

Rapid Response Teams

A Systematic Review and Meta-analysis

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Background: Although rapid response teams (RRTs) increasingly have been adopted by hospitals, their effectiveness in reducing hospital mortality remains uncertain. We conducted a meta-analysis to assess the effect of RRTs on reducing cardiopulmonary arrest and hospital mortality rates.

Methods: We conducted a systematic review of studies published from January 1, 1950, through November 31, 2008, using PubMed, EMBASE, Web of Knowledge, CINAHL, and all Evidence-Based Medicine Reviews. Randomized clinical trials and prospective studies of RRTs that reported data on changes in the primary outcome of hospital mortality or the secondary outcome of cardiopulmonary arrest cases were included.

Results: Eighteen studies from 17 publications (with 1 treated as 2 separate studies) were identified, involving nearly 1.3 million hospital admissions. Implementation of an RRT in adults was associated with a 33.8% reduction in rates of

cardiopulmonary arrest outside the intensive care unit (ICU) (relative risk [RR], 0.66; 95% confidence interval [CI], 0.54-0.80) but was not associated with lower hospital mortality rates (RR, 0.96; 95% CI, 0.84-1.09). In children, implementation of an RRT was associated with a 37.7% reduction in rates of cardiopulmonary arrest outside the ICU (RR, 0.62; 95% CI, 0.46-0.84) and a 21.4% reduction in hospital mortality rates (RR, 0.79; 95% CI, 0.63-0.98). The pooled mortality estimate in children, however, was not robust to sensitivity analyses. Moreover, studies frequently found evidence that deaths were prevented out of proportion to reductions in cases of cardiopulmonary arrest, raising questions about mechanisms of improvement.

Conclusion: Although RRTs have broad appeal, robust evidence to support their effectiveness in reducing hospital mortality is lacking.

Arch Intern Med. 2010;170(1):18-26

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CASES OF IN-HOSPITAL cardiopulmonary arrest are common and are associated with low rates of survival.¹ Previous studies^{2,3} have found that hospital patients often exhibit signs of physiologic deterioration in the hours before cardiopulmonary arrest occurs. Because early detection of these warning signs may provide an opportunity for the prevention of cardiopulmonary arrest and its attendant mortality, the use of a rapid response team (RRT) has been promoted as a means of reduction of in-hospital mortality.



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An RRT is typically a multidisciplinary team of medical, nursing, and respiratory therapy staff charged with the prompt evaluation, triage, and treatment of patients with signs of clinical deterioration not treated in the intensive care unit

(ICU).⁴ Independent of the primary physicians who care for the patient, members of the RRT can order critical laboratory and imaging studies and medications, transfer patients to higher levels of monitoring and care, and discuss end-of-life care with patients. The development of RRTs has grown in parallel with an increasing interest in improvement of hospital quality and outcomes. In fact, the Institute for Healthcare Improvement's 100 000 Lives Campaign⁵ has recommended that hospitals implement RRTs as 1 of 6 strategies to reduce preventable in-hospital deaths. As a result, hundreds of hospitals have implemented these teams as part of their quality improvement initiatives.

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Although the use of RRTs has broad appeal, previous studies⁶⁻⁸ have been limited and have reported mixed results, and individual studies have often not been adequately powered to examine the

clinically meaningful outcome of hospital mortality. Because a primary action of RRTs is to triage sick patients to the ICU, to demonstrate that these interventions not only reduce rates of intermediate outcomes (such as cardiopulmonary arrest outside the ICU) but also reduce hospital-wide mortality is critical before endorsing their widespread adoption.^{8,9} Finally, although meta-analyses of RRTs have been previously performed,^{10,11} they do not include a number of recent studies, have not examined the cumulative temporal trend on outcomes with inclusion of each additional study, and have not addressed the extent to which mortality benefits may be attributable to the interventions of the RRT.

Accordingly, we conducted an updated systematic review and meta-analysis to (1) assess the effect of RRT implementation in reduction of rates of cardiopulmonary arrest and hospital mortality, (2) examine the cumulative temporal trend on outcomes among published studies of RRTs, and (3) evaluate the degree to which observed mortality reductions are explained by lower rates of cardiopulmonary arrest.

METHODS

DATA SOURCES AND SEARCH STRATEGY

We conducted a systematic review of the literature for studies published from January 1, 1950, through November 31, 2008, by the use of PubMed, EMBASE, Web of Knowledge, CINAHL, and all Evidence-Based Medicine Reviews (which include the Cochrane Databases). The search was not restricted by language of articles and used both keywords and Medical Subject Headings in a Boolean search strategy (eAppendix available at <http://www.archinternmed.com>). In addition to these automated searches, we conducted a hand search of bibliographies of key articles and abstracts presented at major scientific conferences between 2006 and 2008, such as the annual meetings of the American Heart Association, the American College of Cardiology, the American College of Chest Physicians, and the American College of Emergency Physicians.

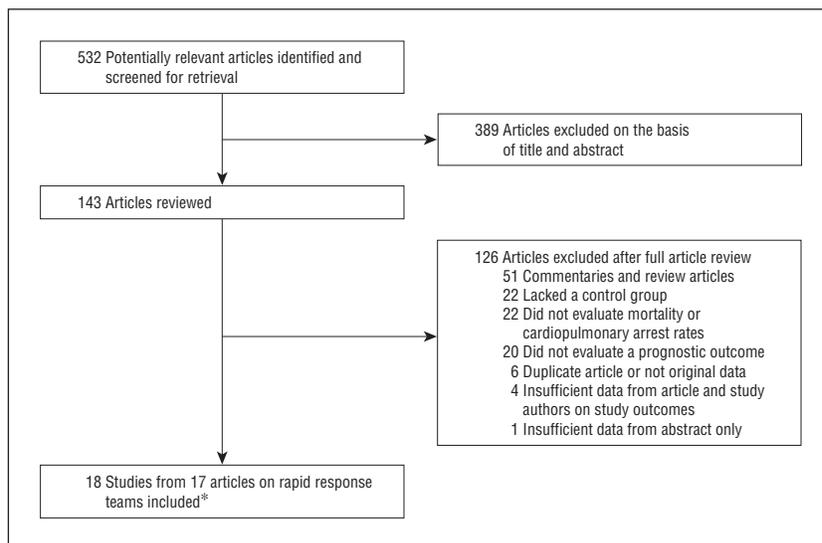


Figure 1. Flowchart of the study selection process. *One publication²⁰ was treated as 2 separate studies.

STUDY INCLUSION CRITERIA AND STUDY OUTCOMES

To be considered for inclusion in this meta-analysis, studies were required to meet 3 inclusion criteria: (1) be randomized clinical trials or prospective active intervention studies of RRTs among hospital inpatients, (2) perform comparisons with a control group or a control period, and (3) provide sufficient quantitative data on either the primary outcome of hospital-wide mortality or the secondary outcome of rates of non-ICU-treated cardiopulmonary arrest. On the basis of the initial search results, 532 titles and abstracts were independently reviewed by at least 2 of the authors (P.S.C., R.J., and/or C.S.), and 389 were immediately excluded. Two reviewers (P.S.C. and R.J.) subsequently reviewed the full text articles of the remaining 143 publications for study inclusion. Agreement between the reviewers for study eligibility was high (weighted $\kappa=0.91$), and disagreements were resolved by discussion. The corresponding authors of 8 studies¹²⁻¹⁹ were contacted by electronic correspondence on at least 3 occasions during a 4-week period (December 2008) to provide additional data on study outcomes to allow for meta-analysis; 5 did not respond and were excluded.¹⁵⁻¹⁹ Additional reasons for study exclusion were nonintervention study (descriptive and review articles; $n=51$), lack of a control group ($n=22$), lack of evaluation of a prognostic outcome ($n=20$) or any of the outcomes of this study ($n=22$), and duplicate studies ($n=6$) (**Figure 1**).

DATA EXTRACTION

Data extraction was independently performed by 2 reviewers (P.S.C. and C.S.)

by the use of a standardized form. From each study, the following variables were abstracted: study outcomes (rates of cardiopulmonary arrest and hospital mortality in control and intervention periods); age group (pediatric or adult); type of study (randomized trial, interrupted time series design with adjustment for preintervention trends, or observational studies with no adjustment for preintervention trends); year of publication; number of sites; academic status of hospitals; duration of control, educational rollout, and intervention periods; sample sizes of control and intervention groups; control for confounders (eg, demographics or case mix); control for preintervention time trends; and frequency of activations per 1000 admissions. We also collected information as to whether a study included or excluded patients with do not resuscitate (DNR) status in its recording of outcomes of hospital mortality. Authors were contacted to clarify study definitions of mortality when it was not clearly defined. Finally, if several estimates for study outcomes were reported, the most fully adjusted estimate was chosen.

CRITERIA USED TO ASSESS QUALITY

Studies that met our inclusion criteria were further evaluated for quality.²¹ Studies were considered high quality if they adjusted for confounding (age, sex, ethnicity, and case mix) between the control and intervention periods and for time trends by the use of either contemporaneous control groups (eg, randomized clinical trials and observational studies with concurrent controls) or an

interrupted time series design with at least 3 data time points before and after intervention. Studies that adjusted only for confounding but not for time trends were categorized as fair quality, whereas studies that did not adjust for either were categorized as low quality.

DATA SYNTHESIS

Outcome data for hospital mortality and non-ICU-treated cardiopulmonary arrest were summarized by the use of basic descriptive statistics (simple counts and proportions). Because of differences in the origin²² and incidence²³ of cardiopulmonary arrest between adults and children, we stratified our quantitative analyses by the study population. Meta-analyses for each outcome were conducted by means of a random-effects model.²⁴ Between-study heterogeneity was evaluated with the I^2 statistic,²⁵ and publication bias was evaluated by means of the Begg test. We also examined the cumulative influence of each study on the pooled estimate over calendar time. Finally, we performed sensitivity analyses to examine the influence of each study on the overall pooled estimate by omission of each estimate one at a time.

Meta-regression²⁶ was conducted to explore the heterogeneity in risk ratios between studies based on predefined study criteria, which included differences in the definition of study outcome (eg, included or excluded patients with DNR status), study quality, and the frequency of RRT use (>10 vs ≤ 10 activations per 1000 admissions). Significant variables identified in meta-regression were further explored with subgroup analyses.

To examine the mechanistic plausibility of mortality gains with RRT implementation, we evaluated the extent to which lower hospital mortality rates were fully attributable to reductions in cardiopulmonary arrest by the RRT intervention. We accomplished this by examination of whether the number of codes averted exceeded the number of deaths prevented among those studies that reported a significant reduction in hospital mortality. For those studies that also reported case-fatality rates for cardiopulmonary arrest before and after RRT intervention, we further determined whether the number of expected deaths prevented (derived from reductions in and improved survival from cardiopulmonary arrest) was comparable to the actual reported number of fewer deaths after RRT intervention.

All statistical tests were 2-sided and were evaluated at a significance

level of .05. We used STATA statistical software, version 10.0 (StataCorp, College Station, Texas) to conduct all analyses.

RESULTS

SEARCH RESULTS

A total of 17 articles^{9,12-14,20,27-38} (of which one study²⁰ was treated as 2 unique studies) met study inclusion criteria (Figure 1). Original data from 1 study¹³ were obtained from study authors to calculate event rates and risk ratios. For a second study,²⁰ an intervention hospital was separately compared with 2 control hospitals (hence its treatment as 2 distinct studies). A third study³⁰ reported outcomes separately for medical and surgical patients, and we combined event rates from both groups for this review.

SYSTEMATIC REVIEW OF RRTs

Description of Studies

The RRT studies had a total sample size of 1 271 864 admissions (580 776 during the control period and 691 088 during the intervention period). All RRT studies were published during or after 2000, with 9 (50.0%) published since 2007 (**Table 1**). A randomized trial design was used in 2 studies (11.1%). Fourteen studies were single-institution studies, 3 involved 2 hospitals, and 1 involved 23 hospitals. Evaluation was performed among adults in 13 studies and among children in 5 studies.

Physicians participated in the RRT assessment of patients in 13 (81.3%) of the 16 studies that reported on team composition. Activation criteria, when reported, were similar across studies. Use of the RRT varied substantially across hospitals, with a median of 15.1 activations (range, 2.5-40.3) per 1000 admissions in adult studies and a median of 7.5 activations (range, 2.8-12.8) per 1000 admissions in pediatric studies.

Quality Assessment and Definition of Outcomes

Of the 18 RRT studies, 6 studies^{9,20,31,34,35} (5 adult and 1 pedi-

atric) were categorized as high quality. These studies included 2 randomized clinical trials, 2 observational studies with contemporaneous control populations, and 2 observational studies that adjusted for preintervention trends.

Sixteen RRT studies reported on rates of cardiopulmonary arrest. Seven studies^{9,12,14,29,35,36,38} defined cardiopulmonary arrest as both respiratory and cardiac arrest, another 8^{13,20,27,30,31,33,37} defined cardiopulmonary arrest as either respiratory or cardiac arrest, whereas 1 study²⁸ included all cardiac arrest calls. Fifteen RRT studies reported on hospital mortality. Ten studies^{9,12-14,27,32-35,37} included patients with DNR status in their mortality outcome, whereas 3 studies^{20,31} excluded patients with DNR status. One study³⁶ reported mortality for only patients not treated in the ICU, whereas 1 study²⁸ did not define mortality or respond to queries for additional information.

META-ANALYSIS OF RRT STUDIES

Cardiopulmonary Arrest

In adults, 7 studies^{9,12,13,27-30} showed a significant reduction in rates of cardiopulmonary arrest, whereas 4 studies^{20,31,33} did not. Collectively, implementation of an RRT in adults was associated with a 33.8% reduction in rates of non-ICU-treated cardiopulmonary arrest (pooled relative risk [RR], 0.66; 95% confidence interval [CI], 0.54-0.80) (**Figure 2**). No evidence of publication bias was seen ($P = .30$ for the Begg test). In subgroup analyses, adult studies identified as high quality reported a more modest 21.1% reduction in rates of non-ICU-treated cardiopulmonary arrest compared with a 47.8% reduction in the other studies (eFigure 1).

Among the 5 pediatric RRT studies, 4 studies^{14,35,36,38} reported a significant reduction in rates of cardiopulmonary arrest outside the ICU. Pooled analyses found that implementation of an RRT was associated with a 37.7% reduction in rates of non-ICU-treated cardiopulmonary arrest (Figure 2) and was robust to subgroup analyses (eFigure 1).

Table 1. Characteristics of the Included Rapid Response Team Studies

Source, Country	Age Group/ Study Design	Sites, No./ Type of Hospital	Control Period/ Rollout Period/ RRT Period, mo	RRT Start Date	Physician on Team	RRT Use Rate per 1000 Admissions	Study Definition of Cardiac Arrest and Mortality	Adjusted For	Study Quality ^a
Baxter et al, ¹² Canada	Adult/before-after	2/NR	24/12/12	Jan 2005	Yes	40.3	All cases of arrest/ Hospital-wide deaths, patients with DNR designation included	No adj	Low
Bellomo et al, ²⁷ Australia	Adult/before-after	1/academic	4/14/4	Nov 2000	Yes	4.7	Cardiac only/ Hospital-wide, patients with DNR designation included	No adj	Low
Brilli et al, ³⁶ United States	Pediatric/before-after	1/academic	16/4/8	Jun 2005	Yes	2.8	All cases of arrest/Non-ICU-treated cases only	No adj	Low
Bristow et al, ²⁰ Australia ^b	Adult/CC	2/NR	NR/NR/6	Jul 1996	Yes	NR	Cardiac only/ Hospital-wide, patients with DNR designation excluded	CC, D	High
Buist et al, ²⁸ Australia	Adult/before-after	1/academic	12/24/12	Jan 1999	Yes	6.7	Cardiac only ^a / Mortality NR	CM	Fair
Dacey et al, ¹³ United States	Adult/before-after	1/community	4/1/12	Oct 2005	No	20.1	Cardiac only/ Hospital-wide, patients with DNR designation included	No adj	Low
DeVita et al, ²⁹ United States	Adult/before-after	1/academic	60/0/20	Jan 2001	Yes	25.8	All cases of arrest/ Mortality NA	CM	Fair
Hillman et al, ³¹ Australia	Adult/clinical trial	23/mixed	NR/NR/NR	NR	NR	8.7	Cardiac only/ Hospital-wide, patients with DNR designation excluded	CM, RCT	High
Hunt et al, ³⁸ United States	Pediatric/before-after	1/academic	12/0/12	Oct 2004	Yes	11.7	All cases of arrest/ Mortality NA	No adj	Low
Jones et al, ³⁰ Australia	Adult/before-after	1/academic	8/14/50	Sep 2000	Yes	NR	Cardiac only/ Mortality NA	No adj	Low
Jones et al, ³² Australia	Adult/before-after	1/academic	12/14/50	Nov 2000	Yes	25.2	NA/ Hospital-wide, patients with DNR designation included	No adj	Low
Kenward et al, ³³ England	Adult/before-after	1/NR	NR/NR/12	Oct 2000	NR	2.5	Cardiac only/ Hospital-wide, patients with DNR designation included	No adj	Low
Priestley et al, ³⁴ England	Adult/clinical trial	1/NR	NR/NR/NR	Apr 2001	Yes	NR	NA/ Hospital-wide, patients with DNR designation included	CM, RCT	High
Sharek et al, ³⁵ United States	Pediatric/time series	1/academic	56/0/19	Sep 2005	Yes	7.5	All cases of arrest/ Hospital-wide, patients with DNR designation included	CM, D, T	High
Tibballs and Kinney, ³⁷ Australia	Pediatric/before-after	1/NR	41/3/48	Dec 2002	Yes	5.8	Cardiac only/ Non-ICU-treated cases only, patients with DNR designation included	No adj	Low
Zenker et al, ¹⁴ United States	Pediatric/before-after	1/academic	23/0/12	Dec 2005	No	12.8	All cases of arrest/ Hospital-wide, patients with DNR designation included	No adj	Low
Chan et al, ⁹ United States	Adult/time series	1/academic	20/4/20	Jan 2006	No	15.1	All cases of arrest/ Hospital-wide, patients with DNR designation included	D, CM, T	High

Abbreviations: CC, concurrent controls; CM, case-mix severity; D, demographics; DNR, do not resuscitate; ICU, intensive care unit; NA, not applicable; No adj, no adjustment; NR, not reported; RCT, randomized clinical trial; RRT, rapid response team; T, time trends.

^aStudy was designated as high quality if adjustments for preintervention trends (CC, RCT, or control for time trends) and for differences between patients in the 2 comparison periods were performed, fair quality if adjustments for differences between patients in the comparison periods but not for preintervention trends were performed, and low quality if no adjustment for either was performed.

^bArticle treated as 2 separate studies.

Hospital Mortality

Significant heterogeneity was found among the 11 adult studies that examined the effect of RRT implementation on hospital mortality ($I^2=91.4\%$, $P<.001$) (**Figure 3**). Two studies^{27,34} reported a significant reduction in hospital mortality, 1 study²⁸ reported a decreased trend, 6 studies^{9,12,13,20,31,33} reported

no effect, 1 study²⁰ reported a trend toward increased mortality, and 1 study³² reported an increase in hospital mortality. Taken together, these studies showed no overall effect on hospital mortality (pooled RR, 0.96; 95% CI, 0.84-1.09).

The cumulative effect of each additional study over calendar time on the pooled mortality estimate in adults is shown in

Figure 4. Although the pooled estimate from initial studies suggested a benefit, with the inclusion of recent studies, the cumulative pooled estimate has trended toward the null and was not associated with lower mortality rates. Collectively, there was no evidence of publication bias ($P=.92$ for the Begg test). Moreover, systematic omission of studies one at

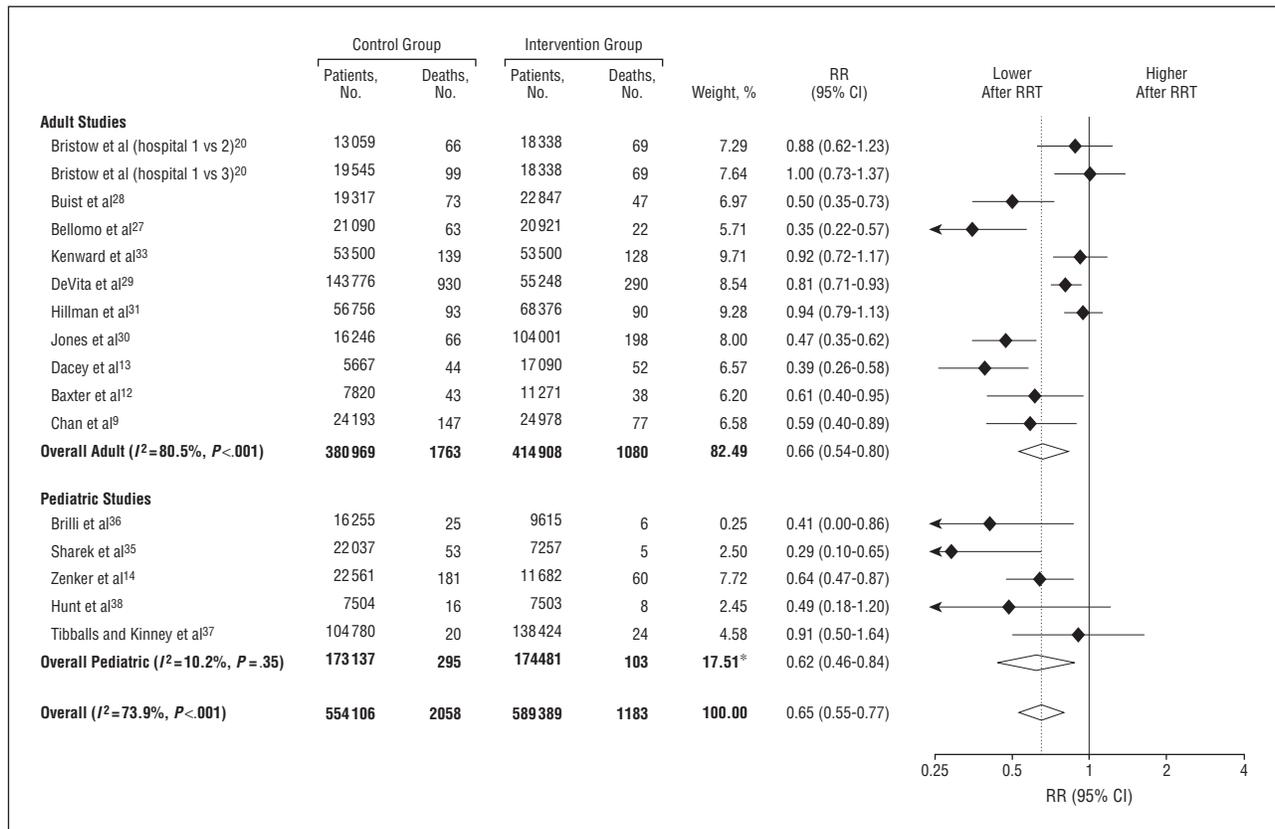


Figure 2. Pooled relative risks (RRs) of cardiopulmonary arrest outside the intensive care unit for adults and children after rapid response team (RRT) implementation. CI indicates confidence interval. *Number owing to rounding error for each of the individual pediatric studies.

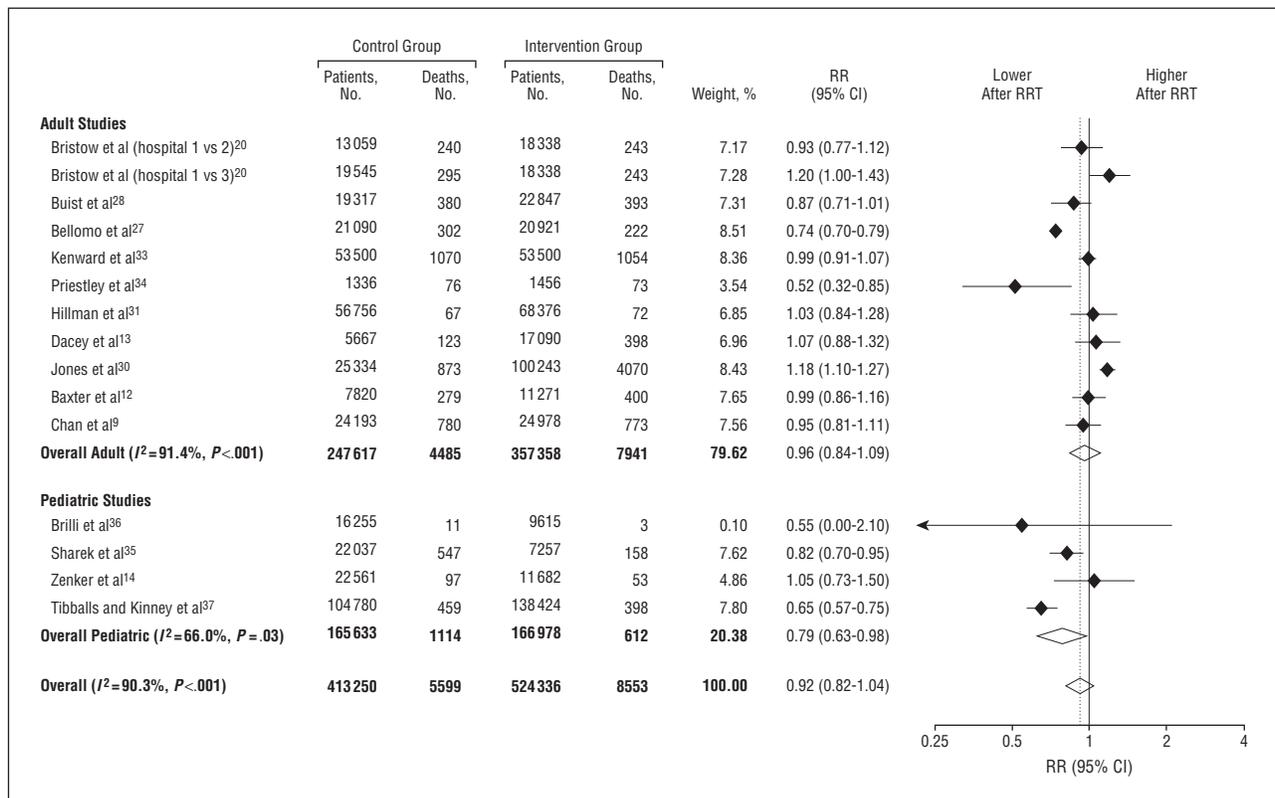


Figure 3. Pooled relative risks (RRs) of hospital mortality for adults and children after rapid response team (RRT) implementation. CI indicates confidence interval.

a time revealed no study whose removal would have meaningfully changed the pooled mortality estimate. Finally, pooled mortality estimates were not different between studies characterized as high vs low quality, studies with high vs low rates of RRT activation, or studies that excluded or included patients with a DNR designation (eFigure 2).

Among the 4 pediatric RRT studies, 2 studies^{35,37} reported a significant reduction in mortality, whereas 2 others^{14,36} found no effect. Implementation of an RRT was associated with lower hospital mortality rates in pediatric patients (pooled RR, 0.79; 95% CI, 0.63-0.98) (Figure 3), but significant heterogeneity was observed ($I^2=66.0\%$, $P=.03$). Importantly, the pooled mortality estimate was sensitive to omission of any 3 of the 4 individual studies³⁵⁻³⁷ (ie, would result in no association with hospital mortality when omitted), which suggests that the association of RRT implementation with lower mortality rates in pediatric hospitals was not robust (eFigure 3). Lastly, when data from adult and pediatric studies were aggregated, implementation of RRTs was not associated with lower hospital mortality rates (pooled RR, 0.92; 95% CI, 0.82-1.04) (Figure 3).

Mechanistic Plausibility

For the 5 studies^{27,28,34,35,37} that reported lower mortality rates after implementation of an RRT, we examined the extent to which this was owing to the interventions of the RRT with regard to cardiopulmonary arrest. One study³⁴ did not report on rates of cardiopulmonary arrest. In the 4 remaining studies,^{27,28,35,37} the number of fewer deaths observed after RRT implementation exceeded by 1.4-fold to more than 100-fold the number of cases of cardiopulmonary arrest averted (Table 2). For the 2 studies^{28,37} that also reported case-fatality rates of cardiopulmonary arrest before and after intervention, the number of averted deaths attributable to the RRT intervention (determined from the lower rate of and improved survival from cardiopulmonary arrest) could not account for the actual number of fewer

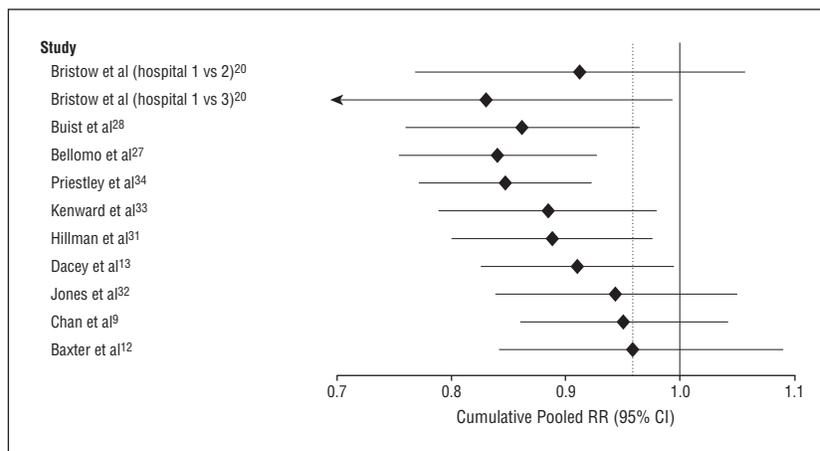


Figure 4. Cumulative pooled estimate for hospital mortality after rapid response team (RRT) implementation in adults. The cumulative effect of each additional study on the pooled mortality estimate in adults is depicted. Because of significant findings in earlier studies, there was a suggestion that RRTs may reduce hospital mortality rates. After inclusion of recent adult studies, however, implementation of RRTs was not found to be associated with lower hospital mortality rates. Dotted vertical line denotes the overall pooled mortality estimate in adults. CI indicates confidence interval; RR, relative risk.

deaths observed during the postintervention period (Table 3). This was particularly the case for the study³⁷ with the greatest weight in the pooled mortality estimate in children, in which 10 deaths were prevented through the direct interventions of the RRT on cardiopulmonary arrest, whereas 214 fewer deaths were reported in the postintervention period. For the other 2 studies,^{27,35} we similarly found that even if we assumed a best-case scenario (100% case-fatality rate before intervention and 0% case-fatality rate after intervention), the number of prevented deaths attributable to the RRT intervention could not account for the actual number of fewer deaths reported during the postintervention period (Table 3).

COMMENT

This systematic review found that implementation of RRTs was associated with substantial reductions in non-ICU-treated cardiopulmonary arrest rates of 33.8% in adults. However, these reductions were not associated with lower overall hospital mortality rates in this group of patients. Notably, the effect of RRT implementation on hospital mortality in adults has shifted toward the null during the past decade, which raises questions about the effective dissemination of relevant information about RRTs or the possibility of initial publication bias. In children, implementation of

an RRT intervention was associated with a pooled reduction in non-ICU-treated cardiopulmonary arrest rates of 37.7% and an overall 21.4% reduction in hospital mortality, but this latter finding was not robust to sensitivity analyses.

In the adult and pediatric studies that reported lower hospital mortality rates after RRT implementation, we also found a disconnect between these improvements and lower rates of or improved survival from cardiopulmonary arrest (see Tables 2 and 3). It is likely that the mortality benefit associated with the RRT intervention was overestimated in these studies. The excess deaths prevented may have been owing to the overall improvement in hospital care quality from RRT training and education, unmeasured secular trends, other quality improvement initiatives during the intervention period, or residual confounding (eg, inadequate control for case mix and preintervention time trends). Collectively, the findings from this review raise questions about the effectiveness and generalizability of RRT implementation, given the lack of a sustained, robust, and plausible mortality benefit.

Our meta-analysis significantly extends the findings of previous studies (including meta-analyses) in several ways. First, this is the most contemporary systematic review of the literature to assess the effect of an

Table 2. Cases of Cardiopulmonary Arrest Averted and Number of Deaths Reduced After Implementation of an RRT in Studies That Show a Mortality Benefit

Study	RRT Calls, No.	RR for Codes	No. of Observed Codes After RRT	No. of Codes Averted With RRT ^a	RR for Deaths	No. of Observed Deaths After RRT	No. of Fewer Deaths After RRT ^b
Bellomo et al ²⁷	99	0.35	22	41	0.74	222	78
Buist et al ²⁸	152	0.50	47	47	0.87	393	59
Priestley et al ³⁴	NR	NA	NA	NA	0.52	83	77
Sharek et al ³⁵	143	0.29	5	12	0.82	158	35
Tibballs and Kinney ³⁷	808	0.91	24	2	0.65	398	214

Abbreviations: NA, not applicable; NR, not reported; RR, relative risk; RRT, Rapid Response Team.

^a Determined by the following equation: (Observed Codes/RR for Codes) – Observed Codes.

^b Determined by the following equation: (Observed Deaths/RR for Death) – Observed Deaths.

Table 3. Case-Fatality Rates and Deaths Prevented by Implementation of a Rapid Response Team (RRT)

Study	Case-Fatality Rate for Codes Before RRT, %	Case-Fatality Rate for Codes After RRT, %	No. of Deaths Prevented by Decreased Code Rate ^a	No. of Deaths Prevented by Increased Code Survival ^b	Total No. of Deaths Prevented by RRT Effect on Codes	No. of Fewer Deaths After RRT ^c
Buist et al ²⁸	76.7	55.3	36	10	46	59
Tibballs and Kinney ³⁷	65.0	26.1	1	9	10	214
Bellomo et al ²⁷	100	0	41 ^d	22 ^d	63	78
Sharek et al ³⁵	100	0	12 ^d	5 ^d	17	35

^a Determined by the following equation: (Codes Averted With RRT From Table 2) × (Case-Fatality Rate Before RRT).

^b Determined by the following equation: (Observed Codes After RRT) × (Difference in Case-Fatality Rate for Codes Before and After RRT).

^c Derived in Table 2.

^d Rates are for best-case scenario for sensitivity analyses.

RRT; as a result, we identified 18 studies of RRTs, many of which were published since 2007, that involved nearly 1.3 million admissions. We also evaluated studies in both adult and pediatric populations and examined studies across time to evaluate for cumulative effects. Finally, we extensively used meta-regression, subgroup, and sensitivity analyses to evaluate the robustness of the pooled estimates.

Several additional aspects of this review deserve comment. First, the studies of RRTs in this review exhibited extensive heterogeneity across their reported outcomes. Our use of random-effects models, meta-regression, and sensitivity analyses explained some of the potential sources of this heterogeneity. However, we also noted significant variation across studies in research design, study quality, and RRT activation rates, which would contribute to study heterogeneity. Moreover, although the activation criteria for RRTs appeared to be comparable among the studies, interventions that were implemented by RRTs for specific clinical scenarios have not been sufficiently described or standardized. Our study suggests that development of more rigorous

study designs and standardized treatment protocols, as well as the adoption of common terms for reporting on outcomes for RRTs (similar to the Utstein criteria for cardiac arrest³⁹⁻⁴¹), would improve future research in this area.

Second, the discordance between a reduction in rates of cardiopulmonary arrest but not of hospital mortality after RRT implementation in adults may be owing to several factors. This may be in part owing to the establishment of DNR status of severely ill patients by the RRT, which thereby removes very ill patients from consideration for the outcome of cardiopulmonary arrest without improving overall mortality rates.^{9,42} Moreover, because RRTs transfer clinically deteriorating patients to the ICU, the measurement of only non-ICU-treated cardiopulmonary arrest rates (rather than hospital-wide rates) may introduce reporting bias and overestimate the effect of the RRT on cardiopulmonary arrest.⁹ Finally, although the RRT intervention may succeed in preventing initial cases of cardiopulmonary arrest, their short-term impact may not be sufficient to alter overall survival in severely ill patients.

In contrast to the findings in adults, implementation of an RRT in pediatric populations was associated with lower hospital mortality rates. This difference may be because respiratory conditions are more frequently the cause of cardiopulmonary arrest in children,²² and children who have cardiac arrest have fewer comorbidities and are more likely to survive than adults.⁴³ Nevertheless, the pooled estimate in children was not robust to sensitivity analyses and was greatly influenced by studies^{35,37} in which the lower number of observed deaths could not be plausibly explained by the direct interventions of the RRT.

Third, our analyses had adequate power to detect a modest reduction in hospital mortality, especially in adults, but may have been limited in their ability to detect smaller improvements. It has been estimated that a sample size of 150 000 patients before and after implementation of an RRT would be required to have 80% power to detect a 5% reduction in hospital mortality rates.⁹ Therefore, it remains possible that an even larger study sample of RRTs than the nearly 1 million patients for the mortality

analysis in this study may have found a significant mortality reduction.

Fourth, there remains to date no formal evaluation of the costs or the cost-effectiveness of RRTs, although significant hospital staff resources are involved in their development and maintenance. It is possible that, by initiating DNR discussions with patients, RRTs may be cost-minimizing because terminally ill patients may decline aggressive treatment. Alternatively, increased triage to the ICU after RRT implementation without observable survival gains may increase hospital costs.

Our meta-analysis should be interpreted in the context of the following limitations. We did not have patient-level data, and our results were therefore analyzed at the study level. Comprehensive information on the characteristics of the hospitals that implement RRTs was not available, including the use of hospitalists. Of the 12 studies that reported on academic status in this meta-analysis, 10 studies involved academic centers and 1 study was a 23-center study of academic and community hospitals. It is possible that the greater presence of medical house staff and hospitalists in academic centers may have blunted the potential benefits of RRT implementation. Our studies did not assess the effect of RRTs on other mortality end points (eg, 30-day or mortality of those treated in the ICU vs those not treated in the ICU). Finally, because most studies did not routinely report on outcomes other than rates of cardiopulmonary arrest and hospital mortality, we were unable to assess the effect of RRTs on issues such as satisfaction among nurses, establishment of DNR status, and prevention of in-hospital complications. Although these outcomes are important, they are not the primary goals for the establishment of RRTs and may possibly be achieved with approaches other than the use of RRTs.

Although RRTs appear to reduce rates of cardiopulmonary arrest outside the ICU, consistent and plausible evidence is not available to demonstrate that they are associated with improved survival—the primary reason for their develop-

ment. Health quality organizations may need to reconsider their promotion of RRTs without robust evidence to support their use.

Accepted for Publication: August 28, 2009.

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Online-Only Material: The eAppendix and eFigures 1, 2, and 3 are available at <http://www.archinternmed.com>.

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