|  |
| --- |
| **Supplemental table 1.** Quality assessment of case-control studies included in this review. |
| CRITERIA | Mazloomi *et al.* (38) | McKeating *et al.* (24) | Dahabiyeh *et al.* (40) | Enebe *et al.* (43) | Eze *et al.* (44) | Lewandowska *et al.* (41) | Bommarito *et al.* (21) | Cinemre *et al.* (50) | Soobramoney *et al.* (47) | Al-Hilli *et al.* (34) | Da Silva *et al.* (48) | Maduray *et al.* (45) | Nnodim *et al.* (46) | Elongi *et al.* (42) | Haque *et al.* (36) | Laine *et al.* (23) | Mistry *et al.* (25) | Rezende *et al.* (49) | Ghaemi *et al.* (22) | Farzin and Sajadi (35) | Katz *et al.* (26) | Kim *et al.* (37) | Negi *et al.* (39) |
| 1. Was the research question or objective in this paper clearly stated and appropriate? | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y |
| 2. Was the study population clearly specified and defined? | N | Y | N | Y | Y | Y | Y | N | N | N | Y | N | Y | Y | Y | Y | Y | N | Y | Y | N | Y | N |
| 3. Did the authors include a sample size justification? | N | N | Y | Y | Y | N | N | N | N | N | Y | N | N | N | N | N | Y | N | Y | Y | N | N | N |
| 4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)? | NR | Y | NR | Y | Y | Y | Y | Y | Y | Y | Y | NR | NR | Y | Y | Y | Y | NR | Y | NR | NR | Y | NR |
| **Supplemental table 1.** (*Continued)* |
| 5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants? | N | Y | N | Y | Y | Y | Y | Y | N | N | Y | N | N | Y | Y | N | Y | Y | Y | Y | N | Y | Y |
| 6. Were the cases clearly defined and differentiated from controls? | Y | Y | Y | Y | N | Y | Y | Y | Y | N | Y | N | Y | Y | Y | Y | Y | Y | Y | N | N | Y | Y |
| 7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible? | NA | CD | NA | NA | NA | N | CD | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | CD | NA | NA | NA | NA |
| 8. Was there use of concurrent controls? | N | N | N | Y | N | N | N | N | N | N | N | N | N | Y | N | N | N | N | N | N | N | N | N |
| **Supplemental table 1.** (*Continued*) |
| 9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case? | N | N | NR | N | N | Y | Y | N | N | N | N | N | N | N | N | N | Y | N | Y | N | N | N | N |
| 10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants? | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y |
| 11. Were the assessors of exposure/risk blinded to the case or control status of participants? | NR | NR | NR | NR | CD | NR | NR | CD | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR |
| **Supplemental table 1.** (*Continued*) |
| 12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis? | Y | Y | N | Y | Y | Y | Y | N | N | Y | N | N | N | Y | N | Y | Y | N | Y | Y | Y | Y | Y |
| Quality Rating (Good, Fair or Poor) | F | G | F | G | G | G | G | F | F | F | G | P | F | G | F | F | G | F | G | F | F | G | F |
| *Abbreviations:* Y, Yes; N, No; CD, cannot determine; NR, not reported; NA, not applicable; G, Good; F, Fair; P, Poor.Score: Questions 3, 8 and 11 – 1 point for each “Yes”; Rest of the questions – 2 points for each “Yes”; -1 point for each “No” and 0 points for “NA, CD or NR” answers. Then, each paper was attributed a pooled classification of “Good”, “Fair” or “Poor”. |
|  |
|  |

|  |
| --- |
|  |

 **Supplemental table 2.** Quality assessment of observational cohort and cross-sectional studies included in this review.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| CRITERIA | Holmquist *et al.* (28) | Ambad *et al.* (31) | Lewandowska *et al.* (29) | Liu *et al.* (30) | McAlpine *et al.* (32) | Choi *et al.* (27) |
| 1. Was the research question or objective in this paper clearly stated? | Y | Y | Y | Y | Y | Y |
| 2. Was the study population clearly specified and defined? | Y | N | Y | Y | Y | Y |
| 3. Was the participation rate of eligible persons at least 50%? | Y | CD | Y | Y | NR | Y |
| 4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants? | Y | CD | Y | Y | Y | Y |
| 5. Was a sample size justification, power description, or variance and effect estimates provided? | N | N | Y | N | N | Y |
| 6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured? | NR | NR | Y | N | NR | NR |
| 7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed? | CD | CD | Y | N | Y | CD |
| **Supplemental table 2.** (*Continued*) |
| 8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)? | Y | N | Y | Y | N | Y |
| 9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants? | Y | N | Y | Y | Y | Y |
| 10. Was the exposure(s) assessed more than once over time? | N | N | N | N | N | N |
| 11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants? | Y | N | Y | Y | Y | Y |
| 12. Were the outcome assessors blinded to the exposure status of participants? | NR | NR | NR | NR | NR | NR |
| 13. Was loss to follow-up after baseline 20% or less? | NA | NA | N | NA | NA | NA |
| 14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)? | Y | N | Y | Y | Y | N |
| Quality Rating (Good, Fair or Poor) | G | P | G | G | F | G |
| *Abbreviations:* Y, Yes; N, No; CD, cannot determine; NR, not reported; NA, not applicable; G, Good; F, Fair; P, Poor. Score: Questions 5 and 12 – 1 point for each “Yes”; Rest of the questions – 2 points for each “Yes”, -1 point for each “No” and 0 points for “NA, CD or NR” answers. Then, each paper was attributed a pooled classification of “Good”, “Fair” or “Poor”. |

|  |
| --- |
|  **Supplemental table 3.** Quality assessment of RCT study included in this review |
| CRITERIA | Rayman *et al.* (33) |
| 1. Was the study described as randomized, a randomized trial, a randomized clinical trial, or an RCT? | Y |
| 2. Was the method of randomization adequate (i.e., use of randomly generated assignment)? | Y |
| 3. Was the treatment allocation concealed (so that assignments could not be predicted)? | Y |
| 4. Were study participants and providers blinded to treatment group assignment? | Y |
| 5. Were the people assessing the outcomes blinded to the participants' group assignments? | Y |
| 6. Were the groups similar at baseline on important characteristics that could affect outcomes (e.g., demographics, risk factors, co-morbid conditions)? | Y |
| 7. Was the overall drop-out rate from the study at endpoint 20% or lower of the number allocated to treatment? | Y |
| 8. Was the differential drop-out rate (between treatment groups) at endpoint 15 percentage points or lower? | Y |
| 9. Was there high adherence to the intervention protocols for each treatment group? | Y |
| 10. Were other interventions avoided or similar in the groups (e.g., similar background treatments)? | Y |
| 11. Were outcomes assessed using valid and reliable measures, implemented consistently across all study participants? | Y |
| 12. Did the authors report that the sample size was sufficiently large to be able to detect a difference in the main outcome between groups with at least 80% power? | Y |
| 13. Were outcomes reported or subgroups analyzed prespecified (i.e., identified before analyses were conducted)? | Y |
| 14. Were all randomized participants analyzed in the group to which they were originally assigned, i.e., did they use an intention-to-treat analysis? | Y |
| Quality Rating (Good, Fair or Poor) | Good |
| *Abbreviations:* Y, Yes; N, No. |

**Supplemental table 4.** Inclusion and/or exclusion criteria of participants of each study included in this review.

|  |
| --- |
| Mazloomi *et al*. (38)* Exclusion criteria: women with previous elective abortions, previous ectopic pregnancies, underlying diseases such as type 2 diabetes, thyroid disease, kidney, liver, respiratory, infectious and heart disease, taking antihypertensive drugs, and alcohol and tobacco.
 |
| McKeating *et al*. (24)* Inclusion criteria: women over the age of 18, with a singleton pregnancy, and normal mid-trimester fetal morphology examination.
 |
| Dahabiyeh *et al*. (40)* Not reported
 |
| Enebe *et al*. (43)* Exclusion criteria: pregnant women with chronic illnesses such as human immunodeficiency virus infection (HIV), diabetes mellitus (DM), malignancy, and tuberculosis; women taking some medications (e.g. magnesium sulfate, etc); and pregnant women with tobacco and/or alcohol consumption. Also, pregnant women who incidentally became pregnant while on copper-containing contraceptive devices, those whose gestational ages could not be ascertained and women with multiple pregnancies were also excluded.
 |
| Eze *et al*. (44)* Inclusion criteria: women with singleton pregnancies.
* Exclusion criteria: pregnant women with chronic diseases such as HIV, infection, chronic renal disease, and DM; pregnant women with multiple gestations; with tobacco and/or alcohol consumption; and women taking medications that could affect their Se levels.
 |
| Lewandowska *et al*. (41), and Lewandowska *et al*. (29)* Inclusion criteria: Polish caucasian women of descent from Wielkopolska; aged 18–45 years (at conception); in the 10–14th week of a single pregnancy without aneuploidy; with delivery of a phenotypically normal child ≥ 25th week of pregnancy.
* Exclusion criteria: women with chronic diseases, including DM, hypertension, immunological and inflammatory diseases, thromboembolism, and kidney or liver diseases.
 |
| Bommarito *et al*. (21)* Inclusion criteria: women with at least 18 years of age, seeking prenatal care before 15 weeks gestation.
 |
| Cinemre *et al*. (50)* Exclusion criteria: tobacco use, twin pregnancies, preexisting maternal chronic diseases, chromosomal or suspected ultrasound fetal abnormalities, maternal heart disease, use of antihypertensive medication, DM, and renal disease at the 1-year follow-up visit.
 |
| **Supplemental table 4.** (*Continued*) |
| Soobramoney *et al*. (47)* Exclusion criteria: Pregnant women with HIV or with other medical conditions, such as gestational diabetes, epilepsy, chronic asthma, cardiac, thyroid, and chronic renal diseases.
 |
| Al-Hilli *et al*. (34)* Exclusion criteria: Pregnant women more than 40 years old, with body mass index > 30, smoking, with prior history of PE, family history of PE, prior hypertension or kidney disease, previous history of vascular disease, and multiple pregnancy.
 |
| Da Silva *et al*. (48)* Inclusion criteria: women with a gestational age between 20 and 41 weeks.
* Exclusion criteria: women with malnutrition, diabetes (gestational or preexisting), thyroid disease, renal impairment, HIV, infection, previous proteinuria, use of vitamin supplements, inflammatory bowel disease, previous bariatric surgery, drug use, fetal malformations, and multiple pregnancies.
 |
| Maduray *et al*. (45)* Not reported
 |
| Nnodim *et al*. (46)* Inclusion criteria: women within the age range of 20-32 years, in the third trimester.
* Exclusion criteria: women with hypertension, DM, and renal disease.
 |
| Elongi *et al*. (42)* Exclusion criteria: nulliparous women, women with chronic and debilitating diseases, smokers, and regular consumers of alcohol.
 |
| Haque *et al*. (36)* Exclusion criteria: women with history of any chronic illness (renal, cardiovascular, liver disease, endocrine disorder).
 |
| Laine *et al*. (23)* Inclusion criteria: pregnant women with periodontal disease.
 |
| Mistry *et al*. (25)* Inclusion criteria: nulliparous women with singleton pregnancies.
* Exclusion criteria: women in at high-risk for preeclampsia, due to underlying medical conditions, pre-existing hypertension, >3 previous miscarriages or terminations.
 |
| **Supplemental table 4.** (*Continued*) |
| Rezende *et al*. (49)* Exclusion criteria: twin or multiple pregnancy cases or any evidence of previous medical illness, including pre-existing hypertension with or without superimposed preeclampsia.
 |
| Ghaemi *et al*. (22)* Inclusion criteria: singleton pregnancy, gestational age between 24 and 28 weeks, no history of chronic hypertension, lack of use of multivitamins containing Se during the previous year, and no history of diseases during pregnancy, such as kidney disease, diabetes, thyroid, etc.
 |
| Farzin and Sajadi (35)* Inclusion criteria: healthy women in a single pregnancy; gestational age of 30 to 40 weeks.
* Exclusion criteria: women with chronic diseases, diagnosis of abnormal embryo in ultrasound, alcohol or drug addiction, smoking, severe stress during pregnancy, gynaecological history, consumption of anti‑cancer, anticoagulants, aspirins, more than 60 mg iron, calcium and medicines, which contain zinc.
 |
| Katz *et al*. (26)* Exclusion criteria: women with multiple pregnancies, chronic diseases or gestational diabetes mellitus.
 |
| Kim *et al*. (37)* Exclusion criteria: women with history of essential hypertension. altered renal function, diabetes or chronic disease, twin pregnancy, recurrent miscarriage, fetal growth retardation, abruptio placenta, and thrombophilia.
 |
| Negi *et al*. (39)* Exclusion criteria: mothers of newborns with history of difficult delivery, genetic disorder, fetal distress, infection, hemolytic disease and major malformations.
 |
| Holmquist *et al*. (28)* Inclusion criteria: women with singleton gestations, who gave birth to a live-born baby at gestational week 22–42.
* Exclusion criteria: women with hypertension before pregnancy, chronic renal disease, systemic lupus erythematosus or any kind of diabetes. The authors also excluded women with reported energy intake < 4500 kJ or > 20,000 kJ per day.
 |
| Ambad *et al*. (31)* Not reported
 |
| **Supplemental table 4.** (*Continued*) |
| Lui *et al*. (30)* Exclusion criteria: multiple-gestation pregnancies, pregnancies resulting from in vitro fertilization, deliveries induced by maternal trauma, or newborns with major birth defects.
 |
| McAlpine *et al*. (32)* Inclusion criteria: women between 180 and 210 days of gestation residing in South East Queensland.
* Exclusion criteria: women were excluded if they did not complete the full MONT survey set, birthed at a nonparticipating hospital, or were outside the target age range (18-44 years).
 |
| Choi *et al*. (27)* Exclusion criteria: women with history of smoking, history of concurrent serious medical disease, twin pregnancy; miscarriage or fetal death in utero.
 |
| Rayman *et al*. (33)* Inclusion criteria: first pregnancy and 12–14 weeks of gestation at randomisation.
* Exclusion criteria: pregnant women under 18 years old; current smokers; taking any supplement containing Se; taking thyroid medication; multiple pregnancy; abnormal fetal anomaly scan; chronic proteinuria; heparin treatment; HIV, Hep-B or Hep-C positive; yeast intolerance (supplement contains yeast); inability or refusal to give informed consent.
 |