Annexes

Annex 1. Search terms for search strategies

Key concepts identified

| P | I | C | O | S |
|---|---|---|---|---|
| pregnant women | chocolate / polyphenolic compounds | preeclampsia | studies design |
| pregnan* | cocoa | dysfunction | endothelium | randomized and non randomized trials |
| women pregnancy | theobromine | endothelial function | all observational studies |
| flavonoids | cardiovascular disease |
| flavanol-rich | hypertension |
| catechin | nitric oxide |
| epicatechin | blood pressure |

----- AND ---->

Strategy combining

| Concepts identified | Other words and spelling variations |
|---------------------|-------------------------------------|
| Pregnant women | Synonyms MeSH |
| Pregnant woman | Woman, pregnant |
| Women, pregnant | Pregnancy |
| Pregnancy | Pregnancies |
| Maternity | Maternal |
| Maternally | Maternalism |
| Prenatal | Delivery |
| Perinatal | Perinatally |
| Puerperium | Postnatal |
| Accouchement | Obstetrical delivery |
# Chocolate / polyphenolic compounds

| Table 1 |
|----------------------|
| **Cacaos** | **Theobroma cacao** |
| **Theobroma cacaos** | **Cacao, theobroma** |
| **Cacaos, Theobroma** | **Cocoa** |
| **Cocoa** | **Chocolate** |
| **Chocolates** | **** |

| Table 2 |
|----------------------|
| **Theobromine** | **3,7-Dimethylxanthine** |
| **Flavanol-rich** | **2-Phenyl-Chromenes** |
| **Flavonoids** | **2-Phenyl-Benzopyrans** |
| **Catechin** | **Epicatechin** |

## Catechin and epicatechin

| Table 3 |
|----------------------|
| **(-)-Cyanidanol** | **Cianidanol** |
| **Catechunic Acid** | **Acid, Catechinic** |
| **Catechueic Acid** | **Acid, Catechuic** |
| **(+)-Catechin** | **3,3',4',5,7-Flavanpentol** |
| **Categen** | **Zyma** |
| **Epicatechin** | **2H-1-Benzopyran-3,5,7-triol, 2-(3,4-dihydroxyphenyl)-3,4-dihydro-,(2R-cis)-** |
| **KB-53** | **KB 53** |
| **KB53** | **Z 7300** |
| **(-)-Cyanidanol-3** | **Cyanidanol-3** |
| **Cyanidanol 3** | **** |

## Preeclampsia

| Table 4 |
|----------------------|
| **Pre Eclampsia** | **EPH Complex** |
| **EPH Gestosis** | **EPH Toxemias** |
| **EPH Toxemia** | **Toxemia, EPH** |
| **Toxemias, EPH** | **Toxemias, Pregnancy** |
| **Hypertension-Edema-Proteinuria Gestosis** | **Gestosis, Hypertension-Edema-Proteinuria** |
| **Hypertension Edema Proteinuria Gestosis** | **Preeclampsia** |
| **Pregnancy Toxemias** | **Pregnancy Toxemia** |
| **Toxemia, Pregnancy** | **Proteinuria-Edema-Hypertension Gestosis** |
| **Gestosis, Proteinuria-Edema-Hypertension** | **Proteinuria Edema Hypertension Gestosis** |
| **Edema-Proteinuria-Hypertension Gestosis** | **Edema Proteinuria Hypertension Gestosis** |
| **Gestosis, Edema-Proteinuria-Hypertension** | **Gestosis, EPH** |
### Complications of pregnancy

#### Table 5

| Condition                                      | Condition                                      |
|-----------------------------------------------|-----------------------------------------------|
| Hypertension, Pregnancy Induced               | Pregnancy-Induced Hypertension                |
| Pregnancy Induced Hypertension                | Hypertensions, Pregnancy Induced               |
| Induced Hypertension, Pregnancy               | Induced Hypertensions, Pregnancy               |
| Gestational Hypertension                      | Hypertension, Gestational                      |
| Transient Hypertension, Pregnancy             | Hypertension, Pregnancy Transient              |
| Pregnancy Transient Hypertension              |                                               |

### Cardiovascular disease

#### Table 6

| Condition                                      | Condition                                      |
|-----------------------------------------------|-----------------------------------------------|
| Complications, Cardiovascular Pregnancy       | Pregnancy, Cardiovascular Complications        |
| Pregnancies, Cardiovascular Complications     | Cardiovascular Pregnancy Complications         |
| Cardiovascular Pregnancy Complication         | Complication, Cardiovascular Pregnancy         |
| Pregnancy Complication, Cardiovascular        |                                               |

### Endothelial function

#### Table 7

| Endothelium | Endotheliums |
|-------------|--------------|

### Blood pressure

#### Table 8

| Pressure, Blood | Systolic Pressure |
|----------------|-------------------|
| Pressure, Systolic | Pressures, Systolic |
| Diastolic Pressure | Pressure, Diastolic |
| Pulse Pressure | Pressure, Pulse |

### Hypertension

#### Table 9

| Blood Pressure, High | Blood Pressures, High |
|----------------------|-----------------------|
| High Blood Pressure | High Blood Pressures  |
| Nitric Oxide |  |
|------------|--|
| **Table 10** |  |
| • Nitric Oxide | • Mononitrogen Monoxide |
| • Monoxide, Mononitrogen | • Nitrogen Monoxide |
| • Monoxide, Nitrogen | • Endogenous Nitrate Vasodilator |
| • Nitrate Vasodilator, Endogenous | • Vasodilator, Endogenous Nitrate |
| • Nitric Oxide, Endothelium-Derived | • Endothelium-Derived Nitric Oxide |
| • Nitric Oxide, Endothelium Derived | • |
Annex 2. Search strategy in PUBMED

Pregnant women

(Pregnant*[Mesh] OR Pregnant*[tiab] OR (“Pregnant woman” OR Woman, pregnant OR “Women, pregnant” OR Pregnant* OR Pregnancy OR Pregnancies OR Maternity OR Maternal OR Maternally OR “Maternalism” OR Prenatal OR Delivery OR Perinatal OR Perinatally OR puerperium OR Postnatal OR accouchement OR Obstetrical delivery) OR ("Hospitals, Maternity"[Mesh] or Maternity[tiab] or Maternity))

AND

Chocolate / polyphenolic compounds

(("Flavonoids"[Mesh] OR Flavanol-rich[tiab] OR Flavonoids[tiab] OR

"Cacao"[Mesh] OR "Cacao"[TIAB] OR "Theobromine"[Mesh] OR "Theobromine"[TIAB] OR Chocolate[Mesh] OR "Chocolate"[TIAB] OR

"Catechin"[Mesh] OR "Catechin"[TIAB] OR "epicatechin-(4beta-8)-epicatechin-(4beta-8,2beta-O-7)-epicatechin-(4beta-8)-epicatechin" [Supplementary Concept] OR "epicatechin gallate" [Supplementary Concept] OR "epicatechin(4beta-8,2beta-O-7)-epicatechin-(4beta-8)-epicatechin" [Supplementary Concept] OR "ixoratannin A-2" [Supplementary Concept] OR "epigallocatechin-(4,8,2-O-7)epicatechin" [Supplementary Concept] OR "davallin" [Supplementary Concept] OR "4-(S-cysteinyl)epicatechin 3-O-gallate" [Supplementary Concept] OR "3'-O-cinnamoylprocyanidin A-2" [Supplementary Concept] OR "procyanidin" [Supplementary Concept] OR "epicatechin 3-(3-O-methylgallate)" [Supplementary Concept] OR "epicatechin 5-gallate" [Supplementary Concept] OR "3-O-(3,4,5-trimethoxybenzoyl)epicatechin" [Supplementary Concept] OR "epicatechin-glucuronide" [Supplementary Concept] OR "(4beta-8)-7-O-beta-D-xylopyranosyl-epicatechin" [Supplementary Concept] OR "epicatechin dimer B2" [Supplementary Concept] OR "4-(S-cysteinyl)catechin" [Supplementary Concept] OR "epicatechin-(3'-O-7')-epiafzelechin" [Supplementary Concept] OR "epicatechin-3'-O-glucuronide" [Supplementary Concept] OR "epicatechin sulfate" [Supplementary Concept] OR "4-(2-aminoethylthio)epicatechin 3-O-gallate" [Supplementary Concept] OR "galactopyranosylepicatechin (2,7,4,8)epicatechin" [Supplementary Concept] OR Cacaos OR Theobroma cacao OR Theobroma cacaos OR cacao, Theobroma OR cacaos, Theobroma OR Cocoa OR Cocoas OR Chocolate OR Chocolates) or (Polypheno* [Mesh] or Polypheno*[tiab] or Polypheno*)

AND

Preeclampsia
("Pre-Eclampsia"[Mesh]) OR ("Pre-Eclampsia"[TIAB]) OR (Pre-Eclampsia) OR ("Hypertension, Pregnancy-Induced"[Mesh]) OR

("Hypertension"[Mesh]) OR ("Vascular Diseases"[Mesh]) OR ("Cardiovascular Diseases"[Mesh]) OR ("Pregnancy Complications, Cardiovascular"[Mesh]) OR ("Hypertension"[TIAB]) OR ("Vascular Diseases"[TIAB]) OR ("Cardiovascular Diseases"[TIAB]) OR

(Pre Eclampsia OR EPH Complex OR EPH Gestosis OR EPH Toxemias OR EPH Toxemia OR Toxemia, EPH OR Toxemias, EPH OR Toxemias, Pregnancy OR Hypertension-Edema-Proteinuria Gestosis OR Gestosis, Hypertension-Edema-Proteinuria OR Hypertension Edema Proteinuria Gestosis OR Pregnancy Toxemias OR Pregnancy Toxemia OR Toxemia, Pregnancy OR Proteinuria-Edema-Hypertension Gestosis OR Gestosis, Proteinuria-Edema-Hypertension OR Proteinuria Edema Hypertension Gestosis OR Edema-Proteinuria-Hypertension Gestosis OR Edema Proteinuria Hypertension Gestosis OR Gestosis, Edema-Proteinuria-Hypertension OR Gestosis, EPH) OR

(Hypertension, Pregnancy Induced OR Pregnancy-Induced Hypertension OR Pregnancy Induced Hypertension OR Hypertension, Pregnancy Induced OR Induced Hypertension, Pregnancy OR Induced Hypertension, Pregnancy OR Gestational Hypertension OR Hypertension, Gestational OR Transient Hypertension, Pregnancy OR Hypertension, Pregnancy Transient OR Pregnancy Transient Hypertension) OR ("Cardiovascular Diseases"[Mesh] or "Cardiovascular Diseases"[tiab] or "Cardiovascular Diseases") OR (Hypertension[Mesh] or Hypertension[tiab] or Hypertension) OR

("Endothelium, Vascular"[Mesh]) OR (endothelium[tiab]) OR (endothelium OR endotheliums) OR "Hypertension"[Mesh] OR "Hypertension"[TIAB] OR (pressure, blood OR systolic pressure OR pressure, systolic OR pressures, systolic OR diastolic pressure OR pressure, diastolic OR pulse pressure OR pressure, pulse) OR (blood pressure, high OR blood pressures, high OR high blood pressure OR high blood pressures) OR

("Nitric Oxide"[Mesh]) OR ("Nitric Oxide"[TIAB]) OR ("Nitric Oxide Synthase"[Mesh]) OR ("Nitric Oxide Synthase"[tiab]) OR

(Oxide, Nitric OR Mononitrogen Monoxide OR Monoxide, Mononitrogen OR Nitrogen Monoxide OR Monoxide, Nitrogen OR Endogenous Nitrate Vasodilator OR Nitrate Vasodilator, Endogenous OR Vasodilator, Endogenous Nitrate OR Nitric Oxide, Endothelium-Derived OR Endothelium-Derived Nitric Oxide OR Nitric Oxide, Endothelium Derived))
### Annex 3. Search strategy in Embase

| No. | Query |
|-----|-------|
| #32 | #11 AND #20 AND #31 |
| #31 | #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 |
| #30 | 'cardiovascular disease'/exp OR 'cardiovascular diseases' |
| #29 | 'nitric oxide'/exp OR 'nitric oxide' |
| #28 | high AND ('blood'/exp OR blood) AND ('pressure'/exp OR pressure) |
| #27 | 'hypertension'/exp OR hypertension |
| #26 | 'blood'/exp OR blood AND ('pressure'/exp OR pressure) |
| #25 | 'endothelium'/exp OR endothelium |
| #24 | cardiovascular AND ('complication'/exp OR complication) AND ('pregnancy'/exp OR pregnancy) |
| #23 | gestational AND ('hypertension'/exp OR hypertension) |
| #22 | 'hypertension pregnancy induced'/exp OR 'hypertension pregnancy induced' |
| #21 | 'preeclampsia'/exp OR preeclampsia |
| #20 | #12 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 |
| #19 | maternally |
| #18 | 'delivery'/exp OR delivery |
| #17 | accouchement |
| #16 | 'obstetrics'/exp OR obstetrics |
| #15 | 'puerperium'/exp OR puerperium |
| #14 | maternity |
| #12 | pregnan* |
| #11 | #3 OR #4 OR #6 OR #8 OR #9 OR #10 |
| #10 | 'epicatechin'/exp OR epicatechin |
| #9 | 'catechin'/exp OR catechin |
| #8 | flavano* OR polyphenol |
| #6 | 'theobromine'/exp OR theobromine |
| #4 | 'chocolate'/exp OR chocolate |
| #3 | 'cacao'/exp OR cacao |
Annex 4. Search strategy in COCHRANE

| ID | Search                                                                 |
|----|------------------------------------------------------------------------|
| #1 | MeSH descriptor: [Cacao] explode all trees                              |
| #2 | MeSH descriptor: [Theobromine] explode all trees                        |
| #3 | MeSH descriptor: [Flavanones] explode all trees                         |
| #4 | MeSH descriptor: [Catechin] explode all trees                           |
| #5 | MeSH descriptor: [Polyphenols] explode all trees                        |
| #6 | #1 or #2 or #3 or #4 or #5                                             |
| #7 | MeSH descriptor: [Pregnant Women] explode all trees                     |
| #8 | MeSH descriptor: [Pregnancy] explode all trees                          |
| #9 | MeSH descriptor: [Hospitals, Maternity] explode all trees               |
| #10| MeSH descriptor: [Puerperal Disorders] explode all trees                |
| #11| MeSH descriptor: [Delivery, Obstetric] explode all trees                |
| #12| #7 or #8 or #9 or #10 or #11                                            |
| #13| MeSH descriptor: [Pre-Eclampsia] explode all trees                      |
| #14| MeSH descriptor: [Hypertension] explode all trees                       |
| #15| MeSH descriptor: [Hypertension, Pregnancy-Induced] explode all trees    |
| #16| MeSH descriptor: [Cardiovascular Diseases] explode all trees            |
| #17| MeSH descriptor: [Blood Pressure] explode all trees                     |
| #18| MeSH descriptor: [Endothelium] explode all trees                        |
| #19| MeSH descriptor: [Hypertension] explode all trees                       |
| #20| MeSH descriptor: [Nitric Oxide] explode all trees                       |
| #21| #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20                    |
| #22| #6 and #12 and #21                                                      |
| #23| #6 and #12                                                             |
| #24| #6 and #21                                                             |
| #25| #12 and #21                                                            |
Annex 5 Data extraction form

1. Publication source

| No. | Variable       | Variable description                     | Options                        | Class       |
|-----|----------------|-----------------------------------------|--------------------------------|-------------|
| 1.1 | IDscreening    | ID number of first screening            | (number)                       | Continuous  |
| 1.2 | StudyID        | ID number data extraction               | (number)                       | Continuous  |
| 1.3 | Title          | Study title of first screening          | (full title)                   | Nominal     |
| 1.4 | Authors        | Names of authors                        | (last name first author, initials first name) | Nominal |
| 1.5 | Year           | Year of study publishing                | (year in numbers)              | Continuous  |
| 1.6 | ReviewID       | Number of review author identification  | (number)                       | Continuous  |
| 1.7 | Contact        | Contact details                         | (name and email contact author; non-reported) | Nominal |
| 1.8 | Journal        | Publication journal                     | (full name)                    | Nominal     |
| 1.9 | City           | Publication city                        | (full name)                    | Nominal     |
| 1.10| Country        | Publication country                     | (full name)                    | Nominal     |

2. Eligibility verification

| No. | Variable       | Variable description                     | Options                        | Class       |
|-----|----------------|-----------------------------------------|--------------------------------|-------------|
| 2.1 | StudyID        | ID number data extraction               | (number)                       | Continuous  |
| 2.2 | Design         | Study design                            | (design)                       | Nominal     |
| 2.3 | Population     | Pregnant women                          | (Y:Yes, N:Not)                 | Dichotomous |
| 2.4 | Intervention   | Chocolate consumption                   | (Y:Yes, N:Not)                 | Dichotomous |
| 2.5 | Outcome        | Preeclampsia                            | (Y:Yes, N:Not)                 | Dichotomous |
| 2.6 | Eligibility    | Verification of eligibility             | (Y:Yes, N:Not)                 | Dichotomous |
| 2.7 | Exclusion      | Reasons for exclusion                   | (population, intervention or outcome) | Nominal |

3. Methods

| No. | Variable       | Variable description                     | Options                        | Class       |
|-----|----------------|-----------------------------------------|--------------------------------|-------------|
| 3.1 | StudyID        | ID number data extraction               | (number)                       | Continuous  |
| 3.2 | Design         | Study design                            | (CC: case control; C: cohort; RCT: randomized) | Nominal     |
3.3 Details of duration

3.3.1 Beginning Date of beginning enrollment 
(Date: mm-yyyy) Date

3.3.2 End Date of ending enrollment 
(Date: mm-yyyy) Date

3.3.3 Duration Duration of enrollment in months 
(number) Continuous

3.4 Inclusion criteria

3.4.1 Singleton Singleton pregnancy 
(Y:Yes, N:No) Dichotomous

3.4.2 Liveborn Birth of a live infant 
(Y:Yes, N:No) Dichotomous

3.5 Exclusion criteria

3.5.1 CHT Presence of chronic hypertension 
(Y:Yes, N:No) Dichotomous

3.5.2 CRD Presence of chronic renal disease 
(Y:Yes, N:No) Dichotomous

3.5.3 Diabetes Presence of diabetes 
(Y:Yes, N:No) Dichotomous

3.5.4 Twin Presence of a twin gestation 
(Y:Yes, N:No) Dichotomous

3.6 Diagnostic criteria of pre eclampsia

3.6.1 Hypertension Diagnostic criteria regarding hypertension of preeclampsia 
(name) Nominal

3.6.2 Proteinuria Diagnostic criteria regarding proteinuria of preeclampsia 
(name) Nominal

3.6.3 Other Other diagnostic criteria considered 
(name) Nominal

3.7 Study size

3.7.1 Screened Number of subjects screened for eligibility 
(number) Continuous

3.7.2 PotEligible Number of potentially eligible subjects 
(number) Continuous

3.7.3 Included Number of subjects included in the study 
(number) Continuous

3.7.4 AnalysedC Number of subjects analysed with regard to chocolate consumption 
(number) Continuous

3.7.5 AnalysedT Number of subjects analysed with regard to serum theobromine concentration 
(number) Continuous

3.8 Setting Setting of care 
(characteristics) Nominal

4. Participants

| No. | Variable   | Variable description                      | Options   | Class     |
|-----|------------|------------------------------------------|-----------|-----------|
| 4.1 | StudyID    | ID number data extraction                | (number)  | Continuous|
| 4.2 | City       | Participant city                         | (name)    | Nominal   |
| 4.3 | Country    | Participant country                      | (name)    | Nominal   |
| 4.4 | Age interval | Percentage of subjects per age interval | (number)  |           |
| 4.4.1| ≤24        | Percentage of subjects of 24 years of age or under | (number)  | Categorical |
### 4. Percentage of subjects by age

| Variable | Description | Options | Class |
|----------|-------------|---------|-------|
| 25-29    | Percentage of subjects of 25-29 years of age | (number) | Categorical |
| 30-34    | Percentage of subjects of 30-34 years of age | (number) | Categorical |
| >35      | Percentage of subjects over 35 years of age | (number) | Categorical |

### 4.5 Percentage of women by ethnicity

| Ethnicity | Description            | Options | Class |
|-----------|------------------------|---------|-------|
| White     | Percentage of women of white ethnicity | (number) | Categorical |
| Non-white | Percentage of women of non-white ethnicity | (number) | Categorical |

### 4.6 Percentage of women by level of education

| Level | Description | Options | Class |
|-------|-------------|---------|-------|
| ≤12   | Percentage of women with 12 years or less of education, corresponding to High School education or less | (number) | Categorical |
| >12   | Percentage of women with more than 12 years of education, corresponding to any education higher than High School | (number) | Categorical |

### 4.7 Percentage of women by parity

| Parity | Description | Options | Class |
|--------|-------------|---------|-------|
| Nulliparous | Percentage of nulliparous women | (number) | Categorical |
| Parous  | Percentage of parous women     | (number) | Categorical |

### 4.8 Percentage of women by body mass index category

| BMI Category | Description | Options | Class |
|--------------|-------------|---------|-------|
| Underweight  | Percentage of women of underweight BMI | (number) | Categorical |
| Normal       | Percentage of women of normal BMI    | (number) | Categorical |
| Overweight   | Percentage of women of overweight BMI | (number) | Categorical |
| Obese        | Percentage of women of obese BMI     | (number) | Categorical |

### 4.9 Percentage of women by smoking status

| Smoking Status | Description | Options | Class |
|----------------|-------------|---------|-------|
| Non-smoker     | Percentage of women reporting not to smoke | (number) | Categorical |
| Smoker         | Percentage of women reporting to be smokers | (number) | Categorical |

### 4.10 Percentage of women affected by gestational diabetes

| Diabetic Status | Description | Options | Class |
|-----------------|-------------|---------|-------|
| Diabetic        | Percentage of women affected by gestational diabetes | (number) | Categorical |
| Non-diabetic    | Percentage of women not affected by gestational diabetes | (number) | Categorical |

### 5. Interventions

| No.  | Variable | Variable description | Options | Class |
|------|----------|----------------------|---------|-------|
| 5.1  | StudyID  | ID number data extraction | (number) | Continuous |
| Section | Description | Parameter | Data Type |
|---------|-------------|-----------|-----------|
| 5.2     | Exposure    | Exposure assessment | (name) Nominal |
| 5.3     | TimingF     | Timing of exposure in 1st trimester evaluated in days | (number) Continuous |
| 5.4     | TimingT     | Timing of exposure in 3rd trimester evaluated in days | (number) Continuous |
| 5.5     | Technique   | Technique used for quantification of theobromine concentration in serum | (name) Nominal |
| 5.6     | Detection   | Limit of detection of theobromine (ng/dl) | (number) Continuous |
| 5.7     | Quantification | Limit of quantification of theobromine (ng/dl) | (number) Continuous |
| 5.8     | Variation   | Intra-assay coefficient of variation (ng/dl) | (number) Continuous |
| 5.9     | Theobromine concentration in 1st trimester | 5.9.1 MedianF | Median theobromine concentration in 1st trimester | (number) Continuous |
|         |             | 5.9.2 Quartile1F | 1st quartile of theobromine concentration in 1st trimester | (interval) Interval |
|         |             | 5.9.3 Quartile2F | 2nd quartile of theobromine concentration in 1st trimester | (interval) Interval |
|         |             | 5.9.4 Quartile3F | 3rd quartile of theobromine concentration in 1st trimester | (interval) Interval |
|         |             | 5.9.5 Quartile4F | 4th quartile of theobromine concentration in 1st trimester | (interval) Interval |
| 5.10    | Theobromine concentration in 3rd trimester | 5.10.1 MedianT | Median theobromine concentration in 3rd trimester | (number) Continuous |
|         |             | 5.10.2 Quartile1T | 1st quartile of theobromine concentration in 3rd trimester | (interval) Interval |
|         |             | 5.10.3 Quartile2T | 2nd quartile of theobromine concentration in 3rd trimester | (interval) Interval |
|         |             | 5.10.4 Quartile3T | 3rd quartile of theobromine concentration in 3rd trimester | (interval) Interval |
|         |             | 5.10.5 Quartile4T | 4th quartile of theobromine concentration in 3rd trimester | (interval) Interval |
| 5.11    | Total women by theobromine quartile in 1st trimester | 5.11.1 TQuartile1F | Total women in 1st quartile of theobromine concentration in 1st trimester | (number) Categorical |
|         |             | 5.11.2 TQuartile2F | Total women in 2nd quartile of theobromine concentration in 1st trimester | (number) Categorical |
|         |             | 5.11.3 TQuartile3F | Total women in 3rd quartile of theobromine concentration in 1st trimester | (number) Categorical |
|         |             | 5.11.4 TQuartile4F | Total women in 4th quartile of theobromine concentration in 1st trimester | (number) Categorical |
| 5.12    | Total women by theobromine quartile in 3rd trimester | 5.12.1 TQuartile1T | Total women in 1st quartile of theobromine concentration in 3rd trimester | (number) Categorical |
5.12.2 TQuartile2T Total women in 2\textsuperscript{nd} quartile of theobromine concentration in 3\textsuperscript{rd} trimester (number) Categorical

5.12.3 TQuartile3T Total women in 3\textsuperscript{rd} quartile of theobromine concentration in 3\textsuperscript{rd} trimester (number) Categorical

5.12.4 TQuartile4T Total women in 4\textsuperscript{th} quartile of theobromine concentration in 3\textsuperscript{rd} trimester (number) Categorical

5.13 Chocolate Assessment of chocolate consumption (Y:Yes, N:No) Dichotomous

5.14 Total women by number of servings of chocolate drinks and foods consumed per week in 1\textsuperscript{st} trimester

5.14.1 T<1F Less than 1 serving of chocolate drinks and foods consumed per week in 1\textsuperscript{st} trimester (number) Categorical

5.14.2 ToccF Occasional consumption of chocolate drinks and foods in 1\textsuperscript{st} trimester (1 to 3-4 servings per week) (number) Categorical

5.14.3 TregF Regular consumption of chocolate drinks and foods in 1\textsuperscript{st} trimester (4-5 or more servings per week) (number) Categorical

5.15 Total women by number of servings of chocolate drinks and foods consumed per week in 3\textsuperscript{rd} trimester

5.15.1 T<1T Less than 1 serving of chocolate drinks and foods consumed per week in 3\textsuperscript{rd} trimester (number) Categorical

5.15.2 ToccT Occasional consumption of chocolate drinks and foods in 3\textsuperscript{rd} trimester (1 to 3-4 servings per week) (number) Categorical

5.15.3 TregT Regular consumption of chocolate drinks and foods in 3\textsuperscript{rd} trimester (4-5 or more servings per week) (number) Categorical

5.16 Source Source of chocolate (name) Nominal

5.17 Caffeine Assessment of consumption or cord concentration (Y:Yes, N:No) Dichotomous

6. Outcomes

| No. | Variable | Variable description | Options | Class |
|-----|----------|----------------------|---------|-------|
| 6.1 | StudyID  | ID number data extraction | (number) | Continuous |
| 6.2 | Preeclampsia | Outcome assessed | (Y:Yes, N:No) | Dichotomous |
| 6.3 | Cases     | Number of cases with preeclampsia | (number) | Continuous |
| 6.4 | Total cases by quartiles of theobromine concentrations in 1\textsuperscript{st} trimester | | | |
| 6.4.1 | CQuartile1F | Total cases in 1\textsuperscript{st} quartile of theobromine concentration in 1\textsuperscript{st} trimester | (number) | Categorical |
| Section | Code | Description | Type | Categorial/Continuous |
|---------|------|-------------|------|-----------------------|
| 6.4.2   | CQuartile2F | Total cases in 2\textsuperscript{nd} quartile of theobromine concentration in 1\textsuperscript{st} trimester | (number) | Categorial |
| 6.4.3   | CQuartile3F | Total cases in 3\textsuperscript{rd} quartile of theobromine concentration in 1\textsuperscript{st} trimester | (number) | Categorial |
| 6.4.4   | CQuartile4F | Total cases in 4\textsuperscript{th} quartile of theobromine concentration in 1\textsuperscript{st} trimester | (number) | Categorial |
| 6.5     | Total cases by quartiles of theobromine concentrations in 3\textsuperscript{rd} trimester | | | |
| 6.5.1   | CQuartile1T | Total cases in 1\textsuperscript{st} quartile of theobromine concentration in 3\textsuperscript{rd} trimester | (number) | Categorial |
| 6.5.2   | CQuartile2T | Total cases in 2\textsuperscript{nd} quartile of theobromine concentration in 3\textsuperscript{rd} trimester | (number) | Categorial |
| 6.5.3   | CQuartile3T | Total cases in 3\textsuperscript{rd} quartile of theobromine concentration in 3\textsuperscript{rd} trimester | (number) | Categorial |
| 6.5.4   | CQuartile4T | Total cases in 4\textsuperscript{th} quartile of theobromine concentration in 3\textsuperscript{rd} trimester | (number) | Categorial |
| 6.6     | Total cases by categories of chocolate consumption in 1\textsuperscript{st} trimester | | | |
| 6.6.1   | C<1F | Total cases for less than 1 serving of chocolate drinks and foods consumed per week in 1\textsuperscript{st} trimester | (number) | Categorial |
| 6.6.2   | CoccF | Total cases for occasional consumption of chocolate drinks and foods (1 to 3-4 servings per week) in 1\textsuperscript{st} trimester | (number) | Categorial |
| 6.6.3   | CregF | Total cases for regular consumption of chocolate drinks and foods (4-5 or more servings per week) in 1\textsuperscript{st} trimester | (number) | Categorial |
| 6.7     | Total cases by categories of chocolate consumption in 3\textsuperscript{rd} trimester | | | |
| 6.7.1   | C<1T | Total cases for less than 1 serving of chocolate drinks and foods consumed per week in 3\textsuperscript{rd} trimester | (number) | Categorial |
| 6.7.2   | CoccT | Total cases for occasional consumption of chocolate drinks and foods (1 to 3-4 servings per week) in 3\textsuperscript{rd} trimester | (number) | Categorial |
| 6.7.3   | CregT | Total cases for regular consumption of chocolate drinks and foods (4-5 or more servings per week) in 3\textsuperscript{rd} trimester | (number) | Categorial |
| 6.8     | OR by quartiles of theobromine concentration | | | |
| 6.8.1   | ORQuartile1 | OR for 1\textsuperscript{st} quartile of theobromine concentration | (number) | Continuous |
| 6.8.2   | ORQuartile2 | OR for 2\textsuperscript{nd} quartile of theobromine concentration | (number) | Continuous |
| 6.8.3   | ORQuartile3 | OR for 3\textsuperscript{rd} quartile of theobromine concentration | (number) | Continuous |
| 6.8.4   | ORQuartile4 | OR for 4\textsuperscript{th} quartile of theobromine concentration | (number) | Continuous |
| Section | Description |
|---------|-------------|
| 6.9     | Adjusted OR by quartiles of theobromine concentration |
| 6.9.1   | aORQuartile1 Adjusted OR for 1<sup>st</sup> quartile of theobromine concentration (number) Continuous |
| 6.9.2   | aORQuartile2 Adjusted OR for 2<sup>nd</sup> quartile of theobromine concentration (number) Continuous |
| 6.9.3   | aORQuartile3 Adjusted OR for 3<sup>rd</sup> quartile of theobromine concentration (number) Continuous |
| 6.9.4   | aORQuartile4 Adjusted OR for 4<sup>th</sup> quartile of theobromine concentration (number) Continuous |
| 6.10    | OR by selected values of theobromine concentration in 1<sup>st</sup> trimester |
| 6.10.1  | OR100F OR for 100 ng/ml in 1<sup>st</sup> trimester (number) Continuous |
| 6.10.2  | OR200F OR for 200 ng/ml in 1<sup>st</sup> trimester (number) Continuous |
| 6.10.3  | OR300F OR for 300 ng/ml in 1<sup>st</sup> trimester (number) Continuous |
| 6.10.4  | OR500F OR for 500 ng/ml in 1<sup>st</sup> trimester (number) Continuous |
| 6.10.5  | OR700F OR for 700 ng/ml in 1<sup>st</sup> trimester (number) Continuous |
| 6.10.6  | OR900F OR for 900 ng/ml in 1<sup>st</sup> trimester (number) Continuous |
| 6.10.7  | OR1500F OR for 1500 ng/ml in 1<sup>st</sup> trimester (number) Continuous |
| 6.11    | Adjusted OR by selected values of theobromine concentration in 1<sup>st</sup> trimester |
| 6.11.1  | aOR100F OR for 100 ng/ml in 1<sup>st</sup> trimester (number) Continuous |
| 6.11.2  | aOR200F OR for 200 ng/ml in 1<sup>st</sup> trimester (number) Continuous |
| 6.11.3  | aOR300F OR for 300 ng/ml in 1<sup>st</sup> trimester (number) Continuous |
| 6.11.4  | aOR500F OR for 500 ng/ml in 1<sup>st</sup> trimester (number) Continuous |
| 6.11.5  | aOR700F OR for 700 ng/ml in 1<sup>st</sup> trimester (number) Continuous |
| 6.11.6  | aOR900F OR for 900 ng/ml in 1<sup>st</sup> trimester (number) Continuous |
| 6.11.7  | aOR1500F OR for 1500 ng/ml in 1<sup>st</sup> trimester (number) Continuous |
| 6.12    | OR by selected values of theobromine concentration in 3<sup>rd</sup> trimester |
| 6.12.1  | OR100T OR for 100 ng/ml in 3<sup>rd</sup> trimester (number) Continuous |
| 6.12.2  | OR200T OR for 200 ng/ml in 3<sup>rd</sup> trimester (number) Continuous |
| 6.12.3  | OR300T OR for 300 ng/ml in 3<sup>rd</sup> trimester (number) Continuous |
| 6.12.4  | OR500T OR for 500 ng/ml in 3<sup>rd</sup> trimester (number) Continuous |
| 6.12.5  | OR700T OR for 700 ng/ml in 3<sup>rd</sup> trimester (number) Continuous |
| 6.12.6  | OR900T OR for 900 ng/ml in 3<sup>rd</sup> trimester (number) Continuous |
| 6.12.7  | OR1500T OR for 1500 ng/ml in 3<sup>rd</sup> trimester (number) Continuous |
| 6.13    | Adjusted OR by selected values of theobromine concentration in 3<sup>rd</sup> trimester |
| 6.13.1  | aOR100T OR for 100 ng/ml in 3<sup>rd</sup> trimester (number) Continuous |
| 6.13.2  | aOR200T OR for 200 ng/ml in 3<sup>rd</sup> trimester (number) Continuous |
| 6.13.3  | aOR300T OR for 300 ng/ml in 3<sup>rd</sup> trimester (number) Continuous |
| 6.13.4  | aOR500T OR for 500 ng/ml in 3<sup>rd</sup> trimester (number) Continuous |
| 6.13.5  | aOR700T OR for 700 ng/ml in 3<sup>rd</sup> trimester (number) Continuous |
| 6.13.6  | aOR900T OR for 900 ng/ml in 3<sup>rd</sup> trimester (number) Continuous |
| 6.13.7  | aOR1500T OR for 1500 ng/ml in 3<sup>rd</sup> trimester (number) Continuous |
| 6.14    | OR by categories of chocolate consumption in 1<sup>st</sup> trimester |
| 6.14.1  | OR<1F OR for less than 1 serving of chocolate drinks and foods consumed per week in 1<sup>st</sup> trimester (number) Continuous |
6.14.2 ORoccF OR for occasional consumption of chocolate drinks and foods (1 to 3-4 servings per week) in 1st trimester

6.14.3 ORregF OR for regular consumption of chocolate drinks and foods (4-5 or more servings per week) in 1st trimester

6.15 Adjusted OR by categories of chocolate consumption in 1st trimester

6.15.1 aOR<1F Adjusted OR for less than 1 serving of chocolate drinks and foods consumed per week in 1st trimester

6.15.2 AORoccF Adjusted OR for occasional consumption of chocolate drinks and foods (1 to 3-4 servings per week) in 1st trimester

6.15.3 AORregF Adjusted OR for regular consumption of chocolate drinks and foods (4-5 or more servings per week) in 1st trimester

6.16 OR by categories of chocolate consumption in 3rd trimester

6.16.1 OR<1T OR for less than 1 serving of chocolate drinks and foods consumed per week in 3rd trimester

6.16.2 ORoccT OR for occasional consumption of chocolate drinks and foods (1 to 3-4 servings per week) in 3rd trimester

6.16.3 ORregT OR for regular consumption of chocolate drinks and foods (4-5 or more servings per week) in 3rd trimester

6.17 Adjusted OR by categories of chocolate consumption in 3rd trimester

6.17.1 aOR<1T Adjusted OR for less than 1 serving of chocolate drinks and foods consumed per week in 3rd trimester

6.17.2 AORoccT Adjusted OR for occasional consumption of chocolate drinks and foods (1 to 3-4 servings per week) in 3rd trimester

6.17.3 AORregT Adjusted OR for regular consumption of chocolate drinks and foods (4-5 or more servings per week) in 3rd trimester

7. Risk of bias

| No. | Variable            | Variable description                                      | Options                                                                 | Class    |
|-----|---------------------|---------------------------------------------------------|------------------------------------------------------------------------|----------|
| 7.1 | StudyID             | ID number data extraction                                | (number)                                                              | Continuous |
| 7.2 | Selection quality of participants in the studies | Can the criteria for inclusion and exclusion clearly identify the study population? | (Y:Yes, N:Not, U:unclear, NR: non-reported; N/A: non-applicable) | Dichotomous |
| 7.2.1 Criteria | Can the criteria for inclusion and exclusion clearly identify the study population? | (Y:Yes, N:Not, U:unclear, NR: non-reported; N/A: non-applicable) | Dichotomous |
| 7.2.2 Control | Was an appropriate control group used? | (Y:Yes, N:Not, U:unclear, NR: non-reported; N/A: non-applicable) | Dichotomous |
| 7.2.3 Flow | Is the flow of participants explained in detail? | (Y:Yes, N:Not, U:unclear, NR: non-reported; N/A: non-applicable) | Dichotomous |
| 7.2.4 Detail | Are the study participants described in detail? | (Y:Yes, N:Not, U:unclear, NR: non-reported; N/A: non-applicable) | Dichotomous |
| 7.3 Information quality regarding of exposure evaluation | 7.3.1 Consumption | Are objective, suitable, and standard criteria used for measurement of chocolate consumption? | (Y:Yes, N:Not, U:unclear, NR: non-reported; N/A: non-applicable) | Dichotomous |
| 7.3.2 Biomarker | Is the biomarker of chocolate consumption used suitable? | (Y:Yes, N:Not, U:unclear, NR: non-reported; N/A: non-applicable) | Dichotomous |
| 7.3.3 Categories | Is the exposition categorized consistently throughout the study? | (Y:Yes, N:Not, U:unclear, NR: non-reported; N/A: non-applicable) | Dichotomous |
| 7.4 Information quality regarding of outcome evaluation | 7.4.1 Preeclampsia | Are objective, suitable, and standard criteria used for measurement of preeclampsia? | (Y:Yes, N:Not, U:unclear, NR: non-reported; N/A: non-applicable) | Dichotomous |
| 7.4.2 Blinded | Were investigators collecting information regarding outcome blinded to exposure status? | (Y:Yes, N:Not, U:unclear, NR: non-reported; N/A: non-applicable) | Dichotomous |
| 7.5 Choice of design | 7.5.1 Appropriate | Is the study design appropriate for the research question? | (Y:Yes, N:Not, U:unclear, NR: non-reported; N/A: non-applicable) | Dichotomous |
| 7.5.2 Data | Did the study use data that hadn’t been originally collected for another purpose? | (Y:Yes, N:Not, U:unclear, NR: non-reported; N/A: non-applicable) | Dichotomous |
| 7.6 Quality of simple size | 7.6.1 Size | Is the sample size adequately calculated? | (Y:Yes, N:Not, U:unclear, NR: non-reported; N/A: non-applicable) | Dichotomous |
| 7.7 Quality of statistical analyses | 7.7.1 Statistical | Are the statistical tests chosen for analysis of the association appropriate? | (Y:Yes, N:Not, U:unclear, NR: non-reported; N/A: non-applicable) | Dichotomous |
| 7.7.2 Non-analysed | Are reasons for exclusion of subjects from statistical analysis explained? | (Y:Yes, N:Not, U:unclear, NR: non-reported; N/A: non-applicable) | Dichotomous |
| 7.7.3 Confounding | Were confounding variables controlled for in the analysis? | (Y:Yes, N:Not, U:unclear, NR: non-reported; N/A: non-applicable) | Dichotomous |
| 7.7.4 Continuous | Do the results clearly report how they had been adjusted for continuous confounders? | (Y:Yes, N:Not, U:unclear, NR: non-reported; N/A: non-applicable) | Dichotomous |
| 7.7.5 OR | Are the estimates of risk (odds ratio) given with CIs? | (Y:Yes, N:Not, U:unclear, NR: non-reported; N/A: non-applicable) | Dichotomous |
| 7.8  | Quality | Overall quality of studies | (L: Low, I:Intermediate, H:High) | Categorical |
|------|---------|---------------------------|---------------------------------|-------------|


## Annex 6 Assessment of quality

| Criteria | Studies |
|----------|---------|
| **Participants** | | |
| Can the criteria for inclusion and exclusion clearly identify the study population? | |
| Was an appropriate control group used? | |
| Is the flow of participants explained in detail? | |
| Are the study participants described in detail? | |
| **Intervention** | | |
| Are objective, suitable, and standard criteria used for measurement of chocolate consumption? | |
| Is the biomarker of chocolate consumption used suitable? | |
| Is the exposition categorized consistently throughout the study? | |
| **Outcome** | | |
| Are objective, suitable, and standard criteria used for measurement of preeclampsia? | |
| Were investigators collecting information regarding outcome blinded to exposure status? | |
| **Design** | | |
| Is the study design appropriate for the research question? | |
| Did the study use data that hadn't been originally collected for another purpose? | |
| **Sample size** | | |
| Is the sample size adequately calculated? | |
| **Statistical analyses** | | |
| Are the statistical tests chosen for analysis of the association appropriate? | |
| Are the reasons for exclusion of subjects from statistical analysis explained? | |
| Were confounding variables controlled for in the analysis? | |
| Do the results clearly report how they had been adjusted for continuous confounders? | |
| Are the estimates of risk (odds ratio) given with CIs? | |
| **Overall quality** | |