	NR	NR
Escobar, 2020[47]	Arm 1	Pre-intervention	Death within 30 days after alert	30 days	28462	NR (20.4)	NR	Ref	Age, sex, season, KFHP coverage, care directive, COPS2, LAPS2 at admission, and diagnosis, first alert value and elapsed hours from admission to the first alert
Escobar, 2020[47]	Arm 2	Intervention cohort	Death within 30 days after alert	30 days	15487	NR (15.8)	NR	Comparison: Arm 1-Pre-intervention cohort Relative risk: 0.84 (95% CI: 0.78 to 0.90), p=NR	Age, sex, season, KFHP coverage, care directive, COPS2, LAPS2 at admission, and diagnosis, first alert value and elapsed hours from admission to the first alert
Escobar, 2020[47]	Arm 1	Pre-intervention	Patients who died in the hospital (%)	NR	28462	NR (14.4)	NR	NR	NR

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Escobar, 2020[47]	Arm 2	Intervention cohort	Patients who died in the hospital (%)	NR	15487	NR (9.8)	NR	NR	NR
Escobar, 2020[47]	Arm 1	Pre-intervention	Death within 30 days after admission (%)	30 days	28462	NR (19.9)	NR	NR	NR
Escobar, 2020[47]	Arm 2	Intervention cohort	Death within 30 days after admission (%)	30 days	15487	NR (15.5)	NR	NR	NR
Sebat, 2018[56]	Arm 1	Control period	Mortality	NR	28914	1083 (3.7)	Observed-to-expected mortality ratio: 1.5 (95% CI: NR), p=NR	Ref	Observed/expected mortality ratio
Sebat, 2018[56]	Arm 2	Intervention period	Mortality	NR	39802	1282 (3.2)	Observed-to-expected mortality ratio: 1 (95% CI: NR), p=NR	Comparison: Arm 1-Control period p-value only: p<0.001	Observed/expected mortality ratio
Vandegrift, 2021[57]	Arm 1	Pre-implementation	Mortality	2000-2005	85	NR (50)	NR	Ref	NR
Vandegrift, 2021[57]	Arm 2	Post-implementation	Mortality	2000-2005	426	NR (10)	NR	Comparison: Arm 1-Pre-MET p-value only: p<0.001	NR
Vandegrift, 2021[57]	Arm 1	Pre-implementation	Mortality	2003-2005	68	NR (51)	NR	Ref	NR

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Vandegrift, 2021[57]	Arm 2	Post-implementation	Mortality	2003-2005	63	NR (27)	NR	Comparison: Arm 1-Pre-MET p-value only: p<0.001	NR
Vandegrift, 2021[57]	Arm 1	Pre-implementation	Mortality	2008-2013	28914	NR (3.8)	NR	Ref	NR
Vandegrift, 2021[57]	Arm 2	Post-implementation	Mortality	2008-2013	39802	NR (3.2)	NR	Comparison: Arm 1-Pre-MET p-value only: p<0.001	NR

CI=confidence interval; COPS2= Comorbidity Point Score, version 2; C-RR=clinician initiated rapid response; FIRR=family initiated rapid response; KFHP= Kaiser Foundation Health Plan coverage; LAPS2= Laboratory-based Acute Physiology Score, version 2; MET=medical emergency team; N=sample size; NR=not reported; p=p-value; Ref=reference arm; RR=rapid response

Evidence Table C-15. Mortality outcome (continuous data) of included studies comparing afferent limb changes

Author, year	Arm	Arm Name	Outcome Definition	Followup Timepoint	N at Analysis	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Weller, 2018[51]	Arm 1	Pre-implementation	Unplanned deaths per 1,000 discharges	5 months prior implementation	889 discharges	Per 1,000 discharges: 4.92	p=NS	NR	NR
Weller, 2018[51]	Arm 2	Post-implementation	Unplanned deaths per 1,000 discharges	5 months post implementation	1069 discharges	Per 1,000 discharges: 2.6	p=NS	NR	NR
Weller, 2018[51]	Arm 1	Pre-implementation	Unplanned deaths per 1,000 discharges	5 months prior implementation	1053 discharges	Per 1,000 discharges: 1.68	p=NS	NR	NR
Weller, 2018[51]	Arm 2	Post-implementation	Unplanned deaths per 1,000 discharges	5 months post implementation	1000 discharges	Per 1,000 discharges: 1.04	p=NS	NR	NR

N=sample size; NR=not reported; NS=not significant; p=p-value

Evidence Table C-16. Transition to higher level of care outcome (categorical data) of included studies comparing afferent limb changes

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bavare, 2018[33]	Arm 1	C-RR (clinician initiated)	Transfer to ICU	NR	1396	NR (60)	NR	Ref	NR
Bavare, 2018[33]	Arm 2	FIRR (family initiated)	Transfer to ICU	NR	46	13 (27)	NR	Comparison: Arm 1-C-RR p-value only: p<0.01	NR
Dean, 2020[49]	Overall	Whole cohort	Unplanned transfer to ICU	NR	NR	NR	NR	Descriptive only Unplanned transfer rates remained stable	NR
Escobar, 2020[47]	Arm 1	Pre-intervention	ICU admission within 30 days after alert	30 days	28462	NR	NR	Ref	Age, sex, season, KFHP coverage, care directive, COPS2, LAPS2 at admission, and diagnosis, first alert value and elapsed hours from admission to the first alert
Escobar, 2020[47]	Arm 2	Intervention cohort	ICU admission within 30 days after alert	30 days	15487	NR	NR	Comparison: Arm 1-Pre-intervention cohort Relative risk: 0.91 (95% CI: 0.84 to 0.98), p=NR	Age, sex, season, KFHP coverage, care directive, COPS2, LAPS2 at admission, and diagnosis, first alert value and elapsed hours from admission to the first alert
Escobar, 2020[47]	Arm 1	Pre-intervention	Patients with any admission to the ICU during current hospitalization (%)	NR	28462	NR (20.9)	NR	NR	NR

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Escobar, 2020[47]	Arm 2	Intervention cohort	Patients with any admission to the ICU during current hospitalization (%)	NR	15487	NR (17.7)	NR	NR	NR
Stellpflug, 2021[48]	Arm 1	Baseline, pre-MEWS	Transferred to ICU as the result of RRT activations	2016	43 (patients with activations)	26 (60)	NR	NR	NR
Stellpflug, 2021[48]	Arm 2	MEWS	Transferred to ICU as the result of RRT activations	2017	43 (patients with activations)	28 (65)	NR	NR	NR
Stellpflug, 2021[48]	Arm 3	MEWS + monitoring	Transferred to ICU as the result of RRT activations	2018	26 (patients with activations)	17 (65)	NR	NR	NR
Stellpflug, 2021[48]	Arm 1	Baseline, pre-MEWS	RRT activations resulting in ICU transfer	2016	43 (patients with activations)	Events: 47	NR	NR	NR
Stellpflug, 2021[48]	Arm 2	MEWS	RRT activations resulting in ICU transfer	2017	43 (patients with activations)	Events: 55	NR	NR	NR
Stellpflug, 2021[48]	Arm 3	MEWS + monitoring	RRT activations resulting in ICU transfer	2018	26 (patients with activations)	Events: 65	NR	NR	NR

CI=confidence interval; COPS2=Comorbidity Point Score, version 2; C-RR=clinician initiated rapid response; FIRR=family initiated rapid response; ICU=intensive care unit; KFHP=Kaiser Foundation Health Plan coverage; LAPS2=Laboratory-based Acute Physiology Score, version 2; MEWS=modified early warning system; N=sample size; NR=not reported; p=p-value; Ref=reference arm; RRT=rapid response team

Evidence Table C-17. Transition to higher level of care outcome (continuous data) of included studies comparing afferent limb changes

Author, Year	Arm	Arm Name	Outcome Definition	Followup Timepoint	N at Analysis	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Danesh, 2019[46]	Arm 1	Traditional rapid response team	Unplanned Intensive Care Unit Transfers, per 1,000 patient days	2010-2011	5875	per 1,000 patient days: 8.85	NR	Ref	Age, gender, charlson comorbidity index, hospital length of stay
Danesh, 2019[46]	Arm 2	EWS with proactive rapid response team	Unplanned Intensive Care Unit Transfers, per 1,000 patient days	2011-2012	6273	per 1,000 patient days: 6.73	NR	Comparison: Arm 1-Traditional rapid response team Odds ratio: 1.392 (95% CI: 1.017 to 1.905), p=0.001	Age, gender, charlson comorbidity index, hospital length of stay
Penney, 2021[50]	Arm 1	Vital Sign–Based System	Rate of PICU transfers per 1000 patient care days	2015 to 2016	NR	Mean: 5.5 (SE 2.2)	NR	Ref	NR
Penney, 2021[50]	Arm 2	PEWS	Rate of PICU transfers per 1000 patient care days	2016 to 2017	NR	Mean: 6.9 (SE 1.6)	NR	Comparison: Arm 1-Vital sign-based p-value only: p=NS	NR
Penney, 2021[50]	Arm 3	m-PEWS	Rate of PICU transfers per 1000 patient care days	2017 to 2018	NR	Mean: 7.7 (SE 1.6)	NR	Comparison: Arm 1-Vital sign-based p-value only: p=NS	NR
Weller, 2018[51]	Arm 1	Pre-implementation	ICU transfers per 1,000 discharges	5 months prior implementation	889 discharges	Per 1,000 discharges: 52.9	p=NS	Comparing study unit and comparative unit encompassing both arms p=0.09	NR

Author, Year	Arm	Arm Name	Outcome Definition	Followup Timepoint	N at Analysis	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Weller, 2018[51]	Arm 2	Post-implementation	ICU transfers per 1,000 discharges	5 months post implementation	1069 discharges	Per 1,000 discharges: 40.2	p=NS	Comparing study unit and comparative unit encompassing both arms p=0.09	NR
Weller, 2018[51]	Arm 1	Pre-implementation	ICU transfers per 1,000 discharges	5 months prior implementation	1053 discharges	Per 1,000 discharges: 50.3	p=NS	Comparing study unit and comparative unit encompassing both arms p=0.09	NR
Weller, 2018[51]	Arm 2	Post-implementation	ICU transfers per 1,000 discharges	5 months post implementation	1000 discharges	Per 1,000 discharges: 43	p=NS	Comparing study unit and comparative unit encompassing both arms p=0.09	NR

CI=confidence interval; EWS=early warning system; ICU=intensive care unit; N=sample size; NR=not reported; NS=not significant; p=p-value; PICU=pediatric intensive care unit; Ref=reference arm; SE=standard error

Evidence Table C-18. Incidence of cardiorespiratory arrest outcome (categorical data) of included studies comparing efferent limb changes

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Mankidy, 2020[53]	Arm 1	RRT	Cardiac Arrest Total	2013-2014	44643	673 (NR)	NR	Ref	NR
Mankidy, 2020[53]	Arm 2	RRT-MET	Cardiac Arrest Total	2014-2017	77898	484 (NR)	NR	Comparison: Arm 1-RRT Odds ratio: 0.4 (95% CI: 0.35 to 0.45), p<0.001	NR
Mankidy, 2020[53]	Arm 1	RRT	Pulseless Electrical Activity	2013-2014	44643	474 (NR)	NR	Ref	NR
Mankidy, 2020[53]	Arm 2	RRT-MET	Pulseless Electrical Activity	2014-2017	77898	273 (NR)	NR	Comparison: Arm 1-RRT Odds ratio: 0.32 (95% CI: 0.28 to 0.37), p<0.001	NR
Mankidy, 2020[53]	Arm 1	RRT	Total Ventricular Fibrillation/ Tachycardia	2013-2014	44643	147 (NR)	NR	Ref	NR
Mankidy, 2020[53]	Arm 2	RRT-MET	Total Ventricular Fibrillation/ Tachycardia	2014-2017	77898	112 (NR)	NR	Comparison: Arm 1-RRT Odds ratio: 0.42 (95% CI: 0.33 to 0.54), p<0.001	NR
Mankidy, 2020[53]	Arm 1	RRT	Intensive Care Unit Cardiac Arrest	2013-2014	44643	445 (NR)	NR	Ref	NR
Mankidy, 2020[53]	Arm 2	RRT-MET	Intensive Care Unit Cardiac Arrest	2014-2017	77898	330 (NR)	NR	Comparison: Arm 1-RRT Odds ratio: 0.41 (95% CI: 0.36 to 0.47), p<0.001	NR
Mankidy, 2020[53]	Arm 1	RRT	Intensive Care Unit Pulseless Electrical Activity	2013-2014	44643	321 (NR)	NR	Ref	NR
Mankidy, 2020[53]	Arm 2	RRT-MET	Intensive Care Unit Pulseless Electrical Activity	2014-2017	77898	185 (NR)	NR	Comparison: Arm 1-RRT Odds ratio: 0.32 (95% CI: 0.27 to 0.38), p<0.001	NR
Mankidy, 2020[53]	Arm 1	RRT	Acute Care Ward Cardiac Arrest	2013-2014	44643	132 (NR)	NR	Ref	NR

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Mankidy, 2020[53]	Arm 2	RRT-MET	Acute Care Ward Cardiac Arrest	2014-2017	77898	91 (NR)	NR	Comparison: Arm 1-RRT Odds ratio: 0.38 (95% CI: 0.29 to 0.50), p<0.001	NR
Mankidy, 2020[53]	Arm 1	RRT	Acute Care Ward Pulseless Electrical Activity	2013-2014	44643	78 (NR)	NR	Ref	NR
Mankidy, 2020[53]	Arm 2	RRT-MET	Acute Care Ward Pulseless Electrical Activity	2014-2017	77898	52 (NR)	NR	Comparison: Arm 1-RRT Odds ratio: 0.37 (95% CI: 0.26 to 0.53), p<0.001	NR
Mankidy, 2020[53]	Arm 1	RRT	Total Emergency Department Cardiac Arrest	2013-2014	44643	60 (NR)	NR	Ref	NR
Mankidy, 2020[53]	Arm 2	RRT-MET	Total Emergency Department Cardiac Arrest	2014-2017	77898	41 (NR)	NR	Comparison: Arm 1-RRT Odds ratio: 0.38 (95% CI: 0.26 to 0.56), p<0.001	NR
Mankidy, 2020[53]	Arm 1	RRT	Emergency Department Pulseless Electrical Activity	2013-2014	44643	53 (NR)	NR	Ref	NR
Mankidy, 2020[53]	Arm 2	RRT-MET	Emergency Department Pulseless Electrical Activity	2014-2017	77898	25 (NR)	NR	Comparison: Arm 1-RRT Odds ratio: 0.26 (95% CI: 0.16 to 0.42), p<0.001	NR

CI=confidence interval; MET = medical emergency team; N=sample size; NR=not reported; p=p-value; Ref=reference arm; RRT=rapid response team

Evidence Table C-19. Incidence of cardiorespiratory arrest outcome (continuous data) of included studies comparing efferent limb changes

Author, Year	Arm	Arm Name	Outcome Definition	Followup Timepoint	N at Analysis	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Mankidy, 2020[53]	Arm 1	RRT	Cardiac Arrest Total, per 1,000 patient days	2013-2014	44643	per 1,000 patient days: 2.2	NR	Ref	NR
Mankidy, 2020[53]	Arm 2	RRT-MET	Cardiac Arrest Total, per 1,000 patient days	2014-2017	77898	per 1,000 patient days: 0.88	NR	Comparison: Arm 1-Control period p-value only: p<0.001	NR
Mankidy, 2020[53]	Arm 1	RRT	Pulseless Electrical Activity, per 1,000 patient days	2013-2014	44643	per 1,000 patient days: 1.55	NR	Ref	NR
Mankidy, 2020[53]	Arm 2	RRT-MET	Pulseless Electrical Activity, per 1,000 patient days	2014-2017	77898	per 1,000 patient days: 0.5	NR	Comparison: Arm 1-Control period p-value only: p<0.001	NR
Mankidy, 2020[53]	Arm 1	RRT	Total Ventricular Fibrillation/ Tachycardia, per 1,000 patient days	2013-2014	44643	per 1,000 patient days: 0.48	NR	Ref	NR
Mankidy, 2020[53]	Arm 2	RRT-MET	Total Ventricular Fibrillation/ Tachycardia, per 1,000 patient days	2014-2017	77898	per 1,000 patient days: 0.2	NR	Comparison: Arm 1-Control period p-value only: p<0.001	NR
Mankidy, 2020[53]	Arm 1	RRT	Intensive Care Unit Cardiac Arrest, per 1,000 patient days	2013-2014	44643	per 1,000 patient days: 1.45	NR	Ref	NR
Mankidy, 2020[53]	Arm 2	RRT-MET	Intensive Care Unit Cardiac Arrest, per 1,000 patient days	2014-2017	77898	per 1,000 patient days: 0.6	NR	Comparison: Arm 1-Control period p-value only: p<0.001	NR

Author, Year	Arm	Arm Name	Outcome Definition	Followup Timepoint	N at Analysis	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Mankidy, 2020[53]	Arm 1	RRT	Intensive Care Unit Pulseless Electrical Activity, per 1,000 patient days	2013-2014	44643	per 1,000 patient days: 1.05	NR	Ref	NR
Mankidy, 2020[53]	Arm 2	RRT-MET	Intensive Care Unit Pulseless Electrical Activity, per 1,000 patient days	2014-2017	77898	per 1,000 patient days: 0.34	NR	Comparison: Arm 1-Control period p-value only: p<0.001	NR
Mankidy, 2020[53]	Arm 1	RRT	Acute Care Ward Cardiac Arrest, per 1,000 patient days	2013-2014	44643	per 1,000 patient days: 0.43	NR	Ref	NR
Mankidy, 2020[53]	Arm 2	RRT-MET	Acute Care Ward Cardiac Arrest, per 1,000 patient days	2014-2017	77898	per 1,000 patient days: 0.17	NR	Comparison: Arm 1-Control period p-value only: p<0.001	NR
Mankidy, 2020[53]	Arm 1	RRT	Acute Care Ward Pulseless Electrical Activity, per 1,000 patient days	2013-2014	44643	per 1,000 patient days: 0.25	NR	Ref	NR
Mankidy, 2020[53]	Arm 2	RRT-MET	Acute Care Ward Pulseless Electrical Activity, per 1,000 patient days	2014-2017	77898	per 1,000 patient days: 0.09	NR	Comparison: Arm 1-Control period p-value only: p<0.001	NR
Mankidy, 2020[53]	Arm 1	RRT	Total Emergency Department Cardiac Arrest, per 1,000 patient days	2013-2014	44643	per 1,000 patient days: 0.2	NR	Ref	NR

Author, Year	Arm	Arm Name	Outcome Definition	Followup Timepoint	N at Analysis	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Mankidy, 2020[53]	Arm 2	RRT-MET	Total Emergency Department Cardiac Arrest, per 1,000 patient days	2014-2017	77898	per 1,000 patient days: 0.07	NR	Comparison: Arm 1-Control period p-value only: p<0.001	NR
Mankidy, 2020[53]	Arm 1	RRT	Emergency Department Pulseless Electrical Activity, per 1,000 patient days	2013-2014	44643	per 1,000 patient days: 0.17	NR	Ref	NR
Mankidy, 2020[53]	Arm 2	RRT-MET	Emergency Department Pulseless Electrical Activity, per 1,000 patient days	2014-2017	77898	per 1,000 patient days: 0.05	NR	Comparison: Arm 1-Control period p-value only: p<0.001	NR
Sawicki, 2021[54]	Arm 1	Pre-implementation	Cardiopulmonary arrests before PICU admission	2017-2019	615	NR	NR	Ref	No
Sawicki, 2021[54]	Arm 2	Post-implementation	Cardiopulmonary arrests before PICU admission	2019-2021	277	NR	NR	Comparison: Arm 1-Pre-implementation p-value only: p=NS	No
Sebat, 2018[56]	Arm 1	Control period	Cardiac arrests, per 1000 discharges	NR	28914	Per 1,000 discharges: 3.1	NR	Ref	NR
Sebat, 2018[56]	Arm 2	Intervention period	Cardiac arrests, per 1000 discharges	NR	39802	Per 1,000 discharges: 2.4	NR	Comparison: Arm 1-Control period p-value only: p=0.04	NR

MET = medical emergency team; N=sample size; NR=not reported; NS=not significant; p=p-value; PICU=pediatric intensive care unit; Ref=reference arm; RRT=rapid response team

Evidence Table C-20. Serious adverse events related to clinical deterioration outcome (categorical data) of included studies comparing efferent limb changes

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Hatlem, 2018[52]	Arm 1	Original RRT	Transferred to a monitored bed	2005-2007	68	4 (5.9)	NR	NR	NR
Hatlem, 2018[52]	Arm 2	Modified RRT	Transferred to a monitored bed	2007-2008	633	31 (4.9)	NR	NR	NR
Hatlem, 2018[52]	Arm 1	Original RRT	Transferred to a step-down bed	2005-2007	68	NR	NR	NR	NR
Hatlem, 2018[52]	Arm 2	Modified RRT	Transferred to a step-down bed	2007-2008	633	25 (3.9)	NR	NR	NR
Hatlem, 2018[52]	Arm 1	Original RRT	Procedure performed	2005-2007	68	NR	NR	NR	NR
Hatlem, 2018[52]	Arm 2	Modified RRT	Procedure performed	2007-2008	633	4 (0.6)	NR	NR	NR
Hatlem, 2018[52]	Arm 1	Original RRT	Transferred to Dialysis	2005-2007	68	NR	NR	NR	NR
Hatlem, 2018[52]	Arm 2	Modified RRT	Transferred to Dialysis	2007-2008	633	1 (0.2)	NR	NR	NR

N=sample size; NR=not reported; RRT=rapid response team

Evidence Table C-21. Serious adverse events related to clinical deterioration outcome (continuous data) of included studies comparing efferent limb changes

Author, Year	Arm	Arm Name	Outcome Definition	Followup Timepoint	N at Analysis	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Sawicki, 2021[54]	Arm 1	Pre-implementation	Critical deterioration events	2017-2019	615	NR	Pre-implemenetation trajectory, number of events per 1000 non-ICU patient days per month.: -0.01 (95% CI: -0.06 to 0.04), p=0.67	Ref	Age, sex, PICU admission after a rapid response, number of CCCs, PRISM 3 score, and a rapid response-PRISM 3 interaction term.
Sawicki, 2021[54]	Arm 2	Post-implementation	Critical deterioration events	2019-2021	277	NR	Post-implemenetation trajectory, number of events per 1000 non-ICU patient days per month.: -0.29 (95% CI: -0.42 to -0.16), p<0.001	Comparison: Arm 1-Pre-implementation Difference between pre and post trajectories: -0.28 (95% CI: -0.40 to -0.16), p<0.001	Age, sex, PICU admission after a rapid response, number of CCCs, PRISM 3 score, and a rapid response-PRISM 3 interaction term.
Sawicki, 2021[54]	Arm 1	Pre-implementation	Non-invasive positive pressure ventilation within 12 hours of PICU admission	2017-2019	615	NR	Pre-implemenetation trajectory, number of events per 1000 non-ICU patient days per month.: -0.01 (95% CI: -0.05 to 0.03), p=0.72	Ref	Age, sex, PICU admission after a rapid response, number of CCCs, PRISM 3 score, and a rapid response-PRISM 3 interaction term.

Author, Year	Arm	Arm Name	Outcome Definition	Followup Timepoint	N at Analysis	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Sawicki, 2021[54]	Arm 2	Post-implementation	Non-invasive positive pressure ventilation within 12 hours of PICU admission	2019-2021	277	NR	Post-implemenetation trajectory, number of events per 1000 non-ICU patient days per month.: -0.22 (95% CI: -0.31 to -0.11), p<0.001	Comparison: Arm 1-Pre-implementation Difference between pre and post trajectories: -0.21 (95% CI: -0.31 to -0.11), p<0.001	Age, sex, PICU admission after a rapid response, number of CCCs, PRISM 3 score, and a rapid response-PRISM 3 interaction term.
Sawicki, 2021[54]	Arm 1	Pre-implementation	Intubation within 12 h of PICU admission	2017-2019	615	NR	Pre-implemenetation trajectory, number of events per 1000 non-ICU patient days per month.: 0 (95% CI: -0.01 to 0.01), p=0.92	Ref	Age, sex, PICU admission after a rapid response, number of CCCs, PRISM 3 score, and a rapid response-PRISM 3 interaction term.
Sawicki, 2021[54]	Arm 2	Post-implementation	Intubation within 12 h of PICU admission	2019-2021	277	NR	Post-implemenetation trajectory, number of events per 1000 non-ICU patient days per month.: -0.1 (95% CI: -0.13 to -0.07), p<0.001	Comparison: Arm 1-Pre-implementation Difference between pre and post trajectories: -0.1 (95% CI: -0.13 to -0.07), p<0.001	Age, sex, PICU admission after a rapid response, number of CCCs, PRISM 3 score, and a rapid response-PRISM 3 interaction term.
Sawicki, 2021[54]	Arm 1	Pre-implementation	Intubation within 1 hour of PICU admission	2017-2019	615	NR	Pre-implemenetation trajectory, number of events per 1000 non-ICU patient days per month.: 0 (95% CI: -0.01 to 0.01), p=0.59	Ref	Age, sex, PICU admission after a rapid response, number of CCCs, PRISM 3 score, and a rapid response-PRISM 3 interaction term.

Author, Year	Arm	Arm Name	Outcome Definition	Followup Timepoint	N at Analysis	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Sawicki, 2021[54]	Arm 2	Post-implementation	Intubation within 1 hour of PICU admission	2019-2021	277	NR	Post-implemenetation trajectory, number of events per 1000 non-ICU patient days per month.: -0.08 (95% CI: -0.11 to -0.05), p<0.001	Comparison: Arm 1-Pre-implementation Difference between pre and post trajectories: -0.08 (95% CI: -0.11 to -0.05), p<0.001	Age, sex, PICU admission after a rapid response, number of CCCs, PRISM 3 score, and a rapid response-PRISM 3 interaction term.

CCC=complex chronic conditions; CI=confidence interval; ICU=intensive care unit; N=sample size; NR=not reported; p=p-value; PICU=pediatric intensive care unit; PRISM=Pediatric Risk of Mortality, Version 3; Ref=reference arm; RRT=rapid response team

Evidence Table C-22. Mortality outcome (categorical data) of included studies comparing efferent limb changes

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Hatlem, 2018[52]	Arm 1	Original RRT	Expired	2005-2007	68	NR	NR	NR	NR
Hatlem, 2018[52]	Arm 2	Modified RRT	Expired	2007-2008	633	4 (0.6)	NR	NR	NR
Hatlem, 2018[52]	Arm 1	Original RRT	Overall mortality	2005-2007	68	NR (2.27)	NR	NR	NR
Hatlem, 2018[52]	Arm 2	Modified RRT	Overall mortality	2007-2008	633	NR (2.21)	NR	NR	NR
Sebat, 2018[56]	Arm 1	Control period	Mortality	NR	28914	1083 (3.7)	Observed-to-expected mortality ratio: 1.5 (95% CI: NR), p=NR	Ref	Observed/expected mortality ratio
Sebat, 2018[56]	Arm 2	Intervention period	Mortality	NR	39802	1282 (3.2)	Observed-to-expected mortality ratio: 1 (95% CI: NR), p=NR	Comparison: Arm 1-Control period p-value only: p<0.001	Observed/expected mortality ratio
Vandegrift, 2021[57]	Arm 1	Pre-implementation	Mortality	2000-2005	85	NR (50)	NR	Ref	NR
Vandegrift, 2021[57]	Arm 2	Post-implementation	Mortality	2000-2005	426	NR (10)	NR	Comparison: Arm 1-Pre-MET p-value only: p<0.001	NR
Vandegrift, 2021[57]	Arm 1	Pre-implementation	Mortality	2003-2005	68	NR (51)	NR	Ref	NR
Vandegrift, 2021[57]	Arm 2	Post-implementation	Mortality	2003-2005	63	NR (27)	NR	Comparison: Arm 1-Pre-MET p-value only: p<0.001	NR
Vandegrift, 2021[57]	Arm 1	Pre-implementation	Mortality	2008-2013	28914	NR (3.8)	NR	Ref	NR

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Vandegrift, 2021[57]	Arm 2	Post-implementation	Mortality	2008-2013	39802	NR (3.2)	NR	Comparison: Arm 1-Pre-MET p-value only: p<0.001	NR

CI=confidence interval; MET = medical emergency team; N=sample size; NR=not reported; p=p-value; Ref=reference arm; RRT=rapid response team

Evidence Table C-23. Mortality outcome (continuous data) of included studies comparing efferent limb changes

Author, Year	Arm	Arm Name	Outcome Definition	Followup Timepoint	N at Analysis	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Factora, 2022[55]	Arm 1	Pre-RRT implementation	In-hospital mortality, trend slope	2005 to 2008	177760	Slope: 0.001 (SE 0.001)	Odds ratio: 1.01 (95% CI: 0.98 to 1.04), p=NR	Ref	Demographic factors and surgical procedures
Factora, 2022[55]	Arm 2	Post-implementation period	In-hospital mortality, trend slope	2009 to 2018	450778	Slope: –0.003 (SE 0)	Odds ratio: 0.961 (95% CI: 0.955 to 0.968), p=NR	Comparison: Arm 1-Post implementation Slope change: –0.004 (SE 0.001), p=0.001	Demographic factors and surgical procedures
Factora, 2022[55]	Arm 1	Pre-RRT implementation	In-hospital mortality, intercept change	2005 to 2008	NR	NR	Odds ratio: 1.01 (95% CI: 0.98 to 1.04), p=NR	Ref	Demographic factors and surgical procedures
Factora, 2022[55]	Arm 2	Post-implementation period	In-hospital mortality, intercept change	2009 to 2018	NR	NR	Odds ratio: 1.17 (95% CI: 1.09 to1.25), p=NR	Comparison: Arm 1-Postimplementation Intercept change: 0.154 (SE 0.036), p<0.001	Demographic factors and surgical procedures
Factora, 2022[55]	Arm 1	Pre-RRT implementation	In-hospital mortality, intercept	2005 to 2008	177760	Intercept: –6.122 (SE 0.072)	Odds ratio: 0.002 (95% CI: 0.002 to 0.003), p=NR	Ref	Demographic factors and surgical procedures
Factora, 2022[55]	Arm 2	Post-implementation period	In-hospital mortality, intercept	2009-2011	NR	NR	NR	Comparison: Arm 1-Postimplementation Intercept change: 0.087 (SE 0.045) Odds Ratio: 1.091 (95% CI: 0.999 to 1.192) p=0.054	Demographic factors and surgical procedures

Author, Year	Arm	Arm Name	Outcome Definition	Followup Timepoint	N at Analysis	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Factora, 2022[55]	Arm 2	Post-implementation period	In-hospital mortality, intercept	2012-2013	NR	NR	NR	Comparison: Arm 1-Postimplementation Intercept change: –0.209 (SE 0.05) Odds Ratio: 0.812 (95% CI: 0.736 to 0.896) p<0.001	Demographic factors and surgical procedures
Factora, 2022[55]	Arm 2	Post-implementation period	In-hospital mortality, intercept	2014-2018	NR	NR	NR	Comparison: Arm 1-Postimplementation Intercept change: –0.136 (SE 0.048) Odds Ratio: 0.872 (95% CI: 0.794 to 0.958) p=0.004	Demographic factors and surgical procedures
Factora, 2022[55]	Arm 1	Pre-RRT implementation	In-hospital mortality, trend slope	2005 to 2008	177760	Slope: 0 (SE 0.001)	Odds ratio: 0.996 (95% CI: 0.002 to 0.003), p=0.782	Ref	Demographic factors and surgical procedures
Factora, 2022[55]	Arm 2	Post-implementation period	In-hospital mortality, trend slope	2009-2011	NR	Slope: 0.003 (0.002)	NR	Comparison: Arm 1-Postimplementation Intercept change: 0.003 (SE 0.002) Odds Ratio: 1.038 (95% CI: 0.992 to 1.088) p=0.111	Demographic factors and surgical procedures
Factora, 2022[55]	Arm 2	Post-implementation period	In-hospital mortality, trend slope	2012-2013	NR	Slope: 0.002 (0.002)	NR	Comparison: Arm 1-Postimplementation Intercept change: –0.001 (SE 0.003) Odds Ratio: 0.812 (95% CI: 0.736 to 0.896) p=0.71	Demographic factors and surgical procedures

Author, Year	Arm	Arm Name	Outcome Definition	Followup Timepoint	N at Analysis	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Factora, 2022[55]	Arm 2	Post-implementation period	In-hospital mortality, trend slope	2014-2018	NR	Slope: -0.001 (0.001)	NR	Comparison: Arm 1-Postimplementation Intercept change: –0.003 (SE 0.002) Odds Ratio: 0.872 (95% CI: 0.794 to 0.958) p=0.26	Demographic factors and surgical procedures
Factora, 2022[55]	Arm 1	Pre-RRT implementation	In-hospital mortality, fully adjusted	2005 to 2008	177760	NR	Odds ratio: 1.16 (95% CI: 1.09 to1.25), p<0.001	Ref	Demographic factors, surgical procedures, patient medical history
Factora, 2022[55]	Arm 2	Post-implementation period	In-hospital mortality, fully adjusted	2009 to 2018	450778	NR	Odds ratio: 0.74 (95% CI: 0.63 to 0.85), p<0.001	Comparison: Arm 1-Postimplementation Odds ratio: 0.96 (95% CI: 0.96 to 0.97), p=<0.001	Demographic factors, surgical procedures, patient medical history

CI=confidence interval; N=sample size; NR=not reported; p=p-value; Ref=reference arm; RRT=rapid response team; SE=standard error

Evidence Table C-24. Transition to higher level of care outcome (categorical data) of included studies comparing efferent limb changes

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Hatlem, 2018[52]	Arm 1	Original RRT	Transferred to ICU	2005-2007	68	45 (66.2)	NR	NR	NR
Hatlem, 2018[52]	Arm 2	Modified RRT	Transferred to ICU	2007-2008	633	192 (30.3)	NR	NR	NR
Hatlem, 2018[52]	Arm 1	Original RRT	Transferred to the Emergency Department	2005-2007	68	1 (1.5)	NR	NR	NR
Hatlem, 2018[52]	Arm 2	Modified RRT	Transferred to the Emergency Department	2007-2008	633	9 (1.4)	NR	NR	NR
Hatlem, 2018[52]	Arm 1	Original RRT	Transferred to Operating Room	2005-2007	68	NR	NR	NR	NR
Hatlem, 2018[52]	Arm 2	Modified RRT	Transferred to Operating Room	2007-2008	633	4 (0.6)	NR	NR	NR

ICU=intensive care unit; N=sample size; NR=not reported; RRT=rapid response team

Evidence Table C-25. Transition to higher level of care outcome (continuous data) of included studies comparing efferent limb changes

Author, Year	Arm	Arm Name	Outcome Definition	Followup Timepoint	N at Analysis	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Sawicki, 2021[54]	Arm 1	Pre-implementation	PICU admissions after a rapid response	2017-2019	615	per 1, 000 non-ICU patient days: 1.09 (13.5%)	NR	NR	NR
Sawicki, 2021[54]	Arm 2	Post-implementation	PICU admissions after a rapid response	2019-2021	277	per 1, 000 non-ICU patient days: 1.79 (23.4%)	NR	NR	NR
Sawicki, 2021[54]	Arm 1	Pre-implementation	Unplanned transfers to the PICU	2017-2019	615	per 1, 000 non-ICU patient days: 8.08	NR	NR	NR
Sawicki, 2021[54]	Arm 2	Post-implementation	Unplanned transfers to the PICU	2019-2021	277	per 1, 000 non-ICU patient days: 7.62	NR	NR	NR

ICU=intensive care unit; N=sample size; NR=not reported; PICU=pediatric intensive care unit

Evidence Table C-26. Barriers, limitations, and facilitators to successfully implementing rapid response systems

Author, Year	Facilitators or Barriers
Hatlem, 2018[52]	Barriers: Barrier to calling RRT was nurses were uncomfortable consulting with a team directed by a physician, preferring instead a peer-to-peer consult.
Stellpflug, 2021[48]	Barriers: Potential barriers to early recognition of patient deterioration include the variable frequency of nursing assessments and vital sign checks, especially during the night, and suboptimal multidisciplinary communication of changes in patient condition.
Winterbottom, 2021[44]	Facilitator: Embedded RRNs improved staff support, standardized practices, and enhanced rapid penetration of clinical changes into routine patient care
Winterbottom, 2021[44]	Facilitator: Fiscal impact of the program demonstrated a return on investment for RRN salaries

RRN=rapid response nurse; RRT=rapid response team

Evidence Table C-27. Strength of evidence of primary studies included

Comparison	Outcome	Population	Number of Primary Studies (Design)	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Strength of Evidence
Comparing Outcomes With and Without a Rapid Response System	Hospital mortality	Adult	4 pre-post studies[40, 44, 45, 55]	High	Direct	Consistent	Precise	Undetected	Low
		Pediatric	3 pre-post studies[41-43]	High	Direct	Consistent	Precise	Undetected	Low
	incidence of cardiorespiratory arrest	Adult	2 pre-post studies[44, 45]	High	Direct	Consistent	Imprecise No statistical analysis provided in Winterbottom, 2021[44]	Undetected	Insufficient
		Pediatric	1 pre-post study[41]	High	Direct	Unknown	Precise	Undetected	Insufficient
	transition to higher level of care	Adult	1 pre-post studies[44]	High	Direct	Unknown	Imprecise No statistical analysis provided in Winterbottom, 2021[44]	Undetected	Insufficient
		Pediatric	1 pre-post studies[43]	High	Direct	Unknown	Precise	Undetected	Insufficient
	other serious adverse events related to clinical deterioration	Adult	1 pre-post study[45]	High	Direct	Unknown	Precise	Undetected	Insufficient
		Pediatric	1 pre-post study[41]	High	Direct	Unknown	Precise	Undetected	Insufficient
Comparing Outcomes	Hospital mortality	Adult	4 pre-post studies[47, 51, 56, 57]	High	Direct	Consistent	Precise	Undetected	Low

Comparison	Outcome	Population	Number of Primary Studies (Design)	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Strength of Evidence
Associated With an Afferent Limb Model Change		Pediatric	1 Observational study with a comparison group**[33] 1 pre-post study[49]	High	Direct	Consistent	Imprecise Lack of comparator data and small sample size in Bavare, 2018, low number of events in Dean, 2020[49]	Undetected	Insufficient
	incidence of cardiorespiratory arrest	Pediatric	1 Observational study with a comparison group**[33] 1 pre-post study[49]	High	Direct	Consistent	Imprecise Lack of comparator data and small sample size in Bavare, 2018[33]	Undetected	Insufficient
	transition to higher level of care	Adults	1 observational study with a comparison group[48] 3 pre-post[46, 47, 51]	High	Direct	Consistent	Precise	Undetected	Low
		Pediatric	1 Observational study with a comparison group**[33] 2 pre-post studies[49, 50]	High	Direct	Consistent	Imprecise Small sample size in Penney, 2021, [50] and Bavare, 2018[33]	Undetected	Insufficient

Comparison	Outcome	Population	Number of Primary Studies (Design)	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Strength of Evidence
	other serious adverse events related to clinical deterioration	Pediatric	1 Pre-post[50]	High	Direct	Unknown	Imprecise Small sample size	Undetected	Insufficient
Comparing Outcomes Associated With an Efferent Limb Model Change	Hospital mortality	Adults	3 pre-post studies[55-57] 1 observational study with a comparison[52]	High	Direct	Consistent	Precise	Undetected	Low
	incidence of cardiorespiratory arrest	Adult	2 pre-post studies[54, 56] 1 observational study with a comparison[53]	High	Direct	Consistent	Precise	Undetected	Low
	transition to higher level of care	Adult	1 observational study with a comparison group[52]	High	Direct	Unknown	Precise	Undetected	Insufficient
		Pediatric	1 pre-post[54]	High	Direct	Unknown	Precise	Undetected	Insufficient
	other serious adverse events related to clinical deterioration	Pediatric	1 pre-post[54]	High	Direct	Unknown	Precise	Undetected	Insufficient

** Bavare, 2018 compares family-initiated activation of their rapid response system to clinician-initiated activation. Given that their results find that the reasons for activation are drastically different between the two (see Section 4.2.5.2 for description of study details in relation to outcomes), it is not possible to reliably compare outcomes based on the two afferent limb options.