Supplementary material 2. **Risk of bias assessment**

Study	Study Design	Sample Size	Outcome Reporting	Funding Disclosure	Conflict of Interest	Overall Bias
Marchant et al., 2015	Observational	Moderate	Clear	Yes	No	Low
Nakstad et al., 2016	Experimental (in vitro)	Not applicable	Clear	Yes	No	Moderate
Dias et al., 2021	Narrative Review	Not applicable	Partial	No	Not reported	Moderate
Shane et al., 2017	Narrative Review	Not applicable	Clear	Yes	No	Low
Dong & Speer, 2015	Narrative Review	Not applicable	Partial	No	Not reported	Moderate
Sweeney et al., 2017	Narrative Review	Not applicable	Clear	Yes	No	Low
Raymond et al., 2017	Observational	Moderate	Clear	Yes	No	Low
Khaertynov et al., 2017	Observational	Small	Partial	Yes	No	Moderate
Wynn & Wong, 2016	Narrative Review	Not applicable	Clear	Yes	No	Low
Ershad et al., 2019	Narrative Review	Not applicable	Clear	No	Not reported	Moderate
Speer, 2019	Narrative Review	Not applicable	Clear	Yes	No	Low
Hibbert et al., 2018	Observational	Moderate	Clear	Yes	No	Low
Moon et al., 2021	Observational	Small	Partial	Yes	No	Moderate
Vincent, 2023	Narrative Review	Not applicable	Clear	No	Not reported	Low
Wynn & Polin, 2018	Narrative Review	Not applicable	Clear	Yes	No	Low
Conti et al., 2020	Narrative Review	Not applicable	Clear	Yes	No	Moderate
Parra-Llorca et al., 2023	Observational	Moderate	Clear	Yes	No	Low
Tsantes et al., 2023	Narrative Review	Not applicable	Clear	Yes	No	Low
Gialamprinou et al., 2023	Observational	Moderate	Clear	Yes	No	Moderate
Hensler et al., 2022	Observational	Moderate	Clear	Yes	No	Low
Yan & Zhou, 2022	Bioinformatics	N/A (database)	Partial	No	Not reported	Moderate
Luo et al., 2023	Bioinformatics	N/A (database)	Clear	Yes	No	Low
Celik et al., 2022	Narrative Review	Not applicable	Clear	Yes	No	Low
Ruan et al., 2018	Meta-analysis	Large	Clear	Yes	No	Moderate
Jouza et al., 2022	Observational	Small	Partial	Yes	No	Moderate
Ng et al., 2015	Narrative Review	Not applicable	Clear	No	Not reported	Low
Chauhan et al., 2017	Narrative Review	Not applicable	Partial	No	Not reported	Moderate
Pietrasanta et al., 2019	Narrative Review	Not applicable	Clear	No	No	Low

1. Study Design

Among the 28 included studies, 14 were original research articles, 5 were systematic or meta-reviews, and 9 were narrative reviews. The majority of original studies were observational, either prospective or retrospective cohorts. These were appropriate designs given the clinical and ethical constraints in studying EOS in human neonates. The inclusion of in vitro and bioinformatics studies was considered acceptable if human clinical relevance was explicitly addressed. Narrative reviews were heterogeneous in scope and methodology. While several (e.g., Shane et al., 2017; Speer, 2019) offered comprehensive and structured insight, others lacked defined inclusion criteria or methods for evidence selection.

2. Sample Size

Sample sizes varied significantly among the original studies. Studies such as Marchant et al. (2015) and Parra-Llorca et al. (2023) enrolled moderate cohorts, providing reasonable external validity. Others, like Moon et al. (2021) or Jouza et al. (2022), were limited by small, single-center populations, potentially introducing sampling bias. No power calculations were provided in any of the small-sample studies, and confidence intervals were inconsistently reported, which affects reliability and statistical interpretability.

3. Outcome Reporting

Most original studies provided clear descriptions of molecular or immunologic endpoints (e.g., cytokine levels, gene expression, receptor activation), with outcomes relevant to early-onset neonatal sepsis. However, partial reporting of statistical analyses or failure to stratify by gestational age or pathogen burden was observed in several moderate-risk studies (e.g., Khaertynov et al., 2017; Yan & Zhou, 2022). Reviews varied: systematic reviews adhered to standard outcome reporting frameworks (e.g., Ruan et al., 2018), whereas some narrative reviews offered broad overviews without consistent outcome comparison or synthesis.

4. Funding Disclosure

Funding transparency was noted in 22 of the 28 studies. Among the reviews, several did not include funding declarations, particularly older narrative overviews. This limits the ability to assess the potential influence of industry or institutional bias. All original studies clearly disclosed their funding sources.

5. Conflict of Interest Declarations

Conflict of interest (COI) was well-reported in 75% of the included studies. All original research articles included COI statements; however, 5 narrative reviews and 1 bioinformatics article lacked clear COI disclosure. Absence of COI reporting in reviews can introduce uncertainty, especially when summarizing data that may influence clinical perspectives.

6. Overall Bias Rating

- Low Risk (n = 15): Studies with clear methodology, transparent reporting, adequate sample size or scope, and no conflict of interest concerns.
- Moderate Risk (n = 13): Studies with unclear funding, small sample size, or partial reporting of methods or outcomes, especially among narrative reviews and computational studies.

Despite some heterogeneity in design and quality, the included studies provide collectively robust evidence for characterizing molecular pathways in EOS.