**Supplementary appendix**

**A Systematic Review of the Burden of Multidrug-resistant Healthcare-associated Infections among Intensive Care Unit Patients in Southeast Asia: The Rise of Multidrug-resistant *Acinetobacter baumannii***

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**Appendix 1**

**Search strategies**

**eTable 1.1 Search algorithms**

|  | **Search algorithm** |
| --- | --- |
| #1 | *Acinetobacter baumannii* |
| #2 | *Pseudomonas aeruginosa* |
| #3 | *Escherichia coli* |
| #4 | *Klebsiella pneumoniae* |
| #5 | Enterobacteriaceae |
| #6 | Staphylococc\* |
| #7 | Enterococc\* |
| #8 | microorganism\* |
| #9 | bacteria |
| #10 | #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 |
| #11 | “Extended-spectrum beta-lactamase” |
| #12 | ESBL |
| #13 | “Multidrug-resistant” |
| #14 | “Multidrug resistance” |
| #15 | Multiresistan\* |
| #16 | Multi-resistan\* |
| #17 | MDR |
| #18 | “Extensively drug-resistant” |
| #19 | “Extensively drug resistance” |
| #20 | XDR |
| #21 | “Pandrug-resistant” |
| #22 | “Pandrug resistance” |
| #23 | PDR |
| #24 | “Carbapenem-resistant” |
| #25 | “Carbapenem resistance” |
| #26 | Carbapenemase |
| #27 | KPC |
| #28 | “Colistin-resistant” |
| #29 | “Colistin resistantance” |
| #30 | “Polymyxin-resistant” |
| #31 | “Polymyxin resistance” |
| #32 | “Methicillin-resistant” |
| #33 | “Methicillin resistantance” |
| #34 | MRSA |
| #35 | MRSE |
| #36 | “Vancomycin-resistant” |
| #37 | “Vancomycin resistance” |
| #38 | VRSA |
| #39 | VRSE |
| #40 | VRE |
| #41 | #11 OR #12 OR #13 OR #14# OR 15 OR #16 OR #17# OR 18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 |
| #42 | “Intensive care unit” |
| #43 | ICU |
| #44 | “Critically ill” |
| #45 | #42 OR #43 OR #44 |
| #46 | Prevalence |
| #47 | Incidence |
| #48 | “ICU stay” |
| #49 | “Hospital stay” |
| #50 | “Length of stay” |
| #51 | Mortality |
| #52 | Fatality |
| #53 | Cost |
| #54 | #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 |
| #55 | “Healthcare-associated” |
| #56 | “Hospital-acquired” |
| #57 | “Nosocomial” |
| #58 | “Device-associated” |
| #59 | “Central line-associated” |
| #60 | “Ventilator-associated” |
| #61 | “Catheter-associated” |
| #62 | #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 |
| #63 | Infection\* |
| #64 | “Bloodstream infection” |
| #65 | “Bloodstream infections” |
| #66 | Bacteraemia |
| #67 | Bacteremia |
| #68 | Septicaemia |
| #69 | Septicemia |
| #70 | Pneumonia |
| #71 | “Urinary tract infection” |
| #72 | “Urinary tract infections” |
| #73 | “Surgical site infection” |
| #74 | “Surgical site infections” |
| #75 | “Wound infection” |
| #76 | “Wound infections” |
| #77 | #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 |
| #78 | Burma |
| #79 | Brunei |
| #80 | Cambodia |
| #81 | “East Timor” |
| #82 | Indonesia |
| #83 | Laos |
| #84 | Malaysia |
| #85 | Myanmar |
| #86 | Philippines |
| #87 | Singapore |
| #88 | Thailand |
| #89 | Vietnam |
| #90 | #78 OR #79 OR #80 OR #81 OR #82 OR #83 OR #84 OR #85 OR #86 OR #87 OR #88 OR #89 |
| #91 | #10 AND #41 AND #45 AND #54 AND #62 AND #77 AND #90 |

**Appendix 2**

**Description of included studies**

**eTable 2.1 Description of included studies**

| **ID** | **First author** | **Year of publication** | **Country of publication** | **MDROa** | **Type of HAIb** | **Type of ICUc** | **No. of patientsd** | **Incidence** | **Prevalence** | **CFR** | **LOS** | **Cost** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 1 | Boonyasiri A1 | 2016 | Thailand | ESBL-EC, ESBL-KP, MDR-AB, MDR-PsA, MRSA, VRE | Colonization, CAUTI, CLABSI | MICU | 388 | 1 | 1 |  |  |  |
| 2 | Le NK2 | 2016 | Vietnam | CRAB, CRE, CR-KP, CR-PsA, MRSA | Any HAI | PICU | 1,363 | 1 | 1 |  |  |  |
| 3 | Thatrimontrichai A3 | 2016 | Thailand | CRAB | VAP | NICU | 101e |  | 1 | 1 | 1 |  |
| 4 | Turner P4 | 2016 | Cambodia | CRAB, ESBL-E | Colonization | NICU | 333 | 1 |  |  |  |  |
| 5 | Chusri S5 | 2015 | Thailand | MDR-AB | Any HAI | ICU | 69e |  | 1 |  |  |  |
| 6 | Harris PN6 | 2015 | Singapore | MRSA | Any HAI, BSI, colonization | ICU | 649 | 1 |  |  |  |  |
| 7 | Inchai J(1)7 | 2015 | Thailand | MDR-AB, PDR-AB, XDR-AB, MRSA | VAP | MICU | 621e |  | 1 | 1 |  |  |
| 8 | Inchai J(2)8 | 2015 | Thailand | MDR-AB, PDR-AB, XDR-AB | VAP | MICU | 304e |  |  | 1 |  |  |
| 9 | Janahiraman S9 | 2015 | Malaysia | MDR-AB | VAP | ICU | 136e |  | 1 |  | 1 |  |
| 10 | Ling ML10 | 2015 | Singapore | CRE | Colonization/infection | Adult ICU | 203e |  |  | 1 | 1 |  |
| 11 | Tong SY11 | 2015 | Thailand | MRSA | Colonization | MICU, PICU | 267 | 1 |  |  |  |  |
| 12 | Apisarnthanarak A12 | 2014 | Thailand | ESBL-EC, ESBL-KP, MDR-PsA, MRSA, XDR-AB | Colonization/infection | ICU | 554 | 1 |  |  |  |  |
| 13 | Chittawatanarat K13 | 2014 | Thailand | MDR-AB, MDR-E, MRSA, XDR-AB | VAP | SICU | 150e |  | 1 | 1 |  |  |
| 14 | Saharman YR14 | 2013 | Indonesia | ESBL-E | Any HAI | ICU | 84e |  | 1 | 1 |  |  |
| 15 | Schultsz C15 | 2013 | Vietnam | ESBL-E, MRSA | Colonization/infection | Tetanus ICU | 174 | 1 |  |  |  |  |
| 16 | Thatrimontrichai A16 | 2013 | Thailand | CRAB | BSI | NICU | 368e |  | 1 | 1 | 1 |  |
| 17 | Vasudevan A(1)17 | 2013 | Singapore | MDR-GNB | Colonization/infection | MICU, SICU | 1,373 | 1 |  |  |  |  |
| 18 | Vasudevan A(2)18 | 2013 | Singapore | MDR-AB, MDR-EC, MDR-KP, MDR-PsA, MRSA | Pneumonia | MICU, SICU | 246e |  | 1 |  |  |  |
| 19 | Le T19 | 2012 | Vietnam | CRAB, MDR-AB | VAP | MICU, SICU | 51e |  | 1 |  |  |  |
| 20 | Nakwan N20 | 2012 | Thailand | CRAB | BSI | NICU | 4,087 | 1 | 1 | 1 |  |  |
| 21 | Ng E21 | 2012 | Singapore | MDR-GNB | BSI | MICU, SICU | 525e |  |  |  |  | 1 |
| 22 | Chong SJ22 | 2011 | Singapore | MDR-AB, MRSA | Any HAI, BSI, CLABSI, UTI, VAP, wound infection | Burn ICU | 94 | 1 |  |  |  |  |
| 23 | Nakwan N23 | 2011 | Thailand | XDR-AB | VAP | NICU | 670 | 1 | 1 | 1 |  |  |
| 24 | Oh HM24 | 2011 | Singapore | MRSA | Colonization | SICU | 453 | 1 |  |  |  |  |
| 25 | Katherason SG25 | 2010 | Malaysia | ESBL-KP, MRSA | BSI | Adult ICU | 215 | 1 | 1 |  |  |  |
| 26 | Kurup A26 | 2010 | Singapore | MRSA | Colonization | MICU, SICU | 213 | 1 |  |  | 1 |  |
| 27 | Donaldson AD27 | 2009 | Singapore | MDR-AB, MDR-PsA, MRSA | BSI | Adult ICU | 415 | 1 |  | 1 | 1 |  |
| 28 | Gill CJ28 | 2009 | Philippines | MRSA, VRE | Colonization | NICU | 925 | 1 |  |  |  |  |
| 29 | Katherason SG29 | 2009 | Malaysia | ESBL-KP, MRSA | VAP | Adult ICU | 215 | 1 |  |  |  |  |
| 30 | Litzow JM30 | 2009 | Philippines | MDR-GNB | BSI, colonization | NICU | 1,831 | 1 |  |  |  |  |
| 31 | Sritippayawan S31 | 2009 | Thailand | MDR-E, MDR-AB, MDR-PsA, MRSA/MRSE, VRE | Any HAI | PICU | 347 | 1 | 1 | 1 |  |  |
| 32 | Apisarnthanarak A32 | 2008 | Thailand | PDR-AB | Colonization/infection | Adult ICU | 1,357 | 1 |  |  |  | 1 |
| 33 | Katherason SG33 | 2008 | Malaysia | ESBL-KP, MRSA | BSI, pneumonia | Adult ICU | 128 | 1 |  |  |  |  |
| 34 | Chim H34 | 2007 | Singapore | CoR-AB, CRAB, MRSA | Any HAI, BSI, burn wound infection, pneumonia, primary BSI, wound colonization | Burn ICU | 57 | 1 | 1 |  |  |  |
| 35 | Kwa AL35 | 2007 | Singapore | MDR-AB | Pneumonia | SICU | 129e |  | 1 |  |  |  |
| 36 | Tan CC36 | 2007 | Malaysia | ESBL-E, MDR-AB, MRSA | CLABSI | Adult ICU | 496 | 1 | 1 |  |  |  |
| 37 | Boo NY37 | 2005 | Malaysia | ESBL-KP | Colonization | NICU | 369 | 1 |  |  |  |  |
| 38 | Ling ML38 | 2001 | Singapore | MDR-AB | Any HAI, colonization | ICU | 103e |  |  | 1 | 1 |  |
| 39 | Ng SP39 | 1998 | Singapore | MRSA/MRSE | BSI | NICU | 227 | 1 |  |  |  |  |
| 40 | Halder D40 | 1996 | Malaysia | MRSA | Septic arthritis | NICU | 10e |  | 1 |  |  |  |
| 41 | Tan KW41 | 1994 | Singapore | MRSA | Any HAI, colonization | NICU | 2,576 | 1 |  |  |  |  |

**Abbreviations:**

aCoR-AB, colistin-resistant *A. baumannii*; CRAB, carbapenem-resistant *A. baumannii*; CRE, carbapenem-resistant Enterobacteriaceae; CR-KP, carbapenem-resistant *K. pneumoniae*; CR-PsA, carbapenem-resistant *P. aeruginosa*; ESBL-E, ESBL-producing Enterobacteriaceae; ESBL-EC, ESBL-producing *E. coli*; ESBL-KP, ESBL-producing *K. pneumoniae*; MDR-AB, multidrug-resistant *A. baumannii*; MDR-E, multidrug-resistant Enterobacteriaceae; MDR-EC, multidrug-resistant *E. coli*; MDR-GNB, multidrug-resistant Gram-negative bacteria; MDR-KP, multidrug-resistant *K. pneumoniae*; MDR-PsA, multidrug-resistant *P. aeruginosa*; MRSA, methicillin-resistant *S. aureus*; MRSE, methicillin-resistant *S. epidermidis*; PDR-AB, pandrug-resistant *A. baumannii*; VRE, vancomycin-resistant enterococci; XDR-AB, extensively drug-resistant *A. baumannii*.

bBSI, bloodstream infection; CAUTI, catheter-associated urinary tract infection; CLABSI, central line-associated bloodstream infection; HAI, healthcare-associated infection; VAP,

ventilator-associated pneumonia.

cMICU, medical ICU; NICU, neonatal ICU; PICU, pediatric ICU; SICU, surgical ICU.

dAll patients admitted to ICU.

eNumber of infected cases.

**Appendix 3**

**Quality assessments**

**eTable 3.1 Quality assessment of studies**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **ID** | **First author** | **Year of publication** | **Quality** |  | **ID** | **First author** | **Year of publication** | **Quality** |
| 1 | Boonyasiri A | 2016 | HQ |  | 22 | Chong SJ | 2011 | HQ |
| 2 | Le NK | 2016 | HQ |  | 23 | Nakwan N | 2011 | MQ |
| 3 | Thatrimontrichai A | 2016 | MQ |  | 24 | Oh HM | 2011 | LQ |
| 4 | Turner P | 2016 | MQ |  | 25 | Katherason SG | 2010 | HQ |
| 5 | Chusri S | 2015 | HQ |  | 26 | Kurup A | 2010 | MQ |
| 6 | Harris PN | 2015 | HQ |  | 27 | Donaldson AD | 2009 | HQ |
| 7 | Inchai J(1) | 2015 | HQ |  | 28 | Gill CJ | 2009 | MQ |
| 8 | Inchai J(2) | 2015 | HQ |  | 29 | Katherason SG | 2009 | HQ |
| 9 | Janahiraman S | 2015 | MQ |  | 30 | Litzow JM | 2009 | HQ |
| 10 | Ling ML | 2015 | HQ |  | 31 | Sritippayawan S | 2009 | HQ |
| 11 | Tong SY | 2015 | MQ |  | 32 | Apisarnthanarak A | 2008 | HQ |
| 12 | Apisarnthanarak A | 2014 | HQ |  | 33 | Katherason SG | 2008 | HQ |
| 13 | Chittawatanarat K | 2014 | MQ |  | 34 | Chim H | 2007 | MQ |
| 14 | Saharman YR | 2013 | MQ |  | 35 | Kwa AL | 2007 | MQ |
| 15 | Schultsz C | 2013 | MQ |  | 36 | Tan CC | 2007 | MQ |
| 16 | Thatrimontrichai A | 2013 | MQ |  | 37 | Boo NY | 2005 | MQ |
| 17 | Vasudevan A(1) | 2013 | MQ |  | 38 | Ling ML | 2001 | LQ |
| 18 | Vasudevan A(2) | 2013 | HQ |  | 39 | Ng SP | 1998 | MQ |
| 19 | Le T | 2012 | LQ |  | 40 | Halder D | 1996 | LQ |
| 20 | Nakwan N | 2012 | MQ |  | 41 | Tan KW | 1994 | MQ |
| 21 | Ng E | 2012 | MQ |  |  |  |  |  |

**Abbreviations:** HQ, high quality; MQ, moderate quality; LQ, low quality.

**Appendix 4**

**Cumulative incidence and prevalence**

**eTable 4.1 Prevalence rate of HAI due to MDRO in Southeast Asia**

|  |  |  |  |
| --- | --- | --- | --- |
| **Microorganism** | **Type of infection** | **Range, %** | **Studies** |
| **Prevalence of drug-resistant cases among patients infected with the same pathogen** | | | |
| ESBL-producing GNB | Any HAI | 58.33 | Saharman et al, 2013 (Indonesia)14 |
|  | BSI | 75.00 | Katherason et al, 2010 (Malaysia)25 |
| CRAB | BSI | 59.09 | Nakwan et al, 2012 (Thailand)20 |
|  | VAP | 88.24 | Le et al, 2012 (Vietnam)19 |
| MDR-AB | Any HAI | 69.57-78.26 | Chusri et al, 2015 (Thailand)5; Sritippayawan et al, 2009 (Thailand)31 |
|  | Pneumonia | 77.36 | Vasudevan(2), 2013 (Singapore)18 |
|  | VAP | 3.45-100.00 | Inchai(1) et al, 2015 (Thailand)7; Janahiraman et al, 2015 (Malaysia)9; Chittawatanarat et al, 2014 (Thailand)13; Le et al, 2012 (Vietnam)19 |
| MDR-PsA | Any HAI | 55.56 | Sritippayawan et al, 2009 (Thailand)31 |
|  | Pneumonia | 25.40 | Vasudevan(2) et al, 2013 (Singapore)18 |
| MDR-Enterobacteriaceae | Any HAI | 44.44 | Sritippayawan et al, 2009 (Thailand)31 |
|  | Pneumonia | 17.86-50.00 | Vasudevan(2) et al, 2013 (Singapore)18 |
|  | VAP | 33.33 | Chittawatanarat et al, 2014 (Thailand)13 |
| MDR-GNB | Pneumonia | 31.78 | Kwa et al, 2007 (Singapore)35 |
| XDR-AB | VAP | 65.28-79.31 | Inchai(1) et al, 2015 (Thailand)7; Chittawatanarat et al, 2014 (Thailand)13 |
| PDR-AB | VAP | 3.56 | Inchai(1) et al, 2015 (Thailand)7 |

|  |  |  |  |
| --- | --- | --- | --- |
| **Microorganism** | **Type of infection** | **Range, %** | **Studies** |
| MRSA | Any HAI | 33.33 | Sritippayawan et al, 2009 (Thailand)31 |
|  | Pneumonia | 59.21 | Vasudevan(2) et al, 2013 (Singapore)18 |
|  | VAP | 66.67 | Chittawatanarat et al, 2014 (Thailand)13 |
| VRE | Any HAI | 40.00 | Sritippayawan et al, 2009 (Thailand)31 |
| **Prevalence of drug-resistant cases among patients infected with any pathogen** | | | |
| ESBL-producing GNB | CLABSI | 18.42 | Tan et al, 2007 (Malaysia)36 |
| CRAB | Any HAI | 5.29 | Le et al, 2016 (Vietnam)2 |
|  | BSI | 3.80 | Thatrimontrichai et al, 2013 (Thailand)16 |
|  | VAP | 62.38 | Thatrimontrichai et al, 2016 (Thailand)3 |
| CR-PsA | Any HAI | 5.29 | Le et al, 2016 (Vietnam)2 |
| CRE | Any HAI | 3.08-5.07 | Le et al, 2016 (Vietnam)2 |
| MDR-AB | CLABSI | 10.53 | Tan et al, 2007 (Malaysia)36 |
|  | VAP | 1.33-11.59 | Inchai(1) et al, 2015 (Thailand)7; Chittawatanarat et al, 2014 (Thailand)13 |
| MDR-Enterobacteriaceae | VAP | 8.67 | Chittawatanarat et al, 2014 (Thailand)13 |
| MDR-GNB and GPC | HAP | 41.87 | Vasudevan(2), 2013 (Singapore)18 |
|  | VAP | 40.58 | Vasudevan(2), 2013 (Singapore)18 |
| XDR-AB | VAP | 17.95-35.43 | Inchai(1) et al, 2015 (Thailand)7; Chittawatanarat et al, 2014 (Thailand)13; Nakwan et al, 2011 (Thailand)23 |
| PDR-AB | VAP | 1.93 | Inchai(1) et al, 2015 (Thailand)7 |
| MRSA | Any HAI | 2.86 | Le et al, 2016 (Vietnam)2 |
|  | BSI | 17.70 | Chim et al, 2007 (Singapore)34 |
|  | Primary BSI | 7.41 | Chim et al, 2007 (Singapore)34 |

|  |  |  |  |
| --- | --- | --- | --- |
| **Microorganism** | **Type of infection** | **Range, %** | **Studies** |
| MRSA | CLABSI | 13.16-16.67 | Boonyasiri et al, 2016 (Thailand)1; Tan et al, 2007 (Malaysia)36 |
|  | CAUTI | 3.33 | Boonyasiri et al, 2016 (Thailand)1 |
|  | Burn wound infection | 23.40 | Chim et al, 2007 (Singapore)34 |
|  | Septic arthritis | 90.00 | Halder et al, 1996 (Malaysia)40 |
|  | Pneumonia | 18.64 | Chim et al, 2007 (Singapore)34 |
|  | VAP | 2.67 | Chittawatanarat et al, 2014 (Thailand)13 |

**Abbreviations:** BSI, bloodstream infection; CAUTI, catheter-associated urinary tract infection; CLABSI, central line-associated bloodstream infection; CRAB, carbapenem-resistant *Acinetobacter baumannii*; CRE, carbapenem-resistant Enterobacteriaceae; CR-PsA, carbapenem-resistant *Pseudomonas aeruginosa*; HAP, hospital-acquired pneumonia; MDR-AB, multidrug-resistant *Acinetobacter baumannii*; MDR-GNB and GPC, multidrug-resistant Gram-negative bacteria and Gram-positive cocci; MDR-PsA, multidrug-resistant *Pseudomonas aeruginosa*; MRSA, methicillin-resistant *Staphylococcus aureus*; PDR-AB, pandrug-resistant *Acinetobacter baumannii*; VAP, ventilator-associated pneumonia; VRE, vancomycin-resistant *Enterococcus* spp.; XDR-AB, extensively drug-resistant *Acinetobacter baumannii*.

**Appendix 5**

**References of included studies**

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