

Supplemental digital content for Effectiveness of automated alerting system compared to usual care for the management of sepsis: a systematic review and meta-analysis

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Supplementary Methods

Searching strategy in relevant databases

The following searching strategy was applied on December 2021

Searching strategy in PubMed

Item number	Searching words	Number of items
1#	((sepsis[Title/Abstract] AND (septic[Title/Abstract])) AND (septicemia[Title/Abstract]))	161461
2#	early warning[Title/Abstract] OR machine learning[Title/Abstract] OR prediction[Title/Abstract] OR artificial intelligence[Title/Abstract] OR detection [Title/Abstract]	1310072
3#	mortality[Title/Abstract] OR length of stay[Title/Abstract]	910594
4#	randomized[Title/Abstract] OR controlled[Title/Abstract] OR observational[Title/Abstract] OR pre-implementation[Title/Abstract] OR pre-post [Title/Abstract]	1374458
5#	1# AND 2# AND 3# AND 4#	394

SCOPUS (n = 498)

TITLE-ABS-KEY (sepsis OR septic) AND TITLE-ABS-KEY ((early AND warning) OR (machine AND learning) OR prediction OR (artificial AND intelligence)) AND TITLE-ABS-KEY (mortality) AND TITLE-ABS-KEY (randomized OR controlled OR pre-implementation OR pre-post) AND (LIMIT-TO (DOCTYPE , "ar"))

WOS (n = 785)

Item number	Searching words	Number of items
1#	((AB=(sepsis)) OR AB=(septic)) OR AB=(septicemia)	209874
2#	(((((AB=(early warning)) OR AB=(machine learning)) OR AB=(prediction)) OR AB=(artificial intelligence)) OR AB=(detection)) OR AB=(automated)	6160275
3#	(AB=(mortality)) OR AB=(length of stay)	1225755
4#	(((((AB=(randomized)) OR AB=(controlled)) OR AB=(observational)) OR AB=(pre-implementation)) OR AB=(pre-post)	18075728
5#	1# AND 2# AND 3# AND 4#	785

MedRxiv (n = 327)

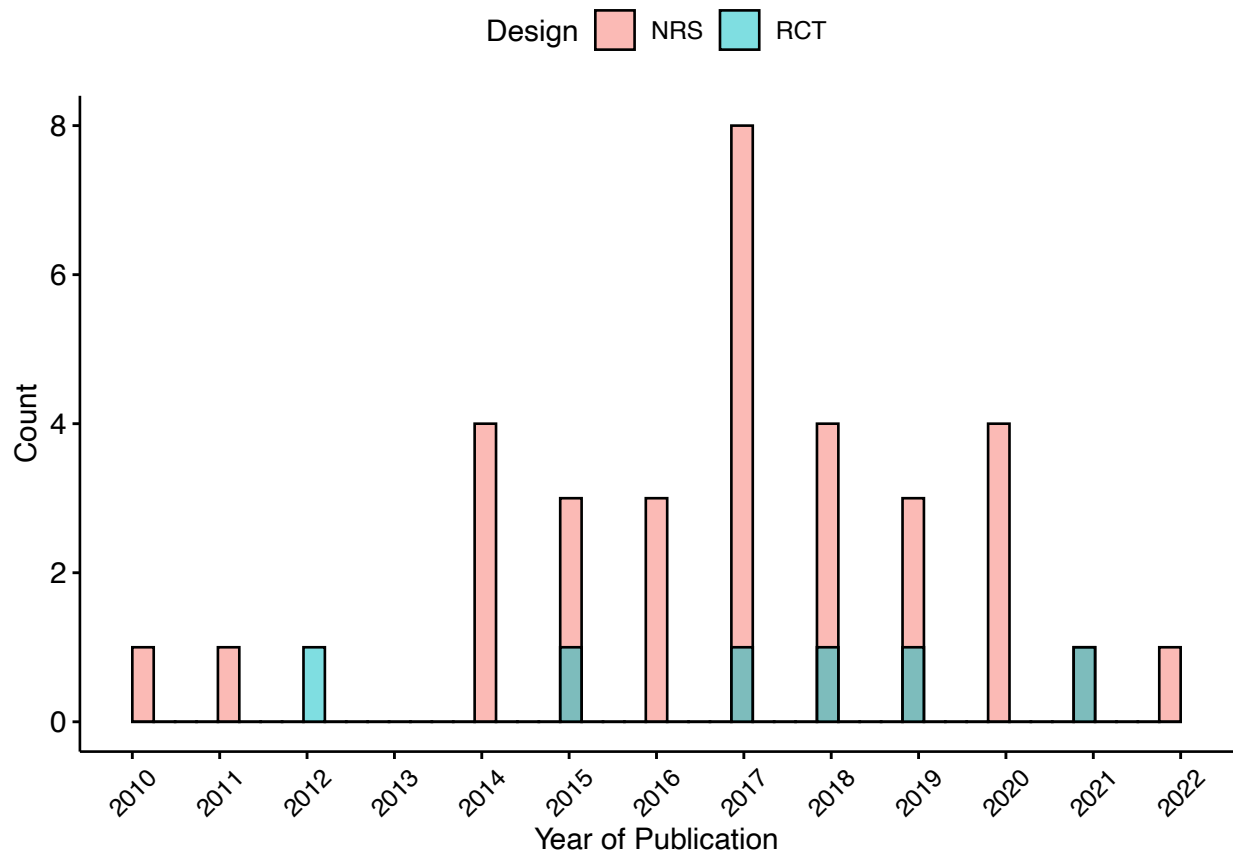
(sepsis OR septic) AND (automated OR alert OR machine learning OR artificial intelligence OR early warning OR prediction) AND (mortality OR length of stay) AND (randomized OR pre-implementation OR pre-post OR controlled OR observational)

Embase under PICO framework (n = 643)

('sepsis'/exp OR 'septicemia'/exp OR 'septic shock'/exp) AND ('prediction'/exp OR 'early warning score'/exp OR 'machine learning'/exp OR 'artificial intelligence'/exp OR automated:ti,ab OR detection:ti,ab) AND ('mortality'/exp OR 'length of stay'/exp) AND ('randomized controlled trial'/exp OR 'observational study'/exp)

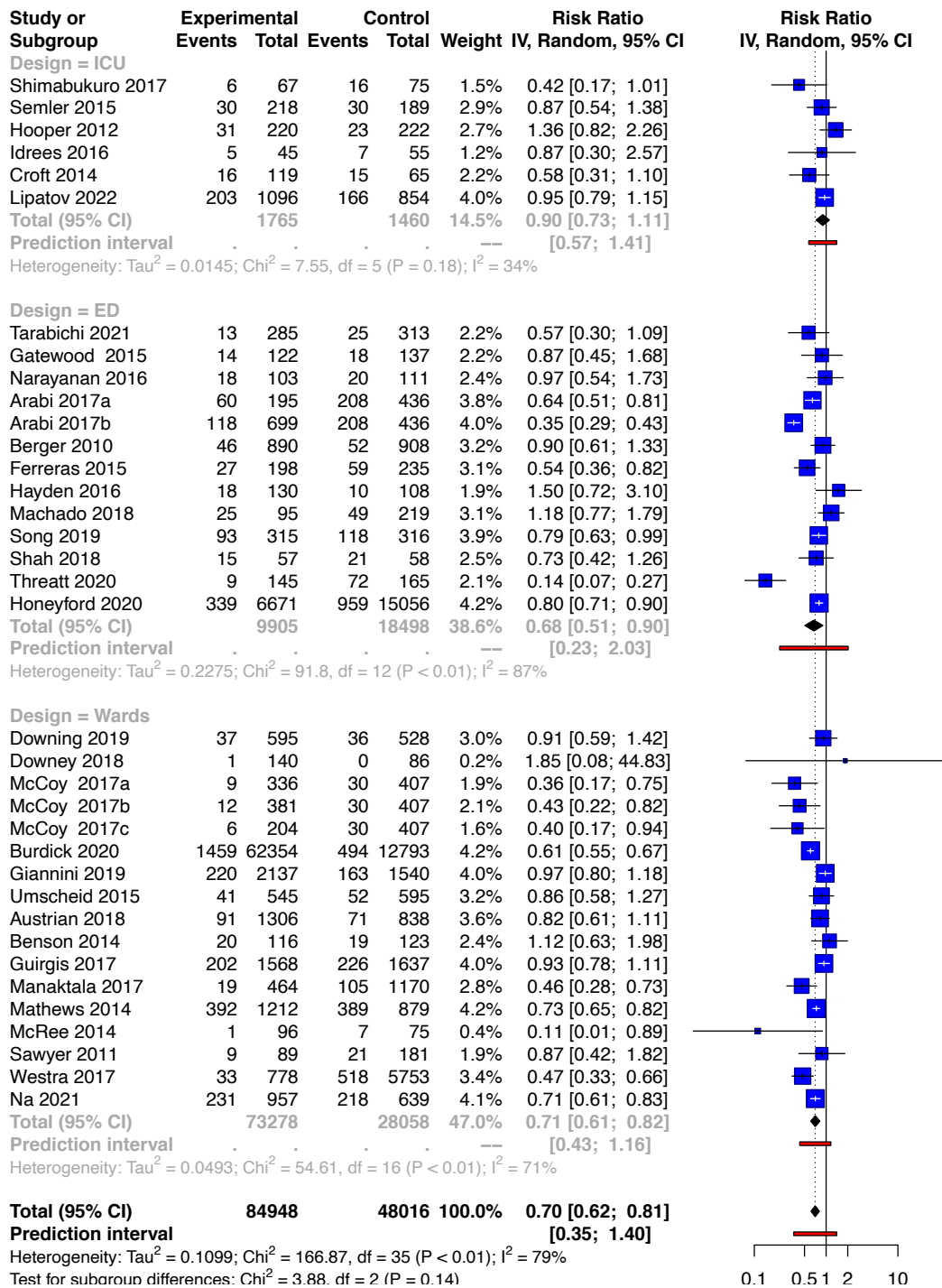
Cochrane Central Register of Controlled Trials (CENTRAL) (n = 801)

"sepsis" OR "septic" OR "septicemia" OR "bacteremia" in Title Abstract Keyword AND "detection" OR "machine learning" OR "early warning" OR "prediction" OR "artificial intelligence" OR "automated" in Title Abstract Keyword AND "mortality" OR "length of stay" in Title Abstract Keyword AND "randomized" OR "controlled" OR "observational" OR "pre-implementation" OR "pre-post" in Title Abstract Keyword - (Word variations have been searched)



Supplementary Figure 1 Trends of the number of publications over time stratified by study design.

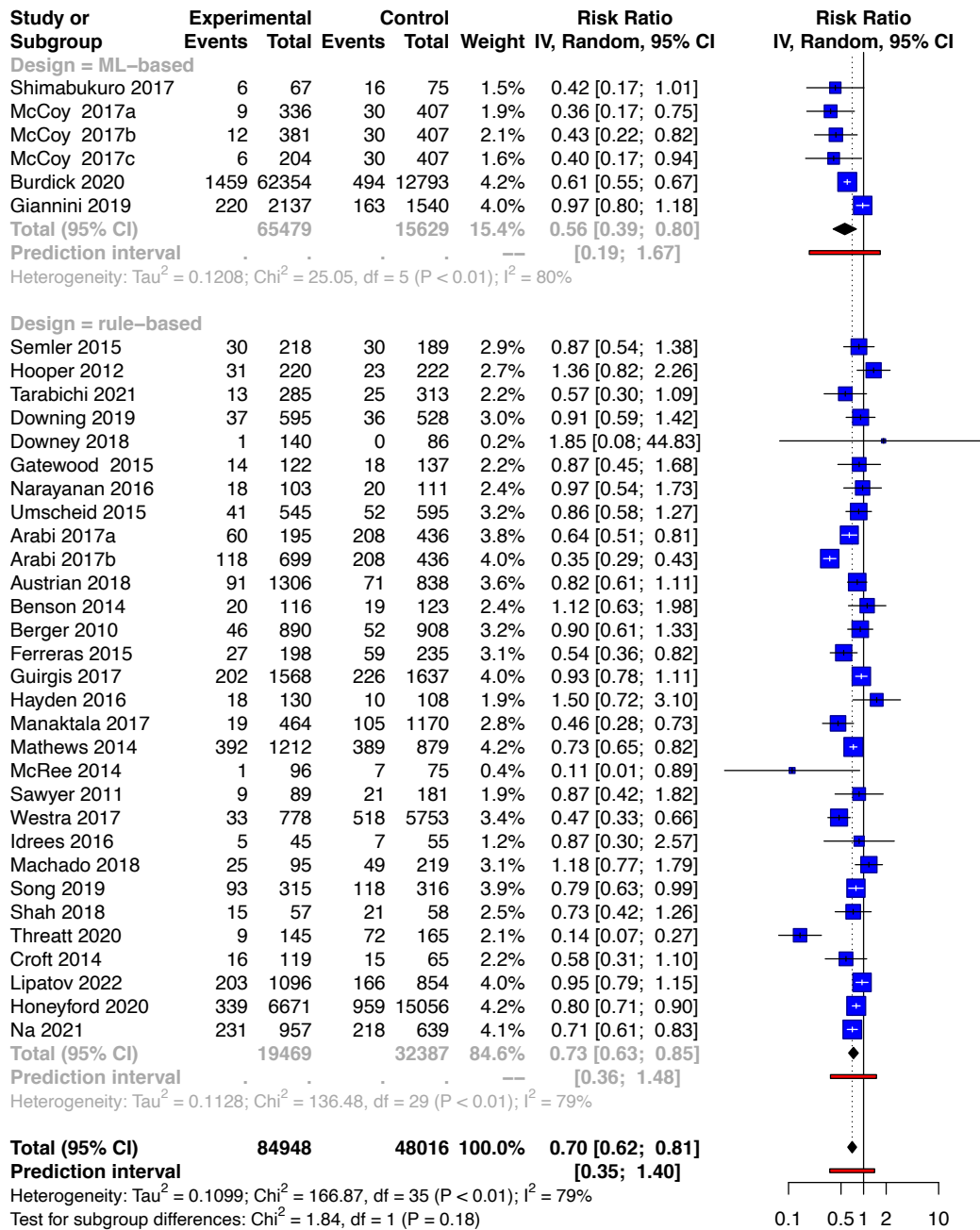
NRS = non-randomized study; RCT = randomized controlled trial



Supplementary Figure 2. Subgroup analysis for mortality outcome stratified by setting.

The size of the blue square indicates the weight of each individual study. The black diamond represents the pooled effect size for each subgroup as well as for the overall effect. The red bars represent the prediction interval.

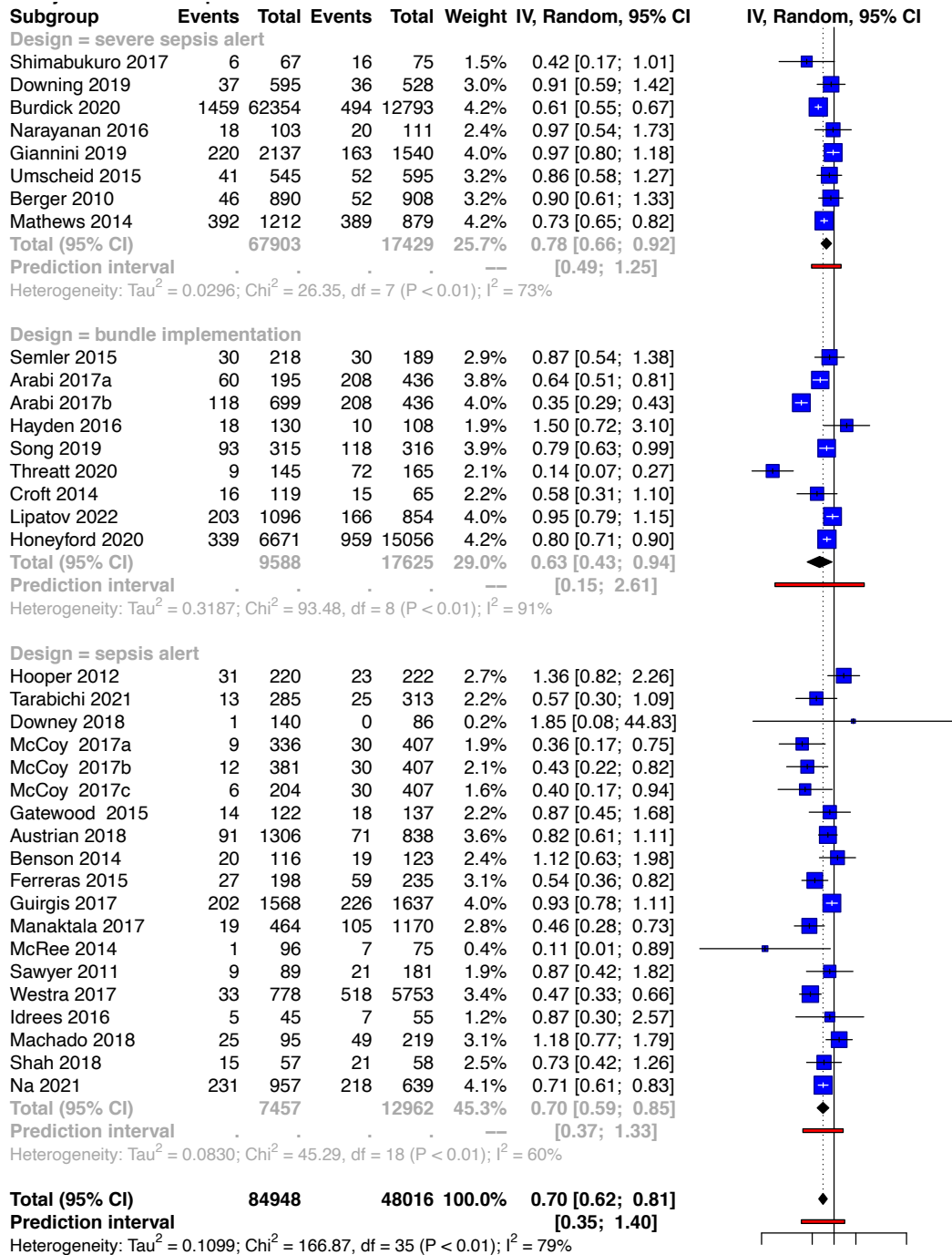
Abbreviations: ED = emergency department; ICU = intensive care unit; CI = confidence interval; IV = inverse variance.



Supplementary Figure 3. Subgroup analysis for mortality outcome stratified by alerting method.

The size of the blue square indicates the weight of each individual study. The black diamond represents the pooled effect size for each subgroup as well as for the overall effect. The red bars represent the prediction interval.

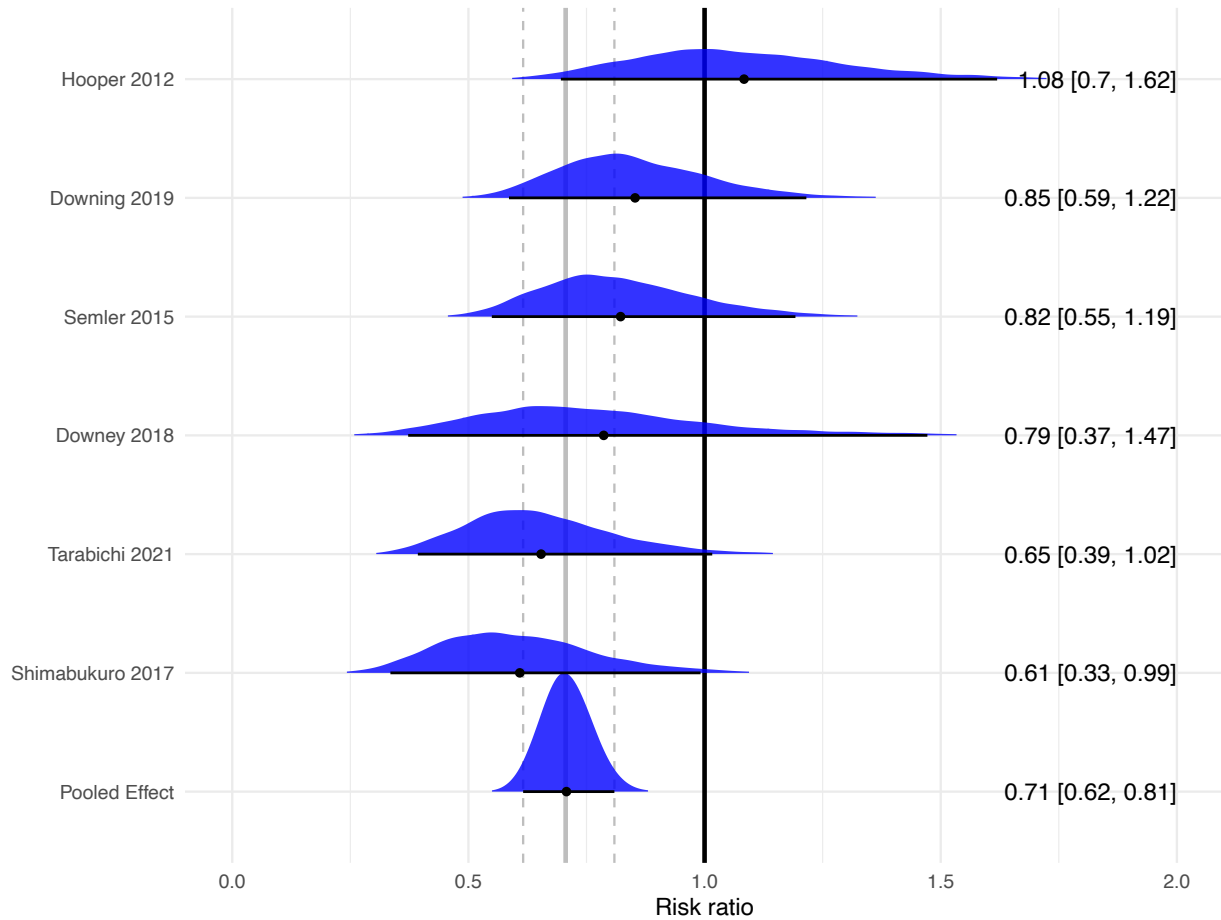
Abbreviations: ED = emergency department; ICU = intensive care unit; CI = confidence interval; IV = inverse variance.



Supplementary Figure 4. Subgroup analysis for mortality outcome stratified by purpose of alerting.

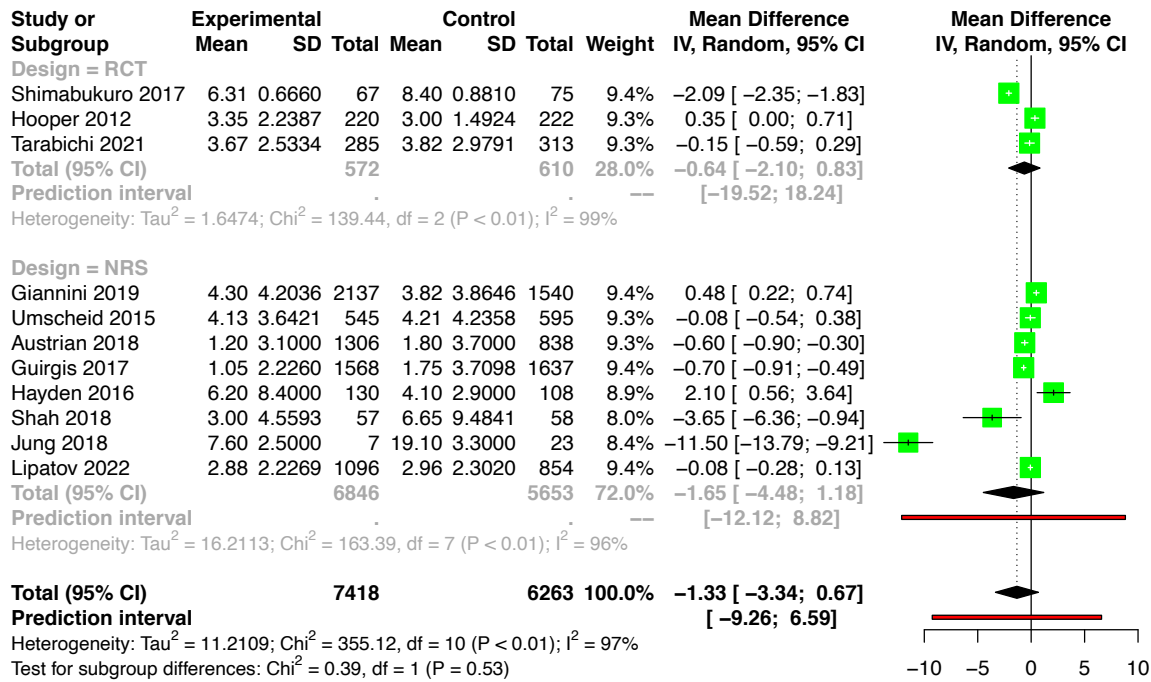
The size of the blue square indicates the weight of each individual study. The black diamond represents the pooled effect size for each subgroup as well as for the overall effect. The red bars represent the prediction interval.

Abbreviations: ED = emergency department; ICU = intensive care unit; CI = confidence interval; IV = inverse variance.



Supplementary Figure 5. Bayesian meta-analysis of RCTs for mortality.

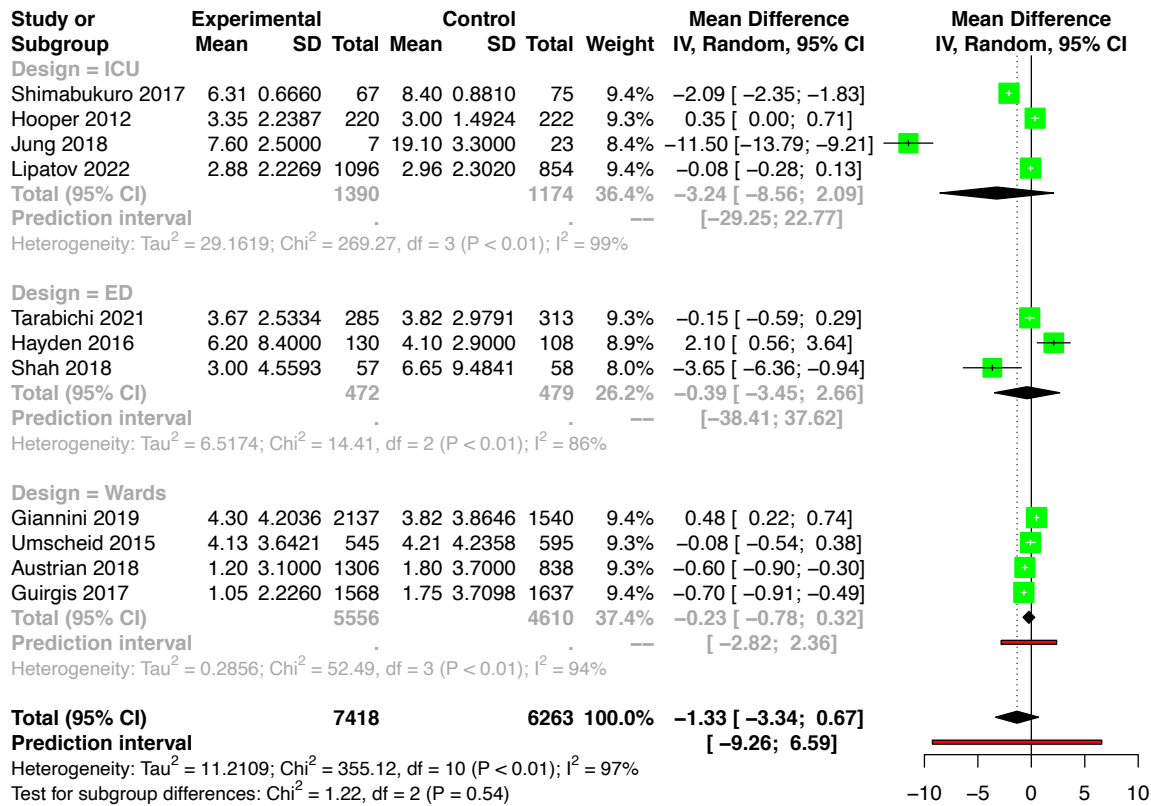
Pooled metrics from non-randomized studies were employed as the prior. The effect measure is the risk ratio, and a value <1 indicates beneficial effect of the automated alerting system. The blue shaded area represents the posterior distribution for each individual study as well as for the pooled effects.



Supplementary Figure 6. Subgroup analysis for ICU length of stay stratified by the study design.

The size of the green square indicates the weight of each individual study. The black diamond represents the pooled effect size for each subgroup as well as for the overall effect. The red bars represent the prediction interval.

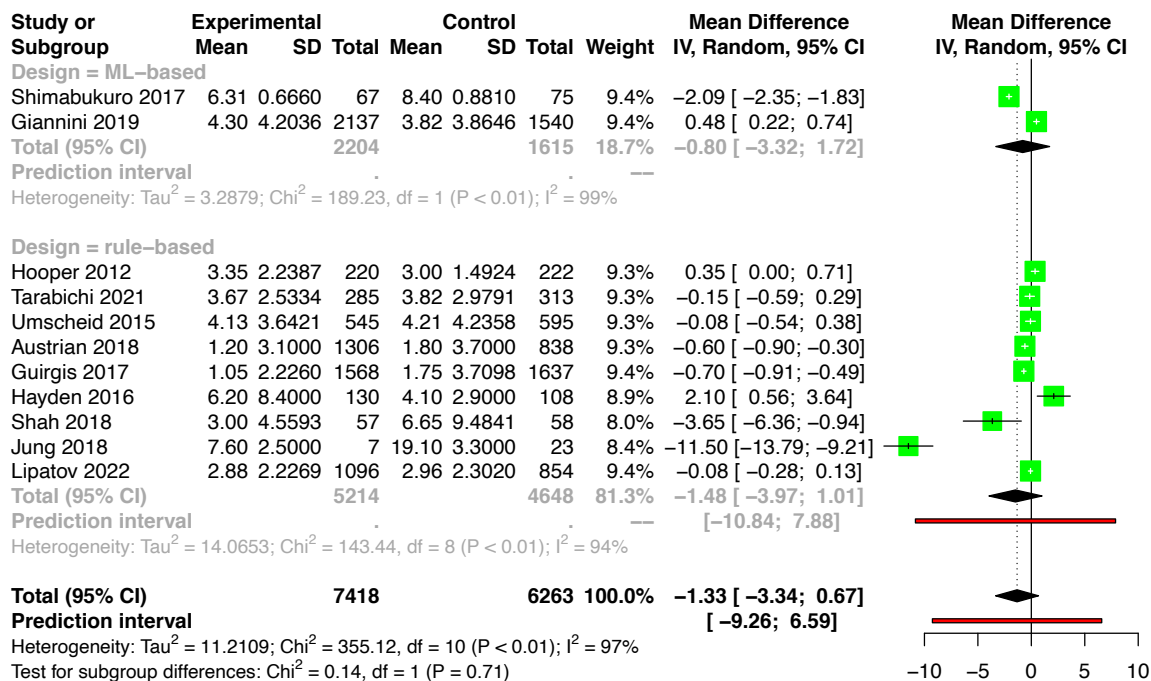
Abbreviations: RCT = randomized controlled trial; ICU = intensive care unit; CI = confidence interval; IV = inverse variance.



Supplementary Figure 7. Subgroup analysis for ICU length of stay stratified by the study setting.

The size of the green square indicates the weight of each individual study. The black diamond represents the pooled effect size for each subgroup as well as for the overall effect. The red bars represent the prediction interval.

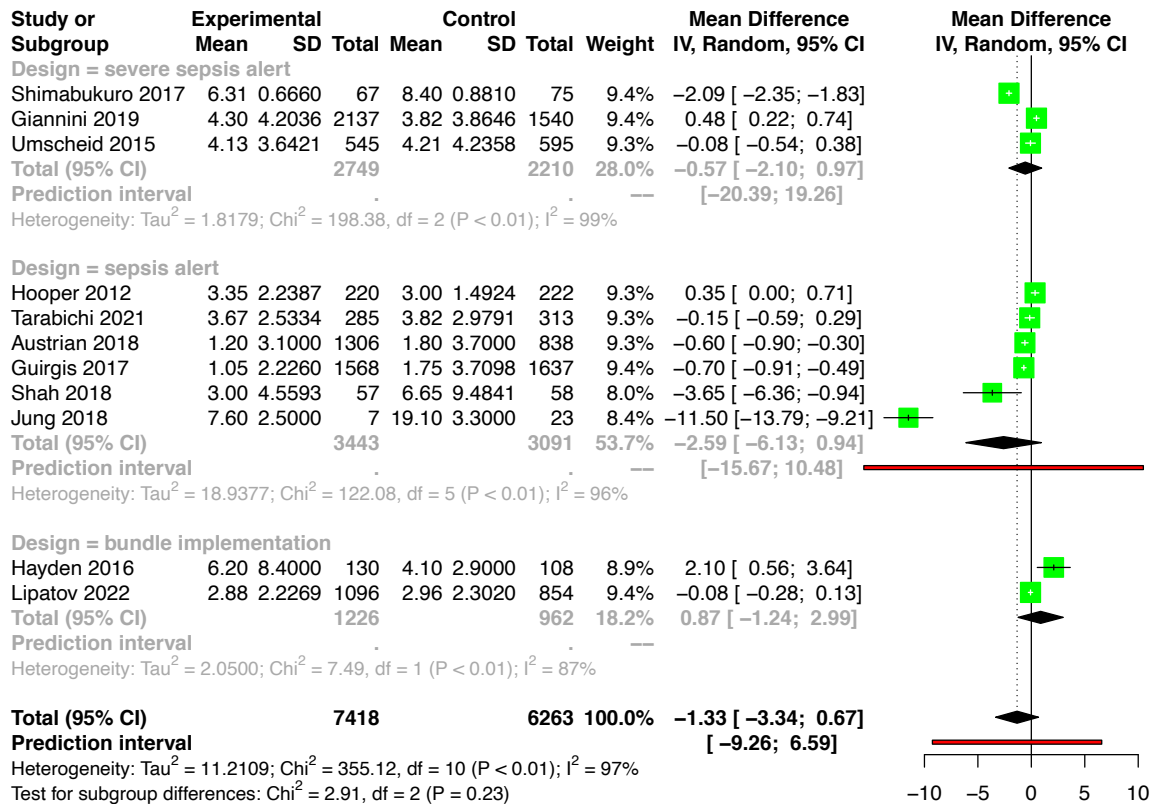
Abbreviations: ED = emergency department; ICU = intensive care unit; CI = confidence interval; IV = inverse variance.



Supplementary Figure 8. Subgroup analysis for ICU length of stay stratified by prediction methods.

The size of the green square indicates the weight of each individual study. The black diamond represents the pooled effect size for each subgroup as well as for the overall effect. The red bars represent the prediction interval.

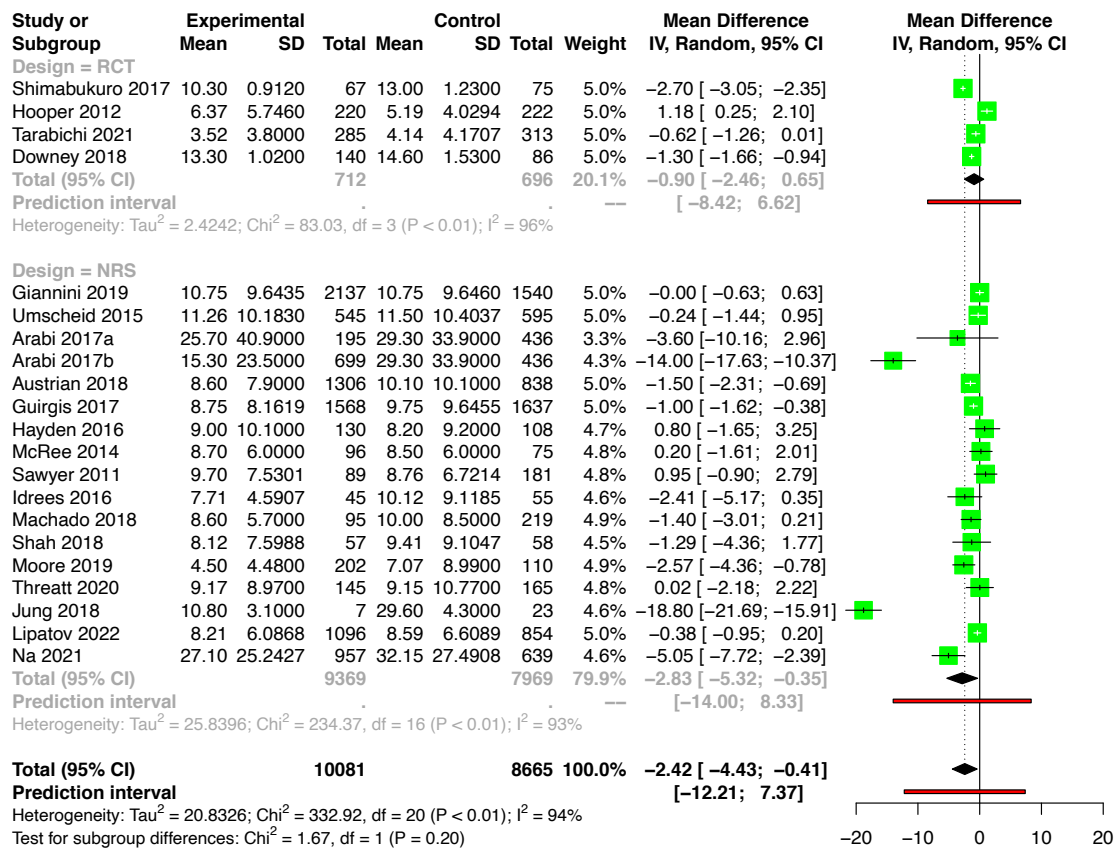
Abbreviations: ML = machine learning; ICU = intensive care unit; CI = confidence interval; IV = inverse variance.



Supplementary Figure 9. Subgroup analysis for ICU length of stay stratified by prediction purpose.

The size of the green square indicates the weight of each individual study. The black diamond represents the pooled effect size for each subgroup as well as for the overall effect. The red bars represent the prediction interval.

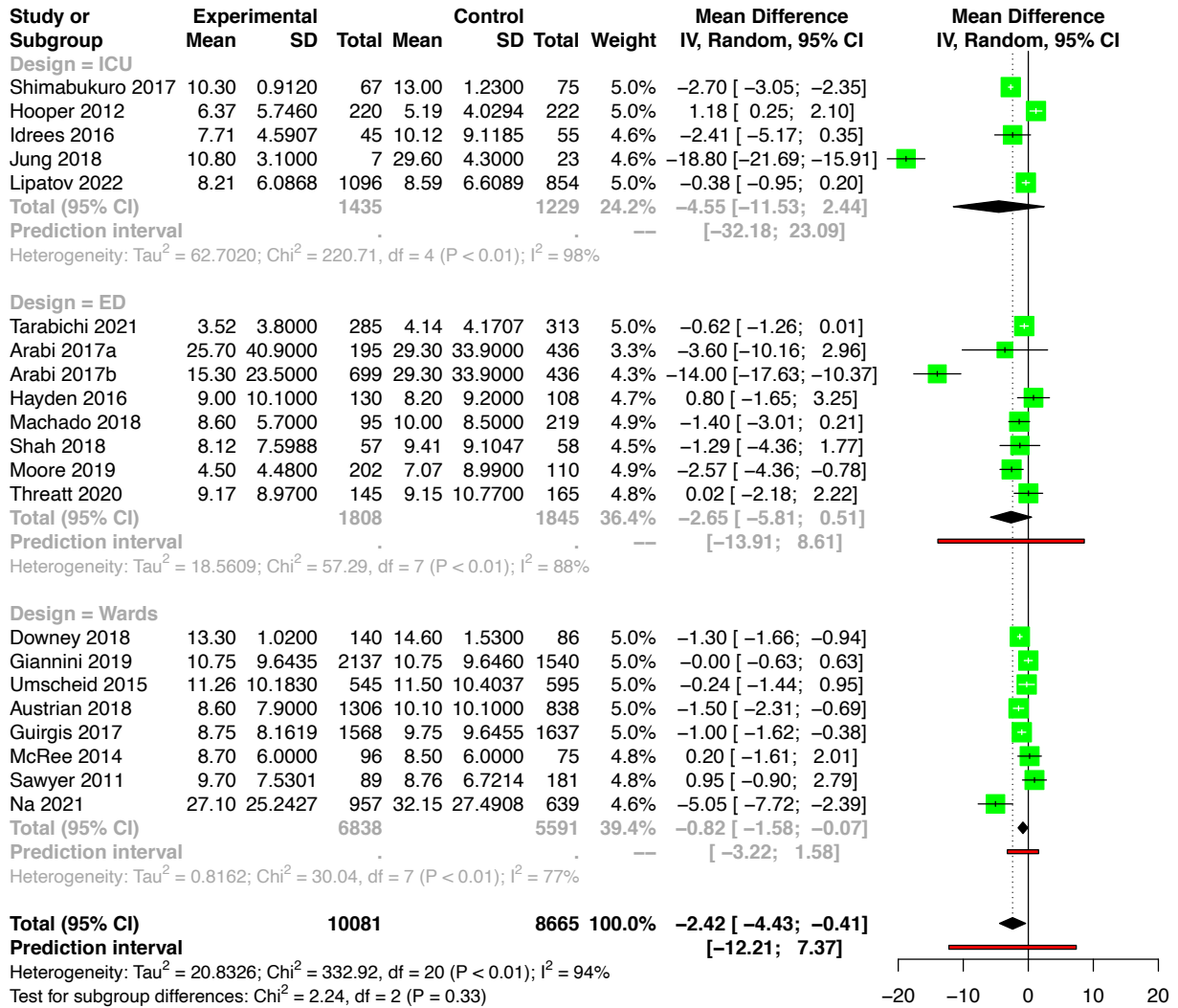
Abbreviations: SD = standard deviation; ICU = intensive care unit; CI = confidence interval; IV = inverse variance.



Supplementary Figure 10. Subgroup analysis for hospital length of stay stratified by study design.

The size of the green square indicates the weight of each individual study. The black diamond represents the pooled effect size for each subgroup as well as for the overall effect. The red bars represent the prediction interval.

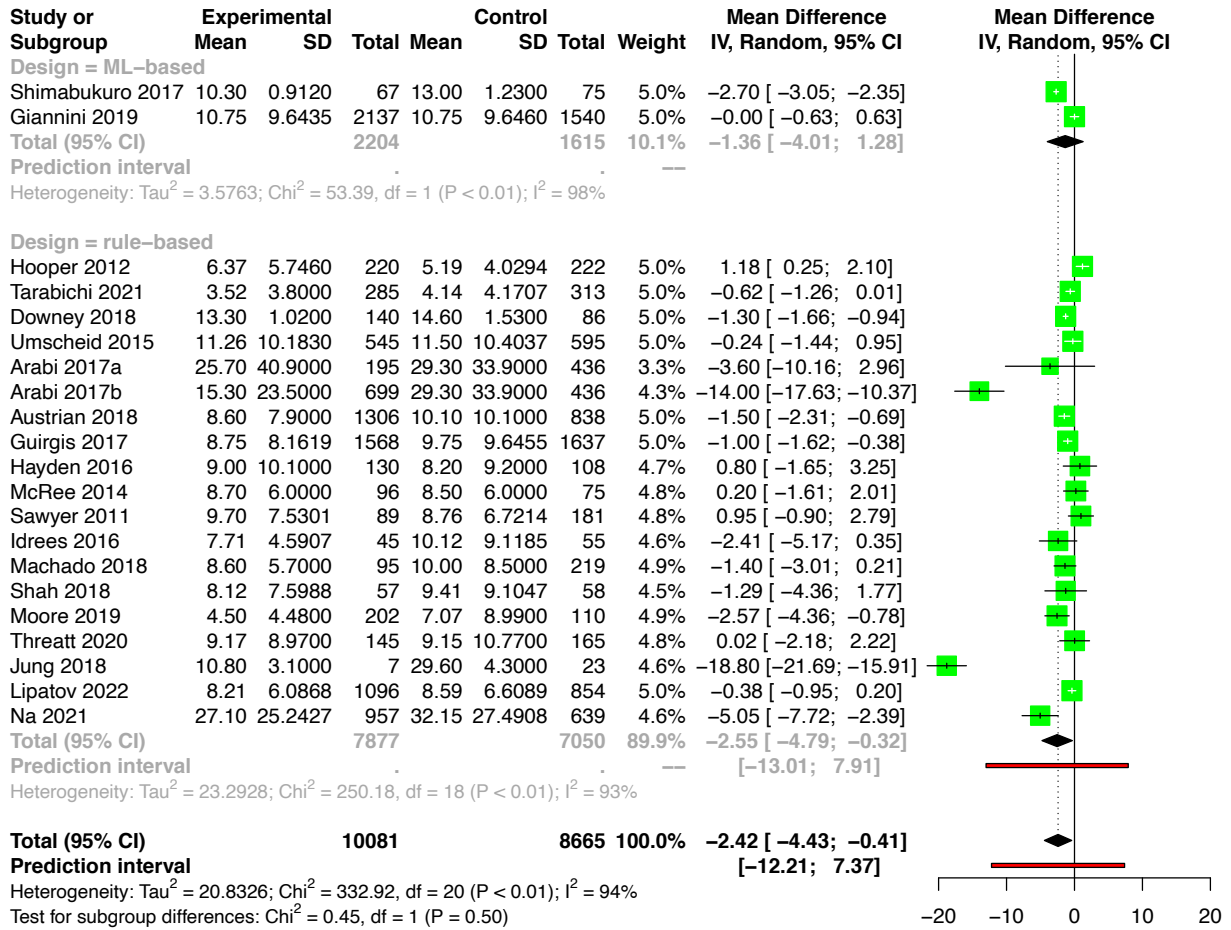
Abbreviations: SD = standard deviation; RCT = randomized controlled trial; CI = confidence interval; IV = inverse variance.



Supplementary Figure 11. Subgroup analysis for hospital length of stay stratified by study setting.

The size of the green square indicates the weight of each individual study. The black diamond represents the pooled effect size for each subgroup as well as for the overall effect. The red bars represent the prediction interval.

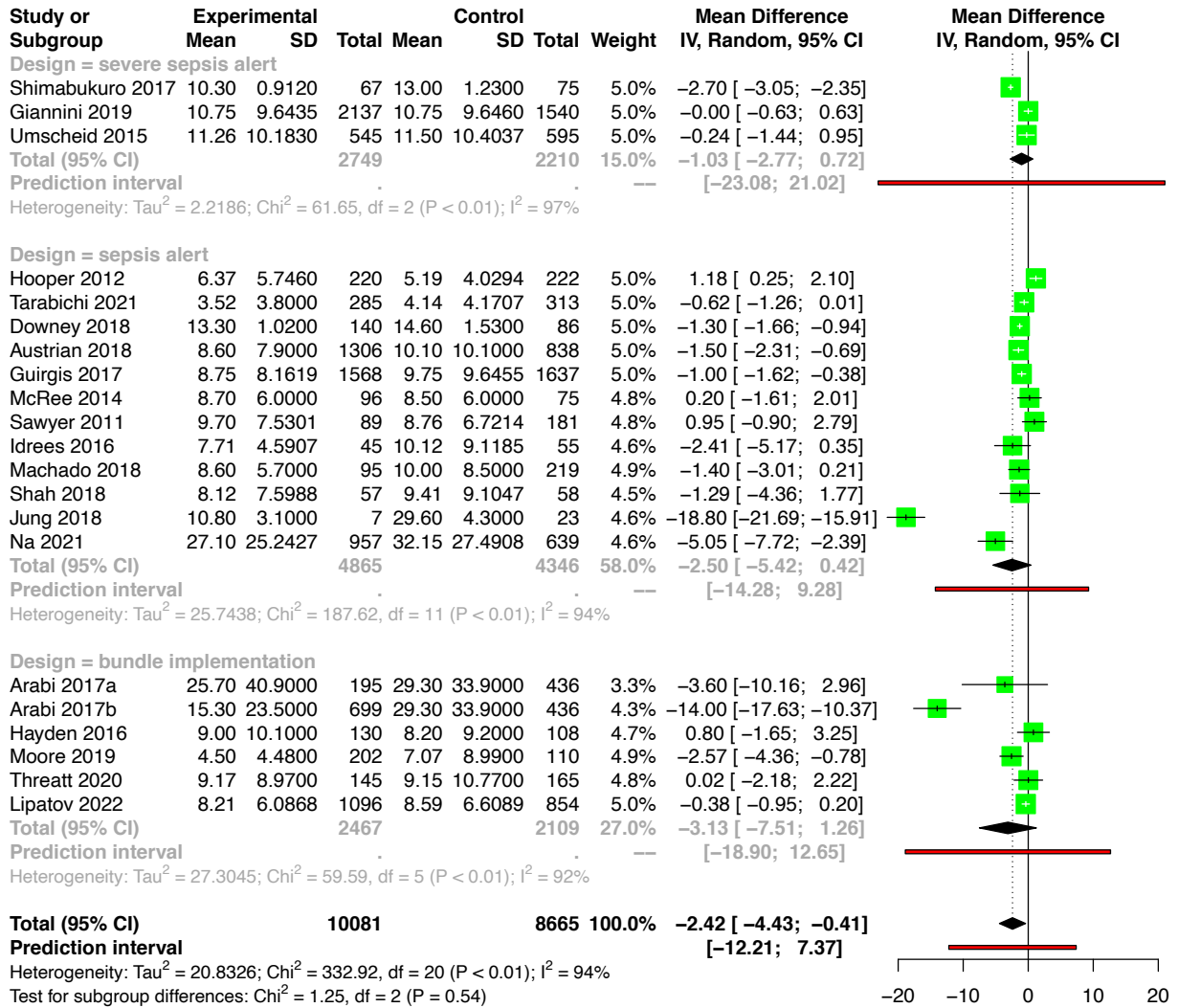
Abbreviations: SD = standard deviation; ED = emergency department; ICU = intensive care unit; CI = confidence interval; IV = inverse variance.



Supplementary Figure 12. Subgroup analysis for hospital length of stay stratified by alerting methods.

The size of the green square indicates the weight of each individual study. The black diamond represents the pooled effect size for each subgroup as well as for the overall effect. The red bars represent the prediction interval.

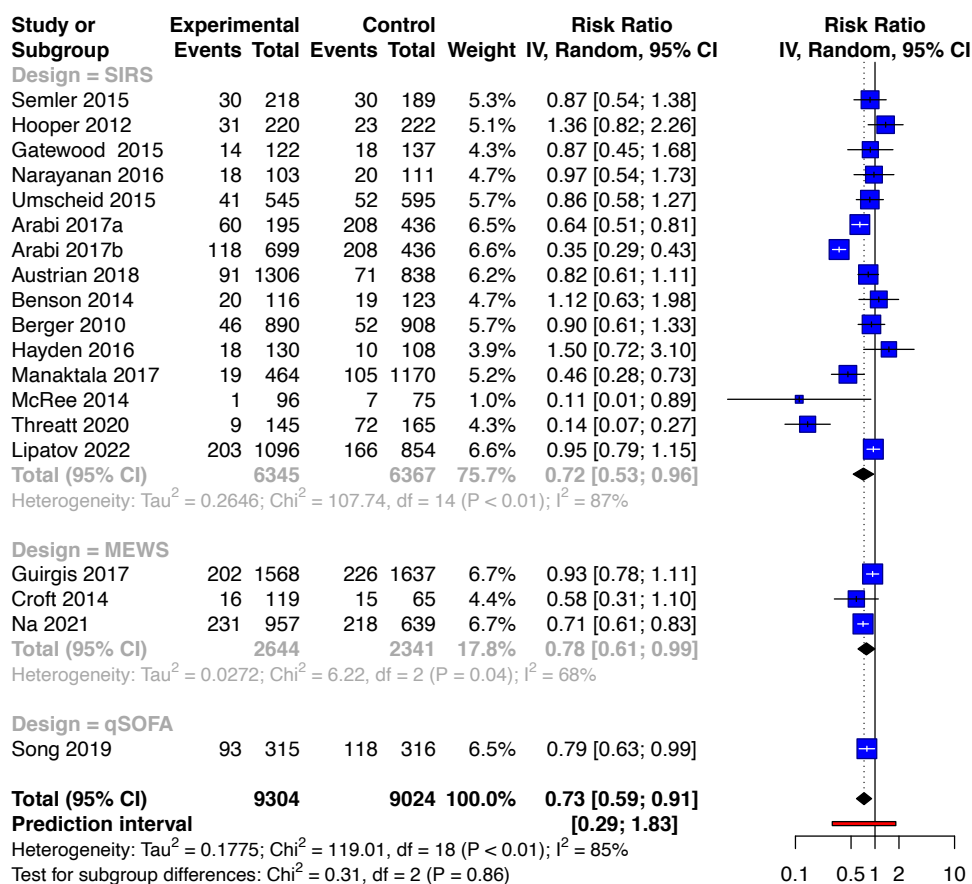
Abbreviations: SD = standard deviation; ML = machine learning; CI = confidence interval; IV = inverse variance.



Supplementary Figure 13. Subgroup analysis for hospital length of stay stratified by alerting purpose.

The size of the green square indicates the weight of each individual study. The black diamond represents the pooled effect size for each subgroup as well as for the overall effect. The red bars represent the prediction interval.

Abbreviations: SD = standard deviation; CI = confidence interval; IV = inverse variance.



Supplementary Figure 14. Subgroup analysis for mortality stratified by different rules to alert sepsis onset.

The size of the green square indicates the weight of each individual study. The black diamond represents the pooled effect size for each subgroup as well as for the overall effect. The red bars represent the prediction interval.

Abbreviations: SD = standard deviation; CI = confidence interval; IV = inverse variance; SIRS = systematic inflammatory response syndrome; qSOFA = quick Sepsis Related Organ Failure Assessment; MEWS = Modified Early Warning Score.