Supplementary tables and figures

**Supplementary Table 1.**  The individual and joint associations of maternal overweight or obesity (OWO) and maternal self-reported smoking during pregnancy (non-smoking, quit-smoking, continuous-smoking) on child’s risk of small and large for gestation (SGA and LGA) in overall sample (all compared to AGA).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Maternal OWO status | Smoking status | N (total = 2351) | Number of SGA children (%) | OR(95%CI) | Number of LGA children (%) | OR(95%CI) |
| Individual associations | | | | | | |
| nonOWO |  | 1109(0.47) | 180(0.16) | Referent | 78(0.07) | Referent |
| OWO |  | 1242(0.53) | 114(0.09) | 0.60(0.46-0.77) | 150(0.121) | 1.52(1.13-2.05) |
|  | non-smoking | 1930(0.82) | 213(0.11) | Referent | 198(0.10) | Referent |
|  | quit-smoking | 188(0.08) | 18(0.10) | 0.79(0.47-1.33) | 16(0.085) | 0.82(0.48-1.42) |
|  | continuous-smoking | 233(0.10) | 63(0.27) | 3.39(2.35-4.90) | 14(0.060) | 0.68(0.37-1.23) |
|  | BMI/IQR | 2351(1.00) | 294(0.13) | 0.75(0.63-0.89) | 228(0.097) | 1.36(1.18-1.57) |
| Joint associations | | | | | | |
| nonOWO | non-smoking | 927(0.39) | 129(0.14) | Referent | 68(0.07) | Referent |
| nonOWO | quit-smoking | 75(0.03) | 12(0.16) | 1.10(0.56-2.13) | 5(0.067) | 0.95(0.36-2.48) |
| nonOWO | continuous-smoking | 107(0.05) | 39(0.36) | 4.30(2.62-7.04) | 5(0.047) | 0.86(0.32-2.28) |
| OWO | non-smoking | 1003(0.43) | 84(0.08) | 0.67(0.50-0.91) | 130(0.130) | 1.61(1.17-2.22) |
| OWO | quit-smoking | 113(0.05) | 6(0.05) | 0.38(0.16-0.89) | 11(0.097) | 1.17(0.59-2.31) |
| OWO | continuous-smoking | 126(0.05) | 24(0.19) | 1.84(1.10-3.08) | 9(0.071) | 0.95(0.45-2.01) |
| p for interaction (OWO\*smoking) | | | 0.224 | | 0.647 | |

Notes: OWO, overweight or obesity; smk, smoking. Models were adjusted for maternal age at delivery, race, education, parity, perceived stress during pregnancy, child age, breastfeeding, gestational or preexisting diabetes.

**Supplementary Table 2.**  The individual and joint associations of maternal OWO and self-reported smoking during pregnancy (non-smoking, quit-smoking, continuous-smoking) on children OWO during childhood in samples stratified by gender.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Maternal OWO status | Smoking status | Number of female children (total =1174) | Number of overweight children (%) | OR(95%CI) | Number of obese children (%) | OR(95%CI) |
| Individual associations | | | | | | |
| nonOWO |  | 553(0.47) | 86(0.16) | Referent | 90(0.16) | Referent |
| OWO |  | 621(0.53) | 109(0.18) | 1.68(1.20-2.35) | 238(0.383) | 3.52(2.61-4.75) |
|  | non-smoking | 969(0.83) | 167(0.17) | Referent | 261(0.27) | Referent |
|  | quit-smoking | 94(0.08) | 14(0.15) | 0.95(0.50-1.78) | 31(0.330) | 1.27(0.78-2.06) |
|  | continuous-smoking | 111(0.09) | 14(0.13) | 0.71(0.37-1.36) | 36(0.324) | 1.16(0.72-1.87) |
|  | BMI/IQR | 1174(1.00) | 195(0.17) | 1.45(1.17-1.79) | 328(0.279) | 2.20(1.85-2.62) |
| Joint associations | | | | | | |
| nonOWO | non-smoking | 474(0.40) | 74(0.16) | Referent | 76(0.16) | Referent |
| nonOWO | quit-smoking | 33(0.03) | 3(0.09) | 0.53(0.15-1.84) | 7(0.212) | 1.15(0.47-2.82) |
| nonOWO | continuous-smoking | 46(0.04) | 9(0.20) | 1.25(0.54-2.88) | 7(0.152) | 1.00(0.41-2.44) |
| OWO | non-smoking | 495(0.42) | 93(0.19) | 1.77(1.23-2.56) | 185(0.374) | 3.50(2.52-4.87) |
| OWO | quit-smoking | 61(0.05) | 11(0.18) | 1.89(0.88-4.05) | 24(0.393) | 3.84(2.06-7.15) |
| OWO | continuous-smoking | 65(0.06) | 5(0.08) | 0.67(0.25-1.84) | 29(0.446) | 3.75(2.05-6.85) |
| p for interaction (OWO\*smoking) | | | 0.347 | | 0.935 | |

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Maternal OWO status | Smoking status | Number of male children (total = 1177) | Number of overweight children (%) | OR(95%CI) | Number of obese children (%) | OR(95%CI) |
| Individual associations | | | | | | |
| nonOWO |  | 556(0.47) | 90(0.16) | Referent | 111(0.20) | Referent |
| OWO |  | 621(0.53) | 115(0.19) | 1.54(1.11-2.14) | 223(0.359) | 2.65(1.98-3.54) |
|  | non-smoking | 961(0.82) | 164(0.17) | Referent | 266(0.28) | Referent |
|  | quit-smoking | 94(0.08) | 13(0.14) | 0.82(0.42-1.59) | 30(0.319) | 1.17(0.72-1.91) |
|  | continuous-smoking | 122(0.10) | 28(0.23) | 1.87(1.10-3.18) | 38(0.311) | 1.40(0.87-2.26) |
|  | BMI/IQR | 1177(1.00) | 205(0.17) | 1.49(1.19-1.86) | 334(0.284) | 2.27(1.88-2.74) |
| Joint associations | | | | | | |
| nonOWO | non-smoking | 453(0.38) | 70(0.15) | Referent | 89(0.20) | Referent |
| nonOWO | quit-smoking | 42(0.04) | 5(0.12) | 0.84(0.31-2.29) | 8(0.190) | 0.89(0.39-2.05) |
| nonOWO | continuous-smoking | 61(0.05) | 15(0.25) | 2.44(1.18-5.03) | 14(0.230) | 1.50(0.73-3.08) |
| OWO | non-smoking | 508(0.43) | 94(0.19) | 1.66(1.15-2.39) | 177(0.348) | 2.59(1.88-3.57) |
| OWO | quit-smoking | 52(0.04) | 8(0.15) | 1.38(0.57-3.37) | 22(0.423) | 3.48(1.80-6.73) |
| OWO | continuous-smoking | 61(0.05) | 13(0.21) | 2.51(1.19-5.32) | 24(0.393) | 3.61(1.90-6.86) |
| p for interaction (OWO\*smoking) | | | 0.993 | | 0.44 | |

Notes: OWO, overweight or obesity; smk, smoking. Models were adjusted for maternal age at delivery, race, education, parity, perceived stress during pregnancy, child age, breastfeeding, gestational or preexisting diabetes.

**Supplementary Table 3.** The individual and joint associations of maternal OWO and self-reported smoking during pregnancy (non-smoking, quit-smoking, continuous-smoking) on children OWO in term-birth and preterm-birth samples.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Maternal OWO status | Smoking status | Number of term-birth children (total = 1708) | | Number of overweight children (%) | OR(95%CI) | | Number of obese children (%) | OR(95%CI) |
| Individual associations | | | | | | | | |
| nonOWO |  | 825(0.48) | | 134(0.16) | Referent | | 150(0.18) | Referent |
| OWO |  | 883(0.52) | | 172(0.19) | 1.72(1.31-2.26) | | 330(0.374) | 3.11(2.44-3.96) |
|  | non-smoking | 1445(0.85) | | 261(0.18) | Referent | | 393(0.27) | Referent |
|  | quit-smoking | 115(0.07) | | 15(0.13) | 0.86(0.47-1.57) | | 44(0.383) | 1.57(1.03-2.41) |
|  | continuous-smoking | 148(0.09) | | 30(0.20) | 1.24(0.77-2.00) | | 43(0.291) | 1.12(0.74-1.71) |
| Joint associations | | | | | | | | |
| nonOWO | non-smoking | 718(0.42) | | 114(0.16) | Referent | | 129(0.18) | Referent |
| nonOWO | quit-smoking | 40(0.02) | | 4(0.10) | 0.69(0.23-2.05) | | 10(0.250) | 1.34(0.62-2.90) |
| nonOWO | continuous-smoking | 67(0.04) | | 16(0.24) | 1.67(0.87-3.20) | | 11(0.164) | 1.00(0.48-2.06) |
| OWO | non-smoking | 727(0.43) | | 147(0.20) | 1.82(1.36-2.44) | | 264(0.363) | 3.04(2.34-3.96) |
| OWO | quit-smoking | 75(0.04) | | 11(0.15) | 1.52(0.73-3.15) | | 34(0.453) | 4.10(2.39-7.02) |
| OWO | continuous-smoking | 81(0.05) | | 14(0.17) | 1.71(0.86-3.36) | | 32(0.395) | 3.37(1.96-5.81) |
| p for interaction (OWO\*smoking) | | | 0.782 | | | 0.994 | | |

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Maternal OWO status | Smoking status | Number of preterm-birth children (total=643) | Number of overweight children (%) | OR(95%CI) | Number of obese children (%) | OR(95%CI) |
| Individual associations | | | | | | |
| nonOWO |  | 284(0.44) | 42(0.15) | Referent | 51(0.18) | Referent |
| OWO |  | 359(0.56) | 52(0.14) | 1.28(0.80-2.07) | 131(0.365) | 2.83(1.89-4.24) |
|  | non-smoking | 485(0.75) | 70(0.14) | Referent | 134(0.28) | Referent |
|  | quit-smoking | 73(0.11) | 12(0.16) | 1.06(0.53-2.16) | 17(0.233) | 0.82(0.45-1.52) |
|  | continuous-smoking | 85(0.13) | 12(0.14) | 1.32(0.62-2.82) | 31(0.365) | 1.72(0.97-3.06) |
| Joint associations | | | | | | |
| nonOWO | non-smoking | 209(0.33) | 30(0.14) | Referent | 36(0.17) | Referent |
| nonOWO | quit-smoking | 35(0.05) | 4(0.11) | 0.75(0.24-2.35) | 5(0.143) | 0.82(0.29-2.32) |
| nonOWO | continuous-smoking | 40(0.06) | 8(0.20) | 2.24(0.83-6.03) | 10(0.250) | 2.27(0.91-5.61) |
| OWO | non-smoking | 276(0.43) | 40(0.14) | 1.38(0.79-2.40) | 98(0.355) | 2.98(1.86-4.79) |
| OWO | quit-smoking | 38(0.06) | 8(0.21) | 2.00(0.77-5.17) | 12(0.316) | 2.77(1.19-6.44) |
| OWO | continuous-smoking | 45(0.07) | 4(0.09) | 1.01(0.31-3.28) | 21(0.467) | 4.43(2.06-9.54) |
| p for interaction (OWO\*smoking) | | | 0.378 | | 0.845 | |

Notes: OWO, overweight or obesity; smk, smoking; IQR, interquartile range. Models were adjusted for maternal age at delivery, race, education, parity, perceived stress during pregnancy, child age, breastfeeding, gestational or preexisting diabetes.

**Supplementary Table 4.** The individual and joint associations of maternal OWO and maternal self-reported smoking during pregnancy (non-smoking, quit-smoking, continuous-smoking) on children OWO in overall samples, with adding the adjustment of fetal growth restriction.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Maternal OWO status | Smoking status | Number of children (total = 2351) | Number of overweight children (%) | OR(95%CI) | Number of obese children (%) | OR(95%CI) |
| Individual associations | | | | | | |
| nonOWO |  | 1109(0.47) | 176(0.16) | Referent | 201(0.18) | Referent |
| OWO |  | 1242(0.53) | 224(0.18) | 1.59(1.26-2.01) | 461(0.371) | 2.87(2.33-3.54) |
|  | non-smoking | 1930(0.82) | 331(0.17) | Referent | 527(0.27) | Referent |
|  | quit-smoking | 188(0.08) | 27(0.14) | 0.90(0.57-1.41) | 61(0.324) | 1.25(0.88-1.77) |
|  | continuous-smoking | 233(0.10) | 42(0.18) | 1.26(0.84-1.89) | 74(0.318) | 1.54(1.09-2.17) |
| Joint associations | | | | | | |
| nonOWO | non-smoking | 927(0.39) | 144(0.16) | Referent | 165(0.18) | Referent |
| nonOWO | quit-smoking | 75(0.03) | 8(0.11) | 0.69(0.32-1.49) | 15(0.200) | 1.05(0.57-1.94) |
| nonOWO | continuous-smoking | 107(0.05) | 24(0.22) | 1.81(1.04-3.12) | 21(0.196) | 1.57(0.89-2.75) |
| OWO | non-smoking | 1003(0.43) | 187(0.19) | 1.68(1.30-2.17) | 362(0.361) | 2.85(2.26-3.59) |
| OWO | quit-smoking | 113(0.05) | 19(0.17) | 1.66(0.94-2.95) | 46(0.407) | 3.50(2.22-5.50) |
| OWO | continuous-smoking | 126(0.05) | 18(0.14) | 1.47(0.82-2.64) | 53(0.421) | 4.01(2.58-6.25) |
| p for interaction (OWO\*smoking) | | | 0.448 | | 0.688 | |

Notes: OWO, overweight or obesity; smk, smoking; IQR, interquartile range. Models were adjusted for maternal age at delivery, race, education, parity, perceived stress during pregnancy, child age, breastfeeding, gestational or preexisting diabetes, fetal growth restriction.

**Supplementary Table 5.** The individual and joint associations of maternal OWO and maternal plasma cotinine levels at delivery on children OWO in samples with maternal cotinine stratified by gender.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Maternal OWO status | Cotinine | Number of male children (total = 660) | Number of overweight children (%) | OR(95%CI) | Number of obese children (%) | OR(95%CI) |
| Individual associations  OR(95%CI)  n(%)  OR(95%CI) | | | | | | |
| nonOWO |  | 307(0.47) | 40(0.13) | Referent | 64(0.21) | Referent |
| OWO |  | 353(0.53) | 54(0.15) | 1.58(0.98-2.54) | 129(0.365) | 2.43(1.65-3.56) |
|  | Q1 | 164(0.25) | 25(0.15) | Referent | 41(0.25) | Referent |
|  | Q2 | 160(0.24) | 19(0.12) | 0.75(0.38-1.50) | 44(0.275) | 0.98(0.58-1.68) |
|  | Q3 | 161(0.24) | 18(0.11) | 0.74(0.37-1.48) | 49(0.304) | 1.21(0.72-2.04) |
|  | Q4 | 175(0.27) | 32(0.18) | 1.89(0.98-3.66) | 59(0.337) | 1.78(1.03-3.06) |
|  | continuous cotinine | 660(1.00) | 94(0.14) | 1.35(1.05-1.75) | 193(0.292) | 1.26(1.04-1.54) |
| Joint associations | | | | | | |
| nonOWO | Q1-3 | 227(0.34) | 24(0.11) | Referent | 47(0.21) | Referent |
| nonOWO | Q4 | 80(0.12) | 16(0.20) | 2.87(1.34-6.15) | 17(0.212) | 1.24(0.63-2.45) |
| OWO | Q1-3 | 258(0.39) | 38(0.15) | 1.81(1.01-3.25) | 87(0.337) | 2.13(1.36-3.32) |
| OWO | Q4 | 95(0.14) | 16(0.17) | 3.44(1.59-7.43) | 42(0.442) | 4.12(2.29-7.42) |

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Maternal OWO status | Cotinine | Number of female children (total = 655) | Number of overweight children (%) | OR(95%CI) | Number of obese children (%) | OR(95%CI) |
| Individual associations | | | | | | |
| nonOWO |  | 302(0.46) | 51(0.17) | Referent | 53(0.18) | Referent |
| OWO |  | 353(0.54) | 63(0.18) | 1.51(0.96-2.35) | 135(0.382) | 3.09(2.07-4.60) |
|  | Q1 | 167(0.25) | 32(0.19) | Referent | 44(0.26) | Referent |
|  | Q2 | 168(0.26) | 25(0.15) | 0.70(0.38-1.29) | 49(0.292) | 0.99(0.59-1.66) |
|  | Q3 | 166(0.25) | 28(0.17) | 0.83(0.45-1.51) | 46(0.277) | 0.96(0.57-1.61) |
|  | Q4 | 154(0.24) | 29(0.19) | 1.04(0.55-1.95) | 49(0.318) | 1.21(0.70-2.10) |
|  | continuous cotinine | 655(1.00) | 114(0.17) | 0.94(0.74-1.19) | 188(0.287) | 1.03(0.85-1.26) |
| Joint associations | | | | | | |
| nonOWO | Q1-3 | 241(0.37) | 41(0.17) | Referent | 40(0.17) | Referent |
| nonOWO | Q4 | 61(0.09) | 10(0.16) | 0.96(0.43-2.17) | 13(0.213) | 1.31(0.62-2.78) |
| OWO | Q1-3 | 260(0.40) | 44(0.17) | 1.36(0.82-2.27) | 99(0.381) | 3.18(2.02-5.02) |
| OWO | Q4 | 93(0.14) | 19(0.20) | 1.92(0.96-3.86) | 36(0.387) | 3.59(1.94-6.65) |

Notes: OWO, overweight or obesity; smk, smoking. Models were adjusted for maternal age at delivery, race, education, parity, perceived stress during pregnancy, child age, breastfeeding, gestational or preexisting diabetes.

**Supplementary Table 6.** The individual and joint associations of maternal OWO and child cord blood cotinine levels at delivery on children OWO in samples with cord cotinine stratified by gender.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Maternal OWO status | Cotinine | Number of male children (toal = 484) | Number of overweight children (%) | OR(95%CI) | Number of obese children (%) | OR(95%CI) |
| Individual associations | | | | | | |
| nonOWO |  | 225(0.46) | 34(0.15) | Referent | 50(0.22) | Referent |
| OWO |  | 259(0.54) | 44(0.17) | 1.47(0.86-2.52) | 91(0.351) | 2.13(1.35-3.35) |
|  | Q1 | 133(0.27) | 21(0.16) | Referent | 39(0.29) | Referent |
|  | Q2 | 104(0.21) | 25(0.24) | 1.57(0.78-3.15) | 22(0.212) | 0.80(0.42-1.53) |
|  | Q3 | 118(0.24) | 11(0.09) | 0.60(0.26-1.38) | 39(0.331) | 1.09(0.60-1.96) |
|  | Q4 | 129(0.27) | 21(0.16) | 1.34(0.63-2.84) | 41(0.318) | 1.27(0.69-2.31) |
|  | continuous cotinine | 484(1.00) | 78(0.16) | 1.06(0.78-1.43) | 141(0.291) | 1.10(0.86-1.40) |
| Joint associations | | | | | | |
| nonOWO | Q1-3 | 161(0.33) | 23(0.14) | Referent | 34(0.21) | Referent |
| nonOWO | Q4 | 64(0.13) | 11(0.17) | 1.80(0.75-4.34) | 16(0.250) | 1.43(0.67-3.06) |
| OWO | Q1-3 | 194(0.40) | 34(0.18) | 1.73(0.92-3.23) | 66(0.340) | 2.24(1.32-3.79) |
| OWO | Q4 | 65(0.13) | 10(0.15) | 1.76(0.71-4.34) | 25(0.385) | 2.73(1.34-5.57) |

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Maternal OWO status | Cotinine | Number of female children (total = 409) | Number of overweight children (%) | OR(95%CI) | Number of obese children (%) | OR(95%CI) |
| Individual associations | | | | | | |
| nonOWO |  | 196(0.48) | 33(0.17) | Referent | 33(0.17) | Referent |
| OWO |  | 213(0.52) | 49(0.23) | 2.48(1.43-4.29) | 82(0.385) | 3.90(2.34-6.50) |
|  | Q1 | 106(0.26) | 20(0.19) | Referent | 31(0.29) | Referent |
|  | Q2 | 104(0.25) | 23(0.22) | 1.07(0.52-2.22) | 23(0.221) | 0.66(0.34-1.30) |
|  | Q3 | 105(0.26) | 21(0.20) | 0.94(0.45-1.95) | 25(0.238) | 0.72(0.37-1.39) |
|  | Q4 | 94(0.23) | 18(0.19) | 1.22(0.53-2.78) | 36(0.383) | 1.25(0.62-2.49) |
|  | continuous cotinine | 409(1.00) | 82(0.20) | 1.12(0.81-1.54) | 115(0.281) | 1.03(0.78-1.36) |
| Joint associations | | | | | | |
| nonOWO | Q1-3 | 164(0.40) | 24(0.15) | Referent | 25(0.15) | Referent |
| nonOWO | Q4 | 32(0.08) | 9(0.28) | 3.09(1.12-8.54) | 8(0.250) | 1.96(0.71-5.43) |
| OWO | Q1-3 | 151(0.37) | 40(0.26) | 3.53(1.90-6.59) | 54(0.358) | 4.35(2.41-7.83) |
| OWO | Q4 | 62(0.15) | 9(0.15) | 1.83(0.71-4.75) | 28(0.452) | 4.43(2.07-9.47) |

Notes: OWO, overweight or obesity; smk, smoking. Models were adjusted for maternal age at delivery, race, education, parity, perceived stress during pregnancy, child age, breastfeeding, gestational or preexisting diabetes.

**Supplementary Figure 1.** Flowchart of the participant selection process for the analysis.



**Supplementary Figure 2.** Density distribution of cotinine, hydroxycotinine, and the sum of them two in both maternal plasma (MP) and cord plasma (CP), stratified by maternal overweight or obesity (OWO).



**Supplementary Figure 3.** Maternal plasma vs cord plasma biomarkers (cotinine, hydroxycotinine, and sum) loess correlation plot. Scatterplots show the bivariate z-scores with a red fitted curve. Absolute values of the correlations are starred by the cor.test. (MP: maternal plasma. CP: cord plasma. Sum\_cotinine\_hydro: the sum of cotinine and hydroxycotinine.)



**Supplementary Figure 4.** Gender difference of the effects of dose biomarkers of in-utero exposure to cigarette smoke (cotinine hydroxycotinine and their sum in maternal and cord plasma) on child OWO risk, stratified by maternal OWO. Notes: MP, maternal plasma; CP, cord plasma; sum, sum of cotinine and hydroxycotinine; all, all samples; F, female; M, male.



**Supplementary Figure 5.** Child OWO prediction performance of three nested models with different input variables. All of model1, model2, and model3 are adjusted with pertinent covariates, except that model1 only include self-reported smoking, model2 is based on model1 but add maternal plasma biomarker measurements (cotinine, hydroxycotinine), and model3 is based on model2 but add cord plasma biomarker measurements (cotinine, hydroxycotinine).

Notes: AUROC = Area Under Receiver Operating Characteristic.

