

**Is age associated with different vital signs in adults presenting to hospital with bacterial infection? A systematic review and meta-analysis.**

**Appendix A: Supplementary Figures**

**Appendix B: Full Search Strategy**

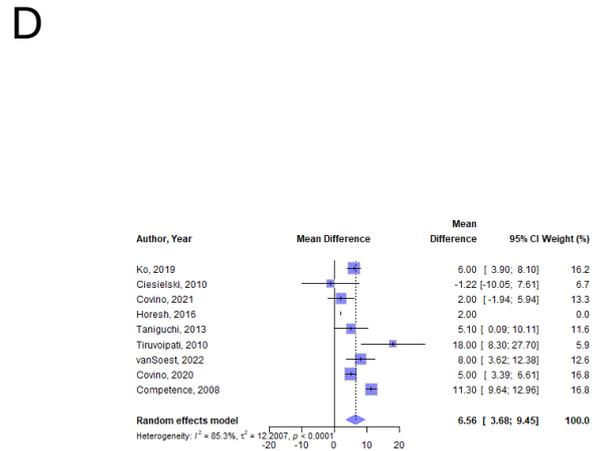
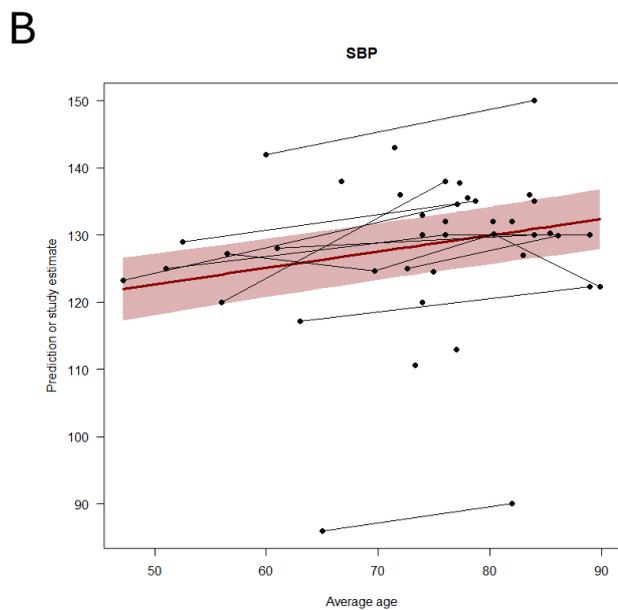
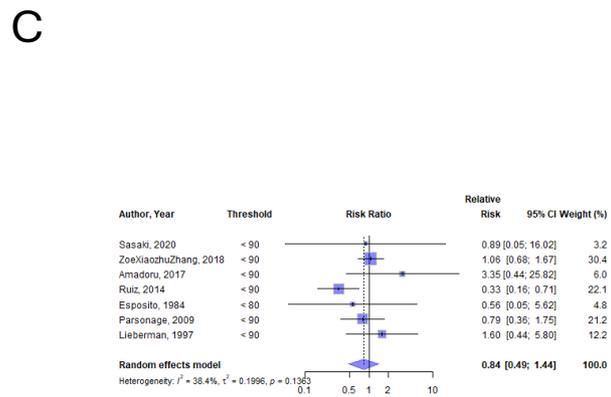
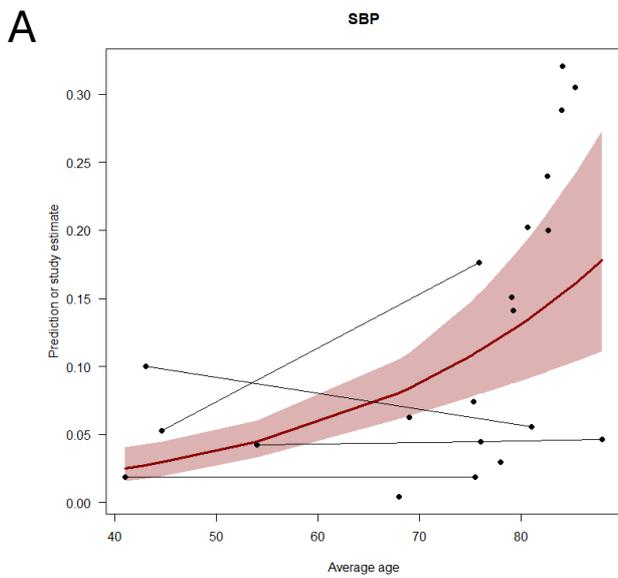
**Appendix C: Quality Assessment Tool**

**Appendix D: Characteristics of Individual Included Studies**

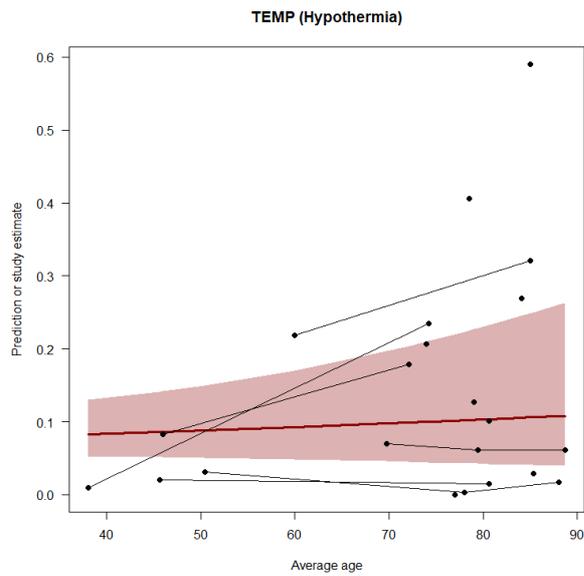
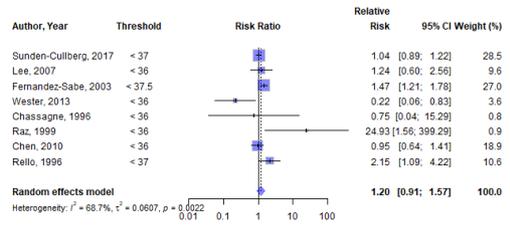
**Appendix E: Data Collection**

**Appendix F: Risk of Bias Assessment of Individual Included Studies**

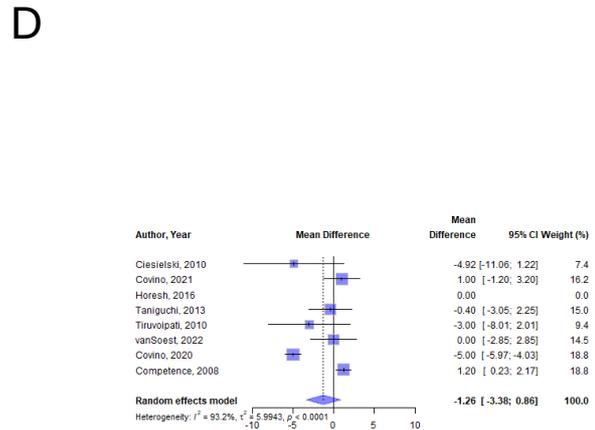
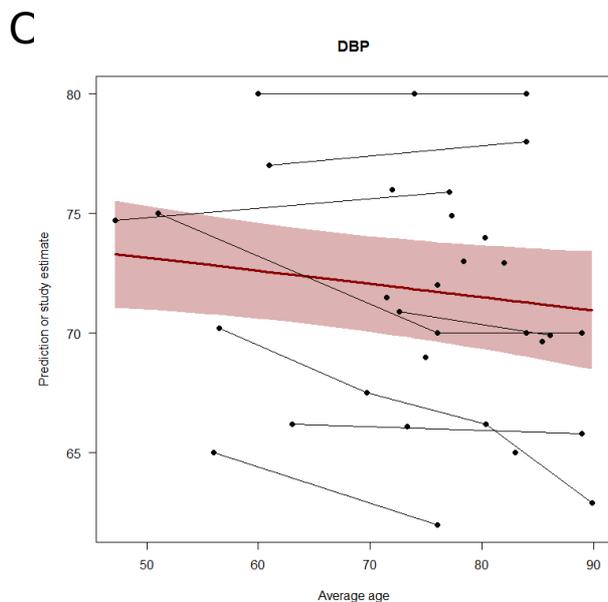
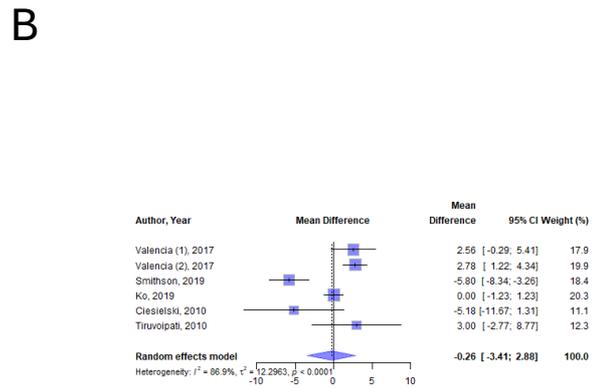
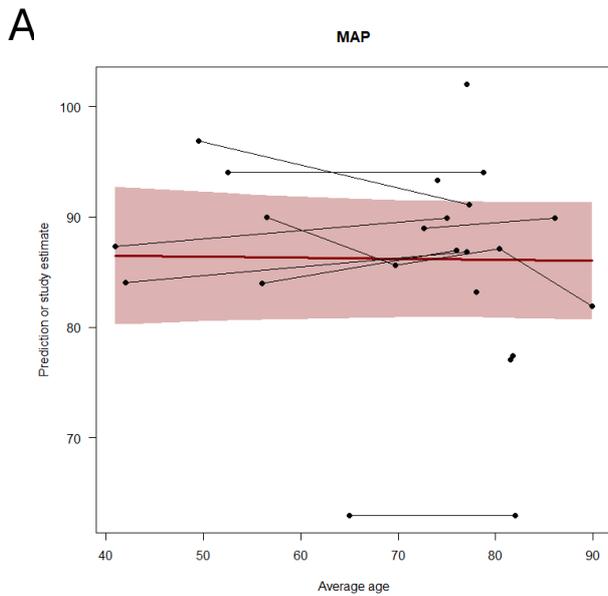
Appendix A: Supplementary Figures



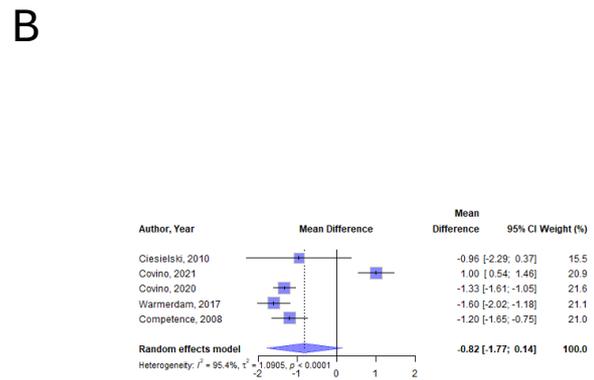
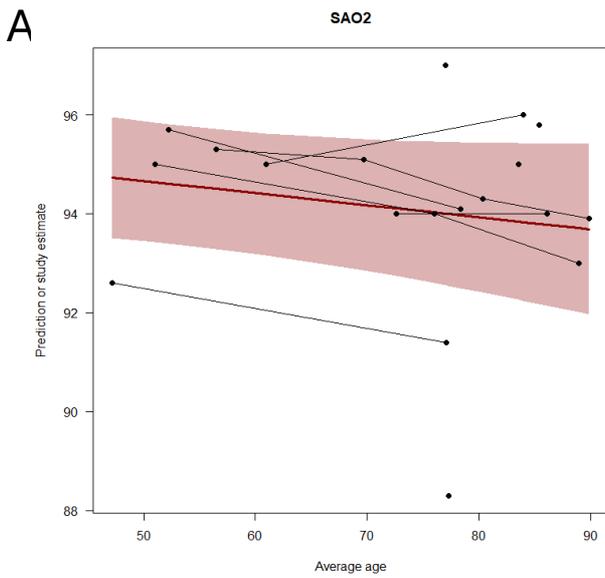
Supplementary Figure 1. [A] Meta-regression showing how proportion of patients with hypotension changes with age;  $n = 15$  studies (6478 patients), slope coefficient 0.045, 95%CI 0.026 to 0.064,  $p < 0.05$ . [B] Meta-regression showing how admission systolic blood pressure changes with age;  $n = 26$  studies (21220 patients), slope coefficient 0.24, 95%CI 0.16 to 0.32,  $p < 0.05$ . [C] Forest plot of the risk ratio of hypotension in older and younger patients;  $n = 7$  studies, RR 0.84, 0.49 to 1.44,  $I^2 = 38.4$ . [D] Forest plot of the mean difference in systolic blood pressure between older and younger patients;  $n = 9$  studies, MD 7mmHg, 4 to 9mmHg,  $I^2 = 85.3$ .

**A****B**

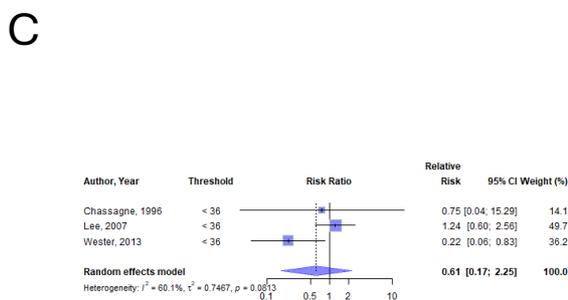
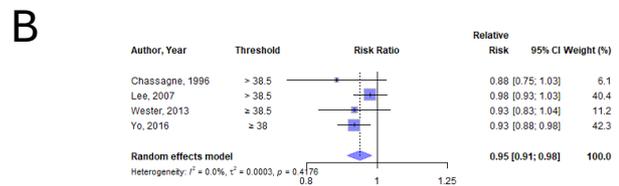
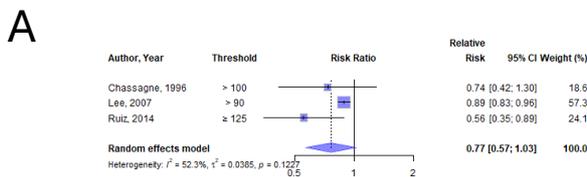
Supplementary Figure 2. [A] Meta-regression showing how proportion of patients with hypothermia changes with age; n = 13 studies (9458 patients), slope coefficient 0.0058 95%CI -0.011 to 0.022, p = 0.49. [B] Forest plot of the risk ratio of hypothermia in older and younger patients; n = 8 studies, RR 1.2, 95%CI 0.91 to 1.57,  $I^2 = 68.7\%$ ).



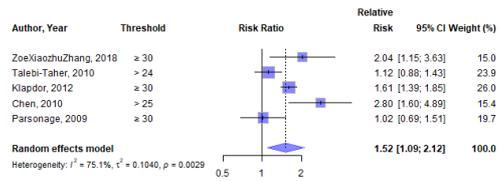
Supplementary Figure 3. [A] Meta-regression showing how admission mean arterial pressure changes with age;  $n = 11$  studies (9797 patients), slope coefficient  $-0.0095$ , 95%CI  $-0.095$  to  $0.076$ ,  $p = 0.83$ . [B] Forest plot of the mean difference in mean arterial pressure between older and younger patients;  $n = 6$  studies, MD  $0$  mmHg,  $-3$  to  $3$  mmHg,  $I^2 = 86.9\%$ . [C] Meta-regression showing how admission diastolic blood pressure changes with age;  $n = 19$  studies (16721 patients), slope coefficient  $-0.055$ , 95%CI  $-0.11$  to  $0.0039$ ,  $p = 0.067$ . [D] Forest plot of the mean difference in diastolic blood pressure between older and younger patients;  $n = 8$  studies, MD  $-1$  mmHg,  $-3$  to  $1$  mmHg,  $I^2 = 93.2\%$ .



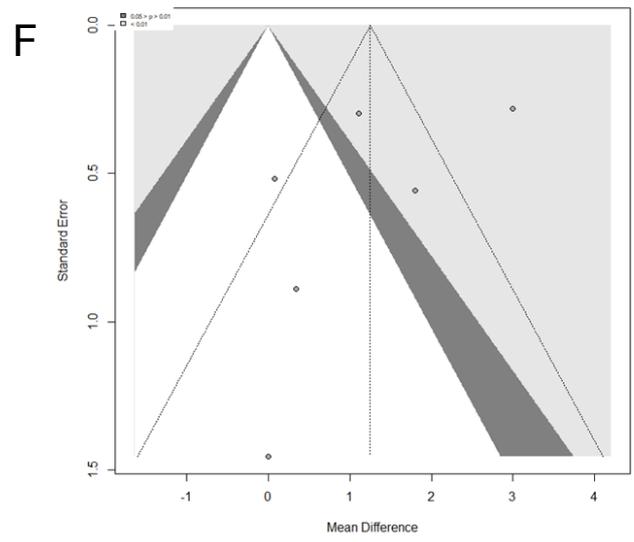
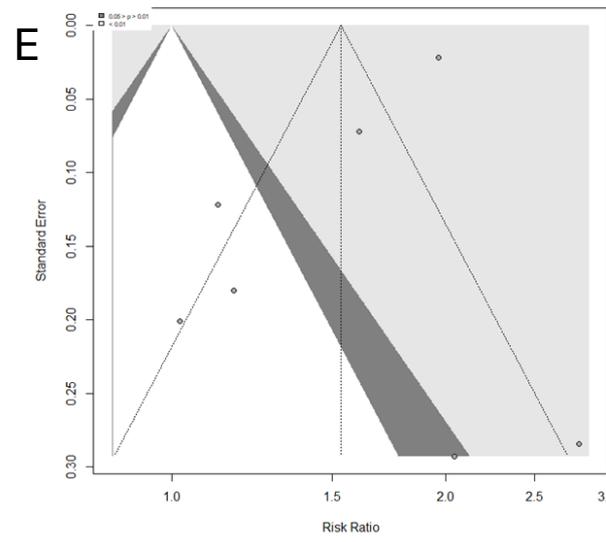
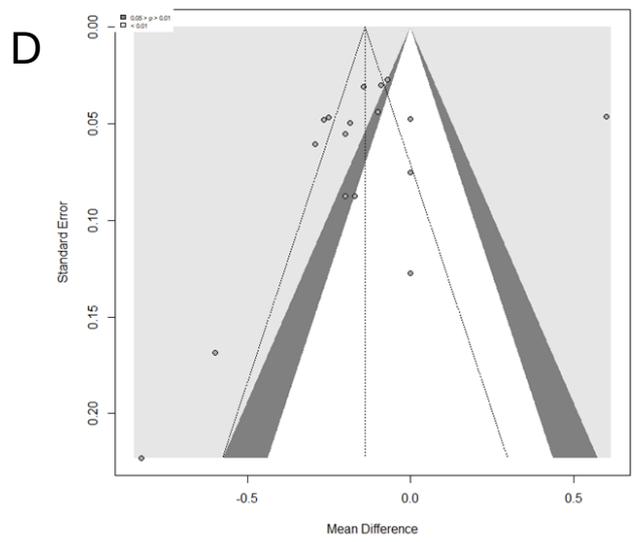
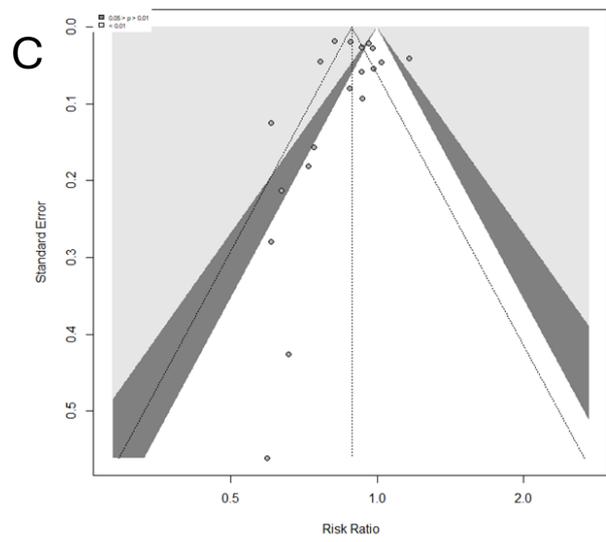
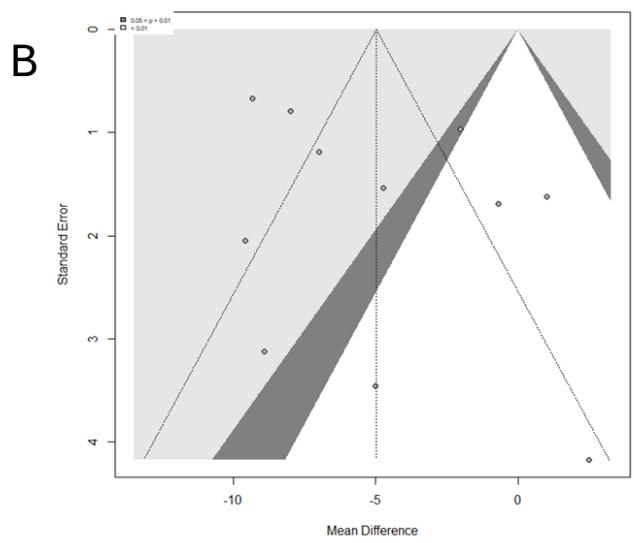
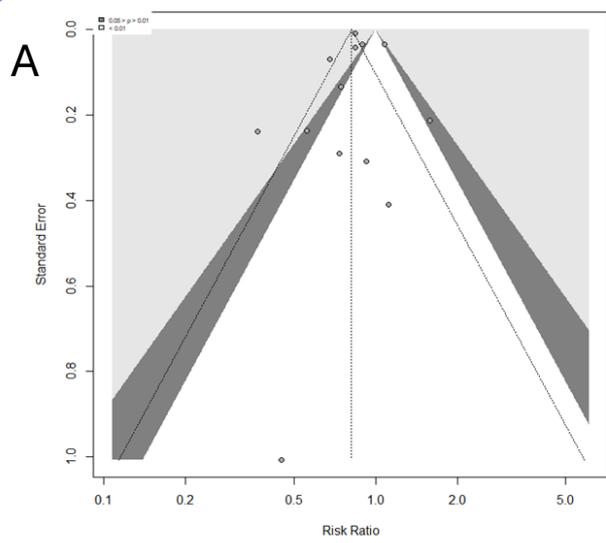
Supplementary Figure 4. [A] Meta-regression showing how admission oxygen saturation changes with age;  $n = 10$  studies (11911 patients), slope coefficient  $-0.024$ , 95%CI  $-0.058$  to  $0.0096$ ,  $p = 0.16$ . [B] Forest plot of the mean difference in oxygen saturation between older and younger patients;  $n = 5$  studies, MD  $-1\%$ ,  $-2$  to  $0\%$ ,  $I^2 = 95.4\%$ .



Supplementary Figure 5. [A] Forest plot of the risk ratio of tachycardia in older and younger patients with bacteraemia;  $n = 3$  studies, RR  $0.77$ ,  $0.57$  to  $1.03$ ,  $I^2 = 52.3\%$ . [B] Forest plot of the risk ratio of fever in older and younger patients with bacteraemia;  $n = 4$  studies, RR  $0.95$ ,  $0.91$  to  $0.98$ ,  $I^2 = 0\%$ . [C] Forest plot of the risk ratio of hypothermia in older and younger patients with bacteraemia;  $n = 3$  studies, RR  $0.61$ ,  $0.17$  to  $2.25$ ,  $I^2 = 60.1\%$ .

**A**

Supplementary Figure 6. [A] Forest plot of the risk ratio of tachypnoea in older and younger patients with respiratory tract infections; n = 5 studies, RR 1.52, 1.09 to 2.12,  $I^2 = 75.1\%$ .



Supplementary Figure 7. Funnel plots for studies reporting [A] HR as dichotomous outcome, [B] HR as continuous outcome, [C] Temp as dichotomous outcome (fever), [D] Temp as continuous outcome, [E] RR as dichotomous outcome, [F] RR as continuous outcome



## Appendix B: Full Search Strategy

### Search strategy for MEDLINE

Medline (Ovid MEDLINE® Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE®) 1946 to present

| #  | Search  | Results |
|----|---|---------|
| 1  | vital signs/ or blood pressure/ or body temperature/ or heart rate/ or respiratory rate/  | 439176  |
| 2  | Oximetry/   | 14418   |
| 3  | consciousness disorders/ or unconsciousness/  | 8146    |
| 4  | Fever/  | 43208   |
| 5  | ("vital sign*" or "heart rate*" or "respiratory rate*" or "blood pressure*" or "body temperature*" or fever* or febrile or afebrile or "oxygen saturation*" or consciousness or "mental status").ab,ti. | 809248  |
| 6  | bacterial infections/ or bacteremia/ or endocarditis, bacterial/ or gram-negative bacterial infections/ or gram-positive bacterial infections/ or pneumonia, bacterial/ or skin diseases, bacterial/    | 155733  |
| 7  | sepsis/ or shock, septic/   | 91111   |
| 8  | Urinary Tract Infections/   | 42646   |
| 9  | Osteomyelitis/  | 22078   |
| 10 | Arthritis, Infectious/  | 12146   |
| 11 | intraabdominal infections/ or appendicitis/ or peritonitis/   | 47196   |
| 12 | Cholecystitis/  | 13132   |
| 13 | Gastroenteritis/  | 16571   |
| 14 | Diverticulitis/   | 3530    |
| 15 | Cellulitis/   | 8073    |
| 16 | Pyelonephritis/   | 14498   |
| 17 | Empyema/  | 4391    |
| 18 | Fasciitis, Necrotizing/   | 3304    |
| 19 | Meningitis, Bacterial/  | 7749    |

|    |  |         |
|----|--|---------|
| 20 | (sepsis or septic*).ab,ti.   | 176886  |
| 21 | (bacteremia* or bacteraemia* or septicemia* or septicaemia*).ab,ti.  | 53968   |
| 22 | (blood* adj2 infection*).ab,ti.  | 21237   |
| 23 | (bacterial adj2 infection*).ab,ti.   | 57087   |
| 24 | cellulitis.ab,ti.  | 10420   |
| 25 | ((((respiratory or chest) adj2 infection*) or (bacterial adj2 pneumonia*))).ab,ti.   | 62418   |
| 26 | ((((intraabdom* or intra-abdom* or abdom*) adj2 infection*) or appendicitis or diverticulitis or cholecystitis).ab,ti.                             | 49082   |
| 27 | ((urin* adj2 infection*) or pyelonephritis).ab,ti.   | 63718   |
| 28 | (bacterial adj2 meningitis).ab,ti.   | 8219    |
| 29 | (bacterial adj2 endocarditis).ab,ti.   | 5248    |
| 30 | (osteomyelitis or septic arthritis).ab,ti.   | 30472   |
| 31 | 1 or 2 or 3 or 4 or 5  | 1040285 |
| 32 | 6 or 7 or 8 or 9 or 10 or 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     | 670187  |
| 33 | 31 and 32  | 51728   |
| 34 | Age Factors/   | 472193  |
| 35 | "Aged, 80 and over"/ or Aged/  | 3451273 |
| 36 | Aging/   | 250314  |
| 37 | Geriatrics/  | 31359   |
| 38 | (aged or geriatric* or elder* or older or ageing or aging or veteran* or septuagenarian* or octogenarian* or nonagenarian* or centenarian*).m_titl | 460466  |
| 39 | 34 or 35 or 36 or 37 or 38   | 4023992 |
| 40 | 33 and 39  | 11843   |
| 41 | limit 40 to animals  | 274     |
| 42 | 40 not 41  | 11569   |
| 43 | "case report* ".m_titl.  | 326807  |
| 44 | Case Reports/  | 2340387 |
| 45 | 43 or 44   | 2393510 |
| 46 | 42 not 45  | 9011    |

|    |  |         |
|----|--|---------|
| 47 | child/ or infant/ or infant, newborn/  | 2643647 |
| 48 | Fetus/   | 82959   |
| 49 | Child, Preschool/  | 988951  |
| 50 | (paediatric* or pediatric* or child* or boy* or girl* or infant* or neonat* or newborn*).m_titl. | 1482670 |
| 51 | 47 or 48 or 49 or 50   | 3136310 |
| 52 | 46 not 51  | 7187    |
| 53 | limit 52 to english language   | 6205    |

### Search strategy for EMBASE

1974 to present

| #  | Search  | Results |
|----|---|---------|
| 1  | *vital sign/  | 1923    |
| 2  | *blood pressure/  | 81247   |
| 3  | *body temperature/  | 11758   |
| 4  | *heart rate/  | 49545   |
| 5  | *breathing rate/  | 4355    |
| 6  | *pulse oximetry/ or *oximetry/  | 6609    |
| 7  | *consciousness/ or *"altered state of consciousness"/ or *consciousness level/ or *consciousness disorder/  | 10850   |
| 8  | *unconsciousness/   | 2160    |
| 9  | ("vital sign*" or "heart rate*" or "respiratory rate*" or "blood pressure*" or "body temperature*" or fever* or febrile or afebrile or "oxygen saturation*" or consciousness or "mental status").ab,ti. | 1165800 |
| 10 | 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9   | 1215846 |
| 11 | *bacterial infection/   | 61934   |

|    |  |        |
|----|--|--------|
| 12 | *bacteremia/   | 17294  |
| 13 | *bacterial endocarditis/   | 19830  |
| 14 | *bacterial pneumonia/  | 6068   |
| 15 | *sepsis/   | 61539  |
| 16 | *septic shock/   | 22111  |
| 17 | *urinary tract infection/  | 40002  |
| 18 | *osteomyelitis/  | 14937  |
| 19 | *bacterial arthritis/  | 5133   |
| 20 | *abdominal infection/  | 2267   |
| 21 | *appendicitis/ or *acute appendicitis/   | 16456  |
| 22 | *bacterial peritonitis/  | 3473   |
| 23 | *cholecystitis/ or *acute cholecystitis/   | 10868  |
| 24 | *acute gastroenteritis/ or *gastroenteritis/   | 11179  |
| 25 | *diverticulitis/   | 3742   |
| 26 | *cellulitis/   | 4929   |
| 27 | *pyelonephritis/ or *acute pyelonephritis/   | 8878   |
| 28 | *empyema/  | 3772   |
| 29 | *necrotizing fasciitis/  | 3914   |
| 30 | *bacterial meningitis/   | 10923  |
| 31 | (sepsis or septic*).ab,ti.   | 264600 |
| 32 | (bacteremia* or bacteraemia* or septicemia* or septicaemia*).ab,ti.  | 70881  |
| 33 | (blood* adj2 infection*).ab,ti.  | 32211  |
| 34 | (bacterial adj2 infection*).ab,ti.   | 78456  |
| 35 | cellulitis.ab,ti.  | 15612  |
| 36 | ((respiratory or chest) adj2 infection*) or (bacterial adj2 pneumonia*).ab,ti.                                       | 94907  |
| 37 | ((intraabdom* or intra-abdom* or abdom*) adj2 infection*) or appendicitis or diverticulitis or cholecystitis).ab,ti. | 62022  |

|    |  |         |
|----|--|---------|
| 38 | ((urin* adj2 infection*) or pyelonephritis).ab,ti.   | 93343   |
| 39 | (bacterial adj2 meningitis).ab,ti.   | 10333   |
| 40 | (bacterial adj2 endocarditis).ab,ti.   | 4674    |
| 41 | (osteomyelitis or septic arthritis).ab,ti.   | 36318   |
| 42 | 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 or 41 | 771402  |
| 43 | 10 and 42  | 76772   |
| 44 | age/   | 587564  |
| 45 | aged/  | 3589886 |
| 46 | aging/   | 314680  |
| 47 | geriatrics/  | 33957   |
| 48 | (aged or geriatric* or elder* or older or ageing or aging or veteran* or septuagenarian* or octogenarian* or nonagenarian* or centenarian*).m_titl.                                    | 581574  |
| 49 | 44 or 45 or 46 or 47 or 48   | 4320400 |
| 50 | 43 and 49  | 14585   |
| 51 | limit 50 to animals  | 58      |
| 52 | 50 not 51  | 14527   |
| 53 | "case report* ".m_titl.  | 404093  |
| 54 | case report/   | 2913725 |
| 55 | 53 or 54   | 2942608 |
| 56 | 52 not 55  | 9569    |
| 57 | child/   | 2105718 |
| 58 | infant/  | 697896  |
| 59 | fetus/   | 214751  |
| 60 | (paediatric* or pediatric* or child* or boy* or girl* or infant* or neonat* or newborn*).m_titl.   | 1766639 |
| 61 | 57 or 58 or 59 or 60   | 3224298 |
| 62 | 56 not 61  | 7954    |
| 63 | limit 62 to english language   | 7199    |
| 64 | limit 63 to conference abstract  | 1623    |
| 65 | 63 not 64  | 5576    |

**Search strategy for CINAHL**

| #  | Search   | Results |
|----|--|---------|
| 1  | MH vital signs   | 3263    |
| 2  | MH blood pressure  | 46211   |
| 3  | MH body temperature  | 4721    |
| 4  | MH heart rate  | 33243   |
| 5  | MH respiratory rate  | 2414    |
| 6  | MH pulse oximetry  | 2438    |
| 7  | MH consciousness   | 3739    |
| 8  | MH consciousness disorders   | 1119    |
| 9  | TI ("vital sign*" or "heart rate*" or "respiratory rate*" or "blood pressure*" or "body temperature*" or fever* or febrile or afebrile or "oxygen saturation*" or consciousness or "mental status") OR AB ("vital sign*" or "heart rate*" or "respiratory rate*" or "blood pressure*" or "body temperature*" or fever* or febrile or afebrile or "oxygen saturation*" or consciousness or "mental status") | 182239  |
| 10 | S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9   | 217578  |
| 11 | MH bacterial infection   | 0       |
| 12 | MH bacterial infection   | 845     |
| 13 | MH bacteremia  | 6405    |
| 14 | MH endocarditis  | 2314    |
| 15 | MH bacterial pneumonia   | 0       |
| 16 | MH pneumonia   | 12585   |
| 17 | MH sepsis or septic or severe sepsis or septic shock   | 31198   |
| 18 | MH urinary tract infection   | 0       |

|    |  |        |
|----|--|--------|
| 19 | MH pyelonephritis  | 1216   |
| 20 | MH osteomyelitis   | 4282   |
| 21 | MH septic arthritis  | 0      |
| 22 | MH appendicitis  | 3984   |
| 23 | MH cholecystitis   | 1658   |
| 24 | MH diverticulitis  | 867    |
| 25 | MH gastroenteritis   | 3074   |
| 26 | MH cellulitis  | 1943   |
| 27 | MH empyema   | 908    |
| 28 | MH necrotizing fasciitis   | 0      |
| 29 | MH meningitis  | 3188   |
| 30 | TI (sepsis or septic*) OR AB (sepsis or septic*)   | 38865  |
| 31 | TI ("urinary tract infection*") OR AB ("urinary tract infection*")   | 11404  |
| 32 | TI (bacteremia* or bacteraemia* or septicemia* or septicaemia*) OR AB (bacteremia* or bacteraemia* or septicemia* or septicaemia*)   | 8314   |
| 33 | TI (meningitis) OR AB (meningitis)   | 8357   |
| 34 | TI (osteomyelitis) OR AB (osteomyelitis)   | 4941   |
| 35 | TI ("infectious arthritis" or "septic arthritis") OR AB ("infectious arthritis" or "septic arthritis")   | 1600   |
| 36 | TI (endocarditis) OR AB (endocarditis)   | 6557   |
| 37 | TI (appendicitis OR cholecystitis OR diverticulitis) OR AB (appendicitis OR cholecystitis OR diverticulitis)   | 7627   |
| 38 | TI (cellulitis) OR AB (cellulitis)   | 2552   |
| 39 | TI (pneumonia) OR AB (pneumonia)   | 34001  |
| 40 | TI (pyelonephritis) OR AB (pyelonephritis)   | 1497   |
| 41 | S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 | 131265 |
| 42 | S10 AND S41  | 11722  |
| 43 | MH aged  | 912862 |

|    |  |         |
|----|--|---------|
| 44 | MH aging   | 54759   |
| 45 | MH geriatric   | 0       |
| 46 | TI (aged or geriatric* or elder* or older or ageing or aging or veteran* or septuagenarian* or octogenarian* or nonagenarian* or centenarian*) | 233636  |
| 47 | S43 OR S44 OR S45 OR S46   | 1017207 |
| 48 | S42 AND S47  | 2536    |
| 49 | TI ((paediatric* or pediatric* or child* or boy* or girl* or infant* or neonat* or newborn*))  | 535064  |
| 50 | S48 NOT S49  | 2476    |
| 51 | TI ("case report* ")   | 71100   |
| 52 | S50 NOT S51  | 2324    |
| 53 | S50 NOT S51, limiters – English Language   | 2292    |

## Appendix C: Quality Assessment Tool

Risk of bias was assessed using an adapted version of the QUADAS (Quality Assessment of Diagnostic Accuracy Studies)-2 tool. It assesses four domains: Patient Selection, Index Test, Reference Standard and Flow and Timing. Each of these domains was scored separately as low risk of bias, high risk of bias or unclear risk of bias (insufficient information to make a judgement).

### Domain 1: Patient Selection

1. Was a consecutive or random sample of patients enrolled?

Studies should describe their method of patient enrolment. If a random sample of patients was used, the method of randomisation should be stated. Convenience sampling or arbitrary recruitment introduces a high risk of bias.

2. Did the study avoid inappropriate exclusions?

Exclusion criteria should be clearly justified.

3. Was the sample size justified?

This prompt only applies to prospective studies

4. Are the characteristics of the study population presented in a table or clearly described?

#### Could the selection of patients have introduced bias?

Low risk of bias: Q1, Q2, Q3, Q4 all answered "yes"

High risk of bias: Any of Q1, Q2, Q3, Q4 answered "no"

Unclear risk of bias: insufficient data reported to permit a judgement

### Domain 2: Index test(s)

1. Were the measurements taken by a healthcare professional or trained personnel?

All studies included in the systematic review are in hospitalised patients; therefore, assume vital signs taken by a healthcare professional.

2. Is a description of the measurement technique included?

The study should either describe sufficient and unambiguous details of the measurement techniques used for vital sign recording; or should state where the measurement was obtained (eg. Patient notes).

3. If a threshold was used, was it pre-specified?

Thresholds for study definitions of tachycardia, bradycardia, hypertension, hypotension, tachypnoea, hypoxia, pyrexia and reduced level of consciousness should be pre-specified.

Not relevant for continuous outcomes.

#### Could the conduct or interpretation of the index test have introduced bias?

Low risk of bias: Q1, Q2, Q3 all answered "yes"

High risk of bias: Any of Q1, Q2, Q3 answered "no"

Unclear risk of bias: insufficient data reported to permit a judgement

### Domain 3: Reference standard

1. Are the criteria used likely to correctly classify the target condition?

#### Could the reference standard, its conduct, or its interpretation have introduced bias?

Low risk of bias: Q1 answered "yes"

High risk of bias: Q1 answered "no"

Unclear risk of bias: insufficient data reported to permit a judgement

**Domain 4: Flow and Timing**

1. Was the study a prospective study?
2. Was there an appropriate interval between vital sign(s) being taken and diagnosis of bacterial infection?
3. Were all patients included in the analysis?

**Could the patient flow have introduced bias?**

Low risk of bias: Q1, Q2, Q3 all answered "yes"

High risk of bias: Any of Q1, Q2, Q3 answered "no"

Unclear risk of bias: insufficient data reported to permit a judgement

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**Appendix D: Characteristics of Individual Included Studies**

| Author       | Year | Citation | Country        | Design                        | Infection      | Infection Definition               | Participants | % Female | Age   |        |       |       |       |
|--------------|------|----------|----------------|-------------------------------|----------------|------------------------------------|--------------|----------|-------|--------|-------|-------|-------|
|              |      |          |                |                               |                |                                    |              |          | mean  | median | sd    | lower | upper |
| Alpay        | 2018 | [1]      | Turkey         | Retrospective cohort          | UTI            | Positive microbiology or pathology | 140          | 53.6     | 78.50 | -      | -     | 65    | 98    |
| Amadoru      | 2017 | [2]      | Australia      | Retrospective cohort          | Spinal         | Clinical diagnosis                 | 53           | 32.1     | 64.70 | -      | -     | 19    | 92    |
| Applefeld    | 1974 | [3]      | United States  | Retrospective cohort          | Endocarditis   | Clinical diagnosis                 | 29           | -        | -     | -      | -     | -     | -     |
| Artero (1)   | 2016 | [4]      | Spain          | Retrospective observational   | UTI            | Positive microbiology or pathology | 196          | 50.5     | 81.74 | -      | 6.62  | -     | -     |
| Artero (2)   | 2016 | [4]      | Spain          | Retrospective observational   | Bacteraemia    | Positive microbiology or pathology | 137          | 62       | 81.52 | -      | 7.07  | -     | -     |
| Barsic       | 1992 | [5]      | Croatia        | Retrospective cohort          | Meningitis     | Positive microbiology or pathology | 70           | 27.1     | -     | -      | -     | 8     | 88    |
| Boonmee      | 2020 | [6]      | Thailand       | Retrospective cohort          | Sepsis         | Clinical diagnosis                 | 1180         | 52.9     | -     | -      | -     | -     | -     |
| Burns        | 1991 | [7]      | United Kingdom | Retrospective cohort          | Endocarditis   | Clinical diagnostic coding         | 19           | 42.1     | 74.00 | -      | -     | 65    | 84    |
| Cabellos     | 2009 | [8]      | Spain          | Prospective cohort            | Meningitis     | Clinical diagnosis                 | 185          | 58.9     | 73.00 | -      | 6.00  | -     | -     |
| Cataudella   | 2017 | [9]      | Italy          | Prospective cohort            | CAP            | Clinical diagnosis                 | 195          | 38.5     | 80.30 | -      | 7.50  | -     | -     |
| Caterino     | 2019 | [10]     | United States  | Prospective observational     | Infection      | Clinical diagnosis                 | 77           | 57       | 74.00 | -      | 7.60  | -     | -     |
| Caterino (1) | 2009 | [11]     | United States  | Prospective cohort            | Infection      | Clinical diagnosis                 | 935          | 57       | 79.10 | -      | 8.30  | -     | -     |
| Caterino (2) | 2009 | [11]     | United States  | Prospective cohort            | Infection      | Clinical diagnosis                 | 2016         | 55.6     | 79.20 | -      | 8.50  | -     | -     |
| Caterino     | 2012 | [12]     | United States  | Prospective cohort            | Infection      | Clinical diagnosis                 | 105          | 53.3     | -     | -      | -     | -     | -     |
| Celikhisar   | 2020 | [13]     | Turkey         | Retrospective cohort          | CAP            | Clinical diagnosis                 | 86           | 72.1     | 73.30 | -      | 19.30 | -     | -     |
| Chassagne    | 1996 | [14]     | France         | Prospective cohort            | Bacteraemia    | Positive microbiology or pathology | 105          | 49.5     | 69.30 | -      | -     | 17    | 96    |
| Ciesielski   | 2010 | [15]     | United States  | Retrospective cohort          | UTI            | Positive microbiology or pathology | 270          | 64       | 76.16 | -      | 12.80 | -     | -     |
| Covino       | 2021 | [16]     | Italy          | Retrospective cohort          | Diverticulitis | Clinical diagnostic coding         | 1139         | 52       | -     | 67.0   | -     | -     | -     |
| Domingo      | 2013 | [17]     | Spain          | Prospective observational     | Meningitis     | Positive microbiology or pathology | 635          | 52.1     | -     | -      | -     | -     | -     |
| Dubost       | 2018 | [18]     | France         | Retrospective cohort          | Spinal         | Clinical diagnosis                 | 152          | 33       | -     | -      | -     | -     | -     |
| Elangovan    | 1996 | [19]     | United States  | Retrospective cross-sectional | Appendicitis   | Positive microbiology or pathology | 74           | 40       | 68.90 | -      | -     | -     | -     |
| Erdem        | 2010 | [20]     | Turkey         | Retrospective cohort          | Meningitis     | Clinical diagnosis                 | 159          | 43.4     | 63.00 | -      | 9.00  | -     | -     |
| Esposito     | 1984 | [21]     | United States  | Prospective cohort            | Bacteraemia    | Positive microbiology or pathology | 38           | 60.5     | 61.00 | -      | -     | -     | -     |
| Ewig (1)     | 2012 | [22]     | Germany        | Prospective cohort            | NHAP           | Clinical diagnosis                 | 518          | 57.3     | -     | 83.3   | -     | -     | -     |

| Author             | Year | Citation | Country       | Design                        | Infection      | Infection Definition               | Participants | % Female | Age   |        |       |       |       |
|--------------------|------|----------|---------------|-------------------------------|----------------|------------------------------------|--------------|----------|-------|--------|-------|-------|-------|
|                    |      |          |               |                               |                |                                    |              |          | mean  | median | sd    | lower | upper |
| Ewig (2)           | 2012 | [22]     | Germany       | Prospective cohort            | CAP            | Clinical diagnosis                 | 2569         | 37.4     | -     | 76.1   | -     | -     | -     |
| Ewig               | 1999 | [23]     | Germany       | Prospective cohort            | CAP            | Clinical diagnosis                 | 168          | 58.9     | 78.00 | -      | 8.00  | -     | -     |
| Fernandez-Sabe     | 2003 | [24]     | Spain         | Prospective cohort            | CAP            | Clinical diagnosis                 | 1474         | 30.1     | -     | -      | -     | -     | -     |
| Finkelstein        | 1983 | [25]     | United States | Retrospective cohort          | Bacteraemia    | Positive microbiology or pathology | 187          | -        | -     | -      | -     | 20    | 93    |
| Fontanarosa        | 1992 | [26]     | United States | Retrospective cross-sectional | Bacteraemia    | Positive microbiology or pathology | 79           | 57       | 80.60 | -      | -     | 68    | 94    |
| Garcia-Ordenez     | 2001 | [27]     | Spain         | Retrospective cohort          | CAP            | Clinical diagnosis                 | 343          | 42       | 76.30 | -      | 7.30  | -     | -     |
| Golcuk             | 2015 | [28]     | Turkey        | Prospective cross-sectional   | CAP            | Clinical diagnosis                 | 100          | 40       | 77.30 | -      | 7.60  | -     | -     |
| Gopal              | 2015 | [29]     | India         | Retrospective cohort          | UTI            | Clinical diagnosis                 | 100          | 47       | 71.50 | -      | 16.30 | -     | -     |
| Guirgis            | 2018 | [30]     | United States | Prospective observational     | Sepsis         | Clinical diagnosis                 | 10           | 50       | 77.00 | -      | 2.00  | -     | -     |
| Hernandez          | 2015 | [31]     | Spain         | Prospective cohort            | Bacteraemia    | Positive microbiology or pathology | 2605         | 47.1     | 78.06 | -      | 7.71  | -     | -     |
| Horattas           | 1990 | [32]     | United States | Retrospective cohort          | Appendicitis   | Positive microbiology or pathology | 96           | 49       | -     | -      | -     | -     | -     |
| Horesh             | 2016 | [33]     | Israel        | Retrospective cross-sectional | Diverticulitis | Not stated                         | 636          | 56.4     | -     | 60.0   | -     | 20    | 98    |
| Hsien-LingChou     | 2016 | [34]     | Taiwan        | Retrospective cohort          | Bacteraemia    | Clinical diagnostic coding         | 20192        | 45.7     | 62.00 | -      | 18.60 | -     | -     |
| Jung               | 2017 | [35]     | South Korea   | Retrospective cohort          | Appendicitis   | Clinical diagnostic coding         | 103          | 49.5     | -     | 72.0   | -     | 65    | 89    |
| Kaser              | 2013 | [36]     | Switzerland   | Retrospective cohort          | Diverticulitis | Clinical diagnosis                 | 282          | 47.5     | 66.70 | -      | 10.80 | -     | -     |
| Kijsirichareanchai | 2015 | [37]     | United States | Retrospective cohort          | Diverticulitis | Clinical diagnostic coding         | 94           | 51.1     | 45.50 | -      | 15.30 | -     | -     |
| Kim                | 2013 | [38]     | South Korea   | Retrospective cohort          | NHAP           | Clinical diagnosis                 | 73           | 53.4     | 79.80 | -      | 9.03  | -     | -     |
| Kim                | 2015 | [39]     | South Korea   | Retrospective cohort          | Sepsis         | Clinical diagnostic coding         | 458          | 47.2     | -     | 78.0   | -     | -     | -     |
| Klapdor            | 2012 | [40]     | Europe        | Prospective cohort            | CAP            | Clinical diagnosis                 | 7803         | 44.4     | 60.90 | -      | 18.50 | -     | -     |
| Ko                 | 2019 | [41]     | Netherlands   | Prospective cohort            | Infection      | Clinical diagnosis                 | 2659         | 43       | 62.10 | -      | 17.10 | -     | -     |
| Laborde            | 2021 | [42]     | France        | Retrospective cohort          | Bacteraemia    | Positive microbiology or pathology | 105          | 61.9     | 85.30 | -      | 5.90  | -     | -     |
| Lee                | 2007 | [43]     | Taiwan        | Prospective cohort            | Bacteraemia    | Positive microbiology or pathology | 890          | 48.5     | -     | -      | -     | -     | -     |
| Lee                | 2013 | [44]     | South Korea   | Prospective cohort            | Sepsis         | Clinical diagnosis                 | 401          | 50.1     | -     | 74.0   | -     | -     | -     |
| Lee                | 2020 | [45]     | South Korea   | Retrospective cohort          | Cholecystitis  | Clinical diagnosis                 | 303          | 46.9     | -     | 74.0   | -     | -     | -     |

| Author         | Year | Citation | Country        | Design                        | Infection       | Infection Definition               | Participants | % Female | Age   |        |       |       |       |
|----------------|------|----------|----------------|-------------------------------|-----------------|------------------------------------|--------------|----------|-------|--------|-------|-------|-------|
|                |      |          |                |                               |                 |                                    |              |          | mean  | median | sd    | lower | upper |
| Lee            | 2020 | [46]     | South Korea    | Retrospective cohort          | Bacteraemia     | Positive microbiology or pathology | 186          | 90.3     | -     | 75.0   | -     | -     | -     |
| Liu            | 2010 | [47]     | Australia      | Prospective cohort            | Infection       | Clinical diagnosis                 | 34           | 62.5     | 85.40 | -      | -     | 71    | 98    |
| Luna           | 2016 | [48]     | International  | Retrospective cohort          | CAP             | Clinical diagnosis                 | 6205         | 38.8     | 66.50 | -      | 17.90 | -     | -     |
| Ma             | 2011 | [49]     | China          | Prospective cohort            | CAP             | Clinical diagnosis                 | 488          | 42.2     | 81.00 | -      | 7.90  | -     | -     |
| Marinella      | 2000 | [50]     | United States  | Retrospective cohort          | Diverticulitis  | Clinical diagnosis                 | 21           | 19       | 34.10 | -      | 5.90  | -     | -     |
| Meyers         | 1989 | [51]     | United States  | Retrospective cohort          | Bacteraemia     | Positive microbiology or pathology | 100          | 63       | -     | -      | -     | -     | -     |
| Myint          | 2005 | [52]     | United Kingdom | Prospective cohort            | CAP             | Clinical diagnosis                 | 100          | 44       | -     | 81.5   | -     | 65    | 96    |
| Mylotte        | 2002 | [53]     | United States  | Retrospective cohort          | Bacteraemia     | Positive microbiology or pathology | 169          | 64.5     | 82.70 | -      | 8.10  | -     | -     |
| Parker         | 1997 | [54]     | United States  | Retrospective cross-sectional | Cholecystitis   | Clinical diagnosis                 | 168          | 48.2     | 74.00 | -      | -     | 65    | 93    |
| Potts          | 1999 | [55]     | United States  | Retrospective cross-sectional | Intra-abdominal | Clinical diagnosis                 | 117          | 52.1     | 85.50 | -      | -     | 80    | 97    |
| Rasmussen      | 1992 | [56]     | Denmark        | Retrospective cohort          | Meningitis      | Clinical diagnosis                 | 48           | 64.6     | -     | 69.0   | -     | -     | -     |
| Raz            | 1999 | [57]     | Israel         | Retrospective cohort          | UTI             | Positive microbiology or pathology | 201          | 100      | 61.00 | -      | 22.10 | -     | -     |
| Riquelme       | 1996 | [58][59] | Spain          | Prospective cohort            | CAP             | Clinical diagnosis                 | 101          | 33.7     | 78.00 | -      | 8.00  | -     | -     |
| Robbins        | 1980 | [60]     | United States  | Retrospective cohort          | Endocarditis    | Clinical diagnostic coding         | 56           | 36       | 71.70 | -      | -     | 65    | 92    |
| Ruiz           | 2014 | [61]     | Spain          | Prospective cohort            | Bacteraemia     | Positive microbiology or pathology | 399          | 32.8     | -     | -      | -     | -     | -     |
| Ryden          | 1983 | [62]     | Sweden         | Retrospective cohort          | Appendicitis    | Clinical diagnosis                 | 672          | -        | -     | -      | -     | -     | -     |
| Salahuddin     | 2012 | [63]     | Pakistan       | Prospective observational     | Appendicitis    | Positive microbiology or pathology | 36           | 44       | 65.50 | -      | 4.20  | -     | -     |
| Sasaki         | 2020 | [64]     | Japan          | Retrospective cohort          | Diverticulitis  | Clinical diagnosis                 | 237          | 34.2     | 44.80 | -      | -     | -     | -     |
| Sheu           | 2007 | [65]     | Taiwan         | Retrospective cohort          | Appendicitis    | Clinical diagnostic coding         | 601          | 52       | 69.90 | -      | 7.50  | -     | -     |
| Shimazui       | 2020 | [66]     | Japan          | Retrospective cohort          | Sepsis          | Clinical diagnosis                 | 1148         | 39.6     | -     | -      | -     | -     | -     |
| Shimoni        | 2021 | [67]     | Israel         | Retrospective cross-sectional | Bacteraemia     | Positive microbiology or pathology | 222          | 58.6     | 84.00 | -      | 8.00  | -     | -     |
| Singler        | 2013 | [68]     | Germany        | Prospective observational     | Infection       | Clinical diagnosis                 | 105          | 64.8     | 83.60 | -      | 4.70  | -     | -     |
| Sirikurnpiboon | 2015 | [69]     | Thailand       | Retrospective cohort          | Appendicitis    | Positive microbiology or pathology | 206          | 62.1     | 68.98 | -      | 7.08  | -     | -     |

| Author           | Year | Citation | Country        | Design                        | Infection        | Infection Definition               | Participants | % Female | Age   |        |       |       |       |
|------------------|------|----------|----------------|-------------------------------|------------------|------------------------------------|--------------|----------|-------|--------|-------|-------|-------|
|                  |      |          |                |                               |                  |                                    |              |          | mean  | median | sd    | lower | upper |
| Smithson         | 2019 | [70]     | Spain          | Ambispective observational    | UTI              | Positive microbiology or pathology | 552          | 0        | 66.10 | -      | 16.70 | -     | -     |
| Sunden-Cullberg  | 2017 | [71]     | Sweden         | Prospective cohort            | Sepsis           | Clinical diagnostic coding         | 2225         | 44       | -     | 68.0   | -     | -     | -     |
| Talebi-Taher     | 2010 | [72]     | Iran           | Prospective cohort            | CAP              | Clinical diagnosis                 | 183          | -        | 59.00 | -      | 24.00 | -     | -     |
| Taniguchi        | 2013 | [73]     | Japan          | Retrospective cross-sectional | Bacteraemia      | Positive microbiology or pathology | 366          | 63.4     | 73.20 | -      | 20.30 | -     | -     |
| Tantarattanapong | 2018 | [74]     | Thailand       | Retrospective cohort          | Appendicitis     | Positive microbiology or pathology | 223          | 55.6     | -     | 68.0   | -     | -     | -     |
| Tantarattanapng  | 2021 | [75]     | Thailand       | Retrospective cross-sectional | Sepsis           | Clinical diagnosis                 | 600          | 50.8     | -     | 78.0   | -     | -     | -     |
| Terpenning       | 1987 | [76]     | United States  | Retrospective cohort          | Endocarditis     | Positive microbiology or pathology | 154          | 31.2     | -     | -      | -     | -     | -     |
| Thiem            | 2009 | [77]     | Germany        | Retrospective cohort          | CAP              | Clinical diagnostic coding         | 391          | 51.2     | 80.00 | -      | 8.00  | -     | -     |
| Tiruvoipati      | 2010 | [78]     | Australia      | Retrospective cohort          | Sepsis           | Clinical diagnosis                 | 175          | 46.9     | -     | -      | -     | -     | -     |
| Tsai             | 2005 | [79]     | Taiwan         | Retrospective cohort          | Empyema          | Clinical diagnosis                 | 132          | 17       | -     | 58.5   | -     | 18    | 89    |
| Valencia (1)     | 2017 | [80]     | Colombia       | Prospective cohort            | Sepsis           | Clinical diagnostic coding         | 765          | 50.7     | 51.62 | -      | 19.96 | -     | -     |
| Valencia (2)     | 2017 | [80]     | Colombia       | Prospective cohort            | Sepsis           | Clinical diagnostic coding         | 1846         | 52.3     | 55.86 | -      | 20.90 | -     | -     |
| Vincent          | 1990 | [81]     | Canada         | Retrospective cohort          | Septic arthritis | Clinical diagnosis                 | 21           | 47.6     | 72.30 | -      | -     | 60    | 92    |
| Warmerdam        | 2018 | [82]     | Netherlands    | Prospective cohort            | Infection        | Clinical diagnosis                 | 833          | 37.6     | 78.40 | -      | 6.30  | -     | -     |
| Wasserman        | 1989 | [83]     | United States  | Prospective cross-sectional   | Infection        | Positive microbiology or pathology | 33           | 68       | 82.00 | -      | -     | -     | -     |
| Weisfelt         | 2006 | [84]     | Netherlands    | Prospective cohort            | Meningitis       | Positive microbiology or pathology | 696          | 50.4     | 50.20 | -      | 19.96 | -     | -     |
| Wester           | 2013 | [85]     | Norway         | Retrospective cohort          | Bacteraemia      | Positive microbiology or pathology | 680          | 57.5     | -     | 75.0   | -     | -     | -     |
| Yahav            | 2015 | [86]     | Israel         | Prospective cross-sectional   | Bacteraemia      | Clinical diagnosis                 | 4308         | -        | -     | -      | -     | -     | -     |
| Yo               | 2016 | [87]     | Taiwan         | Retrospective cohort          | Bacteraemia      | Positive microbiology or pathology | 937          | 47.9     | 63.00 | -      | 17.44 | -     | -     |
| ZoeXiaozhuZhang  | 2018 | [88]     | Singapore      | Retrospective cohort          | CAP              | Clinical diagnosis                 | 1902         | 44.5     | -     | 73.0   | -     | -     | -     |
| Andersson        | 1978 | [89]     | Sweden         | Retrospective cohort          | Appendicitis     | Not stated                         | 68           | 48.5     | 68.54 | -      | -     | 60    | 83    |
| Barkham          | 1996 | [90]     | United Kingdom | Retrospective cross-sectional | Bacteraemia      | Positive microbiology or pathology | 104          | 71.2     | -     | -      | -     | -     | -     |
| CAP-ChinaNetwork | 2020 | [91]     | China          | Retrospective cohort          | CAP              | Not stated                         | 3011         | 45.5     | 77.39 | -      | 7.41  | -     | -     |

| Author       | Year | Citation | Country        | Design                        | Infection        | Infection Definition               | Participants | % Female | Age   |        |       |       |       |
|--------------|------|----------|----------------|-------------------------------|------------------|------------------------------------|--------------|----------|-------|--------|-------|-------|-------|
|              |      |          |                |                               |                  |                                    |              |          | mean  | median | sd    | lower | upper |
| Chen         | 2010 | [92]     | Taiwan         | Prospective observational     | CAP              | Clinical diagnosis                 | 987          | 38.1     | 68.00 | -      | 19.30 | -     | -     |
| Chodak       | 1981 | [93]     | United States  | Retrospective cohort          | Diverticulitis   | Clinical diagnosis                 | 37           | 10.8     | -     | -      | -     | 21    | 40    |
| Choi         | 2022 | [94]     | United States  | Prospective cohort            | UTI              | Clinical diagnosis                 | 61           | 59       | -     | 81.1   | -     | -     | -     |
| Cilloniz (1) | 2023 | [95]     | Spain          | Prospective cohort            | CAP              | Clinical diagnosis                 | 1802         | 42       | -     | 84.0   | -     | -     | -     |
| Cilloniz (2) | 2023 | [95]     | Spain          | Prospective cohort            | CAP              | Clinical diagnosis                 | 204          | 32       | -     | 83.0   | -     | -     | -     |
| Conte        | 1999 | [96]     | United States  | Retrospective cohort          | CAP              | Clinical diagnostic coding         | 2356         | 51.5     | -     | -      | -     | -     | -     |
| Cooper       | 1986 | [97]     | United Kingdom | Retrospective cohort          | Septic arthritis | Clinical diagnosis                 | 21           | 42.9     | 73.80 | -      | 7.00  | -     | -     |
| Cooper       | 1994 | [98]     | United States  | Retrospective cohort          | Intra-abdominal  | Positive microbiology or pathology | 131          | -        | -     | -      | -     | -     | -     |
| Covino       | 2020 | [99]     | Italy          | Retrospective cohort          | CAP              | Clinical diagnosis                 | 4056         | 45       | -     | 76.0   | -     | -     | -     |
| Gorse        | 1984 | [100]    | United States  | Retrospective cohort          | Meningitis       | Positive microbiology or pathology | 86           | -        | -     | -      | -     | -     | -     |
| Habibi       | 2021 | [101]    | Iran           | Retrospective cross-sectional | CAP              | Clinical diagnosis                 | 221          | 28.5     | 81.00 | -      | 6.00  | -     | -     |
| deGroot      | 2017 | [102]    | Netherlands    | Retrospective cohort          | Infection        | Clinical diagnosis                 | 2280         | 42.3     | 61.10 | -      | 17.00 | -     | -     |
| Hall         | 1976 | [103]    | United States  | Retrospective cross-sectional | Appendicitis     | Not stated                         | 50           | 46       | -     | -      | -     | 60    | 95    |
| Hsiao        | 2020 | [104]    | Taiwan         | Retrospective cohort          | UTI              | Positive microbiology or pathology | 1043         | 72.9     | 67.00 | -      | 17.00 | -     | -     |
| Hui          | 2002 | [105]    | United States  | Retrospective cohort          | Appendicitis     | Not stated                         | 95           | 51.6     | 78.00 | -      | 5.60  | -     | -     |
| Joo          | 2022 | [106]    | Canada         | Retrospective cohort          | UTI              | Clinical diagnosis                 | 129          | 58.1     | 85.50 | -      | 7.20  | -     | -     |
| Kim          | 1976 | [107]    | United States  | Retrospective cohort          | Appendicitis     | Not stated                         | 29           | 75.9     | 72.60 | -      | -     | 66    | 90    |
| Laborde      | 2023 | [108]    | France         | Retrospective cohort          | CAP              | Clinical diagnosis                 | 217          | 45       | -     | 85.0   | -     | -     | -     |
| Lieberman    | 1997 | [109]    | Israel         | Prospective cohort            | CAP              | Clinical diagnosis                 | 145          | 48.3     | -     | -      | -     | -     | -     |
| Lim          | 2001 | [110]    | United Kingdom | Retrospective cohort          | CAP              | Clinical diagnosis                 | 156          | -        | 84.10 | -      | 5.39  | -     | -     |
| Mody         | 2002 | [111]    | United States  | Retrospective cohort          | CAP              | Clinical diagnosis                 | 82           | 2        | 72.00 | -      | 9.00  | -     | -     |
| Morrow       | 1978 | [112]    | United States  | Retrospective cohort          | Cholecystitis    | Not stated                         | 39           | -        | 70.50 | -      | -     | -     | -     |
| Ouriel       | 1983 | [113]    | United States  | Retrospective cohort          | Diverticulitis   | Clinical diagnosis                 | 92           | 38       | 33.60 | -      | -     | -     | -     |
| Pagliano     | 2015 | [114]    | Italy          | Prospective cohort            | Meningitis       | Positive microbiology or pathology | 131          | -        | -     | -      | -     | -     | -     |
| Parsonage    | 2009 | [115]    | United Kingdom | Prospective cohort            | CAP              | Clinical diagnosis                 | 428          | 53       | -     | -      | -     | -     | -     |
| Peled        | 2006 | [116]    | Israel         | Retrospective cohort          | Endocarditis     | Not stated                         | 215          | -        | -     | -      | -     | -     | -     |

| Author          | Year | Citation | Country        | Design                        | Infection      | Infection Definition               | Participants | % Female | Age   |        |       |       |       |
|-----------------|------|----------|----------------|-------------------------------|----------------|------------------------------------|--------------|----------|-------|--------|-------|-------|-------|
|                 |      |          |                |                               |                |                                    |              |          | mean  | median | sd    | lower | upper |
| Rebelo          | 2011 | [117]    | Portugal       | Retrospective cohort          | Bacteraemia    | Positive microbiology or pathology | 135          | 45.9     | -     | -      | -     | -     | -     |
| Rello           | 1996 | [118]    | Spain          | Prospective cohort            | CAP            | Clinical diagnosis                 | 251          | 26.3     | -     | -      | -     | -     | -     |
| Salam           | 2018 | [119]    | India          | Retrospective cross-sectional | Appendicitis   | Positive microbiology or pathology | 54           | 44.4     | 72.00 | -      | 9.30  | -     | -     |
| Shah            | 2011 | [120]    | United States  | Retrospective cohort          | Diverticulitis | Clinical diagnosis                 | 76           | 34.2     | 35.40 | -      | -     | 21    | 40    |
| Shchatsko       | 2017 | [121]    | United States  | Retrospective cross-sectional | Appendicitis   | Positive microbiology or pathology | 96           | 58.3     | 73.70 | -      | 1.50  | -     | -     |
| Shirata         | 2021 | [122]    | Japan          | Prospective cohort            | CAP            | Clinical diagnosis                 | 872          | 47.1     | 82.00 | -      | 8.10  | -     | -     |
| Starczewski     | 1988 | [123]    | United Kingdom | Prospective cohort            | CAP            | Clinical diagnosis                 | 100          | 50       | 82.59 | -      | 7.03  | -     | -     |
| Storm-Dickerson | 2003 | [124]    | United States  | Retrospective cohort          | Appendicitis   | Clinical diagnostic coding         | 113          | 51.3     | 71.80 | -      | -     | 60    | 98    |
| vanSoest        | 2022 | [125]    | Netherlands    | Prospective cohort            | Meningitis     | Positive microbiology or pathology | 2140         | 49.6     | -     | -      | -     | -     | -     |
| Whitelaw        | 1992 | [126]    | South Africa   | Prospective cohort            | Bacteraemia    | Positive microbiology or pathology | 121          | 51.2     | 74.00 | -      | -     | 65    | 89    |
| Woodford        | 2009 | [127]    | United Kingdom | Retrospective cohort          | UTI            | Clinical diagnostic coding         | 150          | 68       | 84.50 | -      | -     | -     | -     |
| Young           | 2007 | [128]    | Taiwan         | Retrospective cohort          | Appendicitis   | Clinical diagnostic coding         | 628          | 47.8     | 70.50 | -      | 7.80  | -     | -     |
| Competence      | 2008 | [129]    | Germany        | Prospective cohort            | CAP            | Clinical diagnosis                 | 2647         | 43.9     | -     | -      | -     | -     | -     |
| Warmerdam       | 2017 | [130]    | Netherlands    | Prospective cohort            | Infection      | Clinical diagnosis                 | 2370         | 42.4     | 61.40 | -      | 17.00 | -     | -     |
| Liu (1)         | 2024 | [131]    | China          | Retrospective cohort          | Sepsis         | Not stated                         | 48           | 33.3     | -     | 71.5   | -     | -     | -     |
| Liu (2)         | 2024 | [131]    | China          | Retrospective cohort          | Sepsis         | Not stated                         | 123          | 43.9     | -     | 76.0   | -     | -     | -     |
| Hunold          | 2024 | [132]    | United States  | Prospective cohort            | CAP            | Clinical diagnosis                 | 27           | 48.1     | 75.30 | -      | 8.80  | -     | -     |
| Hsueh (1)       | 2024 | [133]    | Taiwan         | Retrospective cohort          | Bacteraemia    | Positive microbiology or pathology | 912          | 44.5     | -     | 79.0   | -     | -     | -     |
| Hsueh (2)       | 2024 | [133]    | Taiwan         | Retrospective cohort          | Bacteraemia    | Positive microbiology or pathology | 2451         | 51.9     | -     | 77.0   | -     | -     | -     |

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#### Appendix E: Data Collection

Data was extracted independently by two reviewers using a piloted data collection form. Discrepancies were resolved by discussion and recourse to the original data. Data was collected on:

- The report: author, year, funding status, conflicts of interest
- The study: design (e.g. randomised controlled trial, retrospective cohort), dates, country, infection being studied, the method of identifying patients with infection (e.g. microbiological data from cultures, documented admission diagnosis)
- The participants: inclusion and exclusion criteria, number of participants, baseline demographics (age, sex, ethnicity, severity of illness, co-morbidities)
- The comparator: age groups studied
- The outcome: vital signs studied, measurement method, timepoint studied

For each age group we extracted:

- The number of patients in each group
- The average age of the group (mean or median)
- The age variance of the group (SD, IQR, range)
- The upper and lower limits of the group

Eligible outcomes included heart rate, respiratory rate, temperature, blood pressure and oxygen saturation recorded within 24 hours of hospital admission.

- Where data was presented as a dichotomous or categorical outcome we extracted:
  - The outcome categories
  - The timepoint recorded
  - The number of patients falling within each category and the total number of patients studied
  - The number of missing participants
- Where data was presented as a continuous outcome we extracted:
  - The timepoint recorded
  - The average measure (mean or median)
  - The measure of variance (standard deviation, IQR, range)
  - The number of participants
  - The number of missing participants

## **Appendix F: Risk of Bias Assessment of Individual Included Studies**

High = High risk of bias

Low = Low risk of bias

Unclear = Unclear risk of bias

| Author             | Year | Citation | Domain               |                  |                       |                    |
|--------------------|------|----------|----------------------|------------------|-----------------------|--------------------|
|                    |      |          | 1: Patient Selection | 2: Index Test(s) | 3: Reference Standard | 4: Flow and Timing |
| Shimazui           | 2020 | [66]     | Unclear              | Unclear          | Low                   | High               |
| Boonmee            | 2020 | [6]      | Low                  | Low              | Low                   | High               |
| Sasaki             | 2020 | [64]     | Low                  | Low              | Low                   | High               |
| Celikhisar         | 2020 | [13]     | High                 | Low              | Low                   | High               |
| Lee                | 2020 | [45]     | Low                  | Low              | Low                   | High               |
| Sunden-Cullberg    | 2017 | [71]     | High                 | High             | Low                   | Low                |
| Hsien-LingChou     | 2016 | [34]     | Low                  | Low              | High                  | High               |
| Caterino           | 2019 | [10]     | High                 | Low              | Low                   | Low                |
| Warmerdam          | 2018 | [82]     | High                 | High             | Unclear               | High               |
| ZoeXiaoZhuZhang    | 2018 | [88]     | Low                  | Low              | Low                   | High               |
| Cataudella         | 2017 | [9]      | High                 | Low              | Low                   | Low                |
| Jung               | 2017 | [35]     | High                 | Low              | Low                   | High               |
| Amadoru            | 2017 | [2]      | Unclear              | High             | Unclear               | High               |
| Valencia           | 2017 | [80]     | Low                  | Low              | Low                   | High               |
| Smithson           | 2019 | [70]     | High                 | Low              | Low                   | Unclear            |
| Luna               | 2016 | [48]     | Low                  | Low              | Low                   | High               |
| Golcuk             | 2015 | [28]     | High                 | Low              | Low                   | Low                |
| Lee                | 2013 | [44]     | High                 | Unclear          | Low                   | Unclear            |
| Hernandez          | 2015 | [31]     | High                 | Low              | Low                   | Low                |
| Ruiz               | 2014 | [61]     | High                 | High             | Low                   | Low                |
| Kijsirichareanchai | 2015 | [37]     | Low                  | High             | Low                   | High               |
| Ma                 | 2011 | [49]     | High                 | High             | Low                   | Low                |
| Talebi-Taher       | 2010 | [72]     | High                 | Low              | Low                   | Low                |
| Caterino           | 2012 | [12]     | High                 | High             | Low                   | High               |
| Cabellos           | 2009 | [8]      | High                 | High             | Low                   | Low                |
| Ko                 | 2019 | [41]     | Unclear              | Low              | High                  | High               |
| Weisfelt           | 2006 | [84]     | High                 | High             | Low                   | High               |
| Lee                | 2007 | [43]     | High                 | High             | Low                   | Low                |
| Fernandez-Sabe     | 2003 | [24]     | High                 | High             | Low                   | Low                |
| Thiem              | 2009 | [77]     | High                 | Low              | Low                   | High               |
| Myint              | 2005 | [52]     | High                 | High             | Low                   | Low                |
| Rasmussen          | 1992 | [56]     | High                 | High             | Low                   | High               |
| Potts              | 1999 | [55]     | High                 | High             | Low                   | High               |
| Tsai               | 2005 | [79]     | Low                  | High             | Low                   | High               |
| Ciesielski         | 2010 | [15]     | Low                  | Low              | Low                   | High               |
| Tantarattanapng    | 2021 | [75]     | Low                  | Low              | Low                   | High               |
| Laborde            | 2021 | [42]     | Low                  | Low              | Low                   | High               |
| Shimoni            | 2021 | [67]     | High                 | Low              | Low                   | High               |
| Covino             | 2021 | [16]     | Low                  | Low              | Low                   | High               |

| Author           | Year | Citation | Domain               |                  |                       |                    |
|------------------|------|----------|----------------------|------------------|-----------------------|--------------------|
|                  |      |          | 1: Patient Selection | 2: Index Test(s) | 3: Reference Standard | 4: Flow and Timing |
| Lee              | 2020 | [46]     | High                 | High             | Low                   | High               |
| Dubost           | 2018 | [18]     | High                 | High             | Low                   | High               |
| Guirgis          | 2018 | [30]     | High                 | Low              | Low                   | Unclear            |
| Tantarattanapong | 2018 | [74]     | Low                  | High             | Low                   | High               |
| Alpay            | 2018 | [1]      | High                 | High             | Low                   | High               |
| Artero           | 2016 | [4]      | Low                  | Unclear          | Low                   | High               |
| Yo               | 2016 | [87]     | Low                  | Low              | Low                   | High               |
| Horesh           | 2016 | [33]     | High                 | Low              | Unclear               | High               |
| Yahav            | 2015 | [86]     | High                 | Low              | High                  | Low                |
| Singler          | 2013 | [68]     | High                 | Low              | Low                   | Low                |
| Wester           | 2013 | [85]     | Low                  | Low              | Low                   | High               |
| Kim              | 2013 | [38]     | Unclear              | Unclear          | Low                   | Unclear            |
| Domingo          | 2013 | [17]     | High                 | High             | Low                   | High               |
| Kim              | 2015 | [39]     | High                 | Low              | Low                   | High               |
| Gopal            | 2015 | [29]     | High                 | Low              | Low                   | High               |
| Sirikurnpiboon   | 2015 | [69]     | Low                  | High             | Low                   | High               |
| Taniguchi        | 2013 | [73]     | High                 | Low              | Low                   | High               |
| Kaser            | 2013 | [36]     | High                 | High             | Low                   | High               |
| Salahuddin       | 2012 | [63]     | High                 | High             | Low                   | Low                |
| Klapdor          | 2012 | [40]     | Unclear              | High             | Low                   | Low                |
| Ewig             | 2012 | [22]     | High                 | Low              | Low                   | Low                |
| Tiruvoipati      | 2010 | [78]     | Low                  | Low              | Low                   | High               |
| Liu              | 2010 | [47]     | High                 | Low              | Unclear               | Low                |
| Erdem            | 2010 | [20]     | High                 | Low              | Low                   | High               |
| Sheu             | 2007 | [65]     | High                 | High             | Low                   | High               |
| Mylotte          | 2002 | [53]     | Low                  | High             | Low                   | High               |
| Garcia-Ordenez   | 2001 | [27]     | High                 | High             | Low                   | High               |
| Marinella        | 2000 | [50]     | High                 | Low              | Low                   | High               |
| Ewig             | 1999 | [23]     | High                 | Low              | Low                   | Low                |
| Parker           | 1997 | [54]     | High                 | Low              | Low                   | High               |
| Riquelme         | 1996 | [58]     | High                 | Low              | Low                   | Low                |
| Elangovan        | 1996 | [19]     | High                 | High             | High                  | High               |
| Chassagne        | 1996 | [14]     | High                 | Low              | Low                   | Low                |
| Fontanarosa      | 1992 | [26]     | Low                  | High             | Low                   | High               |
| Horattas         | 1990 | [32]     | High                 | High             | Low                   | High               |
| Vincent          | 1990 | [81]     | High                 | High             | Low                   | High               |
| Meyers           | 1989 | [51]     | High                 | High             | Low                   | High               |
| Wasserman        | 1989 | [83]     | High                 | Low              | Low                   | Low                |
| Terpenning       | 1987 | [76]     | Low                  | High             | Low                   | High               |

| Author           | Year | Citation | Domain               |                  |                       |                    |
|------------------|------|----------|----------------------|------------------|-----------------------|--------------------|
|                  |      |          | 1: Patient Selection | 2: Index Test(s) | 3: Reference Standard | 4: Flow and Timing |
| Esposito         | 1984 | [21]     | High                 | Low              | High                  | Unclear            |
| Finkelstein      | 1983 | [25]     | High                 | High             | Low                   | High               |
| Robbins          | 1980 | [60]     | High                 | Unclear          | Low                   | High               |
| Applefeld        | 1974 | [3]      | High                 | Low              | Low                   | High               |
| Caterino         | 2009 | [11]     | High                 | Low              | Unclear               | Low                |
| Raz              | 1999 | [57]     | High                 | Low              | Low                   | High               |
| Barsic           | 1992 | [5]      | High                 | Low              | Low                   | High               |
| Burns            | 1991 | [7]      | High                 | High             | Low                   | High               |
| Ryden            | 1983 | [62]     | High                 | High             | Low                   | High               |
| Cilloniz         | 2023 | [95]     | Low                  | Low              | Low                   | Low                |
| Joo              | 2022 | [106]    | Unclear              | High             | Low                   | High               |
| vanSoest         | 2022 | [125]    | High                 | High             | Low                   | High               |
| Choi             | 2022 | [94]     | High                 | High             | Low                   | Low                |
| Laborde          | 2023 | [108]    | High                 | High             | Low                   | High               |
| Shirata          | 2021 | [122]    | High                 | Low              | Low                   | Low                |
| Habibi           | 2021 | [101]    | High                 | High             | Low                   | High               |
| CAP-ChinaNetwork | 2020 | [91]     | Low                  | High             | Low                   | High               |
| Covino           | 2020 | [99]     | Low                  | Low              | Low                   | High               |
| Hsiao            | 2020 | [104]    | High                 | Low              | Low                   | High               |
| Salam            | 2018 | [119]    | High                 | Low              | Low                   | High               |
| Warmerdam        | 2017 | [130]    | Unclear              | Low              | Low                   | Low                |
| deGroot          | 2017 | [102]    | Low                  | Low              | High                  | High               |
| Shchatsko        | 2017 | [121]    | High                 | Low              | Low                   | High               |
| Pagliano         | 2015 | [114]    | High                 | High             | Low                   | Low                |
| Rebelo           | 2011 | [117]    | Low                  | Low              | Low                   | High               |
| Shah             | 2011 | [120]    | High                 | High             | Low                   | High               |
| Chen             | 2010 | [92]     | High                 | High             | Low                   | Low                |
| Parsonage        | 2009 | [115]    | High                 | Low              | Low                   | Low                |
| Woodford         | 2009 | [127]    | Low                  | Low              | Low                   | High               |
| Competence       | 2008 | [129]    | High                 | Low              | Low                   | Low                |
| Young            | 2007 | [128]    | High                 | Low              | Low                   | High               |
| Peled            | 2006 | [116]    | High                 | Low              | Low                   | High               |
| Hui              | 2002 | [105]    | High                 | Low              | Low                   | High               |
| Mody             | 2002 | [111]    | High                 | Low              | Low                   | High               |
| Lim              | 2001 | [110]    | High                 | High             | Low                   | High               |
| Conte            | 1999 | [96]     | High                 | Low              | Low                   | High               |
| Lieberman        | 1997 | [109]    | High                 | High             | Low                   | Low                |
| Rello            | 1996 | [118]    | High                 | High             | Low                   | Low                |

| Author          | Year | Citation | Domain               |                  |                       |                    |
|-----------------|------|----------|----------------------|------------------|-----------------------|--------------------|
|                 |      |          | 1: Patient Selection | 2: Index Test(s) | 3: Reference Standard | 4: Flow and Timing |
| Barkham         | 1996 | [90]     | High                 | High             | Low                   | High               |
| Cooper          | 1994 | [98]     | High                 | High             | Low                   | High               |
| Whitelaw        | 1992 | [126]    | High                 | Unclear          | Low                   | Low                |
| Starzewski      | 1988 | [123]    | High                 | High             | Low                   | Low                |
| Gorse           | 1984 | [100]    | High                 | High             | Low                   | High               |
| Ouriel          | 1983 | [113]    | High                 | High             | Low                   | High               |
| Chodak          | 1981 | [93]     | High                 | Low              | Low                   | High               |
| Andersson       | 1978 | [89]     | High                 | Low              | Low                   | High               |
| Morrow          | 1978 | [112]    | High                 | High             | Low                   | High               |
| Hall            | 1976 | [103]    | High                 | High             | Low                   | High               |
| Kim             | 1976 | [107]    | High                 | High             | Unclear               | High               |
| Hunold          | 2024 | [132]    | High                 | Unclear          | Low                   | Low                |
| Hsueh           | 2024 | [133]    | Low                  | Low              | Low                   | High               |
| Liu             | 2024 | [131]    | High                 | Low              | Unclear               | High               |
| Storm-Dickerson | 2003 | [124]    | High                 | High             | Low                   | High               |
| Cooper          | 1986 | [97]     | High                 | High             | Low                   | High               |