REVIEWS

Effectiveness of Rapid Response Teams on Rates of In-Hospital Cardiopulmonary Arrest and Mortality: A Systematic Review and Meta-analysis

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BACKGROUND: In 2004, the Institute for Healthcare Improvement's 100,000 Lives Campaign recommended that hospitals implement rapid response teams (RRTs) charged with identifying non-intensive care unit (ICU) patients at risk for rapid deterioration. Although RRTs are now in widespread use, there have been conflicting results regarding the impact of RRTs on hospital mortality and cardiopulmonary arrest.

PURPOSE: To assess the effectiveness of RRTs on reducing hospital mortality and non-ICU cardiopulmonary arrest rates.

DATA SOURCES: We conducted a systematic review using MEDLINE (1966–2014), Cochrane Central Register of Controlled Trials (1898–2014), Cumulative Index to Nursing and Allied Health Literature (1994–2014), and ClinicalTrials.gov (1997–2014) during October 2014. There were no constraints on language or publication status.

DATA EXTRACTION: We included before-after studies, cohort studies, and cluster randomized trials that reported

In 2004, the Institute for Healthcare Improvement (IHI) launched its 100,000 Lives Campaign," a national initiative with a goal of saving 100,000 lives among hospitalized patients through improvements in the safety and effectiveness of healthcare.¹ One of their recommended strategies to reduce preventable inpatient deaths was for hospitals to establish rapid response teams (RRTs).^{2,3} The goal of RRTs, also termed medical emergency teams (METs), is to identify patients at risk for rapid decline in condition and intervene prior to a catastrophic event such as cardiopulmonary arrest.⁴ The basis for recommending RRT/METs was evidence of predictable warning signs occurring in patients prior to cardiopulmonary arrest that could alert physicians.⁵ A pilot study by the IHI,

Received: September 18, 2015; Revised: November 24, 2015; Accepted: January 5, 2016

2016 Society of Hospital Medicine DOI 10.1002/jhm.2554 Published online in Wiley Online Library (Wileyonlinelibrary.com). hospital mortality and/or non-ICU cardiopulmonary arrest for adults hospitalized in a non-ICU setting after the implementation of RRTs and/or medical emergency teams (METs). Data were extracted by 2 sets of 2 independent reviewers using a standardized data-collection form. Disagreements were resolved by a third reviewer. Authors were contacted to obtain any missing data.

DATA SYNTHESIS: Our search identified 691 studies, of which 30 met criteria for inclusion in the analysis. Implementation of an RRT/MET was associated with a significant decrease in hospital mortality (relative risk [RR] = 0.88, 95% confidence interval [CI]: 0.83-0.93, $l^2 = 86\%$, 3,478,952 admissions) and a significant decrease in the number of non-ICU cardiac arrests (RR = 0.62, 95% CI: 0.55-0.69, $l^2 = 71\%$, 3,045,273 admissions).

CONCLUSIONS: Implementation of an RRT/MET is associated with a reduction in both hospital mortality and non-ICU cardiopulmonary arrests. *Journal of Hospital Medicine* 2016;11:438–445. © 2016 Society of Hospital Medicine

including 8 hospitals in the United States and the United Kingdom, found reductions in code calls after implementing RRTs, with 2 hospitals also showing a reduction in mortality.³

In response to the IHI report, many hospitals established RRT/METs.⁶ Proponents for RRT/METs argued that the potential benefit justified immediate implementation, whereas others advocated for further research.⁶ Despite the rapid, widespread adoption of RRT/METs, questions remain regarding their effectiveness in reducing hospital mortality and non–intensive care unit (ICU) cardiopulmonary arrests.^{6,7} In 2010, Chan et al. reported the results of a meta-analysis of studies published through 2008 that demonstrated a reduction in cardiac arrests, but not mortality, following the implementation of RRTs.⁸ An updated systematic review, including studies published through 2012, suggested that RRTs are associated with reduced non-ICU cardiac arrest and reduced mortality.⁹

Since the publication of the Winters et al. systematic review, several new studies have been published.^{9–12} We performed a systematic review and meta-analysis including studies published through 2014 to examine the impact of RRT/METs on hospital mortality and inhospital cardiopulmonary arrest (IHCA).

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Additional Supporting Information may be found in the online version of this article.

METHODS

Search Methods

We conducted a systematic search of publications on RRTs using PubMed (1946–2014), Cumulative Index to Nursing and Allied Health Literature (1937–2014), and the Cochrane Library (issue 10 of 12, 2014). The search used no language restrictions and no limits. Medical Subject Headings with keywords in a Boolean search strategy were employed. The major themes used were cardiopulmonary arrest and rapid response teams. Clinicaltrials.gov (1997-2014) was searched using a similar methodology. A reference review was performed using Web of Science (1900–2014).

Study Eligibility Criteria

Prespecified criteria for determining study eligibility included: before-after studies, cohort studies, nonrandomized control studies, or cluster randomized controlled trials (RCTs); implementation of an RRT and/or a MET as the intervention; adults (based on individual study definition) hospitalized in a non-ICU setting; reported 1 or both prespecified outcomes, hospital mortality, or IHCA. There were no exclusion criteria or language restrictions.

Data Extraction

We prospectively outlined a standard protocol that included the research question, inclusion/exclusion criteria, as well as our outcomes and search approaches. We used standard methodology for analysis in accordance with the guidelines in *Cochrane Handbook for Systematic Reviews of Interventions*.¹³ The protocol can be obtained by request to the authors. All changes to our original protocol were recorded in a protocol amendments table.

The studies identified underwent title and abstract screening by 1 of 2 reviewers (G.S.C., R.S.S.). After irrelevant studies were removed, reviewers independently assessed the remaining studies for eligibility based on full-text review. All disagreements were resolved with consensus and the help of a third reviewer (D.C.B.).

Prior to extracting data, a piloted standardized data-collection form was created. Eligible studies were independently reviewed by each of the 2 reviewers, and the relevant data extracted. Conflicts between the reviewers regarding the data collected for a given study were resolved by a third reviewer. The essential data were total events (hospital deaths and IHCA) and total hospital admissions.

Assessment of Methodological Quality

We utilized design-specific tools to assess the methodological quality of included studies. For nonrandomized control and cohort studies, we used the Newcastle Ottawa Scale. This allowed us to evaluate the representativeness of the intervention cohort, selection of the nonintervention cohort, ascertainment of the intervention, whether or not the outcome was present at the start of the study, comparability of cohorts, assessment of the outcome, and whether there was adequate follow-up.¹⁴ We assigned stars as a measure of rating for each category and tallied the number of stars to assess the methodological quality. The maximum score was 9.¹⁴

For before-after studies, an assessment scale developed by the ECRI (Emergency Care Research Institute) to test the internal validity of each study was utilized.¹⁵ The ECRI Before-After Scale allowed us to evaluate if the study was prospective, inclusion and exclusion criteria were established a priori, consecutive patients were enrolled, the same initial/subsequent treatment was administered, outcomes were objectively measured, follow-up was complete, cohorts were comparable, there were no conflicts of interest, and conclusions were supported by data.¹⁵ We ascertained whether each criterion was met and converted answers to numerical scores. A yes was scored 1, a no was scored -1, and no response was scored -0.5. The sum of these scores was then added to 11, divided by 22, and multiplied by 10 to yield the total quality score. The summary score can range from 0 to 10. A total score <5 was considered unacceptable quality. A score >5 but <7.5 was considered low quality, and a total \geq 7.5 was considered moderate quality.15

To assess the methodological quality of RCTs, we used the Cochrane Risk of Bias Tool.¹³ The tool involves determining whether a study has a high, low, or unclear risk of bias for specific criteria.¹³

Two independent reviewers evaluated the studies using these scales, and discrepancies were resolved by discussion.

Data Analysis

Measure of Treatment Effect

We used relative risk (RR) to summarize outcome data for our prespecified outcomes: hospital mortality and IHCA.

Dealing With Missing Data

If essential data were missing, study authors were contacted. If we did not receive a response, we calculated total events (deaths and IHCAs) using total admissions and event rates per admissions. If total admissions and/or event rates were missing, studies were not included in the analysis.

Data Synthesis

We used Review Manager 5.3 to calculate pooled summary estimates.¹⁶ Meta-analyses for each outcome were conducted by means of a random effects model.

Assessment of Heterogeneity

To assess for heterogeneity, we calculated I^2 and P values. If the $I^2 < 0.50$ or the P > 0.10, then the test

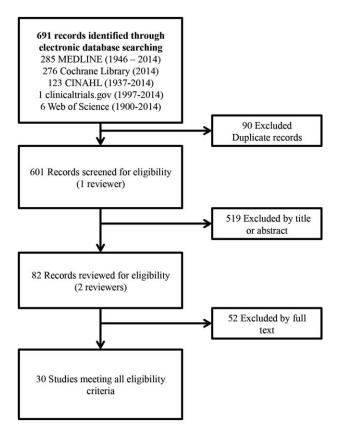


FIG. 1. Study selection flow diagram. Abbreviations: CINAHL, Cumulative Index to Nursing and Allied Health Literature; CENTRAL, Cochrane Central Register of Controlled Trial; MEDLINE = PubMed.

for heterogeneity was passed. If heterogeneity was present, we evaluated each study in an effort to identify outliers. If an outlier was identified, the study was removed from the analysis.

Assessment of Reporting Bias

To assess publication bias, we used a funnel plot of the primary outcome. The findings were arranged by study size and effect size, and the plot was assessed for symmetry.

Subgroup Analyses

Subgroup analyses were performed for study type, RRT/MET composition, and publication year. Study type was grouped by cluster RCT and nonrandomized studies versus cohort/before-after studies. Team composition was grouped by whether or not there was a physician on the RRT/MET. Publication year was grouped by studies published before or after 2010.

Sensitivity Analysis

We conducted sensitivity analyses to evaluate the impact of methodological quality on summary estimates. We compared overall summary estimates to summary estimates based only on before-after studies judged to be low risk for bias. We also conducted an analysis to evaluate the inclusion of studies in which total events were calculated from rates and total admissions. We compared the overall summary estimates to summary estimates based on studies in which we were able to obtain essential data.

RESULTS

Description of Studies

Our search identified 691 studies, of which 90 were duplicates. The remaining studies were screened by title and abstract, identifying 82 potentially eligible studies, of which 30 studies were identified as eligible for inclusion in the meta-analysis (Figure 1).

Of the 30 eligible studies, 10 were excluded from pooled estimates for hospital mortality,^{7,17–28} and 10 were excluded from pooled estimates for IHCA due to missing data.^{17,18,20–27,29,30} For the analysis, 20 studies were included for the hospital mortality analysis and 20 studies were included for the IHCA analysis. The 22 studies included in either or both analyses spanned the years 2000 to 2014. The characteristics of the included studies are summarized in Table 1.

Methodological Quality

The methodological quality of the 4 cohort studies, based on the New Castle Ottawa Scale, was either 8 or 9 stars. Using the ECRI Before-After Scale, the average quality score of the 17 included before-after studies was 8.41 (range, 7.27–9.32). Included before-after studies were of moderate quality, with the exception of 1 of lower quality. The cluster RCT had low risk of bias for random sequence generation, allocation concealment, blinding of participants/personnel, and incomplete outcome data; however, it had unclear risk of bias for blinding of outcome assessment, selective reporting, and sources of bias due to lack of reporting.²⁰ Overall, the 22 studies included ranged from moderate to good quality.

Effect of RRT on Hospital Mortality

Of the 20 studies that reported hospital mortality, 9 favored RRT/METs,^{10,11,30–36} 10 found no difference with RRT/METs,^{12,20,22,28,37–42} and 1 favored RRT/METs for surgical patients while favoring usual care (no RRT/MET) for medical patients²⁹ (Figure 2a). The pooled analysis demonstrated that implementation of RRT/METs was associated with a significant reduction in hospital mortality (RR = 0.88, 95% confidence interval [CI]: 0.83-0.93). There was heterogeneity among the contributing studies ($I^2 = 86\%$).

Effect of RRT on IHCA

Of the 20 studies that reported rates of IHCA, 12 favored RRT/METs ^{7,10–12,31,32,34–39} and 8 found no difference with RRT/METs^{16,19,20,22,28,33,40–42} (Figure 2b). In the pooled analysis, RRT/METs were associated with a significant reduction in IHCA (RR = 0.62, 95% CI: 0.55-0.69). There was moderate heterogeneity among the studies ($I^2 = 71\%$).

Author/Year	Study Design	Setting/Location	Subjects (No.)	Age, y	Description of Intervention	Description of Control	Duration of Study	Outcome(s) of Interest
Al-Qahtani, 2013 ¹⁰	Before-after	Saudi Arabia (tertiary care academic center)	Before: 157,804; after: 98,391	Before: 59.2 \pm 19.2; after: 59 \pm 19.0	RRT Implementation	Before RRT implementation	5 years (January 2006–December 2010)	III mortality, IHCA, ward mortality
Bader, 2009 ⁵⁷ Beitler, 2011 ³¹	berore-arter Before-after	USA (community acute care nospital) USA (tertiary referral public teaching hospital)	Before: 15,949; arter: 16,907 Before: 77,021; after: 79,013	WK Pre-RRT: 40.9 (22.3); post-RRT: 42.0 (22.2)	RRT implementation RRT implementation	before RRT implementation Before RRT implementation	3 years (uctober 2005–June 2008) 5 years (2003–2008)	IHCA, code mortality, ICU transfer IHCA mortality, IHCA, out-of-ICU
								mortality, IH mortality
Bellomo, 2003 ³²	Before-after	Australia (tertiary referral hospital)	Before: 21,090; after: 20,921	Before: 60.7; after: 60.2	MET implementation	Before MET implementation	8 months (before: May 1999-August 1999; after: November 2000-Febnuary 2001)	IHCA, CA-related mortality, I H mortality
Bristow, 2000 ³³	Nonrandomized controlled	Australia (3 public hospitals)	50,942	NR	Hospitals with MET	Hospitals without MET (with conventional CA teams)	5 months (2006)	HCA, IH mortality
Buist, 2002 ³⁸	Before-after	Australia (tertiary referral teaching hospital)	Before: 25,254; after: 28,801	Before: 36.6 (26.0); after: 36.4 (26.0)	MET implementation	Before MET implementation	3 years (1996–1999)	Incidence and outcome of unexpected IHCA
Chan, 2008 ³⁹	Prospective cohort	USA (tertiary care academic hospital)	Before: 24,193; after: 24,978	Before: 56.8 (13.6) in 2004; 56.5 (13.8) in 2005; after: 57.0 (13.9) in 2006; 57.1 (13.8) in 2007	RRT implementation	Standard care	3.5 years (2004-2007)	IHCA, IH mortality
Chen, 2014 ¹¹	Nonrandomized controlled	Australia (teaching hospital)	Before: 1,088,491; after: 479,194	NR	Teaching hospital with a mature RRS	Three teaching hospitals without RRS	8 years (2002–2009)	IHCA, IHCA mortality, IH mortality
Goncales, 2012 ³⁴	Before-after	Brazil (high complexity general hospital)	Before: 40,033; after: 42,796	Before: 73; after: 68	Implementation of RRT called Code Yellow	Before Implementation of RRT—Code Blue	3 years (2005–2008)	IHCA, IHCA mortality, IH mortality
Hatler, 2009 ¹⁹ Hillman, 2005 ²⁰	Before-after Cluster RCT	USA (tertiary care hospital) Australia (23 hospitals)	Before: 24,739; after: 25,470 Control hospitals: 56.756; MET hospitals: 68,376	WR Control hospitals: 56.9; MET hospitals: 55.4	RRT implementation MET implementation	Before RRT implementation Care as usual	2 years (2005–2007) 6 months	HCA IH Mortality, IHCA
Jones, 2005 ⁷ Jones, 2007 ²⁹	Before-after Refore-after	Australia (tertiary care teaching hospital) Australia (teaching hosnital)	Before: 16,246; after: 104,001 Refore: 25,334: after: 100,243	Before: 73.4; after: 70.8 M/R	MET implementation MET implementation	Before MET implementation Refore MET implementation	5 years (1999–2004) 6 yeare (1998–2004)	IHCA, death following cardiac arrest Surnical and medical mortality
Kenward, 2004 ²²	Before-after	UK (general hospital)	Before: 53,500; after: 53,500	Before: N/R; after: 73	MET implementation	Before MET implementation	1 year (2000–2001)	IH mortality, IHCA
Konrad, 2010 ³⁶	Before-after	Sweden (tertiary care center)	Before: 203,892; after 73,825	Before: 53.1; after: 52.4	MET implementation	Before MET implementation	6 years (2000–2006)	IH mortality, IHCA
Lighthall, 2010 ⁺ ° Lim, 2011 ⁴¹	Before-after Before-after	USA (university attilitated VA hospital) South Korea (Samsung Medical Center)	Before: 2,9/5; after: 9,0/7 Before: 33,360; after: 34,699	Before: 65.26; after: 65.56 Before: 64; after: 59	HKI implementation MET implementation	Before RKT implementation Before MET implementation	3 years (2004–2007) 1 year (2008–2009)	IH mortality, IHCA IH mortality, IHCA, unexpected ICII transfers
Moroseos, 2014 ¹²	Before-after	USA (teaching hospital)	Before: 7,092; after: 9,357	Before: 30.1; after: 30.9	Teaching hospital after RRT implementation	Teaching hospital before RRT implementation	10 years (before: January 2000-December 2004; after: January 2007 Docomber 2011)	IH mortality, IHCA, unexpected ICU transfers
Salvatierra, 2014 ³⁰	Observational cohort	USA (10 tertiary care hospitals)	Before: 235,718; after: 235,344	NR	RRT implementation	Before RRT implementation	2007-December 62 months (September 2001-December 2009)	IH mortality
Santamaria, 2010 ³⁵	Before-after	Australia (teaching hospital)	Before (IH mortality): 22,698; before (IHCA): 8,190 after (IH mortality): 74,616; after (IHCA): 81,628	Median: 58-60 (1993-2007)	RRT implementation	Before RRT implementation	14 years (1993-2007)	IH mortality, IHCA
Segon, 2014 ⁴²	Before-after	USA (teaching hospital)	Before: 14,013; after: 14,333	NR	RRT implementation	Before RRT implementation	2 years (January 2004–April 2006)	IH mortality, unexpected ICU transfer, IHCA. ICU length of stav
Shah, 2011 ²⁸	Retrospective cohort	USA (teaching hospital)	Before: 16,244; after: 45,145	WR	RRT implementation	Before RRT implementation	3 years (2005–2008)	HCA, IH mortality, unplanned ICU transfers
TE: Abbreviations: C/	A. cardiac arrest: ICU. inte	NOTE: Abbaviatione: CA cardiac area; COI intensive care init: IH industrial cardiac area; MET marked anamanou team: WB intremoted PCT randomized controlled trid; BBS randy reconces order with learnones team: Wa liderane differences differences and teacher and the concest or the cardiac area of the cardiac are	vardiac arrest: MET medical emernenc	we have a subsection of the second	and the DDC manual and	TOO		

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		RT		RRT		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Al-Qahtani 2013	3191	157804	2214	98391	5.9%	0.90 [0.85, 0.95]	
Bader 2009	292	16907	300	15949	4.2%	0.92 [0.78, 1.08]	
Beitler 2011	1086	79013	1194	77021	5.5%	0.89 [0.82, 0.96]	
Bellomo 2003	222	20921	302	21090	3.9%	0.74 [0.62, 0.88]	
Bristow 2000 (hospital 1 vs 2)	243	18338	240	13059	3.9%	0.72 [0.60, 0.86]	
Bristow 2000 (hospital 1 vs 3)	243	18338	295	19545	4.0%	0.88 [0.74, 1.04]	
Buist 2002	393	28801	380	25194	4.5%	0.90 [0.79, 1.04]	
Chan 2008	773	24978	780	24193	5.3%	0.96 [0.87, 1.06]	+
Chen 2014	5157	404116	14324	942368	6.2%	0.84 [0.81, 0.87]	
Goncales 2012	614	42796	651	40033	5.1%	0.88 [0.79, 0.98]	
Hillman 2005	72	68376	67	\$6756	1.9%	0.89 [0.64, 1.24]	
Jones (Medical) 2007	3489	73807	664	17893	5.5%	1.27 [1.17, 1.38]	-
Jones (Surgical) 2007	581	26436	209	7441	4.2%	0.78 [0.67, 0.91]	
Kenward 2004	1054	53500	1070	\$3500	5.5%	0.99 [0.91, 1.07]	+
Konrad 2010	1214	73825	3847	203892	5.8%	0.87 [0.82, 0.93]	-
Lighthall 2010	203	9077	78	2975	2.7%	0.85 [0.66, 1.10]	
Lim 2011	583	34699	\$69	33360	5.0%	0.99 [0.88, 1.10]	+
Moroseos 2014	31	9357	32	7092	1.1%	0.73 [0.45, 1.20]	
Salvatierra 2014	2423	235344	3183	235718	6.0%	0.76 [0.72, 0.80]	-
Santamaria 2010	551	74616	240	22698	4.3%	0.70 [0.60, 0.81]	
Segon 2014	417	14333	439	14013	4.7%	0.93 [0.81, 1.06]	-
Shah 2011	971	45145	390	16244	4.9%	0.90 [0.80, 1.01]	
3540 2011	3/1	43143	330	10244	4.3/9	0.30 [0.80, 1.01]	
Total (95% CI)		1530527		1948425	100.0%	0.88 [0.83, 0.93]	•
Total events	23803		31468				
Heterogeneity: Tau ² = 0.01; Ch			(P < 0.0	00001); l ^a •	86%		0.2 0.5 1 2
Heterogeneity: Tau ² = 0.01; Ch Test for overall effect: Z = 4.45			(P < 0.0	00001); 1² •	86%		0.2 0.5 1 2 Favours RRT Favours No RRT
	(P < 0.0	0001)			\$6%		Favours RRT Favours No RRT
Test for overall effect: Z = 4.45	(P < 0.0	0001) RT	No	RRT		Risk Ratio	Favours RRT Favours No RRT Risk Ratio
Test for overall effect: Z = 4.45 Study or Subgroup	(P < 0.0) R Events	0001) RT Total	No Events	RRT Total	Weight	M-H, Random, 95% CI	Favours RRT Favours No RRT
Test for overall effect: Z = 4.45 Study or Subgroup Al-Qahtani 2013	(P < 0.0) R Events 144	0001) RT <u>Total</u> 157804	No Events 133	RRT Total 98391	Weight	M-H, Random, 95% CI 0.68 [0.53, 0.85]	Favours RRT Favours No RRT Risk Ratio
Test for overall effect: Z = 4.45 Study or Subgroup Al-Qahtani 2013 Bader 2009	(P < 0.0) R Events 144 17	0001) RT <u>Total</u> 157804 16907	No Events 133 36	RRT Total 98391 15949	Weight 5.9% 2.7%	M-H, Random, 95% CI 0.68 [0.53, 0.85] 0.45 [0.25, 0.79]	Favours RRT Favours No RRT Risk Ratio
Test for overall effect: Z = 4.45 Study or Subgroup Al-Qahtani 2013 Bader 2009 Beitler 2011	(P < 0.0) R Events 144 17 128	00001) RT <u>Total</u> 157804 16907 79013	No Events 133 36 253	RRT 98391 15949 77021	Weight 5.9% 2.7% 6.2%	M-H, Random, 95% CI 0.68 [0.53, 0.85] 0.45 [0.25, 0.79] 0.49 [0.40, 0.61]	Favours RRT Favours No RRT Risk Ratio
Test for overall effect: Z = 4.45 Study or Subgroup Al-Qahtani 2013 Bader 2009 Beilter 2011 Beiltor 2013	(P < 0.0) R Events 144 17 128 22	00001) RT 157804 16907 79013 20921	No Events 133 36 253 63	RRT 98391 15949 77021 21090	Weight 5.9% 2.7% 6.2% 3.3%	M-H, Random, 95% CI 0.68 [0.53, 0.85] 0.45 [0.25, 0.79] 0.49 [0.40, 0.61] 0.35 [0.22, 0.57]	Favours RRT Favours No RRT Risk Ratio
Test for overall effect: Z = 4.45 Study or Subgroup Al-Qahtani 2013 Bader 2009 Beilter 2011 Bellomo 2003 Bristow 2000 (hospital 1 vs 2)	(P < 0.00 R Events 144 17 128 22 69	0001) RT 157804 16907 79013 20921 18338	No Events 133 36 253 63 66	RRT 98391 15949 77021 21090 13059	Weight 5.9% 6.2% 3.3% 4.7%	M-H, Random, 95% CI 0.68 [0.53, 0.85] 0.45 [0.25, 0.79] 0.49 [0.40, 0.61] 0.35 [0.22, 0.57] 0.74 [0.53, 1.04]	Favours RRT Favours No RRT Risk Ratio
Test for overall effect: Z = 4.45 Study or Subgroup Al-Qahtani 2013 Bader 2009 Belter 2011 Bellomo 2003 Bristow 2000 (hospital 1 vs 2) Bristow 2000 (hospital 1 vs 3)	(P < 0.00 R Events 144 17 128 22 69 69	0001) RT 157804 16907 79013 20921 18338 18338	No Events 133 36 253 63 66 99	RRT 98391 15949 77021 21090 13059 19545	Weight 5.9% 2.7% 6.2% 3.3% 4.7% 5.1%	M-H, Random, 95% CI 0.68 [0.53, 0.85] 0.45 [0.25, 0.79] 0.49 [0.40, 0.61] 0.35 [0.22, 0.57] 0.74 [0.53, 1.04] 0.74 [0.55, 1.01]	Favours RRT Favours No RRT Risk Ratio
Test for overall effect: Z = 4.45 Study or Subgroup Al-Qahtani 2013 Bader 2009 Beitier 2011 Bellomo 2003 Bristow 2000 (hospital 1 vs 2) Bristow 2000 (hospital 1 vs 3) Buist 2002	(P < 0.0) R Events 144 17 128 22 69 69 47	0001) RT Total 157804 16907 79013 20921 18338 18338 28801	No Events 133 36 253 63 66 99 73	RRT Total 98391 15949 77021 21090 13059 19545 25194	Weight 5.9% 2.7% 6.2% 3.3% 4.7% 5.1% 4.4%	M-H, Random, 95% CI 0.68 [0.53, 0.85] 0.45 [0.25, 0.79] 0.49 [0.40, 0.61] 0.35 [0.22, 0.57] 0.74 [0.53, 1.04] 0.74 [0.55, 1.01] 0.56 [0.39, 0.81]	Favours RRT Favours No RRT Risk Ratio
Test for overall effect: Z = 4.45 Study or Subgroup Al-Qahtani 2013 Bader 2009 Beilter 2011 Beilomo 2003 Bristow 2000 (hospital 1 vs 2) Bristow 2000 (hospital 1 vs 3) Buist 2002 Chan 2008	(P < 0.0) R Events 144 17 128 22 69 69 47 77	0001) RT Total 157804 16907 79013 20921 18338 18338 18338 28801 24978	No Events 133 36 253 63 66 99 73 147	RRT Total 98391 15949 77021 21090 13059 19545 25194 24193	Weight 5.9% 2.7% 6.2% 3.3% 4.7% 5.1% 4.4% 5.5%	M-H, Random, 95% CI 0.68 [0.53, 0.85] 0.45 [0.25, 0.79] 0.49 [0.40, 0.61] 0.35 [0.22, 0.57] 0.74 [0.53, 1.04] 0.74 [0.55, 1.01] 0.56 [0.39, 0.81] 0.51 [0.39, 0.67]	Favours RRT Favours No RRT Risk Ratio
Test for overall effect: Z = 4.45 Study or Subgroup Al-Qahtani 2013 Bader 2009 Beilter 2011 Bellomo 2003 Bristow 2000 (hospital 1 vs 2) Bristow 2000 (hospital 1 vs 3) Buist 2002 Chan 2008 Chen 2014	(P < 0.00 R Events 144 17 128 22 69 69 69 69 47 77 845	0001) RT Total 157804 16907 79013 20921 18338 18338 28801 24978 404116	No Events 133 36 253 63 66 99 73 147 3741	RRT Total 98391 15949 77021 21090 13059 19545 25194 24193 942368	Weight 5.9% 2.7% 6.2% 3.3% 4.7% 5.1% 4.4% 5.5% 7.6%	M-H, Random, 95% CI 0.68 [0.53, 0.85] 0.45 [0.25, 0.79] 0.49 [0.40, 0.61] 0.35 [0.22, 0.57] 0.74 [0.53, 1.04] 0.74 [0.55, 1.01] 0.56 [0.39, 0.81] 0.51 [0.39, 0.67] 0.53 [0.49, 0.57]	Favours RRT Favours No RRT Risk Ratio
Test for overall effect: Z = 4.45 Study or Subgroup Al-Qahtani 2013 Bader 2009 Belider 2011 Beliomo 2003 Bristow 2000 (hospital 1 vs 2) Bristow 2000 (hospital 1 vs 3) Buist 2002 Chan 2008 Chen 2014 Goncales 2012	(P < 0.0) R Events 144 17 128 22 69 69 69 47 77 845 71	0001) RT Total 157804 16907 79013 20921 18338 18338 28801 24978 40416 42796	No Events 133 36 253 63 66 99 97 3 147 3741 143	RRT Total 98391 15949 77021 21090 13059 19545 25194 24193 942368 40033	Weight 5.9% 2.7% 6.2% 3.3% 4.7% 5.1% 4.4% 5.5% 7.6% 5.3%	M-H, Random, 95% CI 0.68 [0.53, 0.85] 0.45 [0.25, 0.79] 0.49 [0.40, 0.61] 0.35 [0.22, 0.57] 0.74 [0.53, 1.04] 0.74 [0.55, 1.01] 0.56 [0.39, 0.81] 0.51 [0.39, 0.67] 0.46 [0.35, 0.62]	Favours RRT Favours No RRT Risk Ratio
Test for overall effect: Z = 4.45 Study or Subgroup Al-Qahtani 2013 Bader 2009 Beilter 2011 Beilomo 2003 Bristow 2000 (hospital 1 vs 2) Bristow 2002 Chan 2008 Chen 2014 Goncales 2012 Hatler 2009	(P < 0.00 R Events 144 17 128 22 69 69 47 77 845 71 16	0001) RT Total 157804 16907 79013 20921 18338 18338 28801 24978 404116 404116 25470	No Events 133 36 253 63 66 99 73 147 3741 143 23	RRT 98391 15949 77021 21090 13059 19545 25194 24193 942368 40033 24739	Weight 5.9% 2.7% 6.2% 3.3% 4.7% 5.1% 4.4% 5.5% 7.6% 5.3% 5.3% 2.3%	M-H, Random, 95% CI 0.68 [0.53, 0.85] 0.45 [0.25, 0.79] 0.49 [0.40, 0.61] 0.35 [0.22, 0.57] 0.74 [0.53, 1.04] 0.74 [0.55, 1.01] 0.56 [0.39, 0.81] 0.51 [0.39, 0.67] 0.53 [0.49, 0.57] 0.46 [0.35, 0.62] 0.68 [0.36, 1.28]	Favours RRT Favours No RRT Risk Ratio
Test for overall effect: Z = 4.45 Study or Subgroup Al-Qahtani 2013 Bader 2009 Beilter 2011 Beilomo 2003 Bristow 2000 (hospital 1 vs 2) Bristow 2000 (hospital 1 vs 3) Buist 2002 Chan 2008 Chan 2008 Chen 2014 Goncales 2012 Hatler 2009 Hillman 2005	(P < 0.00 R Events 144 17 128 22 69 69 47 77 845 71 16 90	0001) RT Total 157804 16907 79013 20921 18338 18338 28801 24978 404166 42796 40416 42796 68376	No Events 133 36 253 63 66 99 73 147 3741 147 3741 147 3741 23 93	RRT Total 98391 15949 77021 21090 13059 19545 25194 24193 942368 40033 24739 56756	Weight 5.9% 2.7% 6.2% 3.3% 4.7% 5.1% 4.4% 5.5% 7.6% 5.3% 2.3% 5.3%	M-H, Random, 95% CI 0.68 [0.53, 0.85] 0.45 [0.25, 0.79] 0.49 [0.40, 0.61] 0.35 [0.22, 0.57] 0.74 [0.53, 1.04] 0.74 [0.55, 1.01] 0.56 [0.39, 0.81] 0.51 [0.39, 0.67] 0.53 [0.49, 0.57] 0.46 [0.35, 0.62] 0.68 [0.36, 1.28] 0.80 [0.60, 1.07]	Favours RRT Favours No RRT Risk Ratio
Test for overall effect: Z = 4.45 Study or Subgroup Al-Qahtani 2013 Bader 2009 Beilter 2011 Bellomo 2003 Bristow 2000 (hospital 1 vs 2) Bristow 2000 (hospital 1 vs 3) Buist 2002 Chan 2008 Chen 2014 Goncales 2012 Hatler 2009 Hillman 2005 Jones 2005	(P < 0.00 R Events 144 17 128 22 69 69 47 77 845 71 16 90 198	0001) RT Total 157804 16907 79013 20921 18338 18338 18338 28801 24978 404116 42796 25470 68376 104001	No Events 133 63 63 66 99 97 3 147 3741 143 23 93 66	RRT Total 98391 15949 77021 21090 13059 19545 25194 24193 942368 40033 24739 56756 16246	Weight 5.9% 2.7% 6.2% 3.3% 4.7% 5.1% 4.4% 5.5% 7.6% 5.3% 2.3% 5.3% 5.3% 5.4%	M-H, Random, 95% CI 0.68 [0.53, 0.85] 0.45 [0.25, 0.79] 0.49 [0.40, 0.61] 0.35 [0.22, 0.57] 0.74 [0.53, 1.04] 0.74 [0.55, 1.01] 0.56 [0.39, 0.81] 0.51 [0.39, 0.67] 0.45 [0.35, 0.62] 0.68 [0.36, 1.28] 0.80 [0.60, 1.07] 0.47 [0.35, 0.62]	Favours RRT Favours No RRT Risk Ratio
Test for overall effect: Z = 4.45 Study or Subgroup Al-Qahtani 2013 Bader 2009 Beilter 2011 Bellomo 2003 Bristow 2000 (hospital 1 vs 2) Bristow 2000 (hospital 1 vs 2) Bristow 2000 (hospital 1 vs 3) Buist 2002 Chan 2008 Chen 2014 Goncales 2012 Hatler 2009 Hillman 2005 Jones 2005 Kenward 2004	(P < 0.00 R Events 144 17 128 22 69 69 47 77 845 71 16 90 198 128 128	0001) RT Total 157804 16907 79013 20921 18338 18338 28801 24978 40416 42796 25470 68376 104001 55500	No Events 133 63 66 99 73 147 3741 143 23 93 66 139	RRT Total 98391 15949 77021 21090 13059 15552 25194 24193 942368 40033 24739 56756 16246 53500	Weight 5.9% 2.7% 6.2% 3.3% 4.7% 5.1% 4.4% 5.5% 7.6% 5.3% 2.3% 5.3% 5.3% 5.3% 5.9%	M-H, Random, 95% CI 0.68 [0.53, 0.85] 0.45 [0.25, 0.79] 0.49 [0.40, 0.61] 0.35 [0.22, 0.57] 0.74 [0.53, 1.04] 0.74 [0.55, 1.01] 0.56 [0.39, 0.81] 0.51 [0.39, 0.67] 0.46 [0.35, 0.62] 0.68 [0.36, 1.28] 0.80 [0.60, 1.07] 0.47 [0.35, 0.62] 0.92 [0.72, 1.17]	Favours RRT Favours No RRT Risk Ratio
Test for overall effect: Z = 4.45 Study or Subgroup Al-Qahtani 2013 Bader 2009 Beilter 2011 Beilomo 2003 Bristow 2000 (hospital 1 vs 2) Bristow 2000 (hospital 1 vs 3) Buist 2002 Chan 2008 Chen 2014 Goncales 2012 Hatier 2009 Hillman 2005 Jones 2005 Kenward 2004 Konrad 2010	(P < 0.00 R Events 144 17 128 22 69 69 47 77 845 71 16 90 198 128 61	0001) RT Total 157804 16907 79013 20921 18338 18338 24978 404116 42796 25470 68376 104001 53500 73825	No Events 133 36 253 63 63 63 99 73 147 3741 143 23 93 66 139 228	RRT Total 98391 15949 77021 21090 13059 19545 25194 24193 942368 40033 24739 56756 16246 53500 203892	Weight 5,9% 2,7% 6,2% 3,3% 4,7% 5,1% 4,4% 5,5% 7,6% 5,3% 5,3% 5,3% 5,3% 5,3% 5,3% 5,3% 5,4%	M-H, Random, 95% Cl 0.68 [0.53, 0.85] 0.45 [0.25, 0.79] 0.49 [0.40, 0.61] 0.35 [0.22, 0.57] 0.74 [0.53, 1.04] 0.74 [0.55, 1.01] 0.56 [0.39, 0.81] 0.51 [0.39, 0.67] 0.53 [0.49, 0.57] 0.46 [0.35, 0.62] 0.88 [0.36, 1.28] 0.80 [0.60, 1.07] 0.47 [0.55, 0.52] 0.92 [0.72, 1.17] 0.74 [0.56, 0.98]	Favours RRT Favours No RRT Risk Ratio
Test for overall effect: Z = 4.45 Study or Subgroup Al-Qahtani 2013 Bader 2009 Beitler 2011 Bellomo 2003 Bristow 2000 (hospital 1 vs 2) Bristow 2000 (hospital 1 vs 3) Buist 2002 Chan 2008 Chan 2008 Chan 2008 Chan 2014 Goncales 2012 Hatler 2009 Hallman 2005 Jones 2005 Kenward 2004 Konrad 2010 Lighthall 2010	R (P < 0.00 R Events 144 17 128 222 69 69 69 47 77 845 71 16 16 90 198 128 61 74	0001) RT Total 157804 16907 79013 20921 18338 18338 28901 24978 404116 42796 24978 404116 68376 104001 53500 73825 9077	No Events 133 36 253 63 66 99 73 147 3741 143 23 93 66 139 228 35	RRT Total 98391 15949 77021 21090 13059 19545 25194 24193 942368 40033 24739 56756 16246 53500 203892 2975	Weight 5.9% 2.7% 6.2% 3.3% 4.7% 5.1% 4.4% 5.5% 7.6% 5.3% 5.3% 5.3% 5.4% 5.9% 5.9% 5.4%	M-H, Random, 95% Cl 0.68 [0.53, 0.85] 0.45 [0.25, 0.79] 0.49 [0.40, 0.61] 0.35 [0.22, 0.57] 0.74 [0.53, 1.04] 0.74 [0.55, 1.01] 0.56 [0.39, 0.81] 0.51 [0.39, 0.67] 0.53 [0.49, 0.57] 0.46 [0.35, 0.62] 0.68 [0.36, 1.28] 0.80 [0.60, 1.07] 0.47 [0.35, 0.62] 0.92 [0.72, 1.17] 0.74 [0.56, 0.98] 0.69 [0.46, 1.03]	Favours RRT Favours No RRT Risk Ratio
Test for overall effect: Z = 4.45 Study or Subgroup Al-Qahtani 2013 Bader 2009 Beilter 2011 Bellomo 2003 Bristow 2000 (hospital 1 vs 2) Bristow 2000 (hospital 1 vs 3) Buist 2002 Chan 2008 Chan 2008 Chan 2008 Chan 2014 Goncales 2012 Hatler 2009 Hillman 2005 Jones 2005 Kenward 2004 Konrad 2010 Lighthall 2010 Lim 2011	(P < 0.00 R Events 144 17 128 69 69 47 77 845 71 16 90 198 128 61 74 43	0001) RT Total 157804 16907 79013 20921 18338 18338 18338 28801 24978 404116 42796 25470 68376 104001 53500 73825 9077 34699	No Events 133 36 253 66 99 73 147 3741 143 23 93 3741 143 23 93 66 139 228 355	RRT Total 98391 15949 77021 21090 13059 19545 25194 24193 942368 40033 24739 942368 40033 24739 56756 16246 53500 203892 2975 33360	Weight 5.9% 6.2% 3.3% 4.7% 5.1% 4.4% 5.3% 5.3% 5.3% 5.3% 5.4% 5.9% 5.4% 4.1%	M-H, Random, 95% Cl 0.68 [0.53, 0.85] 0.45 [0.25, 0.79] 0.49 [0.40, 0.61] 0.35 [0.22, 0.57] 0.74 [0.53, 1.04] 0.74 [0.55, 1.01] 0.56 [0.39, 0.67] 0.53 [0.49, 0.57] 0.46 [0.35, 0.62] 0.68 [0.36, 1.28] 0.80 [0.60, 1.07] 0.47 [0.35, 0.62] 0.92 [0.72, 1.17] 0.74 [0.56, 0.98] 0.69 [0.46, 1.03] 0.50 [0.47, 1.04]	Favours RRT Favours No RRT Risk Ratio
Test for overall effect: Z = 4.45 Study or Subgroup Al-Qahtani 2013 Bader 2009 Beitier 2011 Beilomo 2003 Bristow 2000 (hospital 1 vs 2) Bristow 2000 (hospital 1 vs 3) Buist 2002 Chan 2008 Chen 2014 Goncales 2012 Hatler 2009 Hillman 2005 Kenward 2004 Konrad 2010 Lighthall 2010 Lim 2011 Moroseos 2014	(P < 0.00 R Events 144 17 1288 69 69 47 77 845 71 16 90 198 128 61 74 43 37	0001) RT Total 157804 16907 79013 20921 18338 18338 28801 24978 404116 42796 42796 68376 104001 53500 73825 9077 34699 9357	No Events 133 36 253 63 66 99 73 147 3741 147 3741 147 3741 147 3741 147 3741 147 3741 147 3741 147 3741 147 3741 147 375 57 57 71	RRT Total 98391 15949 77021 21090 13059 19545 24193 942368 40033 24739 56756 16246 53500 203892 2975 33360 7092	Weight 5.9% 2.7% 6.2% 3.3% 4.7% 5.1% 4.4% 5.5% 7.6% 5.3% 5.3% 5.3% 5.3% 5.4% 4.1%	M-H, Random, 95% CI 0.68 [0.53, 0.85] 0.45 [0.25, 0.79] 0.49 [0.40, 0.61] 0.35 [0.22, 0.57] 0.74 [0.53, 1.04] 0.74 [0.55, 1.01] 0.56 [0.39, 0.81] 0.51 [0.39, 0.67] 0.45 [0.35, 0.62] 0.46 [0.35, 0.62] 0.46 [0.35, 0.62] 0.47 [0.35, 0.62] 0.52 [0.72, 1.17] 0.74 [0.56, 0.98] 0.59 [0.46, 1.03] 0.70 [0.47, 1.04] 0.39 [0.27, 0.59]	Favours RRT Favours No RRT Risk Ratio
Test for overall effect: Z = 4.45 Study or Subgroup Al-Qahtani 2013 Bader 2009 Beilter 2011 Beilomo 2003 Bristow 2000 (hospital 1 vs 2) Bristow 2000 (hospital 1 vs 3) Buist 2002 Chan 2008 Chan 2008 Chan 2008 Chan 2009 Hillman 2005 Jones 2005 Kenward 2004 Konrad 2010 Lighthall 2010 Lim 2011 Moroseos 2014 Santamaria 2010	(P < 0.00 R Events 144 17 128 22 69 69 47 77 845 71 166 90 198 128 61 74 43 37 125	0001) RT Total 157804 16907 79013 20921 18338 18338 18338 24978 404116 42796 25470 68376 104001 53500 73825 9077 34699 9357 81628	No Events 133 36 253 63 66 99 73 147 3741 143 23 66 139 93 66 139 228 35 59 711 24	RRT Total 98391 15949 77021 21090 13059 13059 13059 24193 942368 40033 24739 56756 16246 16246 16246 203892 2975 33360 7092 8190	Weight 5.9% 2.7% 6.2% 3.3% 4.7% 5.1% 4.4% 5.5% 5.3% 5.3% 5.3% 5.4% 5.4% 5.4% 4.1% 4.1% 4.1% 3.7%	M-H, Random, 95% Cl 0.68 [0.53, 0.85] 0.45 [0.25, 0.79] 0.49 [0.40, 0.61] 0.35 [0.22, 0.57] 0.74 [0.53, 1.04] 0.74 [0.55, 1.01] 0.56 [0.39, 0.81] 0.51 [0.39, 0.67] 0.53 [0.49, 0.57] 0.46 [0.35, 0.62] 0.80 [0.60, 1.07] 0.47 [0.35, 0.62] 0.92 [0.72, 1.17] 0.74 [0.56, 0.98] 0.69 [0.46, 1.03] 0.70 [0.47, 1.04] 0.39 [0.27, 0.59] 0.52 [0.34, 0.81]	Favours RRT Favours No RRT Risk Ratio
Test for overall effect: Z = 4.45 Study or Subgroup Al-Qahtani 2013 Bader 2009 Beitler 2011 Bellomo 2003 Bristow 2000 (hospital 1 vs 2) Bristow 2000 (hospital 1 vs 3) Buist 2002 Chan 2008 Chan 2008 Chan 2008 Chan 2008 Chan 2008 Kenward 2014 Konrad 2010 Lighthall 2010 Lighthall 2010 Santamaria 2010 Segon 2014	(P < 0.00 R Events 144 17 128 22 69 69 47 777 845 71 16 90 198 128 61 90 198 128 63 40 144 43 37 125 40	0001) RT Total 157804 16907 79013 20921 18338 18338 28901 24978 404116 42796 24978 404116 68376 104001 53500 73859 9077 34699 9357 815	No Events 133 36 253 63 66 99 73 147 3741 143 23 93 66 139 228 35 59 71 24 24 24 24	RRT Total 98391 15949 77021 21090 13059 19545 25194 24193 942368 40033 24739 56756 16246 55500 203892 2975 33360 7092 8190 14013	Weight 5.9% 2.7% 6.2% 3.3% 5.1% 4.4% 5.5% 7.6% 5.3% 5.3% 5.3% 5.3% 5.4% 5.9% 5.4% 5.9% 5.4% 4.1% 4.1% 3.3% 3.3%	M-H, Random, 95% CI 0.68 [0.53, 0.85] 0.45 [0.25, 0.79] 0.49 [0.40, 0.61] 0.35 [0.22, 0.57] 0.74 [0.53, 1.04] 0.74 [0.55, 1.01] 0.56 [0.39, 0.67] 0.53 [0.49, 0.57] 0.46 [0.35, 0.62] 0.68 [0.36, 1.28] 0.50 [0.60, 1.07] 0.74 [0.55, 0.62] 0.92 [0.72, 1.17] 0.74 [0.56, 0.98] 0.69 [0.46, 1.03] 0.70 [0.47, 1.04] 0.39 [0.27, 0.59] 0.52 [0.34, 0.81] 0.93 [0.60, 1.43]	Favours RRT Favours No RRT Risk Ratio
Test for overall effect: Z = 4.45 Study or Subgroup Al-Qahtani 2013 Bader 2009 Beilter 2011 Beilomo 2003 Bristow 2000 (hospital 1 vs 2) Bristow 2000 (hospital 1 vs 3) Buist 2002 Chan 2008 Chan 2008 Chan 2008 Chan 2009 Hillman 2005 Jones 2005 Kenward 2004 Konrad 2010 Lighthall 2010 Lim 2011 Moroseos 2014 Santamaria 2010	(P < 0.00 R Events 144 17 128 22 69 69 47 77 845 71 166 90 198 128 61 74 43 37 125	0001) RT Total 157804 16907 79013 20921 18338 18338 18338 24978 404116 42796 25470 68376 104001 53500 73825 9077 34699 9357 81628	No Events 133 36 253 63 66 99 73 147 3741 143 23 66 139 93 66 139 228 35 59 711 24	RRT Total 98391 15949 77021 21090 13059 13059 13059 24193 942368 40033 24739 56756 16246 16246 16246 203892 2975 33360 7092 8190	Weight 5.9% 2.7% 6.2% 3.3% 4.7% 5.1% 4.4% 5.5% 5.3% 5.3% 5.3% 5.4% 5.4% 5.4% 4.1% 4.1% 4.1% 3.7%	M-H, Random, 95% Cl 0.68 [0.53, 0.85] 0.45 [0.25, 0.79] 0.49 [0.40, 0.61] 0.35 [0.22, 0.57] 0.74 [0.53, 1.04] 0.74 [0.55, 1.01] 0.56 [0.39, 0.81] 0.51 [0.39, 0.67] 0.53 [0.49, 0.57] 0.46 [0.35, 0.62] 0.80 [0.60, 1.07] 0.47 [0.35, 0.62] 0.92 [0.72, 1.17] 0.74 [0.56, 0.98] 0.69 [0.46, 1.03] 0.70 [0.47, 1.04] 0.39 [0.27, 0.59] 0.52 [0.34, 0.81]	Favours RRT Favours No RRT Risk Ratio
Test for overall effect: Z = 4.45 Study or Subgroup Al-Qahtani 2013 Bader 2009 Beitler 2011 Bellomo 2003 Bristow 2000 (hospital 1 vs 2) Bristow 2000 (hospital 1 vs 3) Buist 2002 Chan 2008 Chan 2008 Chan 2008 Chan 2008 Chan 2008 Kenward 2014 Konrad 2010 Lighthall 2010 Lighthall 2010 Santamaria 2010 Segon 2014	(P < 0.00 R Events 144 17 128 22 69 69 47 777 845 71 16 90 198 128 61 90 198 128 63 40 144 43 37 125 40	0001) RT Total 157804 16907 79013 20921 18338 18338 28901 24978 404116 42796 24978 404116 68376 104001 53500 73859 9077 34699 9357 815	No Events 133 36 253 63 66 99 73 147 3741 143 23 93 66 139 228 35 59 71 24 24 24 24	RRT Total 98391 15949 77021 21090 13059 19545 25194 24193 942368 40033 24739 56756 16246 55500 203892 2975 33360 7092 8190 14013	Weight 5.9% 2.7% 6.2% 3.3% 5.1% 4.4% 5.5% 7.6% 5.3% 5.3% 5.3% 5.4% 5.4% 4.1% 4.1% 4.1% 3.7% 3.8% 5.1%	M-H, Random, 95% CI 0.68 [0.53, 0.85] 0.45 [0.25, 0.79] 0.49 [0.40, 0.61] 0.35 [0.22, 0.57] 0.74 [0.53, 1.04] 0.74 [0.55, 1.01] 0.56 [0.39, 0.67] 0.53 [0.49, 0.57] 0.46 [0.35, 0.62] 0.68 [0.36, 1.28] 0.50 [0.60, 1.07] 0.74 [0.55, 0.62] 0.92 [0.72, 1.17] 0.74 [0.56, 0.98] 0.69 [0.46, 1.03] 0.70 [0.47, 1.04] 0.39 [0.27, 0.59] 0.52 [0.34, 0.81] 0.93 [0.60, 1.43]	Favours RRT Favours No RRT Risk Ratio
Test for overall effect: Z = 4.45 Study or Subgroup Al-Qahtani 2013 Bader 2009 Beilter 2011 Beilomo 2003 Bristow 2000 (hospital 1 vs 2) Bristow 2000 (hospital 1 vs 3) Buist 2002 Chan 2008 Chan 2008 Chan 2008 Chan 2008 Chan 2008 Hillman 2005 Jones 2005 Kenward 2004 Konrad 2010 Lighthall 2010 Lighthall 2010 Lim 2011 Moroseos 2014 Santamaria 2010 Segon 2014 Shah 2011	(P < 0.00 R Events 144 17 128 22 69 69 47 777 845 71 16 90 198 128 61 90 198 128 63 40 144 43 37 125 40	0001) RT Total 157804 16907 79013 20921 18338 18338 28801 24978 404116 42796 25470 68376 104001 53500 73825 9077 34699 9357 81628 14333 45145	No Events 133 36 253 63 66 99 73 147 3741 143 23 93 66 139 228 35 59 71 24 24 24 24	RRT Total 98391 15949 77021 21090 13059 19545 24193 942368 40033 24739 56756 16246 53200 203892 2975 33360 7092 8190 14013 16244	Weight 5.9% 2.7% 6.2% 3.3% 5.1% 4.4% 5.5% 7.6% 5.3% 5.3% 5.3% 5.4% 5.4% 4.1% 4.1% 4.1% 3.7% 3.8% 5.1%	M-H, Random, 95% Cl 0.68 [0.53, 0.85] 0.45 [0.25, 0.79] 0.49 [0.40, 0.61] 0.35 [0.22, 0.57] 0.74 [0.53, 1.04] 0.74 [0.55, 1.01] 0.56 [0.39, 0.81] 0.51 [0.39, 0.67] 0.53 [0.49, 0.57] 0.46 [0.35, 0.62] 0.80 [0.60, 1.07] 0.47 [0.35, 0.62] 0.92 [0.72, 1.17] 0.74 [0.56, 0.98] 0.69 [0.46, 1.03] 0.70 [0.47, 1.04] 0.39 [0.27, 0.59] 0.52 [0.34, 0.81] 0.39 [0.60, 1.43] 0.97 [0.72, 1.32]	Favours RRT Favours No RRT Risk Ratio
Test for overall effect: Z = 4.45 Study or Subgroup Al-Qahtani 2013 Bader 2009 Beitler 2011 Beilomo 2003 Bristow 2000 (hospital 1 vs 2) Bristow 2000 (hospital 1 vs 3) Buist 2002 Chan 2008 Chan 2008 Chan 2008 Chan 2008 Chan 2008 Hillman 2005 Jones 2005 Kenward 2004 Konrad 2010 Lighthall 2010 Lighthall 2010 Segon 2014 Santamaria 2010 Segon 2014 Shah 2011 Total (95% CI)	(P < 0.00 R Events 144 17 128 69 69 47 77 845 71 16 90 198 61 128 61 74 43 37 125 400 157 2458	0001) RT Total 157804 16907 79013 20921 18338 18338 28801 24978 40416 42796 25470 68376 104001 53500 73825 9077 34699 9357 81628 14333 45145 1331423	No Events 133 36 253 63 66 99 97 73 147 3741 143 23 93 66 61 139 228 35 559 71 24 4 258	RRT Total 98391 15949 77021 21090 13059 15545 25194 24193 942368 40033 24739 56756 16246 53500 203892 2975 33360 7092 8190 14013 16244 1713850	Weight 5.9% 2.7% 6.2% 3.3% 4.7% 5.1% 4.4% 5.3% 5.3% 5.3% 5.3% 5.3% 5.3% 5.4% 4.1% 4.1% 4.1% 3.7% 3.3% 5.1% 100.0%	M-H, Random, 95% Cl 0.68 [0.53, 0.85] 0.45 [0.25, 0.79] 0.49 [0.40, 0.61] 0.35 [0.22, 0.57] 0.74 [0.53, 1.04] 0.74 [0.55, 1.01] 0.56 [0.39, 0.81] 0.51 [0.39, 0.67] 0.53 [0.49, 0.57] 0.46 [0.35, 0.62] 0.80 [0.60, 1.07] 0.47 [0.35, 0.62] 0.92 [0.72, 1.17] 0.74 [0.56, 0.98] 0.69 [0.46, 1.03] 0.70 [0.47, 1.04] 0.39 [0.27, 0.59] 0.52 [0.34, 0.81] 0.39 [0.60, 1.43] 0.97 [0.72, 1.32]	Favours RRT Favours No RRT Risk Ratio

FIG. 2. (a) Forest plot of RRT/MET impact on in-hospital mortality. (b) Forest plot of RRT/MET impact on IHCA. Abbreviations: CI, confidence interval; M-H, Mantel-Haenszel; MET, medical emergency team; RRT, rapid response team.

Subgroup Analysis Study Type

For hospital mortality, there was 1 cluster RCT and 2 nonrandomized studies^{11,20,33} (RR = 0.83, 95% CI: 0.80-0.87) and 17 cohort/before-after studies^{10,12,22,28–32,34–42} (RR = 0.89, 95% CI: 0.83-0.96). The cluster RCT and non-randomized studies had minimal heterogeneity (I^2 = 7%), and the cohort/before-after studies exhibited substantial heterogeneity (I^2 = 88%). The test for subgroup differences (I^2 = 54.7%) indicates that study type may have an impact on hospital mortality.

For IHCA, there was 1 cluster RCT and 2 nonrandomized studies^{11,20,33} (RR = 0.68, 95% CI: 0.52-0.88) and 17 before-after studies^{7,10,12,19,22,28,31,32,34-42} (RR = 0.60, 95% CI: 0.52-0.69). The cluster RCT and nonrandomized studies had substantial heterogeneity ($I^2 = 79\%$), whereas the cohort/before-after studies had moderate heterogeneity ($I^2 = 69\%$). The test for subgroup differences $(I^2 = 0\%)$ indicates that study type had no impact on IHCA.

RRT/MET Team Composition

For hospital mortality, there were 14 studies^{10,20,29,31–38,40–42} of RRTs with physicians (RR = 0.88, 95% CI: 0.82-0.95) and 4 studies^{12,28,30,39} without physicians (RR = 0.85, 95% CI: 0.74-0.99). Both groups exhibited substantial heterogeneity ($I^2 = 85\%$ for both). The test for subgroup differences ($I^2 = 0\%$) indicates that team composition had no impact on hospital mortality.

Similarly, for IHCA there were 14 studies^{7,10,20,31–38,40–42} of RRTs with physicians (RR = 0.61, 95% CI: 0.54-0.69) and 4 studies^{12,19,28,39} without (RR = 0.60, 95% CI: 0.39-0.92). The studies with physicians on the RRT had moderate heterogeneity ($I^2 = 55\%$), whereas studies without a physician

on the RRT had substantial heterogeneity ($I^2 = 81\%$). The test for subgroup differences ($I^2 = 0\%$) indicates that team composition had no impact on IHCA.

Publication Year

Publication year had no impact on hospital mortality. Studies published 2010 or earlier had an RR of 0.88 (95% CI: 0.80-0.97), whereas studies published after 2010 had an RR of 0.87 (95% CI: 0.83-0.92). Both groups had substantial heterogeneity (I^2 of 88% and 75%, respectively). The test for subgroup differences ($I^2 = 0\%$) indicates publication year had no impact on hospital mortality.

Publication year had no impact on IHCA. Studies published in 2010 or earlier had an RR of 0.63 (95% CI: 0.54-0.73), whereas studies published after 2010 had an RR of 0.60 (95% CI: 0.50-0.72). The 2010 or earlier group had moderate heterogeneity ($I^2 = 60\%$), whereas the post-2010 group had substantial heterogeneity ($I^2 = 77\%$). The test for subgroup differences ($I^2 = 0\%$) indicates that publication year had no impact on IHCA.

Sensitivity Analysis

A sensitivity analysis was performed excluding studies with low methodological quality from the analysis. For hospital mortality there were no studies of low methodological quality. For IHCA there was no major change in the summary estimate or the heterogeneity (RR = 0.59, 95% CI: 0.53-0.67, $I^2 = 66\%$).

A sensitivity analysis was performed excluding studies only reporting rates and/or average annual admissions from the analysis. For hospital mortality, there was no major change in the summary estimate or the heterogeneity (RR = 0.87, 95% CI: 0.82-0.93, I^2 = 87%). For IHCA there was no major change in the summary estimate, but there was a decrease in heterogeneity (RR = 0.59, 95% CI: 0.53-0.66, I^2 = 63%).

Publication Bias

Funnel plots generated for the effect of RRTs on hospital mortality and on IHCA did not indicate publication bias. Our search of clinicaltrials.gov found 1 potentially eligible study that did not meet our inclusion criteria.

DISCUSSION

We found implementation of RRT/METs was associated with reductions in hospital mortality and IHCA. Our analysis extends the meta-analysis of Chan et al. and is consistent with the recent systematic review by Winters et al.^{8,9} These findings provide support for the IHI recommendation that hospitals implement RRT/METs.¹

Following the 2004 IHI recommendations, RRT/ METs were widely implemented, with over 50% of hospitals having some form of RRT by 2010.⁶ The adoption of RRT/METs occurred despite limited evidence on the effectiveness of RRT/METs. A metaanalysis of studies published through 2008 demonstrated a reduction in cardiac arrests, but no reduction in mortality after implementation of RRT/METs.⁸ More recently a systematic review that included studies through 2012 suggested that RRT/METs are associated with reduced IHCA and reduced mortality.9 Our analvsis addressed the conflicting results of the prior reviews and included 13 studies published after the Chan et al. meta-analysis and several studies published after the Winters et al. systemic review.^{8,9} The studies included in our analysis were completed in hospitals across multiple countries and settings, increasing the generalizability of the results. Most studies were performed in teaching hospitals; thus, the results may not be as applicable to community hospitals.

We found publication year did not impact either outcome. However, this may reflect our use of 2 broad publication periods rather than smaller periods, as 5 of the 6 newly included studies favor RRT interventions. Additionally, if the studies missing data had been included in our analysis, they may have shown that publication year impacts the outcomes. We noted that a physician on a RRT/MET did not affect outcomes, contrary to suggestions by Winters et al.⁹ This may reflect the skill of nonphysician providers and/or the collaboration of the RRT/MET with critical care teams. However, very few RRTs did not include a physician, limiting the conclusion that can be drawn regarding team composition.

Many patients exhibit observable clinical deterioration or measurable changes that could identify them prior to an event such as cardiac arrest.^{5,43} Measurable physiologic parameters, in fact, are the basis of medical early warning systems and recent automated systems.^{44,45} Similarly, delayed transfer to the ICU has been shown to be associated with increased mortality.⁴⁶ Therefore, RRTs, either by identifying patients at risk for clinical deterioration and/or facilitating transfer of patients to the ICU earlier, could result in improved clinical outcomes. We did not specifically look at ICU transfer or ICU codes in our analysis. However, in a recent single-center before-after study, RRT implementation increased ICU admission rates and the transfer of less severely ill patients to the ICU without improvement in severity of illness-adjusted outcomes.47 This finding may reflect the ICU organization of the particular institution; however, given limited ICU resources, admitting an increased number of less severely ill patients without clear clinical benefit is a potential concern. More studies are needed to better understand the mechanism of benefit as well as potential trade-offs associated with RRT implementation. It is possible that institutional factors determine the benefit that can be achieved through RRTs.

Our study has several limitations. Although the methodological quality of the included studies was

moderate to good, confounding and biases can be an issue with before-after trials and cohort studies. Most studies were before-after observational trials, lacking a concurrent control group making it difficult to draw causal relationships. This is particularly the case for hospital mortality, which has been independently falling since 2000.48 Thus, changes in observed hospital mortality may simply reflect the general trend independent of the RRT intervention. However, this does not appear the case for cardiopulmonary arrest, which has been increasing in incidence since 2000.49 There were several studies eligible for inclusion in our analysis, but could not be included because of insufficient data. It is possible that the inclusion of these studies could influence the results of our analysis. Finally, there was heterogeneity among the studies for both outcomes, particularly in-hospital mortality. This likely reflects variations in hospital characteristics and case-mix indices. There may also be other factors impacting teams such as how hospitals handled deteriorating patients before RRT implementation, education periods, and differing mechanisms and criteria for RRT activation.

In conclusion, RRT/METs are effective in decreasing both IHCA and hospital mortality. Our findings support the 2004 IHI recommendations for the implementation of RRTs in hospitals. Additional studies are still required to explore team composition, activation criteria, activation mechanism, and implementation strategies.

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