Supplementary materials

Appendix 1

Construct search strategy example:

MEDLINE Search Strategy

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE (R) Daily and Ovid MEDLINE (R) <1948 to Present>

1. Children.ti.
2. Children.ab.
3. Infants.ti.
4. Infants.ab.
5. Breast fed children.ti.
6. Breast fed children.ab.
7. Atopic children.ti.
8. Atopic children.ab.
9. High risk atopic infants.ti.
10. High risk atopic infants.ab.
11. Severe eczema infants.ti.
12. severe eczema infants.ab.
13. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12
14. Food allergy.ti.
15. Food allergy.ab.
16. allergy.ti.
17. allergy.ab.
18. Allergenic food.ti.
19. Allergenic food.ab.
20. Food Hypersensitivity.ti.
21. Food Hypersensitivity.ab.
22. Food tolerance.ti.
23. Food tolerance.ab.
24. Food intolerance.ti.
25. Food intolerance.ab.
26. Primary prevention of food allergy.ti.
27. Primary prevention of food allergy.ab.
28. 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
29. 13 and 28
30. Randomized controlled trial.ti.
31. Randomized controlled trial.ab.
32. Controlled clinical trial.ti.
33. Controlled clinical trial.ab.
34. Double blind method.ti.
35. Double blind method.ab.
36. Single blind method.ti.
37. Single blind method.ab.
38. Clinical trial.ti.
39. Clinical trial.ab.
40. 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39
41. 29 and 40

Appendix 2

Title & Abstract Screening Form

1. Is the article about humans?
   * + *If no, EXCLUDE*
     + *If yes or unclear, go to the next question*

Population

1. Is the article about atopic high risk infants or normal risk infants or breast fed infants assist for food allergy?
   * + *If no, EXCLUDE*
     + *If yes or unclear, go to the next question*
2. 3. Does the article compare early introduction of allergenic food to exclusive breast

Intervention and comparison

1. feeding till 4 to 6 month of age?

Note: Allergenic foods are; formula milk, egg, peanut, nuts, wheat, soy,

sesame, fish and shellfish.

* + - *If no, EXCLUDE*
    - *If yes or unclear, go to the next question*

Outcomes

4. Does the article report any of the following outcomes: food allergy, allergy

sensitization, asthma, allergic rhinitis, eczema, and/or anaphylaxis?

* + - *If no, EXCLUDE*
    - *If yes or unclear, go to the next question*

Study design

5. Is the article a randomized controlled trial?

* + - *If no, EXCLUDE*
    - *If yes or unclear, INCLUDE*

Appendix 3

Full text screening form

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Early introduction of allergenic foods and the development of food allergy in children** | | | | | | | |
| Article | | Limits | | Population | Intervention and comparison | Outcome | Decision (include, exclude or uncertain) |
| ID | Author/ date | Study in human | RCT | On atopic high risk infants or normal risk infants or breast fed infants | Does the article compare early introduction of allergenic food to exclusive breastfeeding till 6 month of age | Does the article report any of the following outcomes: food allergy, allergy sensitization, asthma, allergic rhinitis, eczema, and/or anaphylaxis |
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Appendix 4

Data extraction form

1. Source:

|  |  |  |
| --- | --- | --- |
| 1 | Reviewer: |  BKA  STS |
| 2 | Ref ID: | \_\_ \_\_ \_\_ \_\_ |
| 3 | Journal name: |  |
| 4 | Frist author last name: |  |
| 5 | Year of publication: |  |
| 6 | Language of Publication: |  English   Non- English ,specify: ----------------------- |
| 7 | Country where study took place: |  USA  Australia  UK   Japan  Other |
| 8 | Number of centers |  |
| 9 | Funding: |  Public  Private  Both  Unclear |
| 10 | Are eligibility criteria reported? |  Explicit  Not explicit  Not reported |
| 11 | Inclusion criteria |  |
| 12 | Exclusion criteria |  |

1. Methods

|  |  |  |  |
| --- | --- | --- | --- |
| 13 | Study design | |  parallel group  cross over  factorial   other |
| 14 | Study follow up duration | |  Weeks   Months   years |
| 15 | Number of patients screened | |  Not Reported |
| 16 | Number of patients eligible | |  Not Reported |
| 17 | Number of patients randomized | |  Not Reported |
| 18 | Sequence generation (Randomization)  Risk of bias:   High   Low   Unclear | |  Random number table   Computer random-number generator   Coin tossing   Rolling die   Picking allocation from a hat/box   Minimization/dynamic allocation   Other methods: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_   Methods not described |
| 19 | Allocation sequence concealment  Risk of bias:   High   Low   Unclear | |  Central randomization   Numbered, opaque, sealed envelopes   Envelopes, with at least one of the following not specified: opaque, sealed, and numbered   Clearly not concealed   Unclear if rigorous concealment method was used |
| 20 | Blinding  Risk of bias:   High   Low   Unclear | |  Yes  No  unclear |
| 21 | Who was blinded | | |
| Patients |  Clearly stated that patient is blind   Not reported   Stated that patients not blinded | |
| Health care provider |  Clearly stated that health care provider is blind   Not reported   Stated that health care provider not blinded | |
| Data collectors |  Clearly stated that data collector is blind   Not reported   Stated that data collectors not blinded | |
| Assessors of outcomes |  Clearly stated that assessors of outcomes  is blind   Not reported   Stated that assessors of outcomes not blinded | |
| Data analysts |  Clearly stated that data analysts is blind   Not reported   Stated that data analysts not blinded | |

1. Participants

|  |  |  |  |
| --- | --- | --- | --- |
|  | | Control | Intervention |
| 22 | Age of patients: Mean/median (SD, range) |  |  |
| 23 | Female |  |  |
| 24 | Number randomized |  |  |
| 25 | Number of females randomized |  |  |
| 26 | Number lost to followed at all |  |  |
| 27 | Number followed; not included |  |  |
| 28 | Number first-degree relative history of allergic disease |  |  |
| 29 | Number of participants with eczema |  |  |
| 30 | Number of breast-fed infants |  |  |
| 31 | How was loss to F/U dealt with? |  Analysis of only the available data (i.e. ignoring the missing data)   Imputing the missing data with replacement values  \_\_ last observation carried forward  \_\_ best/worst case scenario  \_\_ imputing the mean  \_\_ using predicted values from a regression analysis   Multiple imputation   Statistical models   Uncertain/not reported | |
| 32 | Intention-to-treat analysis or modified intention to treat |  Reported |  Not reported |
| 33 | Per protocol analysis |  Reported |  Not reported |

1. Interventions

|  |  |  |
| --- | --- | --- |
|  | Control group | Intervention group |
| 34 |  Exclusive breast-feeding   Rice powder   Placebo   avoidance   Not specified   Other \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |  Cow milk  Egg  Peanut  Sesame   Fish  Wheat  All  (Check all that apply) |
| 35 | Amount |  Gram of protein   Not Reported |
| 36 | Frequency |  Day   Week   Not Reported |
| 37 | Duration |  Months   Not Reported |
| 38 | Authors’ affiliated with commercial industry? | Yes   No   Uncertain/not reported |
| 39 | Participant compliance assessed? |  Yes: \_\_\_High; \_\_\_ Moderate; \_\_\_ Low   No   Uncertain |
| 40 | Was trial stopped early? |  Yes   No   Uncertain |

1. Outcome:

|  |  |  |
| --- | --- | --- |
| 41 | Age at Outcome  Assessment | years |
| 42 | Food allergy  (a reproducible hypersensitivity reaction to a food)  (Check all that apply) |  Oral food challenge   Specific IgE to egg ≥ 0.35 kU/L   Allergy skin test ≥ 3 mm of negative control |
| 43 | Allergic sensitization  (the presence of specific IgE to an allergen)  (Check all that apply) |  Specific IgE to egg ≥ 0.35 kU/L   Allergy skin test ≥ 3 mm of  negative control |
| 44 | Secondary outcome  (Check all that apply) |  Eczema   Asthma   Allergic rhinitis   Anaphylaxis |

Results

|  |  |  |  |
| --- | --- | --- | --- |
| Food allergy to egg | | Control | Intervention group |
| 45 | Number of randomized |  |  |
| 46 | Number of participants with the outcome of interest (%) |  |  |
| 47 | Relative risk |  | |
| 48 | 95 % confidence interval |  |  |
| 49 | Absolut risk reduction |  |  |
| 50 | Number need to treat |  |  |

|  |  |  |  |
| --- | --- | --- | --- |
| Allergic sensitization to egg | | Control | Intervention group |
| 51 | Number of randomized |  |  |
| 52 | Number of participants with the outcome of interest (%) |  |  |
| 53 | Relative risk |  | |
| 54 | 95 % confidence interval |  |  |
| 55 | Absolut risk reduction |  |  |
| 56 | Number need to treat |  |  |

|  |  |  |  |
| --- | --- | --- | --- |
| Eczema | | Control | Intervention group |
| 57 | Number of randomized |  |  |
| 58 | Number of participants with the outcome of interest (%) |  |  |
| 59 | Relative risk |  | |
| 60 | 95 % confidence interval |  |  |
| 61 | Absolut risk reduction |  |  |
| 62 | Number need to treat |  |  |

|  |  |  |  |
| --- | --- | --- | --- |
| Allergic rhinitis | | Control | Intervention group |
| 63 | Number of randomized |  |  |
| 64 | Number of participants with the outcome of interest (%) |  |  |
| 65 | Relative risk |  | |
| 66 | 95 % confidence interval |  |  |
| 67 | Absolut risk reduction |  |  |
| 68 | Number need to treat |  |  |

|  |  |  |  |
| --- | --- | --- | --- |
| Anaphylaxis | | Control | Intervention group |
| 75 | Number of randomized |  |  |
| 76 | Number of participants with the outcome of interest (%) |  |  |
| 77 | Relative risk |  | |
| 78 | 95 % confidence interval |  |  |
| 79 | Absolut risk reduction |  |  |
| 80 | Number need to treat |  |  |

**NOTES:**

Appendix 5

PRISMA Flowchart

Identification

Identified records through systematic database searching in

MEDLINE, EMBASE and Cochrane Central

Up to November 2016 (N=416)

Number of records screened (N=416)

Number of records excluded (N=56) for duplicate

Screening for title and abstract

Number of records screened (N=360)

Number of records excluded (N=336)

Eligibility

Number of articles excluded on reading full-text (N=18)

Number of full-text articles assessed for eligibility (N=24)

Included

Number of articles included (N=6)