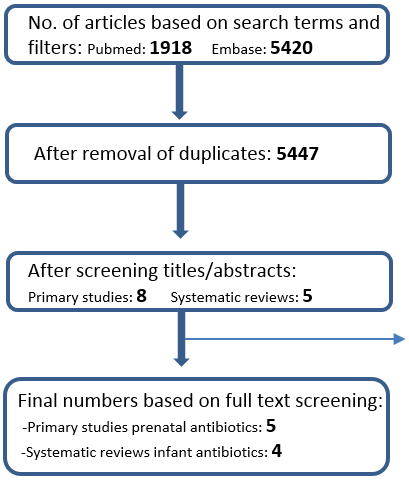
**Box S1**. Search strategy used for Pubmed and Embase

|  |  |  |
| --- | --- | --- |
| Pubmed  "Fetus"[Mesh] OR "Infant"[Mesh] OR "Child"[Mesh] OR pregnancy "[Mesh] OR " maternal-fetal exchange "[Mesh] OR " labor, obstetric mesh OR fetus\*[tiab] OR foetus\*[tiab] OR fetal[tiab] OR foetal[tiab] OR maternal[tiab] OR perinatal[tiab] OR prenatal[tiab] OR intrapartum[tiab]) OR early life[tiab] OR in utero[tiab] OR infant\*[tiab] OR baby[tiab] OR babies[tiab] OR neonat\*[tiab] OR newborn\*[tiab] OR neonatal[tiab] OR postnatal[tiab] OR child[tiab] OR children[tiab]  **AND**  "Anti-Bacterial Agents"[Mesh] OR "Anti-Bacterial Agents" [Pharmacological Action] OR antibacterial\*[tiab] OR anti- bacterial\*[tiab] OR antibiotic\*[tiab] OR antimicrobial[tiab] OR anti-microbial[tiab] OR anti-infective[tiab] OR antiinfective[tiab]  **AND**  "Overweight"[Mesh] OR "Obesity"[Mesh] OR "Weight Gain"[Mesh] OR "Body Mass Index"[Mesh] OR obese\*[tiab] OR overweight\*[tiab] OR obesit\*[tiab] OR body mass index[tiab] OR bmi[tiab] OR weight[tiab] OR body weight change\*[tiab]  Filter: period 01-01-2008 to 01-12-2018 |  | Embase  'fetus'/exp OR fetus OR 'pregnancy'/exp OR pregnancy:ab,ti,kw OR 'childbirth'/exp OR childbirth:ab,ti,kw OR fetal:ab,ti,kw OR foetal:ab,ti,kw OR maternal:ab,ti,kw OR pregnan\*:ab,ti,kw OR intrapartum:ab,ti,kw OR delivery:ab,ti,kw OR 'in utero':ab,ti,kw OR infant\*:ab,ti,kw OR babies:ab,ti,kw OR children:ab,ti,kw OR child:ab,ti,kw OR 'infant'/exp OR infant:ab,ti,kw OR baby:ab,ti,kw OR 'childhood'/exp OR 'early life':ab,ti,kw OR 'infancy'/exp OR infancy:ab,ti,kw OR neonat\*:ab,ti,kw OR newborn\*:ab,ti,kw OR neonatal:ab,ti,kw OR postnatal:ab,ti,kw OR perinatal:ab,ti,kw OR prenatal:ab,ti,kw  **AND**  'antibiotic agent'/exp OR 'antibiotic agent' OR antibacterial\*:ab,ti,kw OR 'anti-bacterial\*:ab,ti,kw OR antibiotic\*:ab,ti,kw OR antimicrobial:ab,ti,kw OR 'anti-microbial':ab,ti,kw  **AND**  'obesity'/exp OR obesity:ab,ti,kw OR obese:ab,ti,kw OR 'overweight'/exp OR overweight:ab,ti,kw OR obesit\*:ab,ti,kw OR 'body weight gain' OR 'body weight change'/exp OR 'body mass index':ab,ti,kw OR bmi:ab,ti,kw OR weight:ab,ti,kw OR 'weight gain'/exp OR 'weight gain':ab,ti,kw  **AND**  [1-1-2008]/sd NOT [2-12-2018]/sd AND ([article]/lim OR [review]/lim) NOT ([animals]/lim NOT [humans]/lim)  Filters: period 01-01-2018 to 01-12-2018, only articles and reviews and only humans. |

**Figure S1**. Search process for publications on early

life antibiotic exposure and overweight/obesity



-1 systematic review excluded as antibiotics was one of many possible exposures associated with overweight / obesity and not much information was available52

-2 primary studies excluded due to outcome measuring symptoms of cardiovascular risk, but not overweight/obesity53 and marker of body weight (cord blood leptin)54; 1 study examined characteristics associated with perinatal antibiotics as outcome, but no mention of childhood overweight/obesity55

**Box S2.** Publications included in the systematic reviews examining infant antibiotic exposure

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Publications reviewed** | **Miller, 2018 (n=17)** | **Partap, 2018 (n=13)** | **Rasmussen, 2018 (n=13)** | **Shao, 2017**  **(n=12)** |
| **Infant antibiotic exposure** | | | | |
| Ajslev et al., *2*011 | \* | \* | \* | \* |
| Azad et al., 2014 | \* | \* | \* | \* |
| Bailey et al., 2014 | \* | \* | \* | \* |
| Gerber et al., 2016 | \* | \* | \* | \* |
| Gürpinar et al., 1997 | \* |  |  |  |
| Kalliomaki et al., 2008 | \* |  |  |  |
| Korpela et al., 2016 | \* |  |  |  |
| Krenz-Niedbala et al., 2015 | \* |  |  |  |
| Li et al., 2017 | \* | \* | \* | \* |
| Mbakwa et al., 2016 | \* | \* | \* | \* |
| Murphy et al., 2013 | \* |  | \* | \* |
| Murphy et al., 2014 | \* | \* | \* |  |
| Poulsen et al., 2017 (also prenatal antibiotics) | \* |  | \* | \* |
| Rogawski et al, 2015 |  | \* |  |  |
| Rogawski et al, 2017 |  | \* |  |  |
| Saari et al., 2014 | \* |  |  |  |
| Saari et al., 2015 | \* | \* | \* | \* |
| Scott et al., 2016 | \* | \* | \* | \* |
| Schwartz et al., 2016 |  | \* |  |  |
| Trasande et al., 2013 | \* | \* | \* | \* |
| Ville et al., 2017 |  |  | \* | \* |

**Table S1a.** Critical appraisal checklist for methodology (Aromatis et al., 2015)24

NA: not applicable

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Systematic review** | **Miller**  **2018** | **Partap**  **2018** | **Rasmussen 2018** | **Shao**  **2017** |
| Is the review question clearly and explicitly stated? | Yes | Yes | Yes | Unclear |
| Were the inclusion criteria appropriate for the review question? | Yes | Yes | Yes | Unclear |
| Was the search strategy appropriate? | Yes | Yes | Yes | Unclear |
| Were the sources and resources used to search for studies adequate? | Yes | Yes | Yes | Unclear |
| Was critical appraisal conducted by two or more reviewers independently? | Yes | Unclear | Unclear | Unclear |
| Were the methods used to combine studies appropriate? | Unclear | Unclear | Unclear | Unclear |
| Was the likelihood of publication bias assessed? | Yes | NA | Yes | Yes |

**Table S1b.** Risk of bias in systematic reviews (ROBIS)25 Low/medium/high: low/medium/high risk of bias

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **ROBIS assessment** | **Shao, 2017** | **Rasmussen, 2018** | **Miller, 2018** | **Partap, 2018** |
| **Domain 1:** Study eligibility criteria | low | low | low | low |
| **Domain 2:** Identification and selection of studies | low | low | low | low |
| **Domain 3:** Data collection and study appraisal | medium | medium | low/ unclear | medium / unclear |
| **Domain 4:** Synthesis and findings | high | medium | low / unclear | low |
| **Main issues** | -Combining of heterogeneous studies  -No information of how NOS assessment was carried out  -Unclear if two researchers conducted quality assessments  -Findings of meta analyses over-emphasized | -Unclear whether data extraction and quality assessments were also conducted by two reviewers.  -Infections not included as necessary confounders in the NOS assessments.  -Meta-analysis on heterogeneous studies, i.e. included studies did not all adjust for important confounders. | -Not stringent with regard to confounding criteria in NOS assessment  -Heterogeneous studies in meta-analysis, (including combining unadjusted ORs with adjusted ORs, and entering overweight and obesity from one study separately into a meta-analysis)  -Unclear whether >1 reviewer extracted and compared the data | -Unclear if >1 reviewer carried out data extraction and quality assessment independently  -Quality assessment not carried out with validated tool, therefore unclear if appraisal method was sufficient. |
| **Overall risk of bias** | medium / high | low/medium | low | low |