**Supplementary material**

**Preconception and early-pregnancy risk prediction for birth complications: development of prediction models within a population-based prospective cohort** *Running title: Risk prediction of birth complications*

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**Supplementary Figure S1. Flow chart of the study participants**

n= 8663Mothers enrolled during early-pregnancy

n=323Twin pregnancy n= 94

Induced abortion n= 29

Intrauterine fetal death n= 74

Loss to follow up n= 42

No information on gestational

age or weight at birth n= 84

n= 8340
Women with singleton live births with information available on at least one characteristic in preconception or early-pregnancy

**Supplementary Methods S1. Literature search**

((“pregnancy” [mesh]) or pregnancy or (preconception) or (prenatal))

AND (“risk factors” [Mesh] OR “Life Style” [mesh] or “health behavior” [mesh] and (risk factor\*) or (life style) or (diet\*))

AND (“premature birth” [Mesh] or “Infant, Low Birth Weight” [mesh] or “Pregnancy Complications” [mesh] or (pregnancy outcome) or (birth) or (growth restriction) OR (low birth weight) or macrosom\*)

AND ((meta-analysis [Publication Type] OR review [Publication Type] OR systematic review [Publication Type]) AND (english[Language]) AND (("2010"[Date - Publication] : "3000"[Date - Publication])))

**Supplementary Table S1. Categories of candidate predictors**

|  |  |  |
| --- | --- | --- |
|  | Variable | Categories |
| *Basic preconception characteristics* | Age | <25 |
| 25-35 |
| >35 |
| Ethnicity | Dutch or European |
| Surinamese |
| Turkish |
| Moroccan |
| Cape Verdian or Dutch Antilles |
| Other |
| *Missing* |
| Parity | Nulliparity |
| Multiparous |
| *Missing* |
| Prepregnancy BMI | <25.0 kg/m2  |
| 25.0; 29.9.0 kg/m2  |
| 30.0; 35.0 kg/m2  |
| >35.0 kg/m2 |
| *Missing* |
| Smoking | No  |
| Yes |
| *Missing* |
| *Socio-demographic characteristics* | Education | Low  |
| High |
| *Missing* |
| Income | Low |
| High |
| *Missing* |
| Marital status | Married/living together |
| No partner/unstable relationship |
| *Missing* |
| Occupation | Currently employed |
| Applying for a job |
| Unemployed and not applying for a job |
| *Missing* |
| Pregnancy planning | Planned pregnancy |
| Unplanned pregnancy |
| *Missing* |
| *Lifestyle characteristics* | Alcohol consumption | Never or ≤ 1 drink/week |
| >1 drink/week |
| *Missing* |
| Multivitamin supplementation  | Yes |
| No |
| *Missing* |
| Folic acid supplementation  | yes |
| No |
| *Missing* |
| Caffeine consumption  | *<2/day* |
| ≥2/day |
| *Missing* |
| Fruit consumption  | ≥200 grams/day |
| <200 grams/day |
| *Missing* |
| Vegetable consumption  | ≥250 grams/day  |
| <250 grams/day |
| *Missing* |
| Fatty fish consumption | <1x/week |
| 1-2x/week |
| >2x/week |
| *Missing* |
| Dietary glycemic index | per 1 increase |
| Stress | BSI score ≤0.71 |
| BSI score >0.71 |
| *Missing*  |
| *Medical history characteristics* | History of a chronic disease  | No |
| Yes |
| *Missing* |
| Obstetric complications in history | No |
| Yes |
| *Missing* |
| IVF or ICSI pregnancy  | No |
| Yes |
| *Missing* |
| Consanguinity with planned biological father | No |
| Yes |
| *Missing* |
| *Early-pregnancy clinical characteristics* | Systolic blood pressure | per 10 mmHg increase |
| Diastolic blood pressure  | per 10 mmHg increase |
| Hb  | First quintile (3.9; 7.0 mmol/l) |
| Second quintile (7.1; 7.4 mmol/l) |
| Third quintile (7.5; 7.6 mmol/l) |
| Fourth quintile (7.7; 8.0 mmol/l) |
| Fifth quintile (8.10; 11.30 mmol/l) |
| *Missing* |
| Random Glucose  | per 1 mmol/L increase |
| Total cholesterol | Per 1 mmol/L increase |
| HDL | per 1 mmol/L increase |
| Triglycerides | per 1 mmol/L increase |
| Ferritine  | First quintile (1.5; 26.4 ug/l) |
| Second quintile (26.4; 42.5 ug/l) |
| Third quintile (42.5; 62.8 ug/l) |
| Fourth quintile (62.8; 95.8 ug/l) |
| Fifth quintile (95.9; 390.4 ug/l) |
| *Missing* |
| Vitamin D  | per 10 nmol/l increase |
| Omega-3 fatty acids  | per 10 mg/l increase |
| *Paternal characteristics* | Age  | <25 |
| 25-35 |
| >35 |
| Ethnicity | Dutch or European |
| Surinamese |
| Turkish |
| Moroccan |
| Cape Verdian or Dutch Antilles |
| Other |
| *Missing* |
| Prepregnancy BMI | <25.0 kg/m2  |
| 25.0; 29.9.0 kg/m2  |
| >30 kg/m2  |
| *Missing* |
| Smoking | No  |
| Yes |
| *Missing* |
| Alcohol consumption in past two months | No  |
| Yes |
| *Missing* |
| Systolic blood pressure | per 10 mmHg increase |
| Diastolic blood pressure  | per 10 mmHg increase |

Green represents the reference category, grey represents the missing category.

**Supplementary Table S2. Characteristics not selected into prediction models according to birth outcomes**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **No adverse birth outcome\***(n=6333) | **Preterm birth/small-for-gestational-age\*** (n=1207) | **Large-for-gestational-age\*** (n=834) |
| **Maternal preconception characteristics** |  |  |  |
| Marital status, n no partner/stable relation (%) | 789 (13.6) |  244 (22.5) | 65 (8.5) |
| History of any obstetric complication, n yes (%)† | 2027 (95.0) | 390 (97.3) | 258 (95.2) |
| IVF/ICSI pregnancy, n yes (%) | 45 (0.7) | 9 (0.9) | 6 (0.8) |
| Consanguinity with biological father, n yes (%) | 225 (4.1) | 33 (3.2) | 30 (4.1) |
| Fruit consumption, n <200grams/day (%) | 2970 (63.9) | 590 (68.4) | 390 (60.5) |
| Daily dietary glycemic index, mean (SD) | 58.2 (3.4) | 58.5 (3.6) | 57.9 (3.2) |
| Folic acid supplementation, n no (%) | 1343 (28.4) | 312 (35.9) | 140 (22.2) |
| Psychological distress, n yes (%) | 510 (10.4) | 120 (13.5) | 57 (8.7) |
| Total cholesterol concentrations, mean (SD), mmol/L  | 4.81 (0.85) | 4.80 (0.88) | 4.82 (0.89) |
| HDL-concentrations, mean (SD), mmol/L | 1.77 (0.35) | 1.77 (0.35) | 1.73 (0.35) |
| Omega-3 fatty acids concentrations, mean (SD), mg/L | 104.1 (27.7) | 100.6 (26.9) (26.1) | 106.2 (26.1) |

\*Of large-for-gestational-age newborns, n=34 were preterm, due to which there is overlap between the columns of preterm birth/small-for-gestational-age and large-for-gestational-age

**Supplementary Table S3. Socio-demographic characteristics of subsets for calibration**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Subset 1** (n=4091) | **Subset 2** (n=3035) | **Subset 3** (n=1214) |
| **Maternal socio-demographic characteristics** |  |  |  |
| Ethnicity  |  |  |  |
|  Dutch or European, n (%) | 1772 (43.3) | 2215 (73.0) | 553 (45.6) |
|  Surinamese, n (%) | 403 (9.9) | 196 (6.5) | 123 (10.1) |
|  Turkish, n (%) | 506 (12.4) | 110 (3.6) | 116 (9.6) |
|  Moroccan, n (%) | 369 (9.0) | 102 (3.4) | 69 (5.7) |
|  Cape Verdean or Dutch Antilles, n (%) | 364 (8.9) | 98 (3.2) | 145 (11.9) |
|  Other, n (%) | 702 (17.2) | 495 (16.3) | 217 (17.9) |
| Education, n higher education (%)  | 1939 (47.4) | 1644 (54.2) | 346 (28.5) |
| Income, n high (%) | 1633 (39.9) | 720 (23.7) | 561 (46.2) |
| Occupational status, employed n (%) | 1924 (47.0) | 2016 (66.4) | 492 (40.5) |
| Marital status, n no partner/stable relation (%) | 468 (11.4) | 150 (4.9) | 111 (9.1) |
| Planned pregnancy, n no (%) | 1162 (28.4) | 562 (18.5) | 388 (32.0) |
| **Birth outcomes** |  |  |  |
| Preterm birth | 217 (5.3) | 128 (4.2) | 80 (6.6) |
| Small-for-gestational-age | 436 (10.7) | 254 (8.4) | 144 (11.9) |
| Large-for-gestational-age | 370 (9.0) | 356 (11.7) | 108 (8.9) |

**Supplementary Table S4. Paternal characteristics** *(n=6062)*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **No adverse birth outcome\***(n=4631) | **Preterm birth\***(n=285) | **Small-for-gestational-age\*** (n=545) | **Large-for-gestational-age\*** (n=601) |
| **Paternal characteristics** |  |  |  |  |
| Age, mean (SD), years | 32.8 (5.7) | 32.2 (6.1) | 31.8 (6.0) | 33.4 (5.1) |
| Ethnicity  |  |  |  |  |
|  Dutch or European, n (%) | 2711 (58.5) | 155 (54.4) | 248 (45.5) | 431 (71.7) |
|  Surinamese, n (%) | 277 (6.0) | 23 (8.1) | 73 (13.4) | 12 (2.0) |
|  Turkish, n (%) | 311 (6.7) | 21 (7.4) | 37 (6.8) | 27 (4.5) |
|  Moroccan, n (%) | 185 (4.0) | 9 (3.2) | 26 (4.8) | 19 (3.2) |
|  Cape Verdean or Dutch Antilles, n (%) | 235 (5.3) | 16 (5.6) | 45 (8.2) | 17 (2.8) |
|  Other, n (%) | 395 (9.0) | 24 (9.0) | 46 (9.0) | 44 (7.6) |
| Body Mass Index, mean (SD), kg/m2  | 25.3 (3.5) | 25.3 (3.5) | 24.9 (3.5) | 25.6 (3.5) |
| Education, n. higher education (%)  | 1985 (42.9) | 105 (36.8) | 168 (30.8) | 316 (52.6) |
| Smoking, n yes (%) | 1653 (35.7) | 106 (37.2) | 216 (39.6) | 202 (33.6) |
| Alcohol consumption in past 2 months, n yes (%) | 3173 (68.5) | 176 (61.8) | 353 (64.8) | 451 (75.0) |
| Mean systolic blood pressure, mean (SD), mmHg | 130 (14) | 130 (13) | 129 (13) | 130 (13) |
| Mean diastolic blood pressure, mean (SD), mmHg | 73 (11) | 73 (12) | 72 (11) | 73 (10) |

**Supplementary Table S5. Model performance for the core model for secondary outcomes**

|  |
| --- |
| **Maternal pregnancy complications and adverse birth outcomes** |
| **4a. Model performance for gestational hypertension and preeclampsia (n total population=8136, ncases=495)** |
| **Models** | **AUC (95% CI)** | **Sensitivity at specificity (%)** |
|  |  | **70%** | **80%** | **90%** |
| Corea  | 0.70 (0.67; 0.72) | 60 | 43 | 28 |
| **4b. Fetal distress (n total population=8030, ncases=598)** |  |
| **Models** | **AUC (95% CI)** | **Sensitivity at specificity (%)** |
|  |  | **70%** | **80%** | **90%** |
| Corea  | 0.70 (0.67; 0.72) | 60 | 43 | 28 |
| **4c. Model performance for caesarean section (n total population=7587, ncases=917)** |  |
| **Models** | **AUC (95% CI)** | **Sensitivity at specificity (%)** |
|  |  | **70%** | **80%** | **90%** |
| Corea  | 0.64 (0.63; 0.66) | 48 | 38 | 22 |
| **4d. Model performance for low birthweight (n total population=8340, ncases=403)** |
| **Models** | **AUC (95% CI)** | **Sensitivity at specificity (%)** |
|  |  | **70%** | **80%** | **90%** |
| Corea  | 0.66 (0.63; 0.69) | 52 | 38 | 22 |
| **4e. Model performance for macrosomia (n total population=8340, ncases=189)** |
| **Models** | **AUC (95% CI)** | **Sensitivity at specificity (%)** |
|  |  | **70%** | **80%** | **90%** |
| Corea  | 0.68 (0.64; 0.72) | 56 | 44 | 33 |

aCore model includes age, ethnicity, prepregnancy Body Mass Index, parity and smoking