



VI Convegno Nazionale GAVePed

Un progetto scientifico educativo GAVeCeLT
'Gli Accessi Venosi Centrali a Lungo Termine'



Quando è possibile il *trattamento conservativo* delle *infezioni catetere-correlate* nel *bambino*

Daniele G. Biasucci

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TOR VERGATA
UNIVERSITÀ DEGLI STUDI DI ROMA



9TH EDITION
REVISED 2024

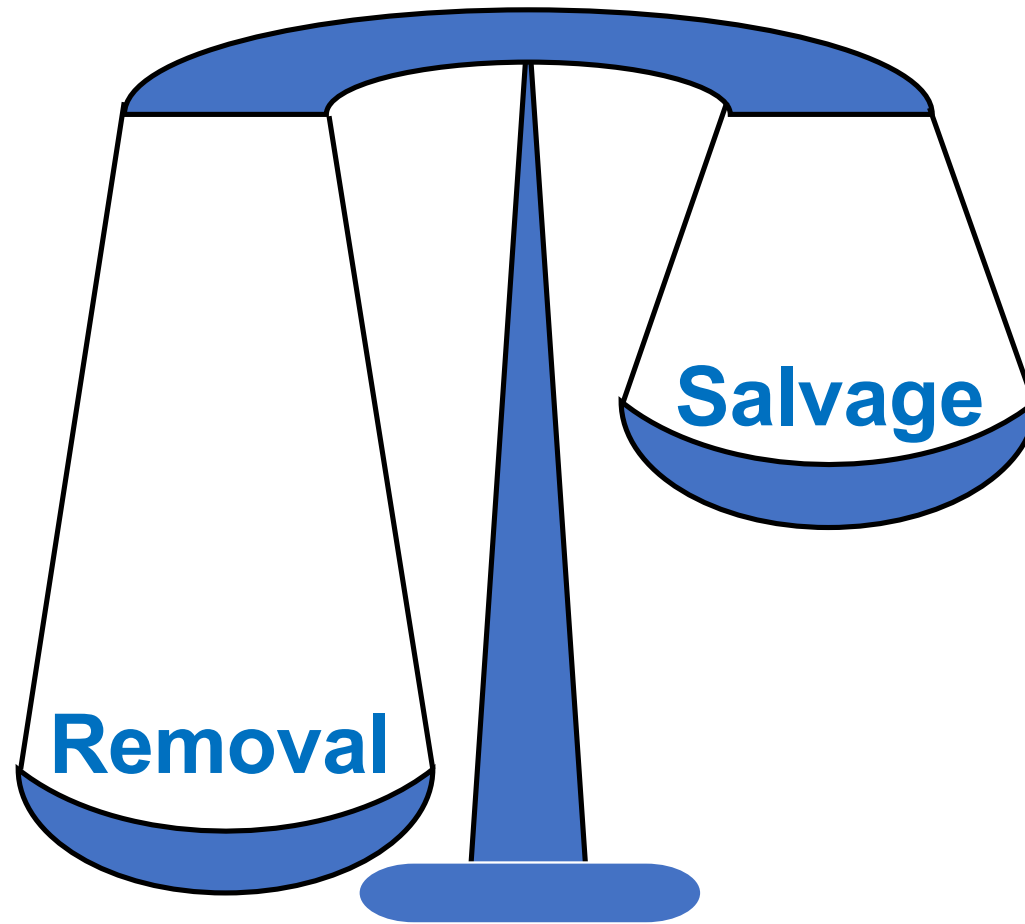
Infusion Therapy Standards of Practice

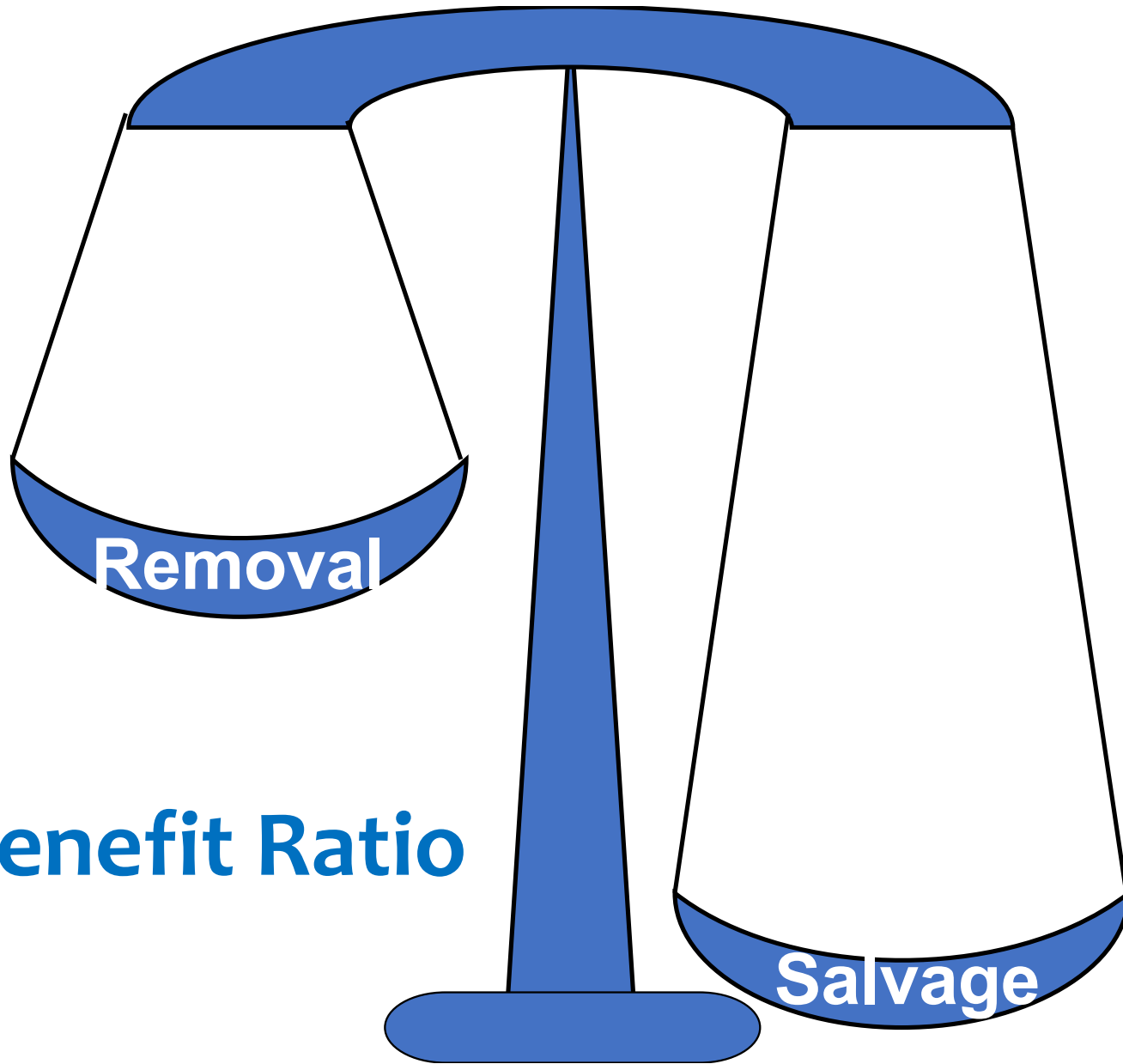


- Assess the *risk and benefit* of CVAD *removal or catheter salvage* based on:
 - the type of CVAD
 - long-term vs short-term
 - infecting organism
 - ability to insert replacement CVAD if necessary

Evidence Rating	Evidence Description ^a
I	Meta-analysis, systematic literature review, guideline based on randomized controlled trials (RCTs), or at least 3 well-designed RCTs.
II	Two well-designed RCTs, 2 or more well-designed, multicenter clinical trials without randomization, or systematic literature review of varied prospective study designs.

Risk/Benefit Ratio



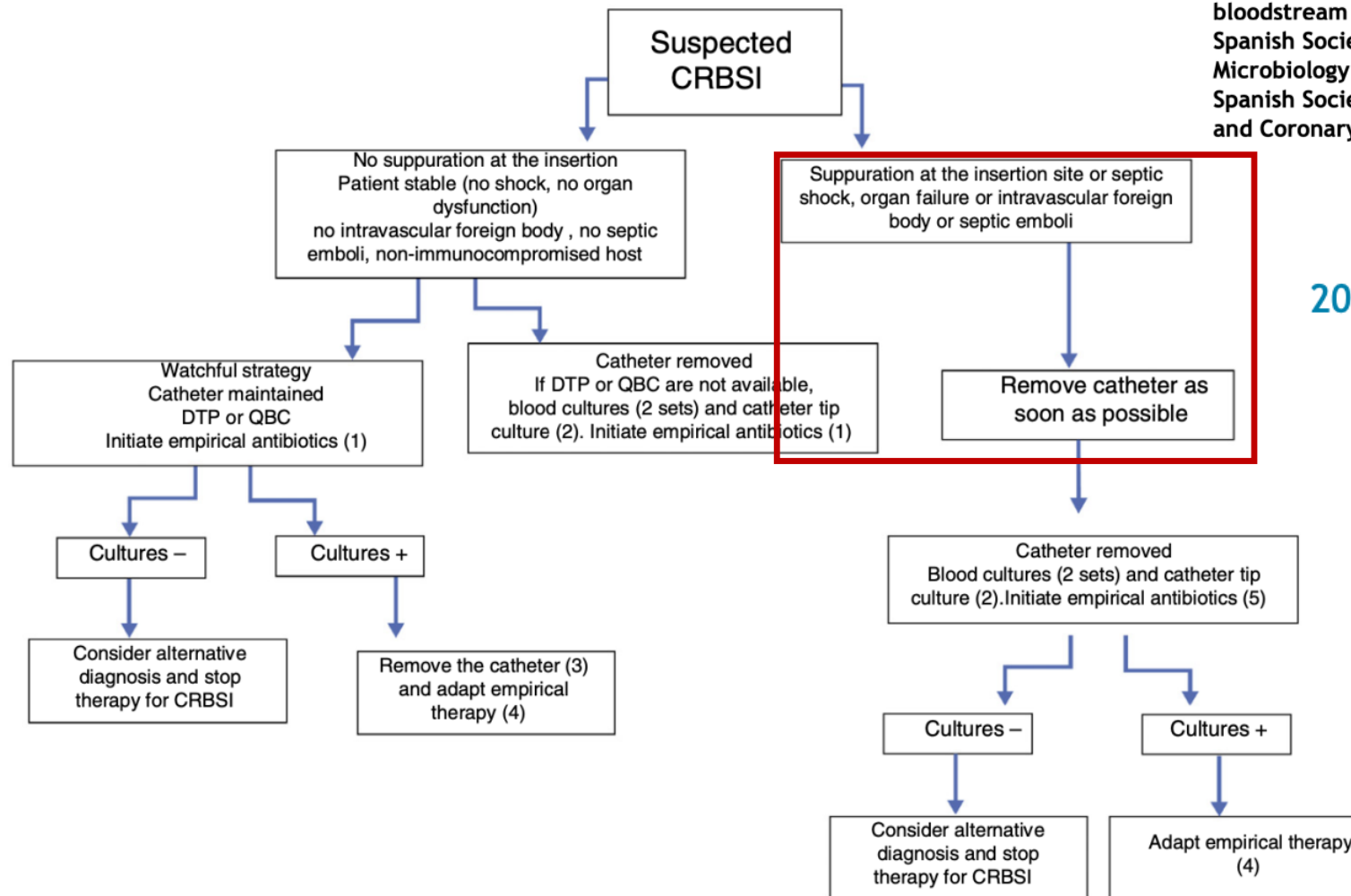


Risk/Benefit Ratio

CONSENSUS STATEMENT

Diagnosis and treatment of catheter-related bloodstream infection: Clinical guidelines of the Spanish Society of Infectious Diseases and Clinical Microbiology and (SEIMC) and the Spanish Society of Intensive and Critical Care Medicine and Coronary Units (SEMICYUC)[☆]

2018;42(1):5–36



GUIDELINES

Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021



Intensive Care Med (2021) 47:1181–1247
<https://doi.org/10.1007/s00134-021-06506-y>



Resuscitation &
Hemodynamic Management



Start Antibiotic treatment
(within 1 h)



Source infection
identification and control

Clinical Practice Guidelines for the Diagnosis
and Management of Intravascular Catheter-Related
Infection: 2009 Update by the Infectious Diseases
Society of America

IDSA GUIDELINES

Leonard A. Mermel,¹ Michael Allon,² Emilio Bouza,³ Donald E. Craven,³ Patricia Flynn,⁴ Naomi P. O'Grady,⁵
Issam I. Raad,⁶ Bart J. A. Rijnders,¹⁰ Robert J. Sherertz,⁷ and David K. Warren⁸

- Indicazioni (generali) per la rimozione del VAD in caso di diagnosi confermata di CRBSI
 - Shock Settico (*tutti*)
 - Instabilità Emodinamica!
 - Endocardite (*cateteri a lungo termine*)
 - Osteomielite grave (*cateteri a lungo termine*)
 - Trombosi Suppurativa Catetere-Relata (*tutti*)
 - Batteriemia persistente dopo > 72 ore di trattamento efficace (*tutti*)

9TH EDITION
REVISED 2024

Infusion Therapy Standards of Practice



- Remove the CVAD if:
 - Clinical deterioration
 - Persisting bacteremia
 - Relapsing bacteremia

Evidence Rating	Evidence Description ^a
I	Meta-analysis, systematic literature review, guideline based on randomized controlled trials (RCTs), or at least 3 well-designed RCTs.
II	Two well-designed RCTs, 2 or more well-designed, multicenter clinical trials without randomization, or systematic literature review of varied prospective study designs.

Clinical Practice Guidelines for the Diagnosis and Management of Intravascular Catheter-Related Infection: 2009 Update by the Infectious Diseases Society of America

Leonard A. Mermel,¹ Michael Allon,² Emilio Bouza,³ Donald E. Craven,³ Patricia Flynn,⁴ Naomi P. O'Grady,⁵ Issam I. Raad,⁶ Bart J. A. Rijnders,¹⁰ Robert J. Sherertz,⁷ and David K. Warren⁸

WHAT ARE THE UNIQUE ASPECTS OF TREATING PEDIATRIC PATIENTS WITH CATHETER-RELATED INFECTION?

Recommendations

49. Indications for catheter removal for children are similar to those for adults (see recommendations 30–32), unless there are unusual extenuating circumstances (e.g., no alternative catheter insertion site). However, the benefits of catheter removal must be weighed against the difficulty of obtaining alternate venous access for an individual patient (A-II).

IDSA GUIDELINES

51. In general, empirical antibacterial therapy for children with CRBSI should be similar to that for adults (see recommendations 21–23) (A-II).

52. Antibiotic lock therapy should be used for catheter salvage (B-II); however, if antibiotic lock therapy cannot be used in this situation, systemic antibiotics should be administered through the colonized catheter (C-III).

50. Children treated without catheter removal should be closely monitored with clinical evaluation and additional blood cultures; the device should be removed if there is clinical deterioration or persistent or recurrent CRBSI (B-III).

Peculiarità del paziente pediatrico

- Ridotte possibilità di reperire vasi di calibro adeguato al posizionamento di VAD idonei
 - Meno frequente con l'uso sistematico dell'ecografia ma possibile
- Necessità di Analgo-sedazione Profonda o, meno frequentemente, di Anestesia Generale
 - Per tale motivo necessità di sala procedura idonea e attrezzata
- *Gravi Alterazioni della Coagulazione e/o della funzione piastrinica*
 - Es. pazienti oncoematologici
- *Difficoltà ad eseguire la diagnosi differenziale tra CLABSI e CRBSI*
 - Difficoltà di esecuzione emocolture da vena periferica per DTP

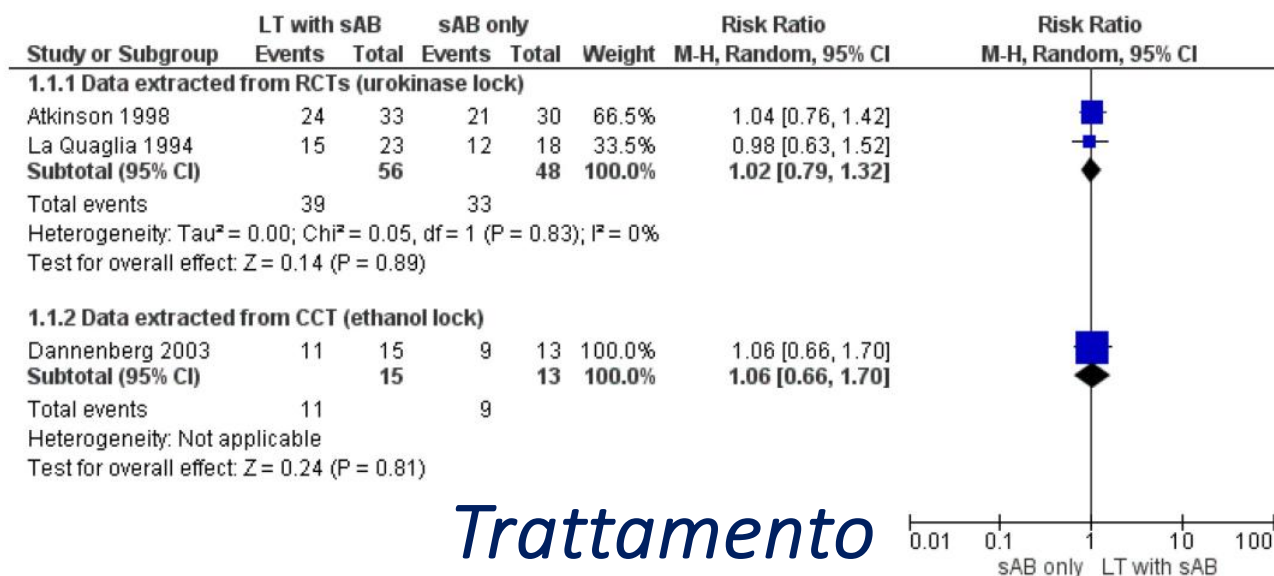
Problemi Aperti

- E' sempre sicuro salvare il VAD nel paziente pediatrico emodinamicamente stabile?
- Quale il trattamento più efficace?
 - Quale il ruolo della *lock therapy* o della terapia di associazione?
- Vi sono agenti eziologici specifici che rappresentano una controindicazione alla strategia conservativa del salvataggio del catetere?
- Se sì, quali?

Antibiotic and other lock treatments for tunnelled central venous catheter-related infections in children with cancer (Review)

Schoot RA, van Dalen EC, van Ommen CH, van de Wetering MD

Figure 3. Forest plot of comparison: 1 Lock treatment with systemic antibiotics versus systemic antibiotics only, outcome: 1.1 Number of patients cured from CVC related infection.



Random sequence generation (selection bias)

Allocation concealment (selection bias)

Incomplete outcome data (attrition bias)

Selective reporting (reporting bias)

Blinding of participants and personnel (performance bias)

Blinding of outcome assessment (detection bias)



Cochrane Database of Systematic Reviews

2013

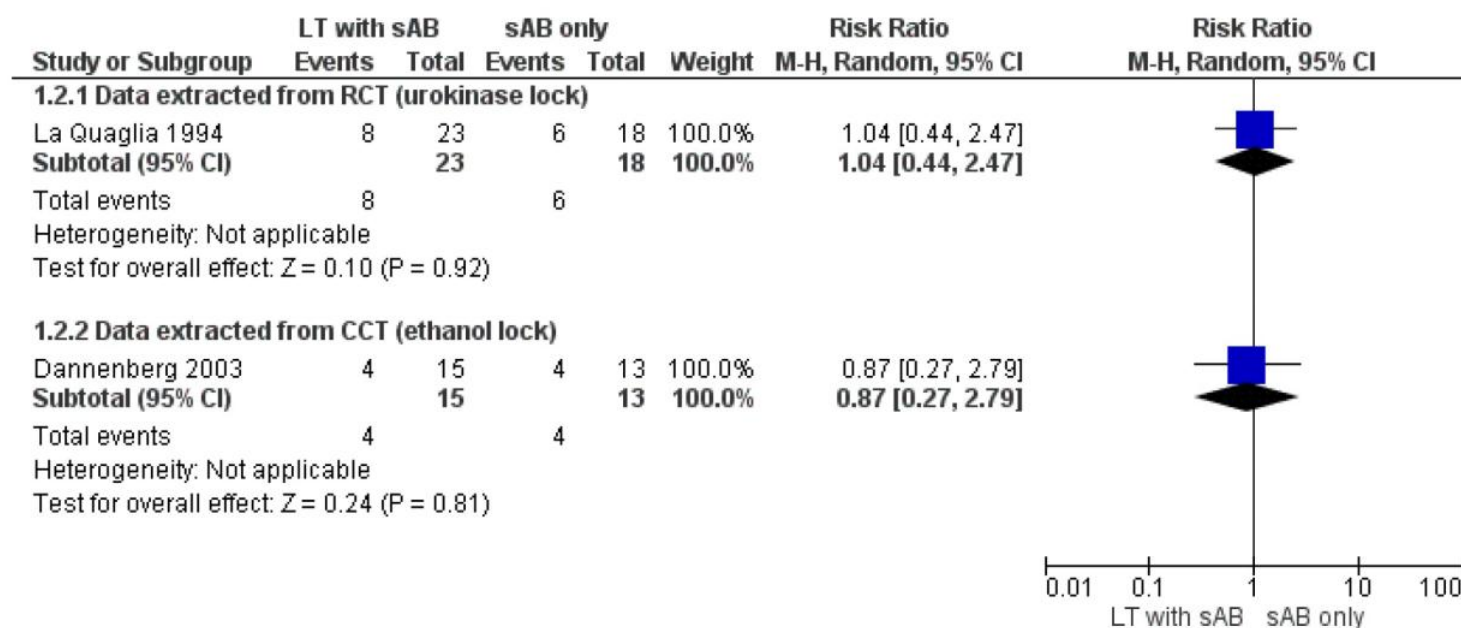
Atkinson 1998
Dannenberg 2003
La Quaglia 1994

Atkinson 1998	?	?	+	+	-	-
Dannenberg 2003	-	-	+	+	-	-
La Quaglia 1994	?	?	+	+	+	+

Antibiotic and other lock treatments for tunnelled central venous catheter-related infections in children with cancer (Review)

Schoot RA, van Dalen EC, van Ommen CH, van de Wetering MD

Figure 4. Forest plot of comparison: 1 Lock treatment with systemic antibiotics versus systemic antibiotics only, outcome: 1.2 Number of patients with a recurrence of the CVC-related infection.





venous catheter related infections AND salvage AND children



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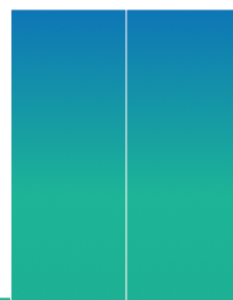
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Reset



2011



2024



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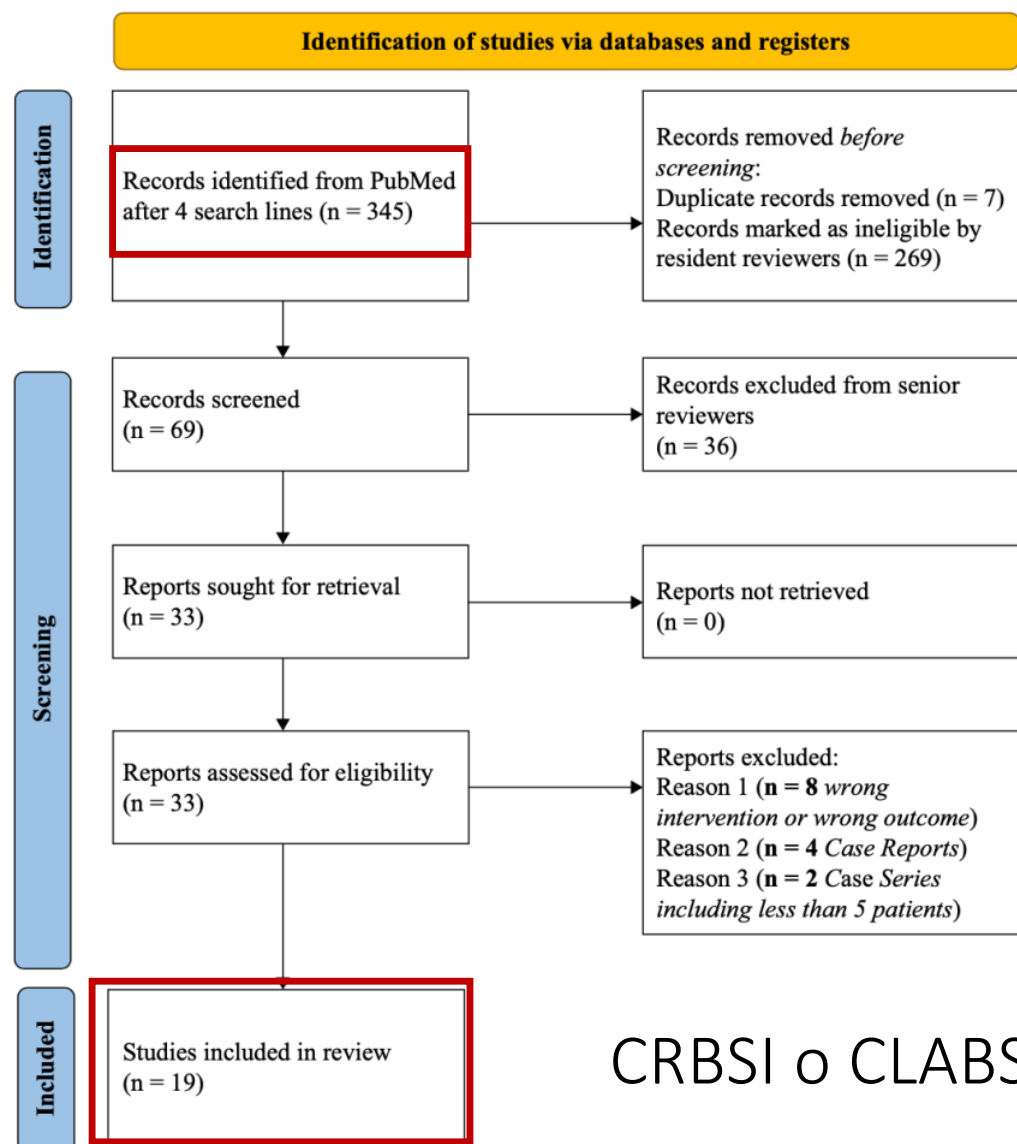
Journal of Hospital Infection

journal homepage: www.elsevier.com/locate/jhin



Catheter salvage strategies in children with central venous catheter-related or -associated bloodstream infections: a systematic review and meta-analysis

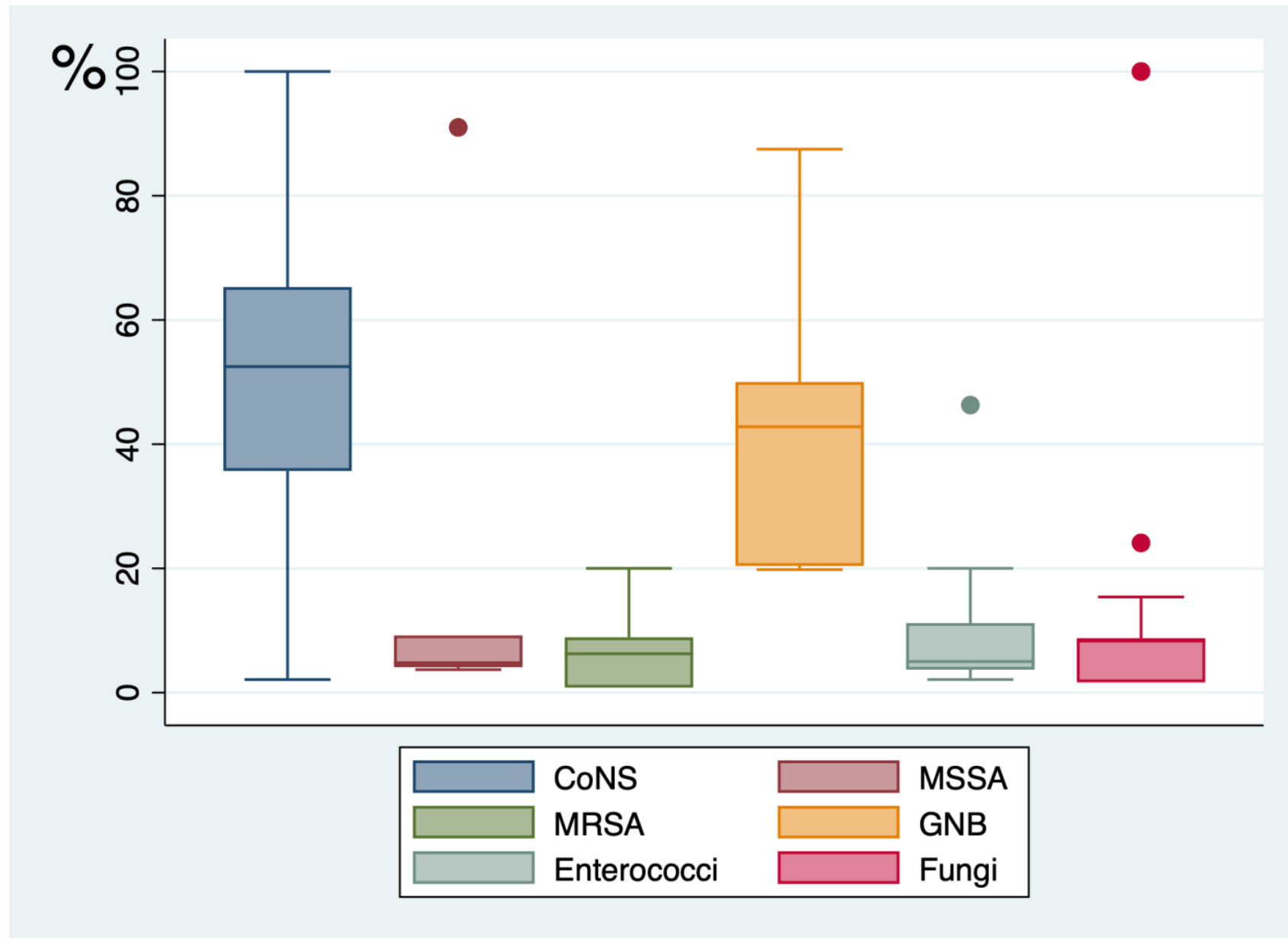
D. Buonsenso^{a,b,c,*}, G. Salerno^d, G. Soderò^d, F. Mariani^d, L. Pisapia^e,
C. Gelormini^e, M. Di Nardo^f, P. Valentini^a, G. Scoppettuolo^g, D.G. Biasucci^{e,**}



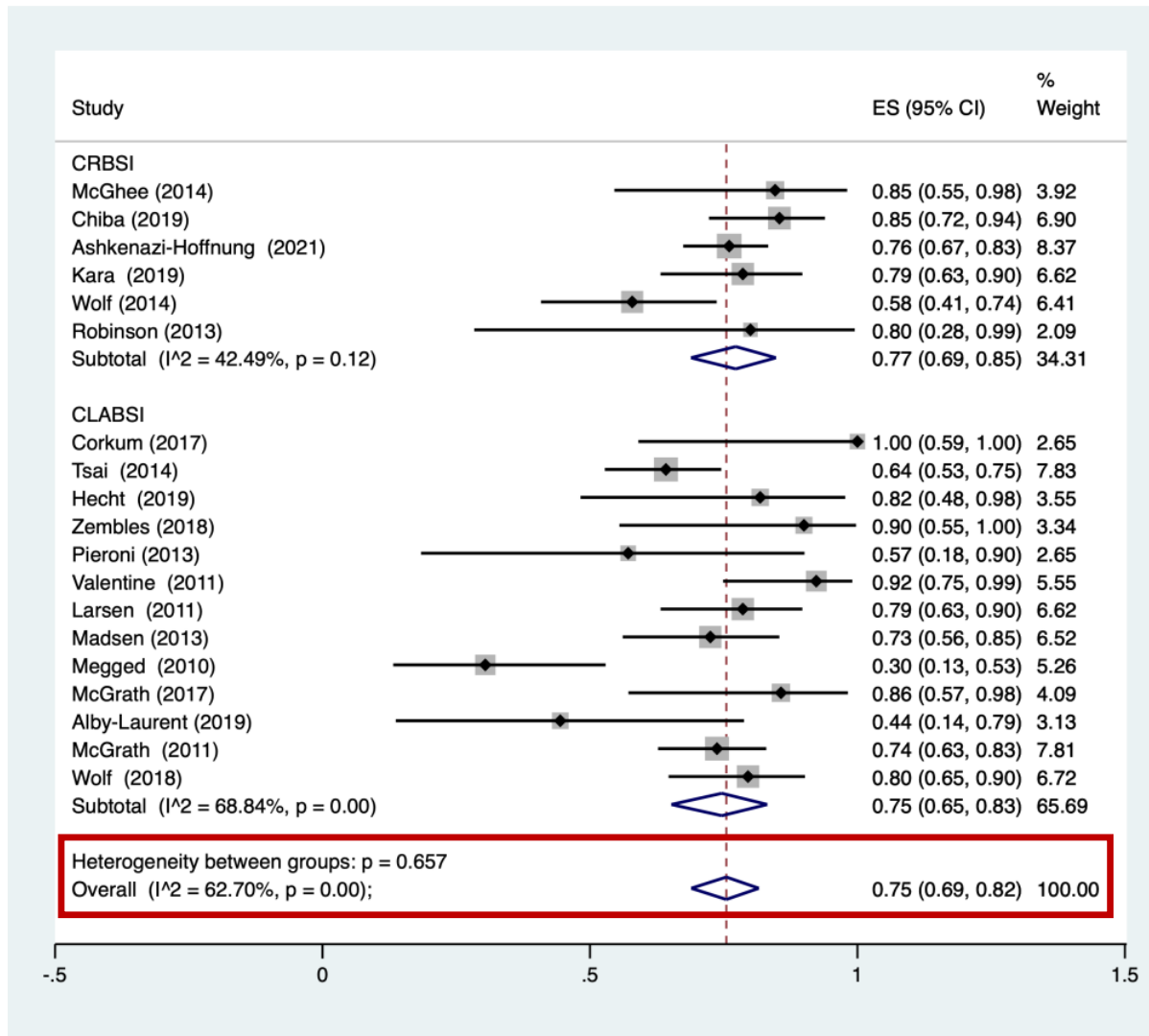
CRBSI o CLABSI?

- Periodo: da gennaio 2010
- **1138 casi (CRBSI/CLABSI)**
 - **6 studi → CRBSI**
 - **13 studi → CLABSI**
- Metodologia
 - 2 RCTs, 4 osservazionali prospettici, 11 retrospettivi, 2 case series (>5 pazienti)
- Trattamenti
 - Lock + Terapia Sistemica (13)
 - Solo Terapia Sistemica (6)
- Popolazione
 - Oncoematologici
 - Trapianti
 - Terapia Intensiva
 - No neonati

Eziologia



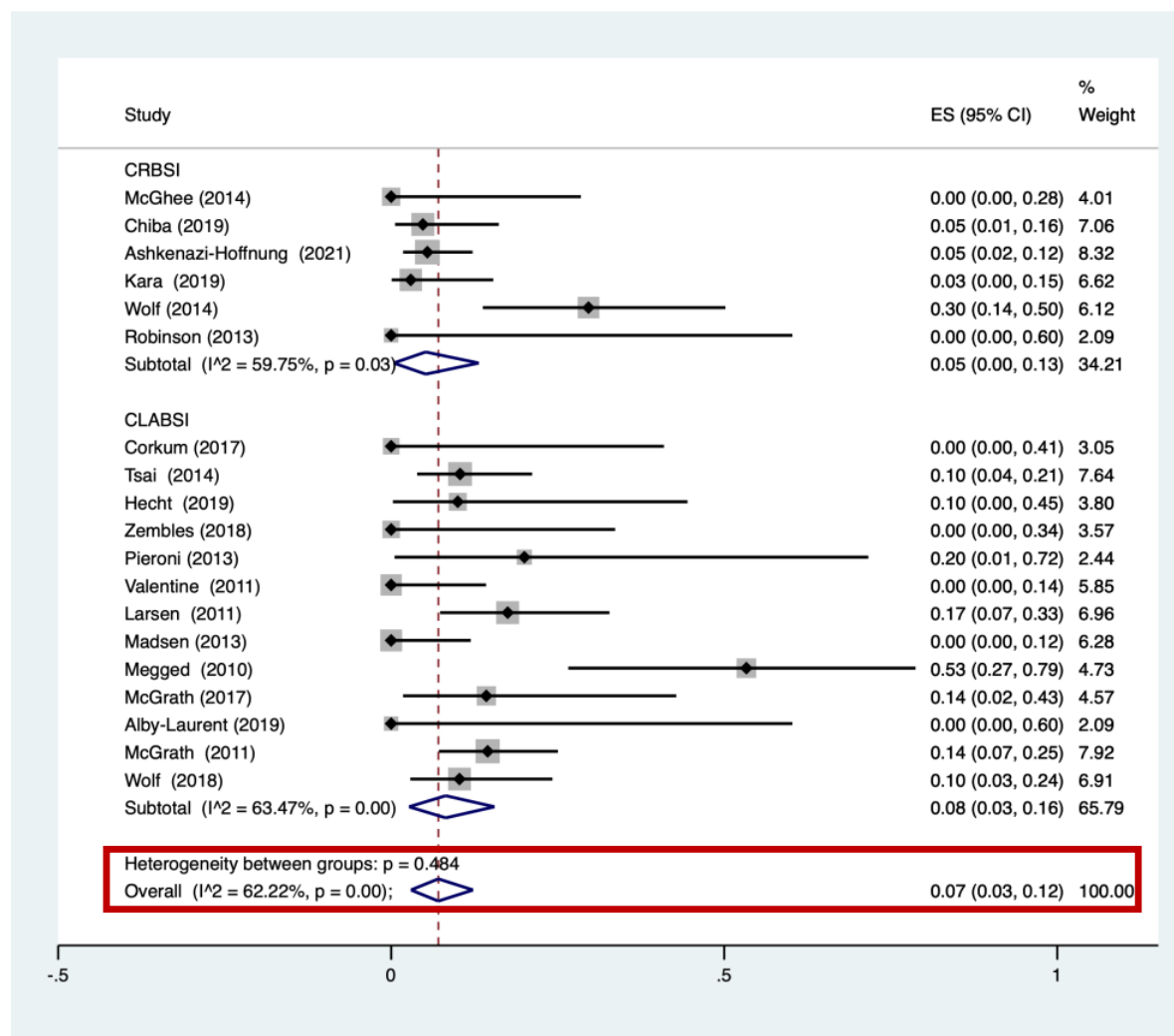
Successo della strategia conservativa



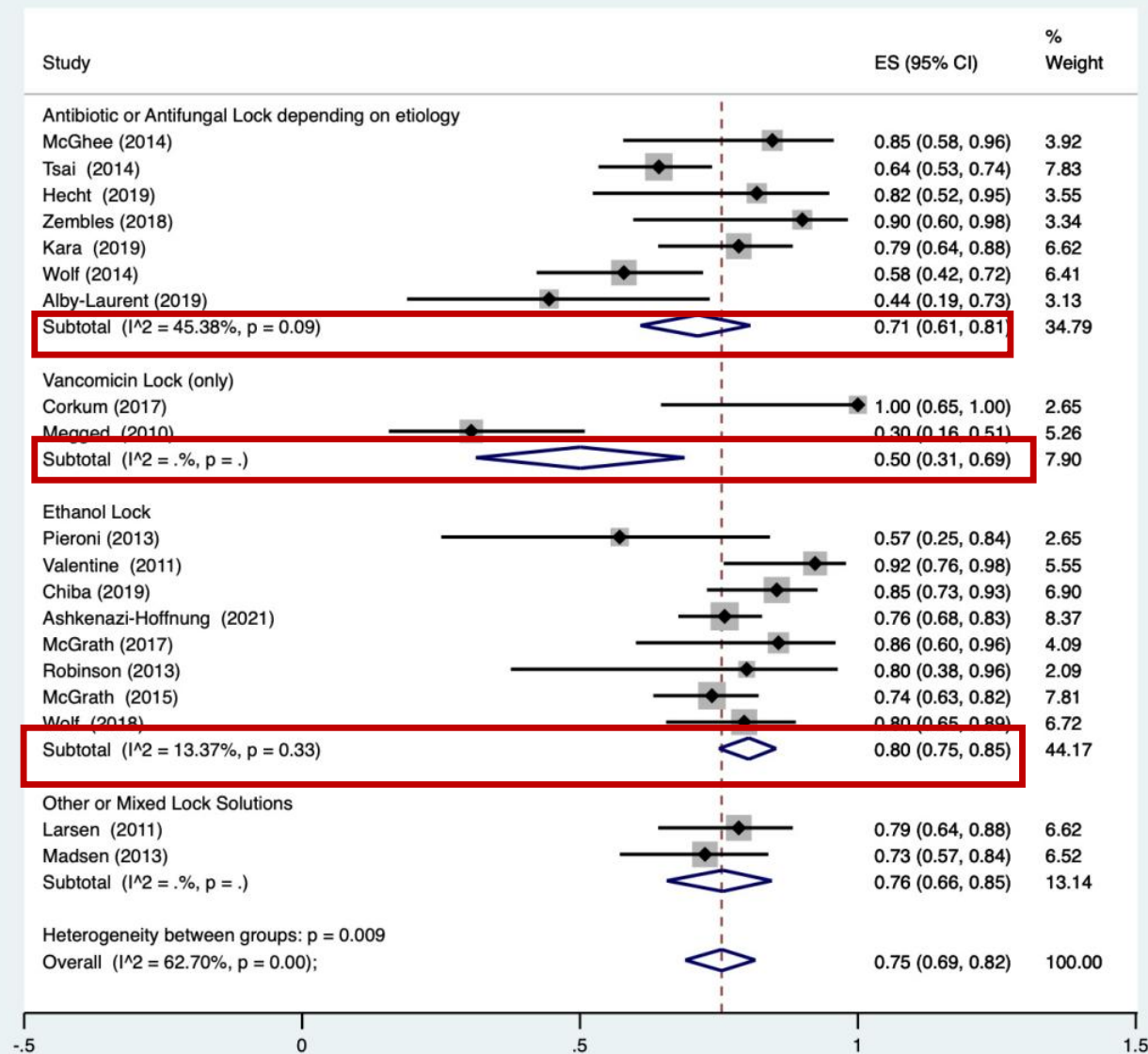
- Successo finale globale
 - ATB + Lock
 - Solo ATB
- Pazienti emodinamicamente stabili

'Recurrence'

Positive blood cultures for the same pathogen more than 30 days after an initial successful conservative treatment.



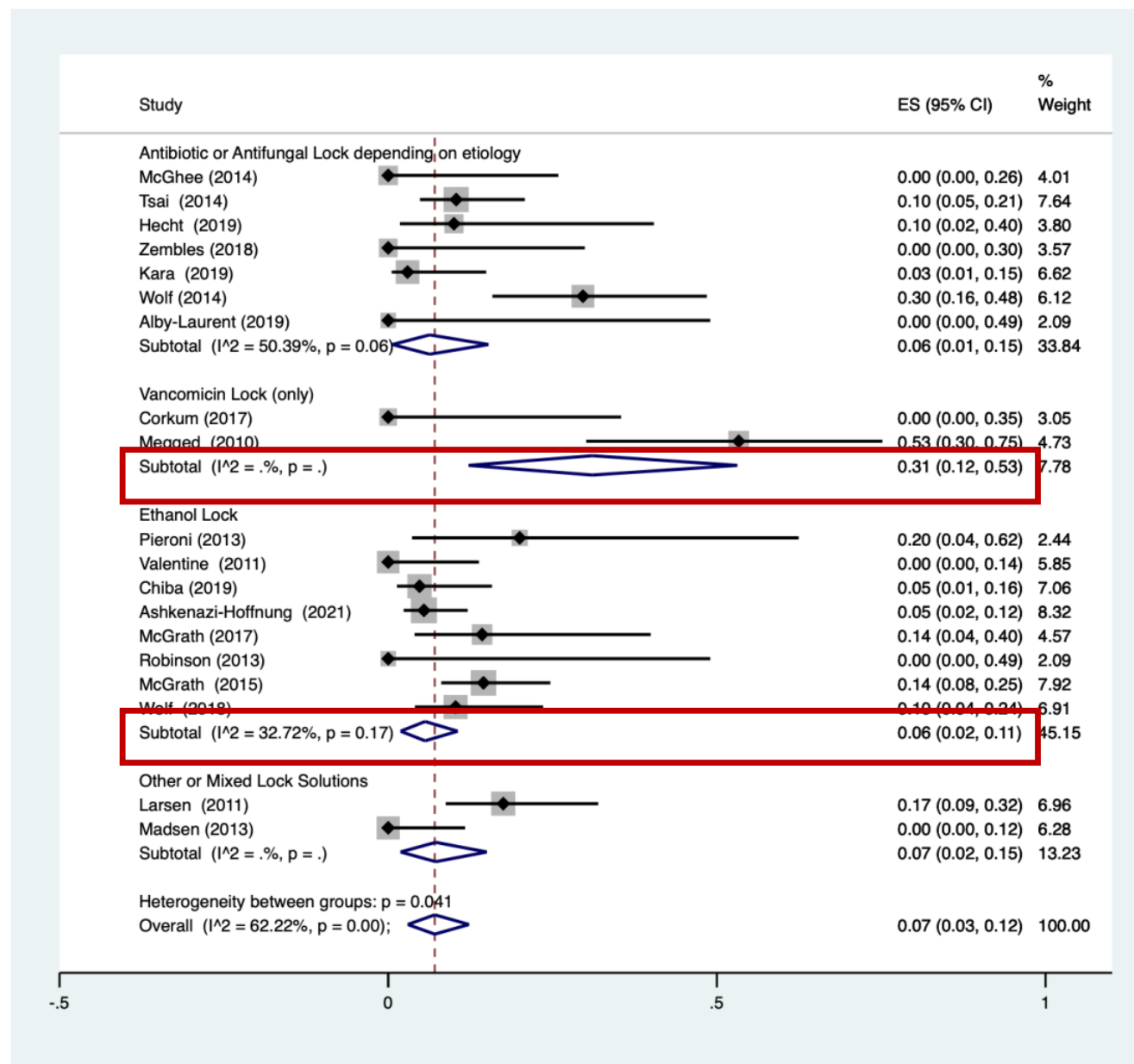
Successo per tipo di Lock



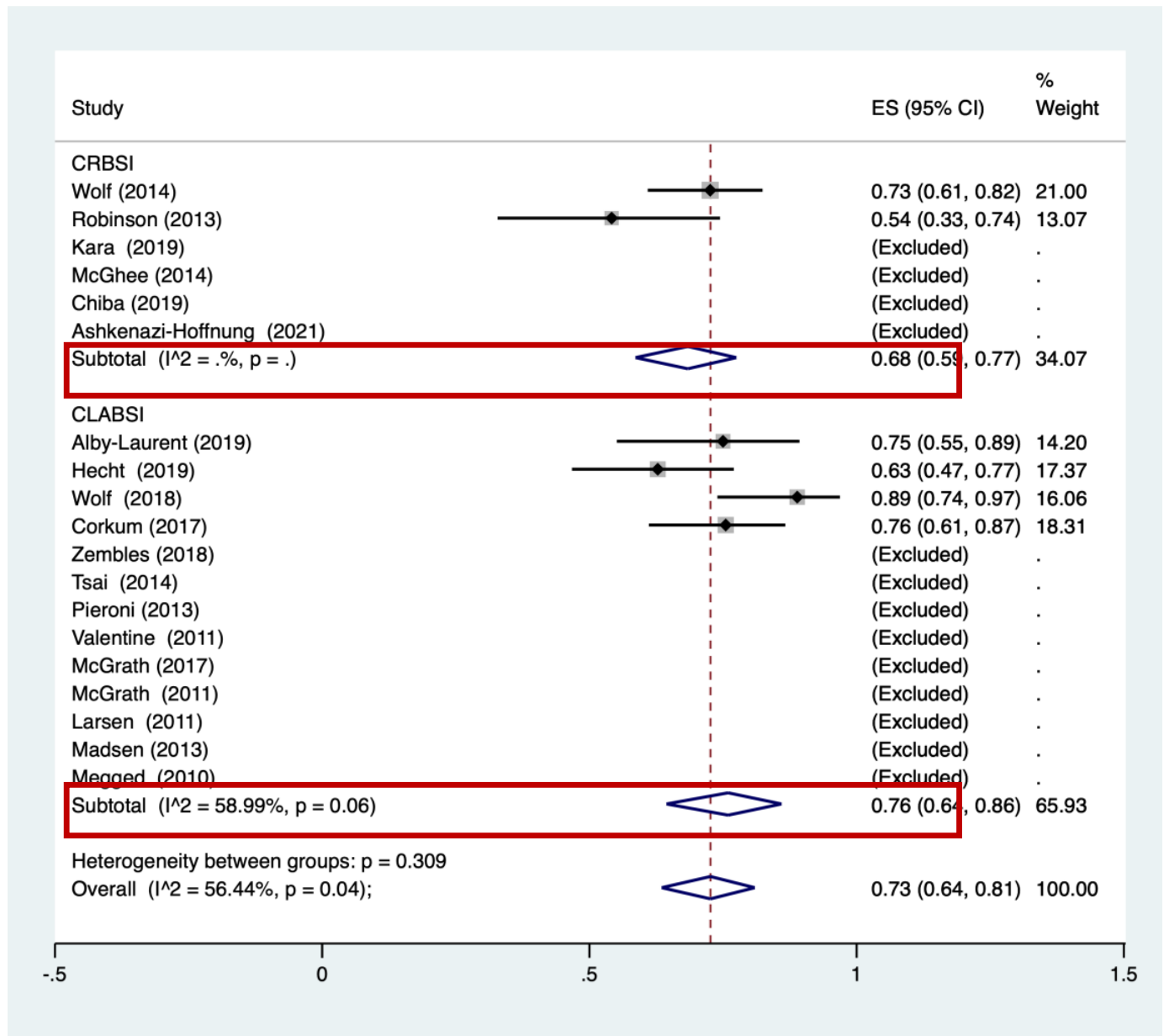
Antibiotic and dosage	Heparin or saline, IU/mL	Reference(s)
Vancomycin, 2.5 mg/mL	2500 or 5000	[100, 275]
Vancomycin, 2.0 mg/mL	10	[275]
Vancomycin, 5.0 mg/mL ^a	0 or 5000	[276, 277]
Ceftazidime, 0.5 mg/mL	100	[123]
Cefazolin, 5.0 mg/mL	2500 or 5000	[100, 277]
Ciprofloxacin, 0.2 mg/mL ^b	5000	[130]
Gentamicin, 1.0 mg/mL	2500	[100]
Ampicillin, 10.0 mg/mL	10 or 5000	[275]
Ethanol, 70% ^c	0	[131]

L-AmB concentration = 2 mg/mL

‘Recurrence’ per tipo di Lock



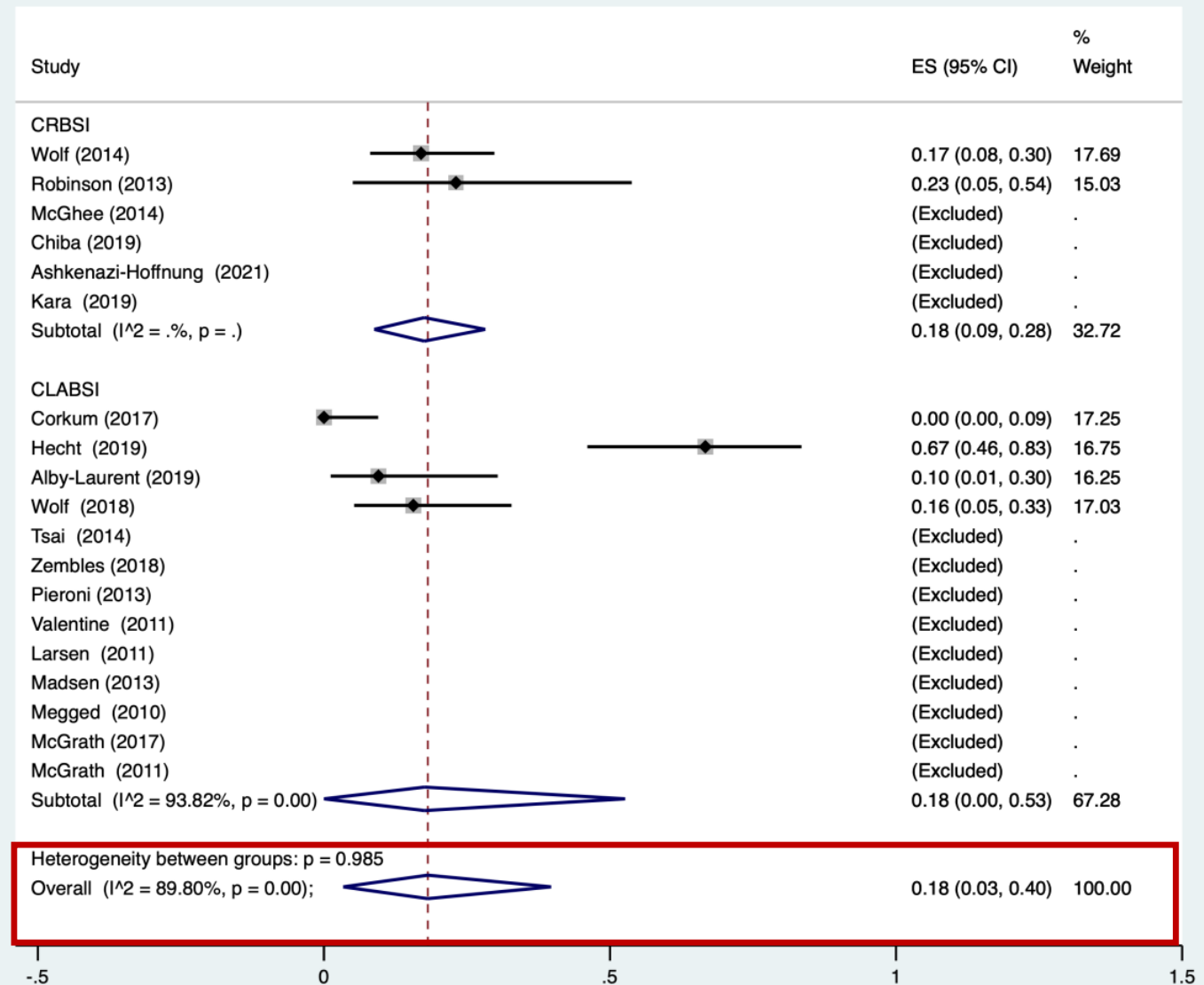
Successo per Antibiotico Sistemico Solo



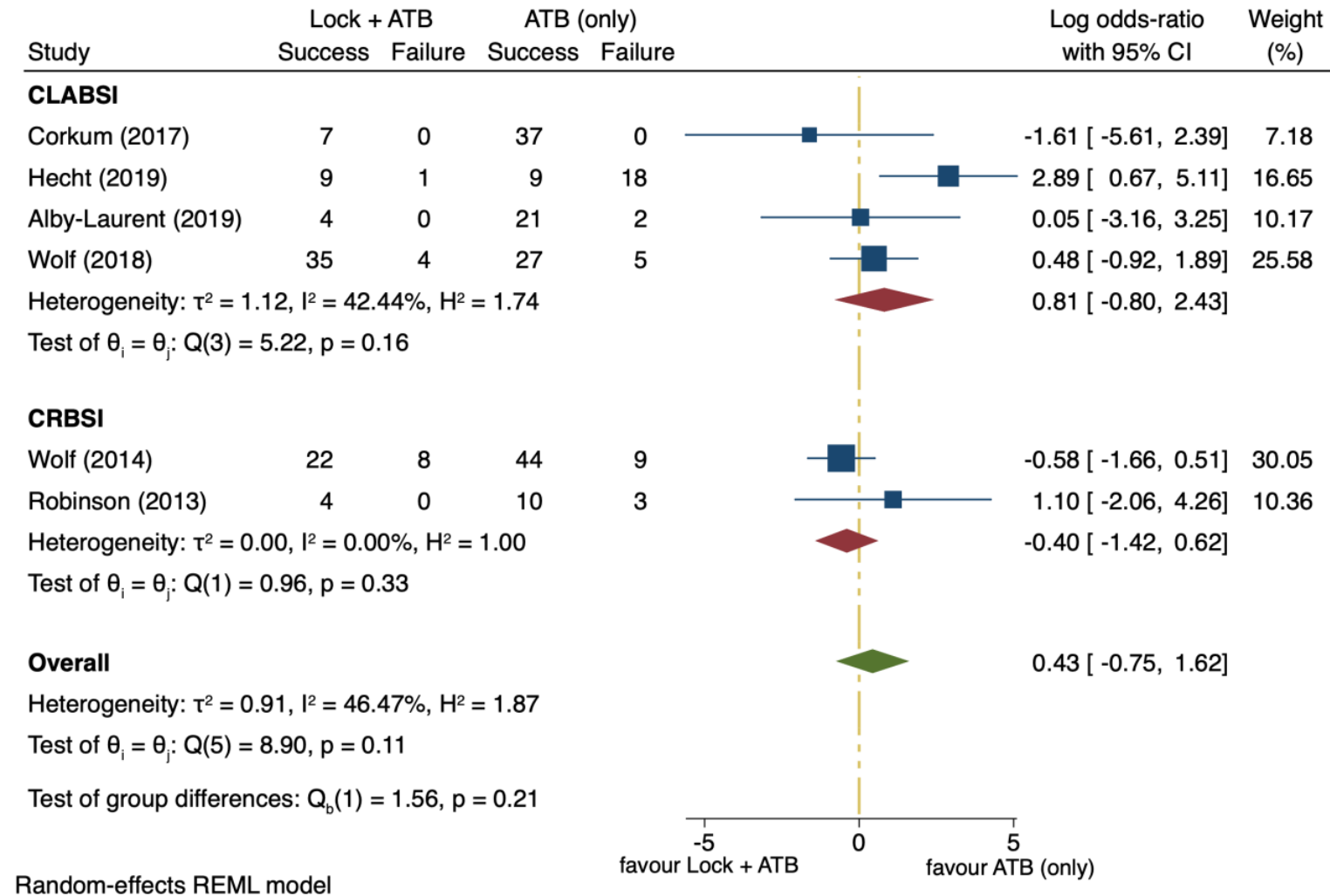
‘Recurrence’ per Antibiotico Sistemico Solo

Troppo Alta: 18%

Elevata Eterogeneità: I^2 89.8%!



Lock + Antibiotico vs Antibiotico Sistemico



Safety and Efficacy of Ethanol for Catheter Salvage and Central Line-Associated Bloodstream Infection Prophylaxis in Polyurethane Catheters in the PICU

Mark D. Weber, MSN, RN,
CPNP-AC, FCCM¹

Charlotte Woods-Hill, MD, MSHP²

Karla Resendiz, PharmD, BCPPS³

Eileen Nelson, BSN, RN⁴

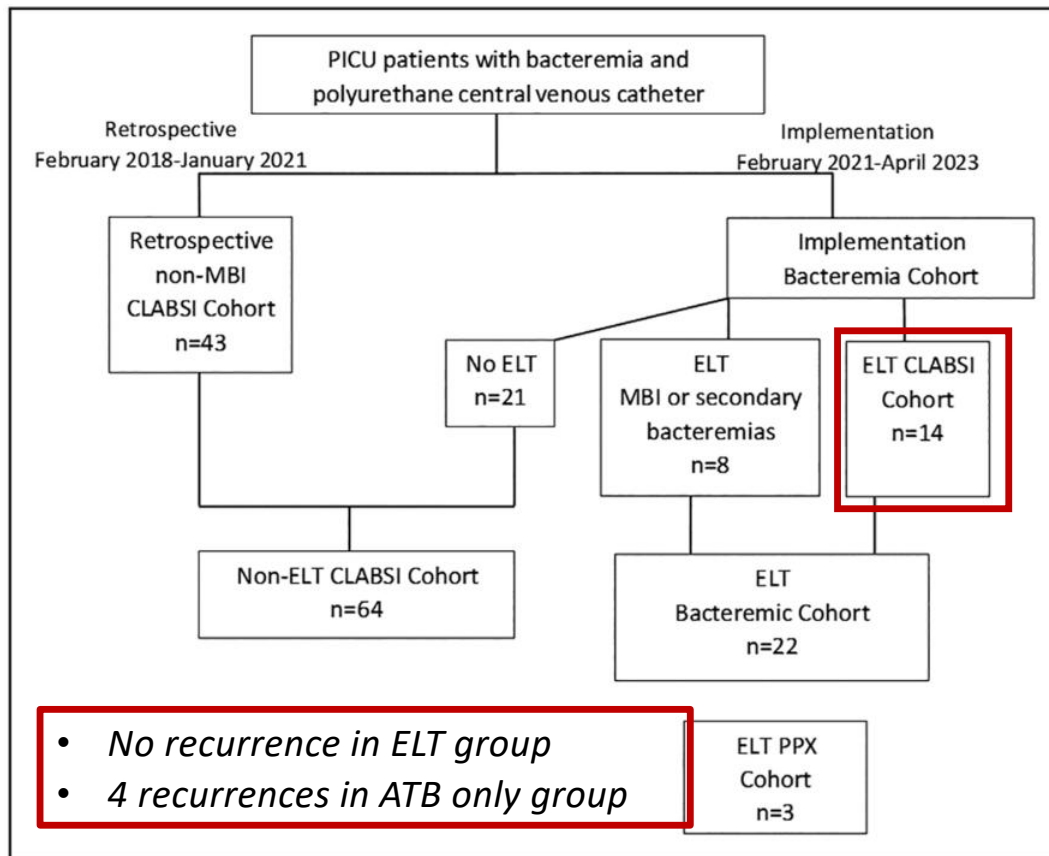
Monica Ryan, BSN, RN⁴

Lauren Brennan, MHA, RT(R)⁵

Abhay Srinivasan, MD⁶

Thomas Conlon, MD²

January
2024



- Ethanol locks can be used in a wide range of polyurethane catheters commonly used in PICU patients.

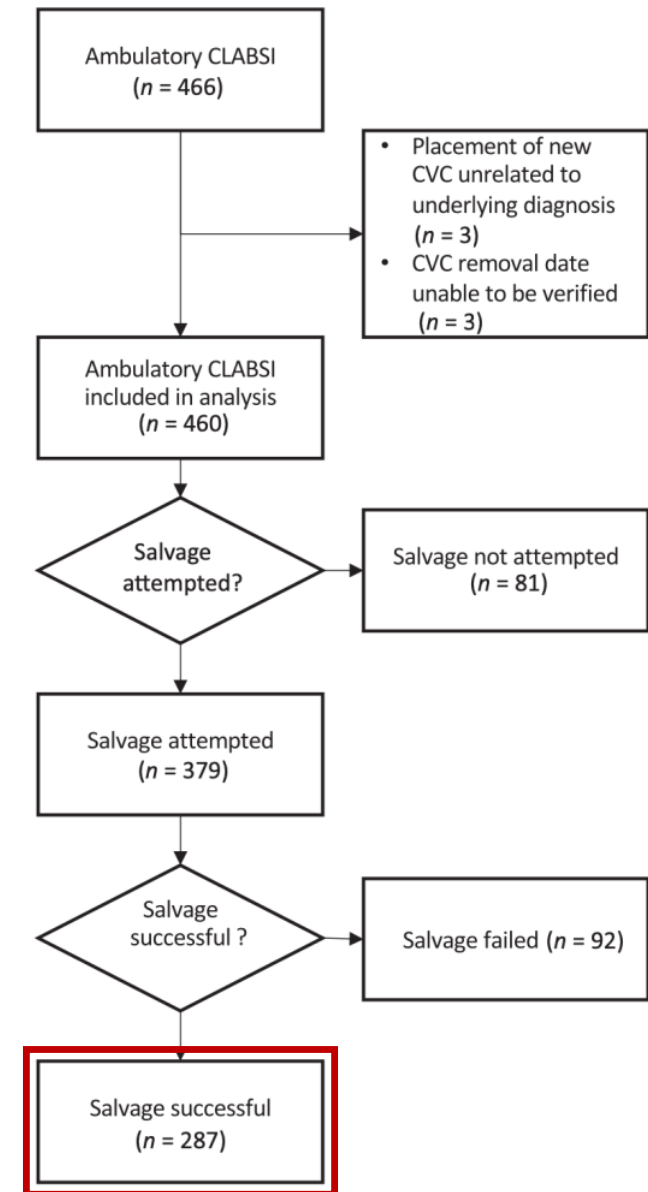
- The success of catheter salvage therapy increased from 62% using systemic antibiotics alone to 92% following the implementation of ethanol locks.

- Given the high success rate, ethanol catheter salvage therapy should be considered in PICU patients with central line-associated bloodstream infection in conjunction with systemic antibiotics.

Central Venous Catheter Salvage in Ambulatory Central Line–Associated Bloodstream Infections **2021**

William J.H. Ford,^a David G. Bundy, MD, MPH,^b Suzette Oyeku, MD,^{c,d} Moonseong Heo, PhD,^e Lisa Saiman, MD,^f Rebecca E. Rosenberg, MD,^g Patricia DeLaMora, MD,^a Barbara Rabin,^h Philip Zachariah, MD,^f Parsa Mirhaji, MD, PhD,^d Elizabeth Klein,^d Oghale Obaro-Best,ⁱ Michael Drasher,^j Alexandre Peshansky, MS,^d Michael L. Rinke, MD, PhD^{c,d}

- Factors associated to **SUCCESS**
 - Tunneled compared to non-tunneled PICCs or totally implanted → (adj OR 2.83 [95% CI 1.21–6.59])
 - Primary diagnosis of Intestinal Failure
- Factors associated to **FAILURE**
 - Malignancy (aOR 0.38 [95% CI 0.17–0.84])
 - *Candidemia* (aOR 0.03 [95% CI 0.004–0.29])



Catheter salvage from central line-related bloodstream infections in pediatric intestinal failure

Catherine Larson-Nath¹ | Linder Wendt² | Riad Rahhal³

2023

- IV antimicrobial therapy most commonly included vancomycin (97%), cefepime (46%), and piperacillin/ tazobactam (29%)
- Ethanol locks were included in 42% of salvage attempts.
- No difference in salvage success Ethanol vs Antibiotic only → OR = 1.88, p = 0.694
- **Successful salvage occurred in 91.7%**
 - Gram-positive 97%
 - Gram-negative 92%
 - ***fungal infections 60%***



Article

Effectiveness of Antimicrobial Lock Therapy for the Treatment of Catheter-Related and Central-Line-Associated Bloodstream Infections in Children: A Single Center Retrospective Study

Claudia Signorino ¹, Eleonora Fusco ¹ , Luisa Galli ² and Elena Chiappini ^{2,*}

- ALT success rate 67.6% (25/37)
- Reasons for treatment failure
 - *persistent bacteremia* (3/12; 25%)
 - clinical or laboratory *findings of infection* (3/12; 25%) despite at least 72 h of appropriate lock therapy
 - *recurrence* (3/12; 25%), or *reinfection* (3/12; 25%) within 90 days after
- Pathogens responsible for the lock failure
 - *Klebsiella pneumoniae* (2/12; 16.7%)
 - CoNS (2/12; 16.7%)
 - *Candida parapsilosis* (2/12; 16.7%)

Use of 2% taurolidine lock solution for treatment and prevention of catheter-related bloodstream infections in neonates: a feasibility study

Journal of Hospital Infection

I. Savarese^a, S. Yazami^b, D.U. De Rose^a, K. Carkeek^b, F. Campi^a, C. Auriti^a,
O. Danhaive^b, F. Piersigilli^{b,*}

- 21 Taurolidine lock + ATB
- 18 Successes

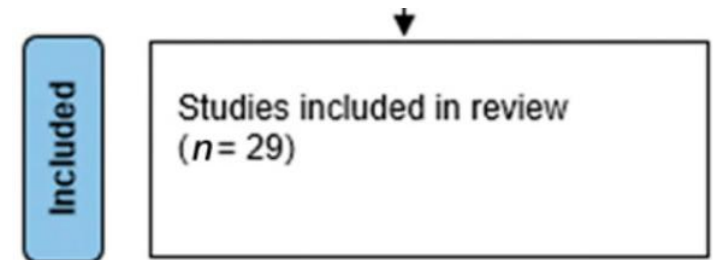
Table I

Types of infections in the therapeutic group

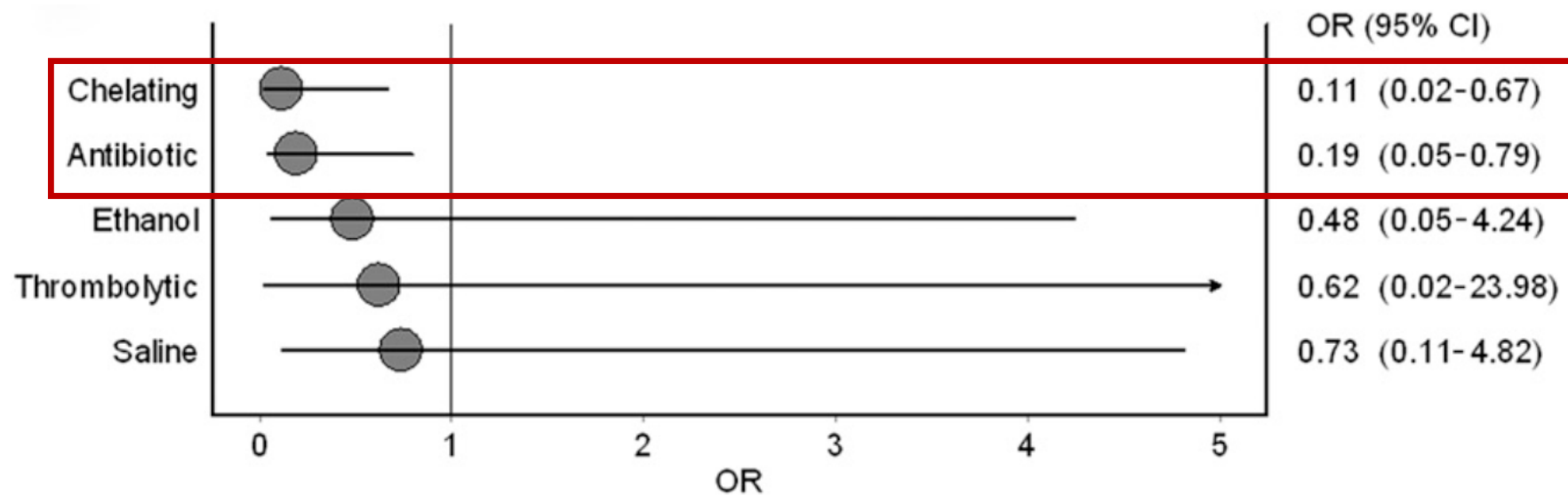
Organism	N
<i>Escherichia coli</i>	2
<i>Pseudomonas aeruginosa</i>	2
<i>Staphylococcus aureus</i>	2
<i>Staphylococcus epidermidis</i>	2
<i>Staphylococcus haemolyticus</i>	1
<i>Enterococcus faecium</i>	3
<i>Klebsiella oxytoca</i>	3
<i>Candida albicans</i>	2

Pediatric Central Venous Access Device Lock Solutions: A Network Meta-analysis

Mari Takashima, M.Epi,^{a,b,c} Yukiko Ezure, M.Epi,^d Luis Furuya-Kanamori, PhD,^d Joshua Wolf, PhD,^{e,f} Mitchell Dufficy, RN,^a Victoria Gibson, RN,^a Julia Clark, PhD, FRACP, Amanda Ullman, PhD^{a,b,c}



Prevention



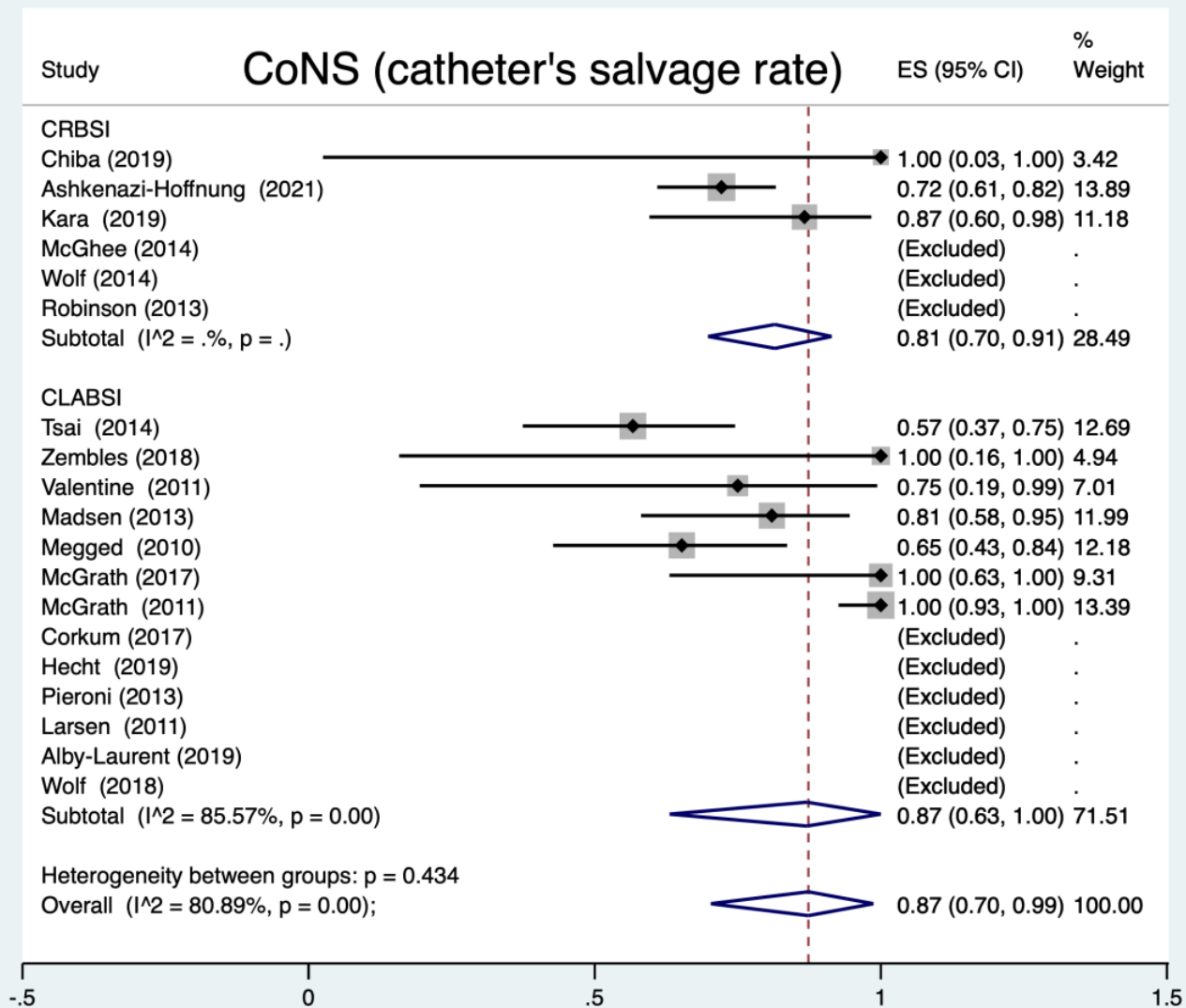
Pediatric Central Venous Access Device Lock Solutions: A Network Meta-analysis

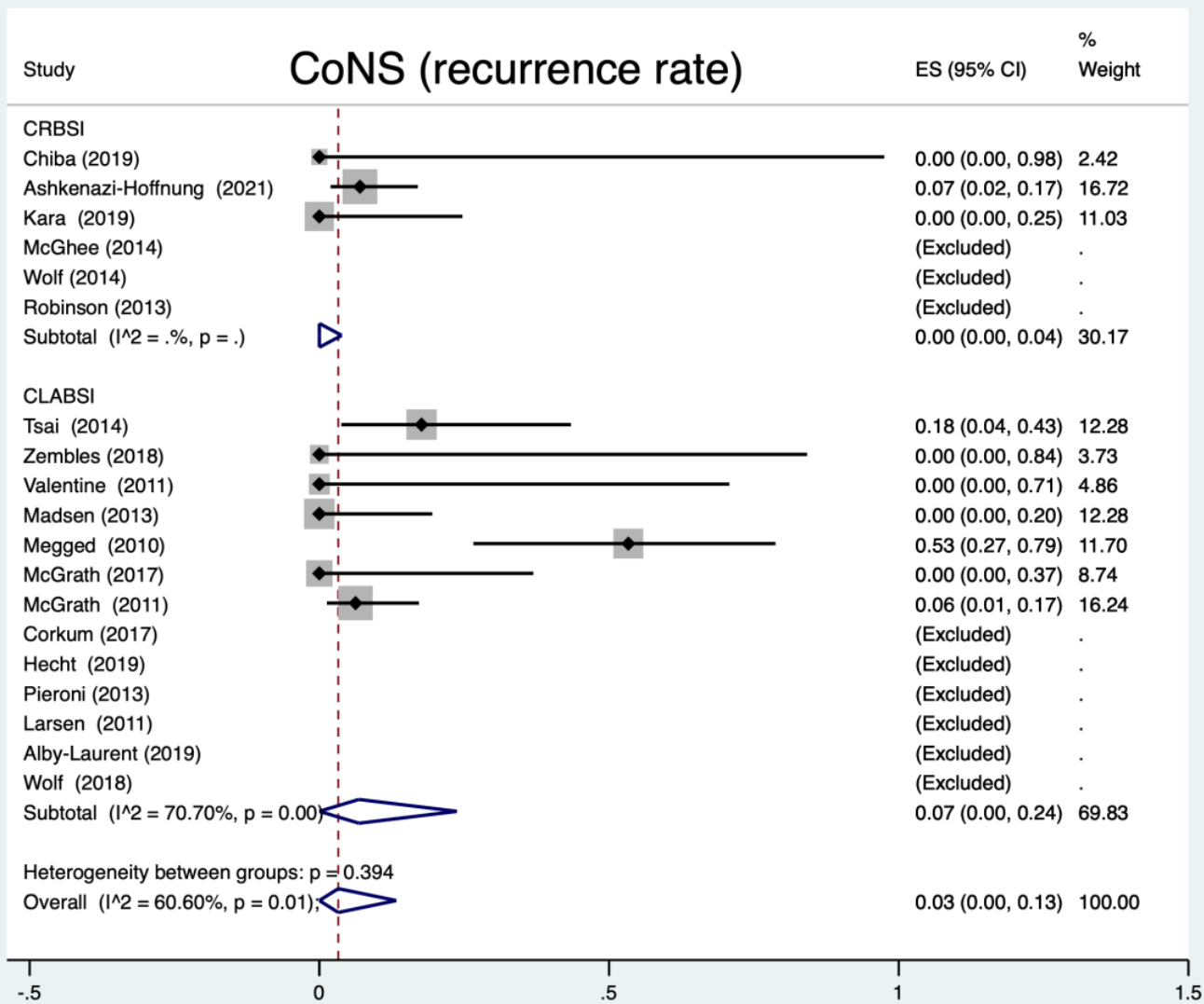
Conservative Treatment

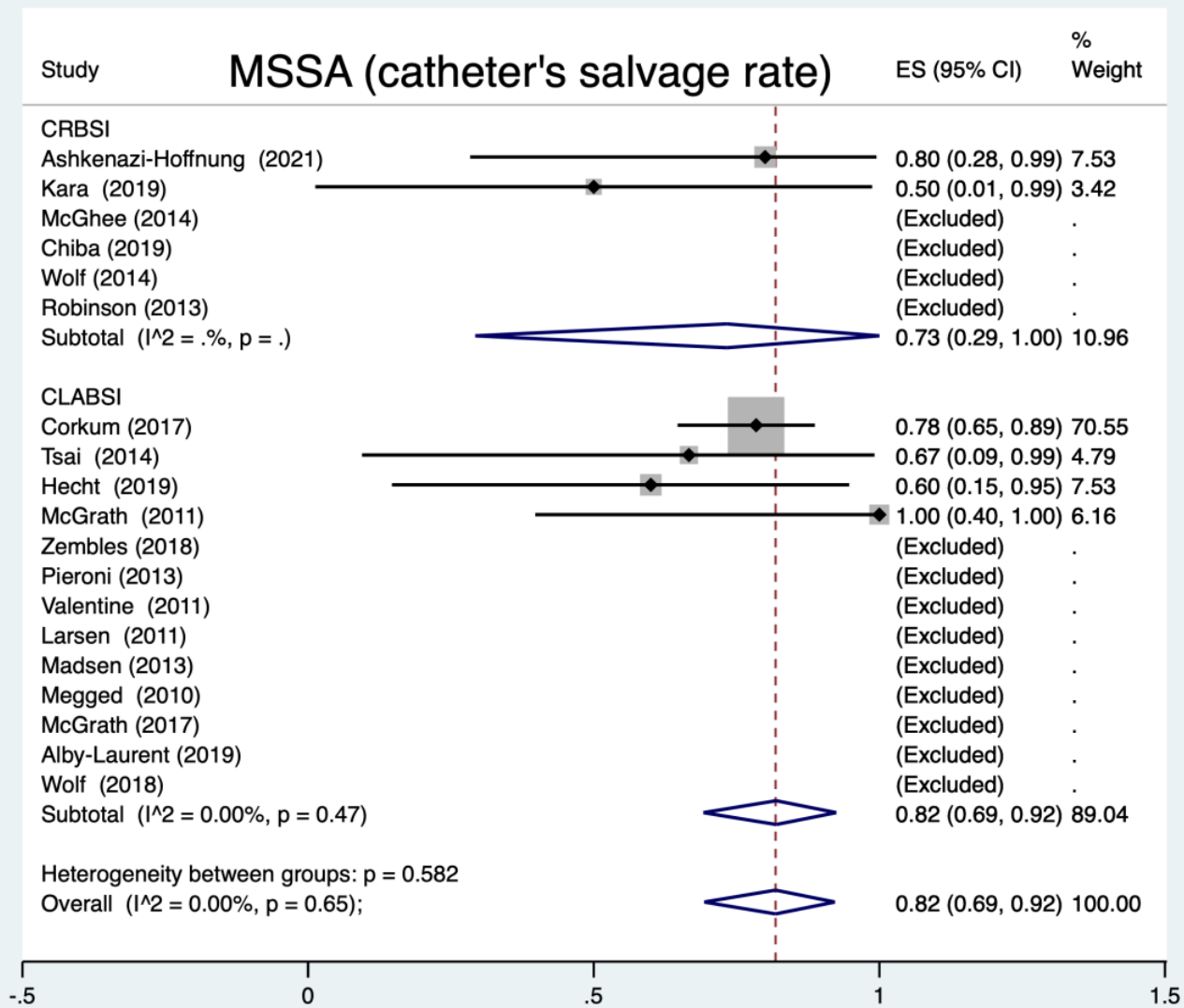
Mari Takashima, M.Epi,^{a,b,c} Yukiko Ezure, M.Epi,^d Luis Furuya-Kanamori, PhD,^d Joshua Wolf, PhD,^{e,f} Mitchell Dufficy, RN,^a
Victoria Gibson, RN,^a Julia Clark, PhD, FRACP, Amanda Ullman, PhD^{a,b,c}

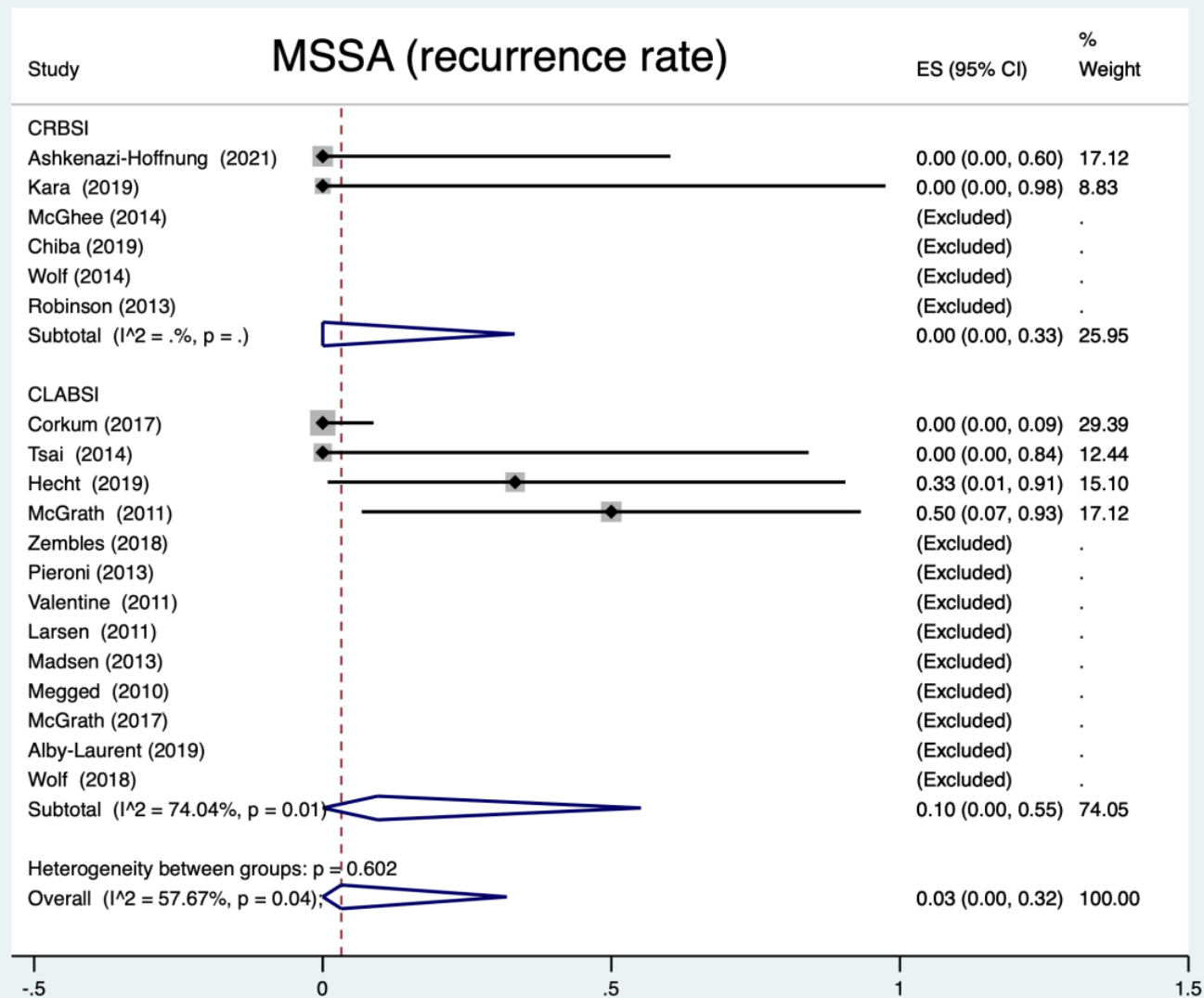
TABLE 3 Summary Table of the Odds Ratio of Lock Solutions Category for Multiple Outcomes (Reference Group: Heparinized Saline)

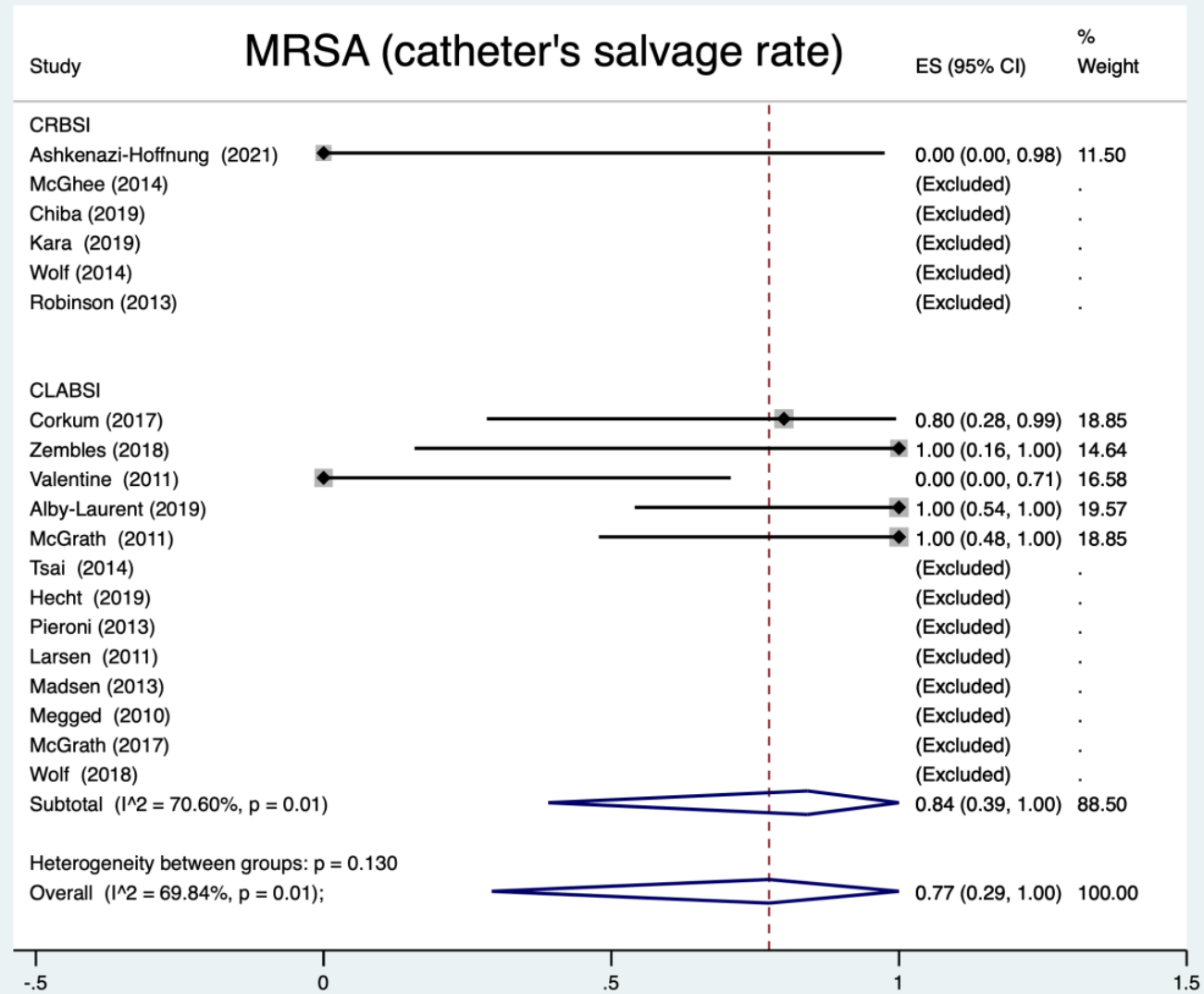
	Outcomes, Odds Ratio (95% CI), and Certainty of the Evidence (GRADE)					
	CVAD-Associated BSI (prevention)	CVAD-Associated BSI Treatment Failure ^d (Supplemental Fig 1)	CVAD-associated Thrombosis (Prevention) ^d (Supplemental Fig 2)	CVAD Occlusion (Prevention) ^d (Fig 3)	CVAD Failure ^d (Supplemental Fig 3)	Mortality ^d (Supplemental Fig 4)
Heparin	Comparator	Comparator	Comparator	Comparator	Comparator	Comparator
Chelating	0.11 (0.02–0.67) ⊕⊕⊕⊖moderate ^a	—	2.27 (0.52–9.97) ⊕⊕⊖⊖low ^b	—	1.52 (0.79–2.94) ⊕⊕⊖⊖low ^b	1.71 (0.26–11.26) ⊕⊕⊖⊖low ^b
Antibiotic	0.19 (0.05–0.79) ⊕⊕⊕⊕high	2.81 (0.04–194.42) ⊕⊕⊖⊖low - imprecision ^b	—	0.88 (0.10–7.74) ⊕⊕⊖⊖low ^b	—	1.34 (0.54–3.35) ⊕⊖⊖⊖very low ^{b,c}
Ethanol	0.48 (0.05–4.24) ⊕⊕⊖⊖low ^b	1.33 (0.42–4.19) ⊕⊕⊖⊖low ^b	0.74 (0.25–2.20) ⊕⊕⊖⊖low ^b	2.84 (1.31–6.16) ⊕⊕⊕⊕high	1.63 (0.71–3.76) ⊕⊕⊖⊖low ^b	0.50 (0.09–2.75) ⊕⊕⊖⊖low ^b
Thrombolytic	0.62 (0.02–23.98) ⊕⊕⊖⊖low ^b	1.00 (0.02–54.46) ⊕⊕⊖⊖low ^b		0.64 (0.44–0.93) ⊕⊕⊖⊖low ^c	0.95 (0.12–7.73) ⊕⊕⊖⊖low ^b	—
Saline	0.73 (0.11–4.82) ⊕⊕⊖⊖low ^b	1.05 (0.02–62.55) ⊕⊖⊖⊖very low ^{b,c}	3.71 (0.51–26.87) ⊕⊕⊖⊖low ^b	0.54 (0.10–3.05) ⊕⊕⊖⊖low ^b	1.05 (0.56–1.95) ⊕⊕⊖⊖low ^b	1.68 (0.19–15.20) ⊕⊕⊖⊖low ^b
Other	—	—	5.14 (0.33–80.81) ⊕⊕⊖⊖low ^b	0.44 (0.05–4.21) ⊕⊕⊖⊖low ^b	1.09 (0.46–2.62) ⊕⊕⊖⊖low ^b	—
Number of studies	22	5	9	12	10	5

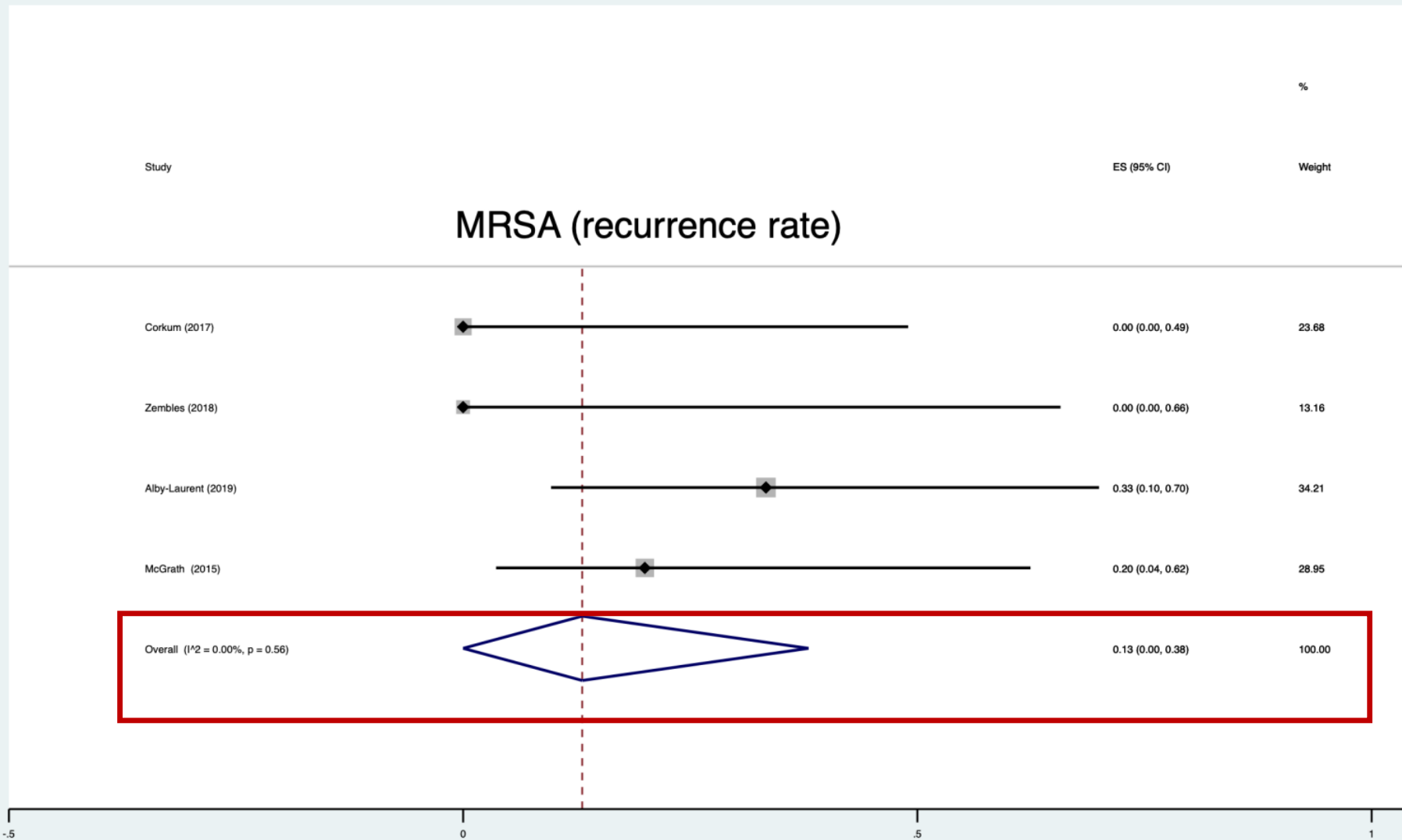








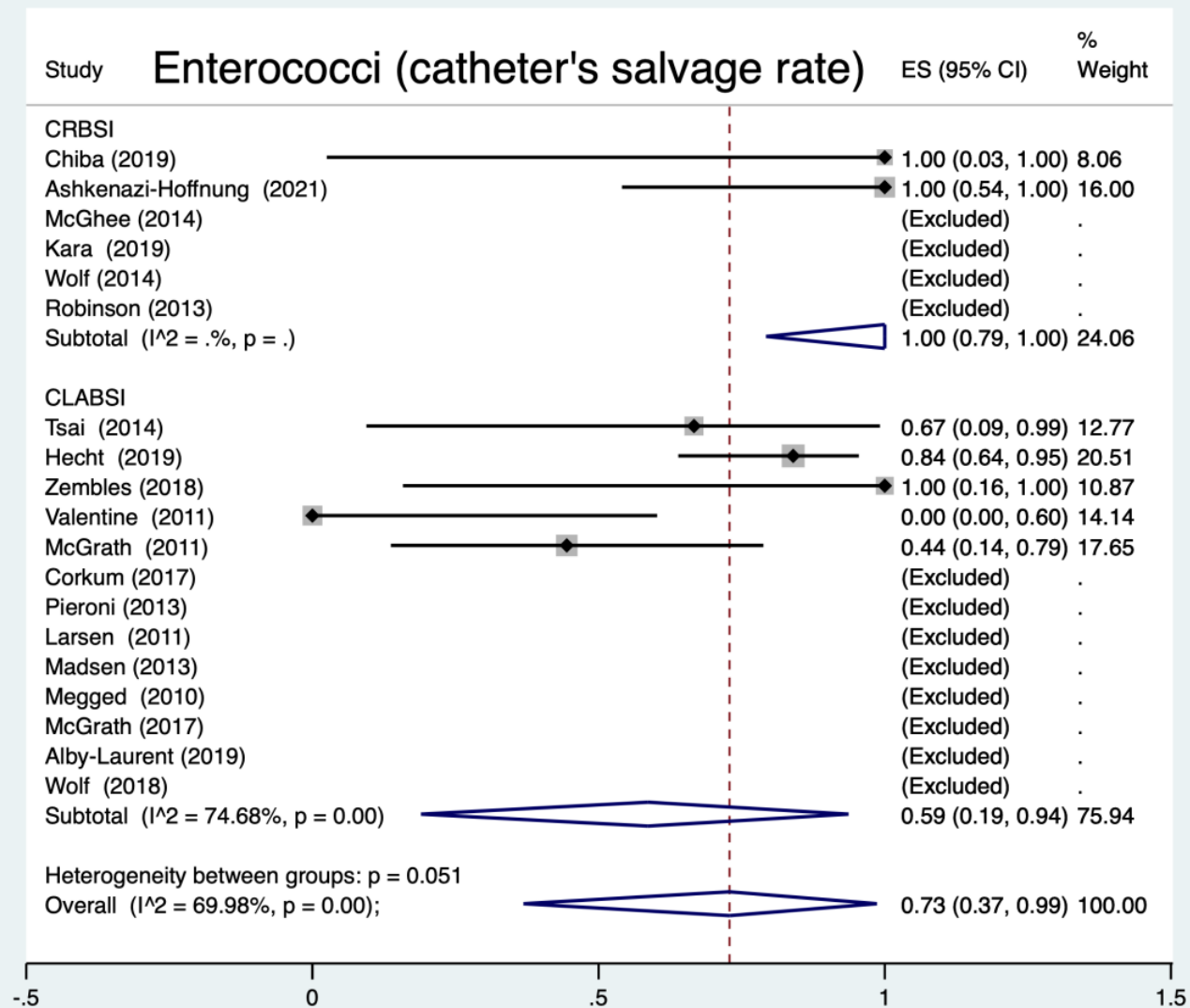


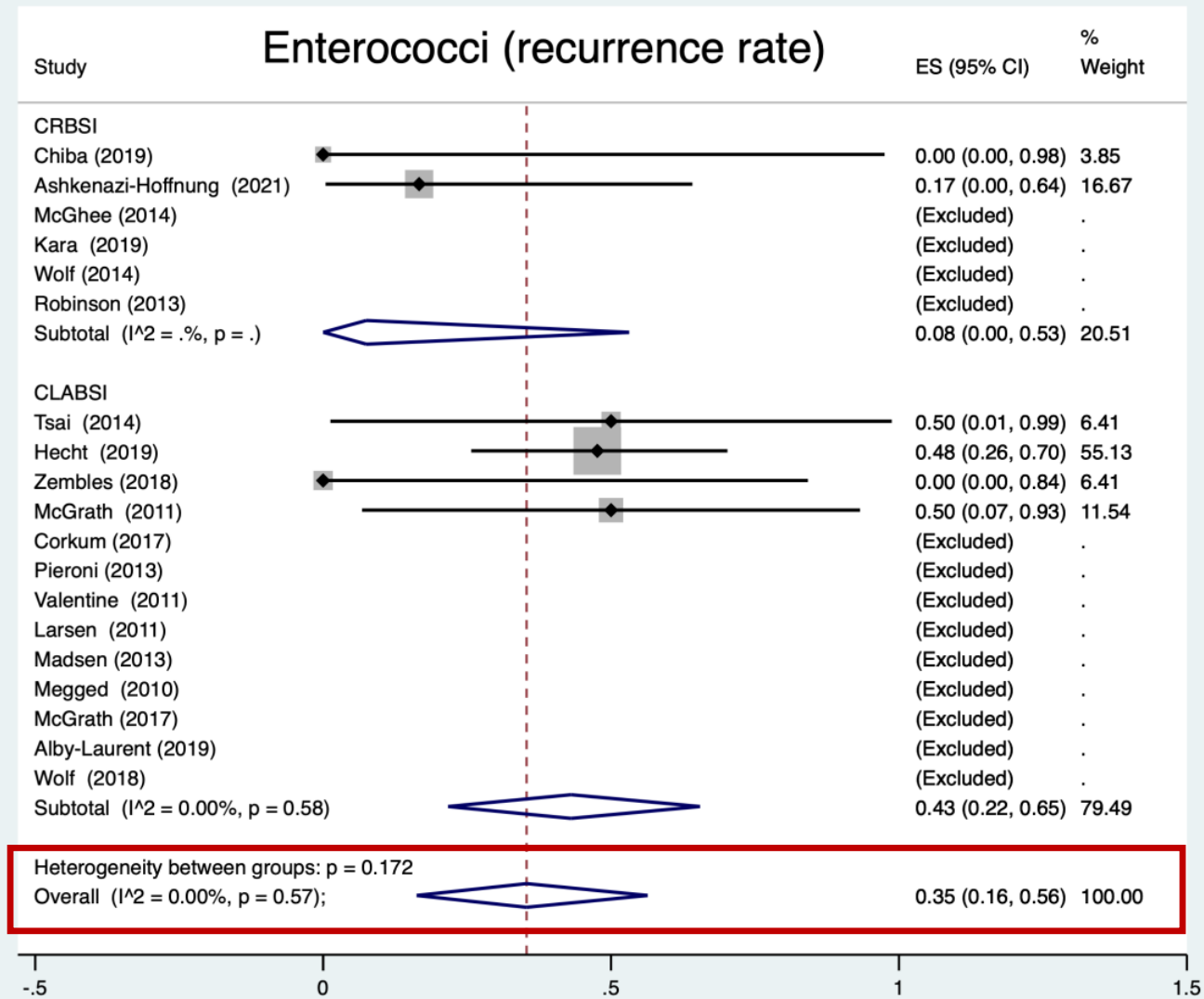


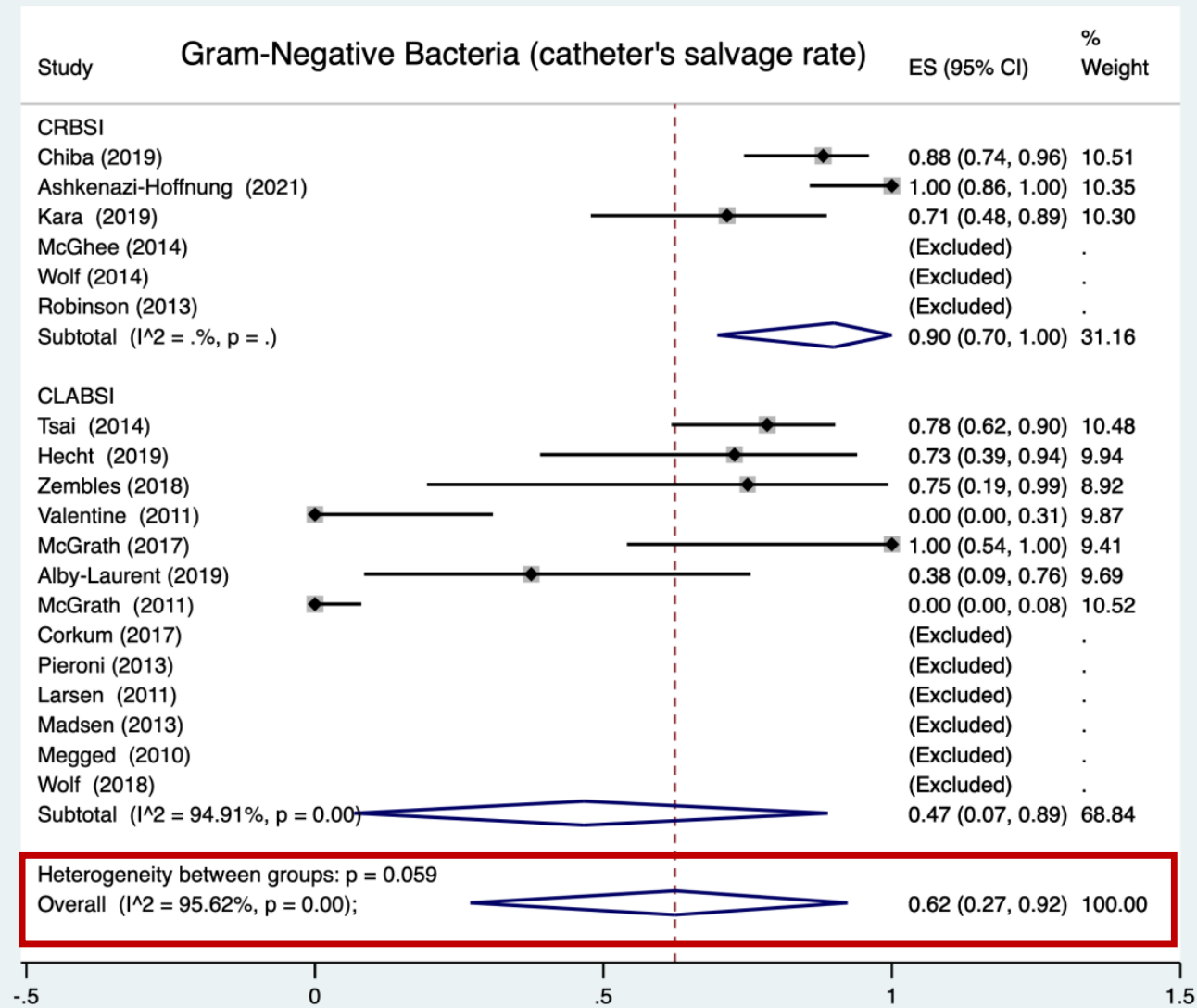
Catheter salvage or removal in catheter-related bloodstream infections with *Staphylococcus aureus* in children with chronic intestinal failure receiving home parenteral nutrition and the use of prophylactic taurolidine catheter lock solution: A descriptive cohort study

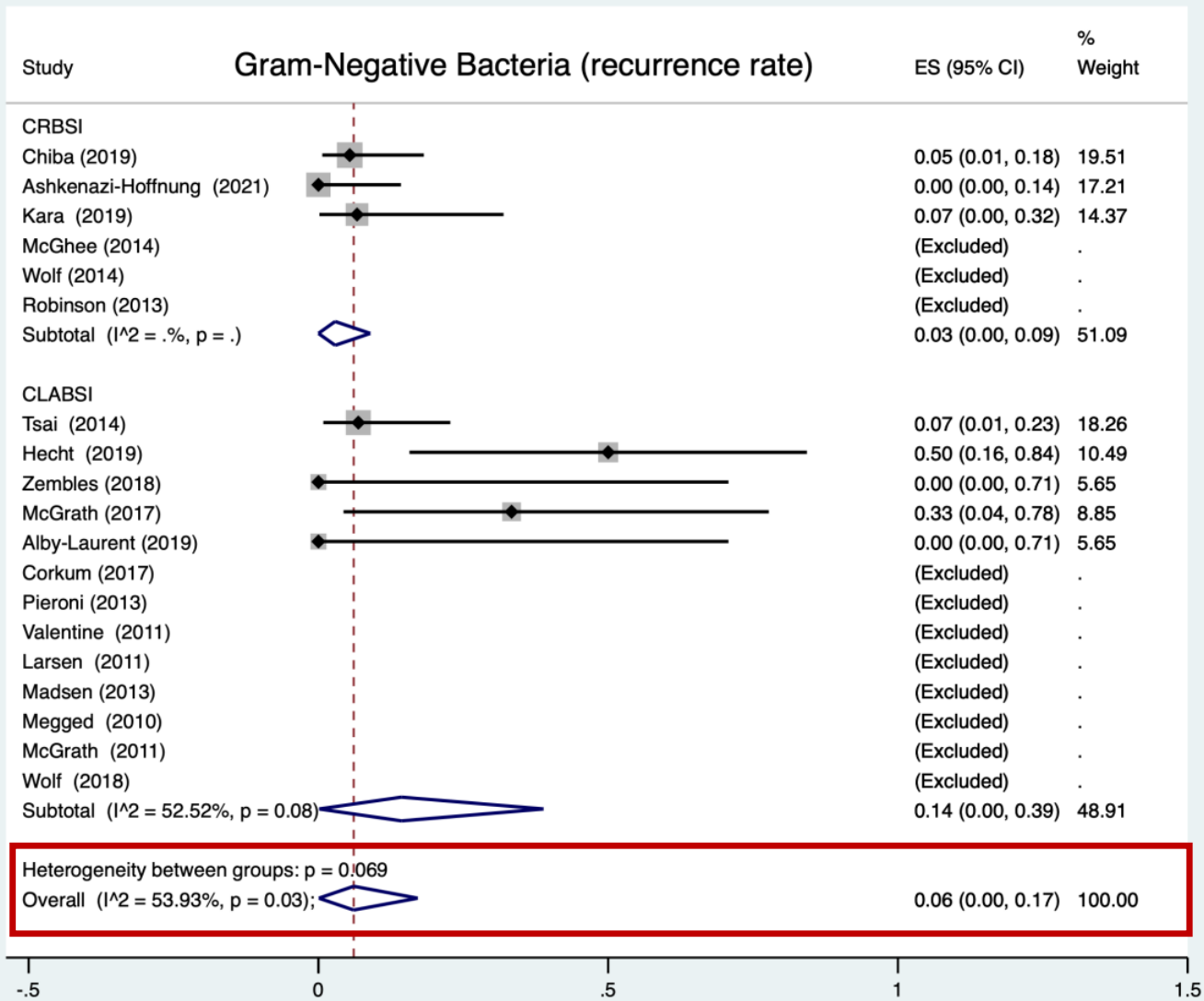
Aysenur Demirok MD¹  | David H. C. Illy BS¹ | Sietse Q. Nagelkerke MD, PhD² |
Michiel F. Lagerweij MS³ | Marc A. Benninga MD, PhD¹ | Merit M. Tabbers MD, PhD¹

- The catheter salvage was attempted in 44% (23/52)
- All *Staph. Aureus* infections
- Treated with intravenous systemic antibiotics
- Successful catheter salvage rate of 100% (23/23)
- No relapse (reinfection within 30 days) of bacteremia
- No removal was needed after catheter salvage in all 23 episodes





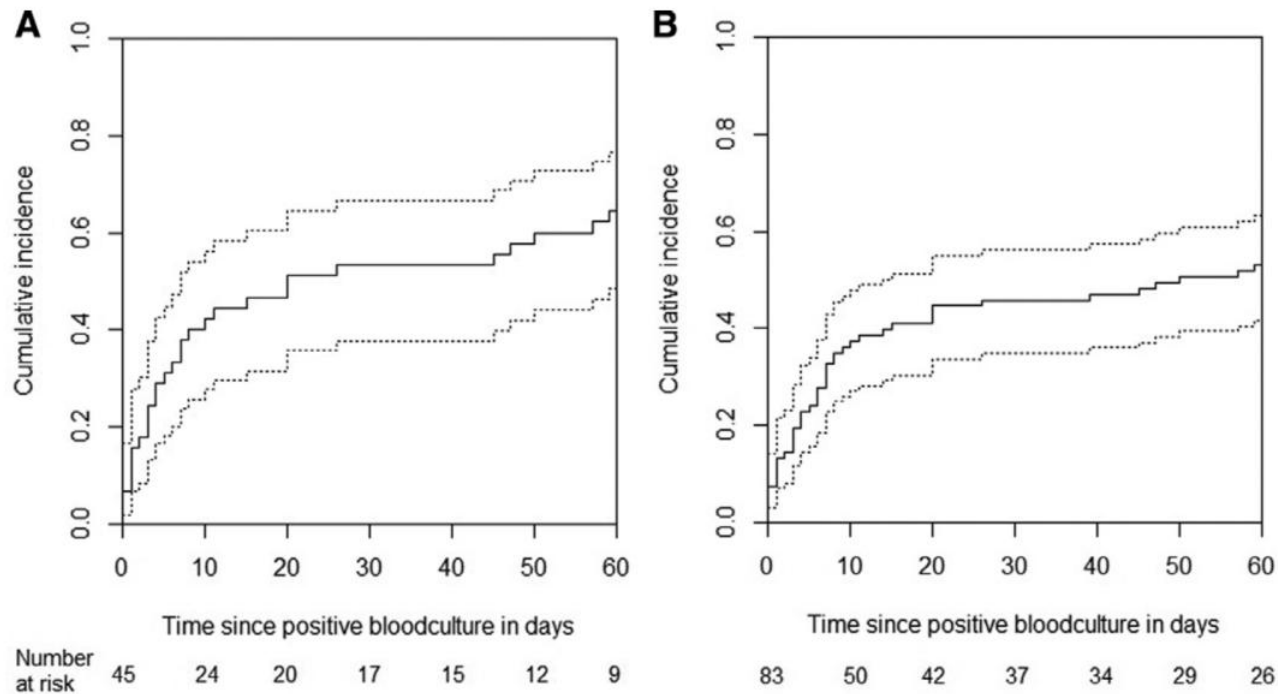


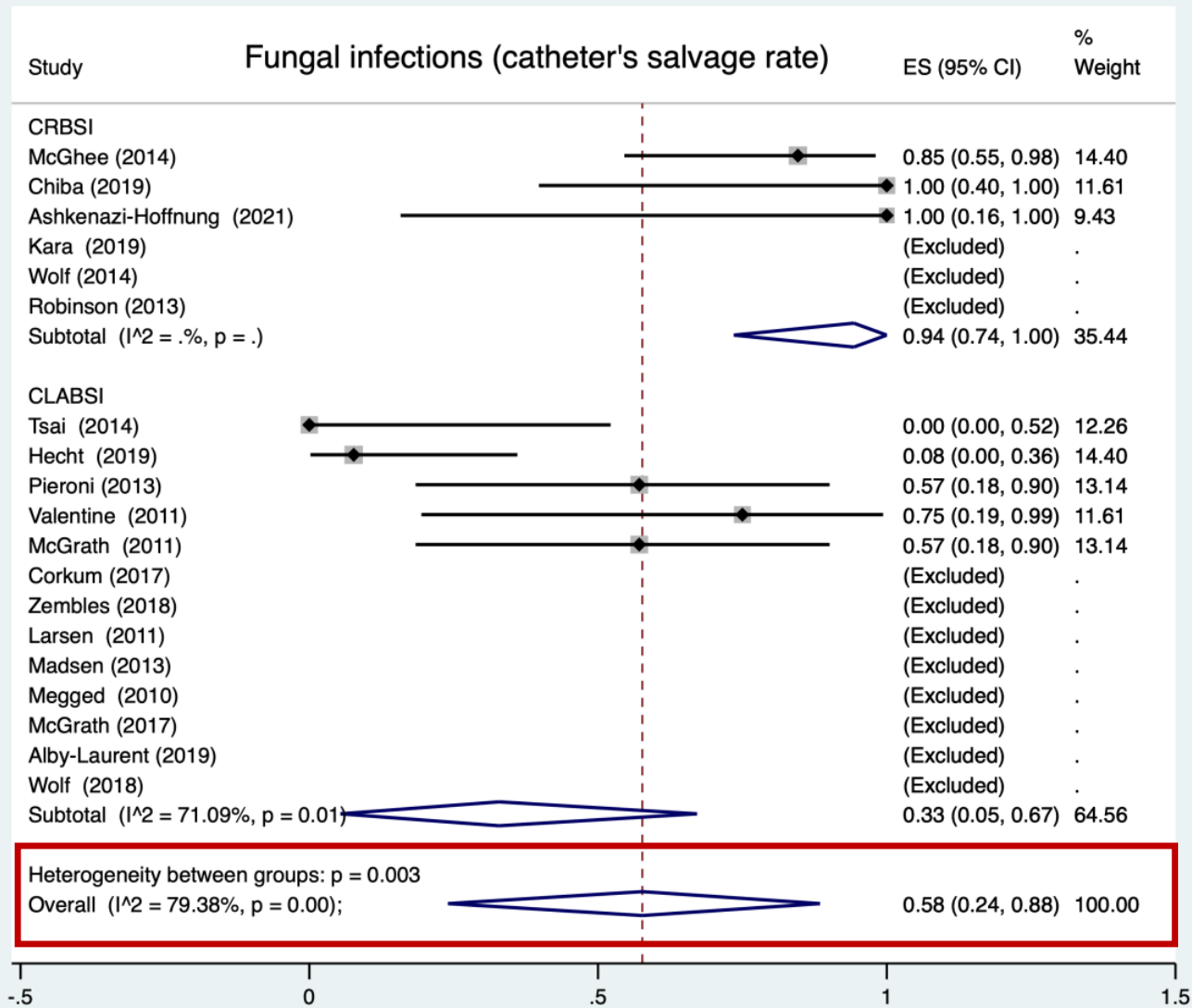


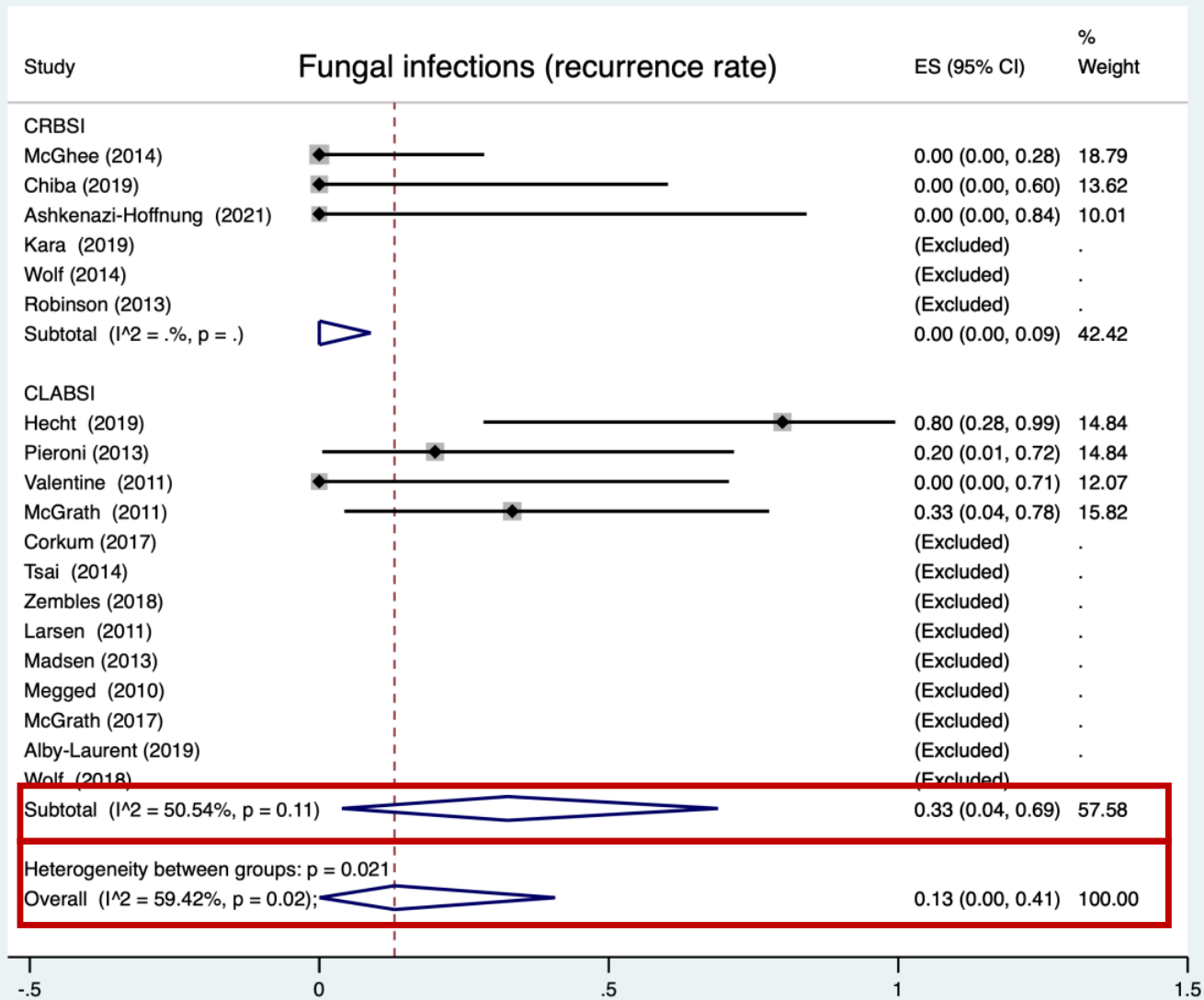
Central Venous Catheter-related Bloodstream Infections Caused by *Enterobacterales* in Pediatric Oncology Patients

Catheter Salvage or Removal

Ceder H. van den Bosch^{ID}, MD,* Aranka L. Kops, BSc,* Yvette G. T. Loeffen, MD,†
Alida F. W. van der Steeg, MD, PhD,* Marianne D. van de Wetering, MD, PhD,* Marta F. Fiocco,*‡§
Miquel B. Ekkelenkamp, MD, PhD,¶ and Tom F. W. Wolfs, MD, PhD†







Conclusioni

- E' fondamentale identificare correttamente la vera CRBSI!
- Ogni strategia conservativa deve includere, ove possibile, la *lock therapy* associata alla terapia antibiotica sistemica
- La lock therapy ha dimostrato efficacia significativa nelle vere CRBSI ma non nelle CLABSI
- Il lock con Etanolo 70% sembrerebbe essere molto efficace e sicuro
 - alta % di successo
 - bassa probabilità di '*recurrence*'
 - bassa eterogeneità degli studi
- Il trattamento conservativo con antibiotico sistemico solo è efficace nelle CLABSI ma non è sicuro per l'elevata probabilità di '*recurrence*' a 30 giorni in quelle che invece sono vere CRBSI non correttamente diagnosticate

Conclusioni

- In merito all'eziologia
 - Infezioni sostenute da **CoNS** e **MSSA** sono state trattate efficacemente con bassa probabilità di 'recurrence' con la terapia combinata lock therapy + antibiotico sistemico
 - *Strategia conservativa fattibile e sicura anche per MSSA*
 - **Warning!** La strategia conservativa delle infezioni sostenute da **MRSA** presenta una % di successi modesta con una % di 'recurrence' inaccettabilmente alta
 - *Rimuovere il VAD!*
 - **Warning!** Sulla base delle evidenze attuali, in caso di infezione sostenuta da *Miceti* *rimuovere il VAD!*
- Riguardo alle infezioni sostenute da Enterococchi e GNB, dai dati che emergono dagli studi inclusi non si possono trarre considerazioni conclusive ma vi è necessità di ulteriori studi, possibilmente RCT
 - Sulla base delle evidenze attuali considerare la rimozione del VAD anche in caso di infezione sostenuta da Enterococchi e GNB

Grazie



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