**Appenix A**

**Complete search strategy**

**embase.com**

('sepsis'/exp OR 'infection'/exp OR pneumonia/exp OR (sepsis OR septic\* OR Bacteremia OR Bacteraemia OR fungemia OR fungaemia OR urosepsis OR infection\* OR pneumonia\* OR meningitis\* OR meningoencephalitis\*):ab,ti) AND ('emergency ward'/exp OR 'emergency patient'/de OR 'emergency health service'/de OR 'hospital emergency service'/de OR 'emergency care'/de OR 'emergency physician'/de OR 'emergency medicine'/de OR (((emergency) NEAR/6 (ward\* OR department\* OR room OR unit OR cent\* OR patient\* OR care OR healthcare OR physician\* OR medicine)) OR 'acute care' OR ed):ab,ti) AND ('biological marker'/exp OR 'marker'/de OR 'molecular marker'/de OR 'disease marker'/de OR 'blood level'/de OR 'lactate blood level'/de OR 'protein blood level'/de OR (((biological\* OR bio\* OR inflammat\* OR diagnos\* OR molecul\* OR disease) NEAR/3 marker\*) OR biomarker\* OR ((serum OR blood) NEAR/6 (concentrate\* OR level\* OR marker\* OR lactate OR protein\* OR elevat\*))):ab,ti) NOT ('case report'/de OR (case-report\*):ti) NOT ([Conference Abstract]/lim) AND [English]/lim NOT ((juvenile/exp OR pediatrics/exp OR 'newborn sepsis'/de OR 'pediatric emergency medicine'/de OR (child\* OR adolescen\* OR infan\* OR newborn\* OR neonat\*):ti) NOT (adult/exp OR (adult\*):ti)) NOT ([animals]/lim NOT [humans]/lim)

**Medline Ovid**

(exp Sepsis/ OR exp Infection/ OR exp Pneumonia/ OR (sepsis OR septic\* OR Bacteremia OR Bacteraemia OR fungemia OR fungaemia OR urosepsis OR infection\* OR pneumonia\* OR meningitis\* OR meningoencephalitis\*).ab,ti.) AND (Emergency Medical Services/ OR Emergency Service, Hospital/ OR Emergency Medicine/ OR (((emergency) ADJ6 (ward\* OR department\* OR room OR unit OR cent\* OR patient\* OR care OR healthcare OR physician\* OR medicine)) OR acute care OR ed).ab,ti.) AND (exp Biomarkers/ OR blood.fs. OR (((biological\* OR bio\* OR inflammat\* OR diagnos\* OR molecul\* OR disease) ADJ3 marker\*) OR biomarker\* OR ((serum OR blood) ADJ6 (concentrate\* OR level\* OR marker\* OR lactate OR protein\* OR elevat\*))).ab,ti.) NOT (case reports/ OR (case-report\*).ti.) AND english.la. NOT ((exp child/ OR exp infant/ OR Pediatrics/ OR Neonatal Sepsis/ OR Pediatric Emergency Medicine/ OR (child\* OR adolescen\* OR infan\* OR newborn\* OR neonat\*).ti.) NOT (exp adult/ OR (adult\*).ti.)) NOT (exp animals/ NOT humans/)

**Web of science**

TS=(((sepsis OR septic\* OR Bacteremia OR Bacteraemia OR fungemia OR fungaemia OR urosepsis OR infection\* OR pneumonia\* OR meningitis\* OR meningoencephalitis\*)) AND ((((emergency) NEAR/5 (ward\* OR department\* OR room OR unit OR cent\* OR patient\* OR care OR healthcare OR physician\* OR medicine)) OR "acute care" OR ed)) AND ((((biological\* OR bio\* OR inflammat\* OR diagnos\* OR molecul\* OR disease) NEAR/2 marker\*) OR biomarker\* OR ((serum OR blood) NEAR/5 (concentrate\* OR level\* OR marker\* OR lactate OR protein\* OR elevat\*))))) NOT TI=(((child\* OR adolescen\* OR infan\* ORnewborn\* OR neonat\*)) NOT ((adult\*))) AND DT=(article) AND LA=(english)

**Cochrane CENTRAL**

((sepsis OR septic\* OR Bacteremia OR Bacteraemia OR fungemia OR fungaemia OR urosepsis OR infection\* OR pneumonia\* OR meningitis\* OR meningoencephalitis\*):ab,ti) AND ((((emergency) NEAR/6 (ward\* OR department\* OR room OR unit OR cent\* OR patient\* OR care OR healthcare OR physician\* OR medicine)) OR 'acute care' OR ed):ab,ti) AND ((((biological\* OR bio\* OR inflammat\* OR diagnos\* OR molecul\* OR disease) NEAR/3 marker\*) OR biomarker\* OR ((serum OR blood) NEAR/6 (concentrate\* OR level\* OR marker\* OR lactate OR protein\* OR elevat\*))):ab,ti) NOT (((child\* OR adolescen\* OR infan\* OR newborn\* OR neonat\*):ti) NOT ((adult\*):ti))

**Google scholar**

sepsis|septic|Bacteremia|Bacteraemia|fungemia|fungaemia|urosepsis|infection|pneumonia|meningitis|meningoencephalitis "emergency ward|department|room"|"acute care" "biological|bio|inflammatory marker|markers"|biomarker|biomarkers -child -infant –newborn

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author, year** | **Domain 1: participants** | **1.1** | **1.2** | **1B** | **DOMAIN 2: Predictors** | **2.1** | **2.2** | **2.3** | **2B** | **DOMAIN 3: Outcome** | **3.1** | **3.2** | **3.3** | **3.4** | **3.5** | **3.6** | **3B** |
| Zhao, 2018 | High | Yes | No | No | Low | Yes | Yes | Yes | No | Low | Yes | Yes | Yes | Yes | Yes | Yes | No |
| Duplessis, 2018 | Low | Yes | Yes | No | Low | Yes | Yes | Yes | No | Low | Yes | Yes | Yes | Yes | Yes | Yes | No |
| Niño, 2017 | Low | Yes | Yes | No | Low | Yes | Yes | Yes | No | Low | Yes | Yes | Yes | Yes | Yes | Yes | No |
| Zhang, 2016 | Low | Yes | Yes | No | Low | Yes | Yes | Yes | No | Low | Yes | Yes | Yes | Yes | Yes | Yes | No |
| Carpio, 2015 | Low | Yes | Yes | No | Low | Yes | Yes | Yes | No | Low | Yes | Yes | Yes | Yes | Yes | Yes | No |
| Zhang, 2014 | Low | Yes | Yes | No | Low | Yes | Yes | Yes | No | Low | Yes | Yes | Yes | Yes | Yes | Yes | No |
| Wang, 2014 | Low | Yes | Yes | No | Low | Yes | Yes | Yes | No | Low | Yes | Yes | Yes | Yes | Yes | Yes | No |
| Chen, 2014 | Low | Yes | Yes | No | Low | Yes | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No |
| Chen, 2019 | Low | Yes | Yes | No | Low | Yes | Yes | Yes | No | Low | Yes | Yes | Yes | Yes | Yes | Yes | No |
| Zhao, 2013 | Low | Yes | Yes | No | Low | Yes | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No |
| Kofoed, 2008 | Low | Yes | Yes | No | Low | Yes | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No |
| Yamamoto, 2015 | Low | Yes | Yes | No | Low | Yes | Yes | Yes | No | Low | Yes | Yes | Yes | Yes | Yes | Yes | No |
| Yin, 2013 | Low | Yes | Yes | No | Low | Yes | Yes | Yes | No | Low | Yes | Yes | Yes | Yes | Yes | Yes | No |
| Liu, 2013 | Low | Yes | Yes | No | Low | Yes | Yes | Yes | No | Low | Yes | Yes | Yes | Yes | Yes | Yes | No |
| Viallon, 2008 | Low | Yes | Yes | No | Low | Yes | Yes | Yes | No | Low | Yes | Yes | Yes | Yes | Yes | Yes | No |
| Henning, 2019 | Low | Yes | Yes | No | Low | Yes | Yes | Yes | No | Low | Yes | Yes | Yes | Yes | Yes | Yes | No |
| Song, 2019 | Low | Yes | Yes | No | Low | Yes | Yes | Yes | No | Low | Yes | Yes | Yes | Yes | Yes | Yes | No |
| Yu, 2019 | Low | Yes | Yes | No | Low | Yes | Yes | Yes | No | Low | Yes | Yes | Yes | Yes | Yes | Yes | No |

**Supplemental table 1:** Extended PROBAST checklist

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author, year** | **DOMAIN 4: Analysis** | **4.1** | **4.2** | **4.3** | **4.4** | **4.5** | **4.6** | **4.7** | **4.8** | **4.9** |
| Zhao, 2018 | Low | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Duplessis, 2018 | High | No | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |
| Niño, 2017 | High | Yes | Yes | Yes | Unknown | Yes | Yes | Yes | No | Yes |
| Zhang, 2016 | Low | Yes | Yes | Yes | Unknown | Yes | Yes | Yes | Yes | Yes |
| Carpio, 2015 | High | No | Yes | Yes | Unknown | Yes | Yes | Yes | No | Yes |
| Zhang, 2014 | High | Yes | Yes | Yes | Unknown | Yes | Yes | Yes | No | Yes |
| Wang, 2014 | High | No | Yes | Yes | Unknown | Yes | Yes | Yes | No | Yes |
| Chen, 2014 | Low | Yes | Yes | Yes | Unknown | Yes | Yes | Yes | Yes | Yes |
| Chen, 2019 | Low | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Zhao, 2013 | Low | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Kofoed, 2008 | High | No | Yes | Yes | Unknown | No | Yes | Yes | No | Yes |
| Yamamoto, 2015 | Low | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Yin, 2013 | High | Yes | Yes | Yes | Unknown | Yes | Yes | Yes | Yes | Yes |
| Liu, 2013 | High | Yes | Yes | Yes | Unknown | Yes | Yes | Yes | Yes | Yes |
| Viallon, 2008 | High | No | Yes | Yes | Unknown | No | Yes | Yes | No | Yes |
| Henning, 2019 | High | No | Yes | No | Yes | No | Yes | Yes | No | Yes |
| Song, 2019 | High | No | Yes | Yes | Unknown | Yes | Yes | Yes | No | Yes |
| Yu, 2019 | Low | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |

**Supplemental table 1:** Extended PROBAST checklist

|  |  |
| --- | --- |
| **1.1** | Were appropriate data sources used, e.g. cohort, RCT or nested case-control study data? |
| 1.2 | Were all inclusions and exclusions of participants appropriate? |
| 1B | Concern that the included participants and setting do not match the review question |
| 2.1 | Were predictors defined and assessed in a similar way for all participants? |
| 2.2 | Were predictor assessments made without knowledge of outcome data? |
| 2.3 | Are all predictors available at the time the model is intended to be used? |
| 2B | Concern that the definition, assessment or timing of predictors in the model do not match the review question |
| 3.1 | Was the outcome determined appropriately? |
| 3.2 | Was a pre-specified or standard outcome definition used? |
| 3.3 | Were predictors excluded from the outcome definition? |
| 3.4 | Was the outcome defined and determined in a similar way for all participants? |
| 3.5 | Was the outcome determined without knowledge of predictor information? |
| 3.6 | Was the time interval between predictor assessment and outcome determination appropriate? |
| 3B | Concern that the outcome, its definition, timing or determination do not match the review question |
| 4.1 | Were there a reasonable number of participants with the outcome? |
| 4.2 | Were continuous and categorical predictors handled appropriately? |
| 4.3 | Were all enrolled participants included in the analysis? |
| 4.4 | Were participants with missing data handled appropriately? |
| 4.5 | Was selection of predictors based on univariable analysis avoided? |
| 4.6 | Were complexities in the data (e.g. censoring competing risks sampling of controls) accounted for appropriately? |
| 4.7 | Were relevant model performance measures evaluated appropriately? |
| 4.8 | Were model overfitting and optimism in model performance accounted for? |
| 4.9 | Do predictors and their assigned weights in the final model correspond to the results from multivariable analysis? |

**Supplemental table 2:** Signaling questions used in PROBAST checklist