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Impact of female obesity and assisted reproduction on uncomplicated pregnancies and healthy births: a study of 428 336 births in Flanders

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STUDY QUESTION: What is the impact of BMI on uncomplicated pregnancies and healthy births in women who did or did not have medically assisted reproduction (MAR, i.e. ART or hormonal stimulation without manipulation of eggs or embryos) in the Flanders region (Belgium)?

SUMMARY ANSWER: Women with a higher BMI who use MAR are at the highest risk of pregnancy and birth complications.

WHAT WE KNOW ALREADY: Medically assisted reproduction (MAR) is used increasingly worldwide and is associated with increased risk of adverse perinatal outcomes. Obesity is also increasing globally and obese women are more likely to seek MAR since obesity is associated with infertility. When obese women undergo MAR, the risk of adverse outcomes may be enhanced but it is not clear to what extent.

STUDY DESIGN, SIZE, DURATION: We conducted a registry-based study using the data from the Study Centre for Perinatal epidemiology database for years 2009–2015, region of Flanders, Belgium. This included 428 336 women.

PARTICIPANTS/MATERIALS, SETTING, METHODS: The average age was 30.0 years (SD 4.78), 194 061 (45.31%) were nulliparous, and 6.3% (n = 26 971) conceived with MAR. We examined the association of BMI and MAR with the following composite primary outcomes: 'uncomplicated pregnancy and birth' and 'healthy baby'. We conducted Poisson regression and adjusted for maternal age, parity, gestational weight gain, smoking and previous caesarean section.

MAIN RESULTS AND THE ROLE OF CHANCE: In our study, 36.80% (n = 157 623) of women had an uncomplicated pregnancy and birth according to the definition used. The predicted probability of having an uncomplicated pregnancy and birth for women with a BMI of 25 kg/m^2 who conceived spontaneously was 0.33 (0.32 to 0.35), while it was 0.28 (0.24 to 0.32) for women who used hormonal stimulation and 0.26 (0.22 to 0.29) for women who used IVF/ICSI. This probability reduced with increasing BMI category for both MAR and non-MAR users. For women with a BMI of 30 kg/m^2, the predicted probability of having an uncomplicated pregnancy and birth was 0.28 (0.26 to 0.30) for women who conceived spontaneously, and 0.22 (0.16 to 0.29) and 0.20 (0.14 to 0.26) for women who used hormonal stimulation only or IVF/ICSI, respectively. The predicted probability of having a healthy baby for women with a BMI of 25 kg/m^2 who conceived spontaneously was 0.92 (0.91 to 0.93), 0.89 (0.87 to 0.92) for women who used hormonal stimulation only and 0.85 (0.84 to 0.87) for women who used IVF/ICSI.

LIMITATIONS, REASONS FOR CAUTION: The database did not include data on socio-economic status, pre-pregnancy morbidities and paternal BMI. Subsequently, we could not adjust for these factors in the analysis.

WIDER IMPLICATIONS OF THE FINDINGS: Obese women who use MAR are at the highest risk of pregnancy and birth complications. This increase in interventions also has cost and resource implications which is relevant for funding policies. Weight loss interventions prior to MAR seem plausible but their (cost-) effectiveness needs urgent investigation.

STUDY FUNDING/COMPETING INTEREST(S): F.W. received an Erasmus Plus training grant to visit A.B., L.A. and R.D. and conducted this study during this visit. The authors have no competing interest to declare.

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Key words: assisted reproductive technology / body mass index / perinatal outcomes / pregnancy complications / healthy births

Introduction

Medically assisted reproduction (MAR) is used worldwide and is associated with increased risk of adverse perinatal outcomes (Pinborg *et al.*, 2013). Multiple embryos transfer led to an increase in multiple pregnancies and hence increased complications (Blondel and Kaminski, 2002). However, even with the introduction of elective single embryo transfer, ART singletons have a higher risk of adverse perinatal outcomes (Helmerhorst *et al.*, 2004; Jackson *et al.*, 2004; McDonald *et al.*, 2009; Sazonova *et al.*, 2011; Goldsmith *et al.*, 2018). Why MAR leads to increased pregnancy and birth complications is multifactorial and not yet fully understood. The population seeking MAR may have underlying conditions that are linked to pregnancy complications; nevertheless, research on gestational surrogates does demonstrate that at least part of the negative impact relates to MAR itself (Woo *et al.*, 2017). MAR is increasingly being used worldwide. In 2016, 918 159 treatment cycles were reported in Europe, a 8% increase compared to the year before (Wyns *et al.*, 2020). This is a further increase compared to 776 556 treatments in 2014 (De Geyter *et al.*, 2018), and 458 759 treatment cycles in 2006 (de Mouzon *et al.*, 2010). The increasing maternal age will likely lead to a continuing increasing trend of MAR use.

Obesity is also increasing worldwide. Subsequently, the prevalence of women of reproductive age who are overweight/obese is increasing (Goldstein *et al.*, 2017; Slack *et al.*, 2019). The World Health Organization (WHO) estimates that in Europe 23% of women are obese (WHO Data and Statistics, 2013). Overweight and obese women are at increased risk of adverse pregnancy and birth outcomes (Catalano and Shankar, 2017). An increased body mass index (BMI) has been associated with pre-eclampsia, gestational diabetes, stillbirth, caesarean section, preterm birth, shoulder dystocia, Neonatal Intensive Care Unit (NICU) stay, perinatal, neonatal and infant death (Aune *et al.*, 2014; Schummers *et al.*, 2015). Higher rates of co-morbidities in overweight and obese women increase the probability of negative perinatal outcomes in this group even further (Mariona, 2016). A high BMI is also linked with reduced fertility that results from the uterine and ovarian changes associated with obesity (Catalano and Shankar, 2017); therefore, this group of women is more likely to seek MAR.

A raised BMI lowers the success rates of MAR. In a systematic review on the correlations between raised BMI and MAR outcomes, the authors concluded that a raised BMI is associated with poorer MAR outcomes (lower birth rates and a higher miscarriage rate) (Supramaniam *et al.*, 2018). Another review looking specifically at miscarriage after IVF, found an increased miscarriage rate in overweight and obese women (Bellver, 2022). Kasim and Roshdy (2014) found that the negative effect of BMI on pregnancy rate was modified by maternal age, infertility type and the number of embryos transferred. Women seeking MAR also have higher rates of other co-morbidities (e.g. asthma, diabetes, etc.) that may coincide with obesity, and that negatively impact on fertility, pregnancy and birth outcomes (Livshits and Seidman, 2009; Vejen Hansen *et al.*, 2019; Nørgård *et al.*, 2021).

We know that a high BMI is associated with increased adverse perinatal outcomes and that MAR treatment also poses risk compared to spontaneous conception. When obese women undergo MAR treatment, the risk of adverse pregnancy and birth outcomes may be enhanced but it is unclear to what extent. In the current context of the increasing trends of MAR use and obesity worldwide, the objective of this study was to examine the impact of BMI on uncomplicated pregnancies and healthy births by the use of MAR or not, including different types of MAR, in women in Flanders (Belgium).

Materials and methods

We analysed data from the database of the Study Centre for Perinatal Epidemiology (SPE) in Flanders (years 2009–2015). All care providers who assist births, both at maternity hospitals, at home or in birth centres, complete a birth registration as well as a statistical form with the medical birth data using an online platform (eBirth). For births in Flanders, these pseudonymised medical data are sent via the Agency for Care and Health of the Flemish government to the SPE for further analysis. The database includes all women who gave birth in the Flanders region (Belgium) to a live baby with a gestation of $\geq$22 weeks (Devlieger *et al.*, 2019). We excluded women with a gestation $<$22 weeks and $>$44 weeks (data inputting errors).

Variables

The factors of interest were pre-pregnancy BMI and MAR. We classified pre-pregnancy BMI according to the WHO classification system (BMI $<$18.5 kg/m^2 (underweight); BMI 18.5–24.99 kg/m^2 (reference category); BMI 25–29.99 kg/m^2 (overweight); BMI 30–34.99 kg/m^2 (obese class I); BMI 35–39.99 kg/m^2 (obese class II); BMI $\geq$40 kg/m^2 (obese class III)). We examined BMI as categorical and continuous variable. ART was classified into ART-IVF, ART-ICSI and hormonal stimulation (ovarian stimulation with timed intercourse or IUI). Our data did not specify the regimen of controlled ovarian stimulation (clomiphene citrate, letrozole, human menopausal gonadotropins, recombinant FSH). In case of artificial insemination, we were not able to distinguish between inseminations with donor or partner semen. We compared MAR versus no MAR, as well as comparing different methods of MAR. We adjusted for age (continuous variable), parity (primiparous/

multiparous), smoking during current pregnancy (yes/no/stopped), previous caesarean section (yes/no), induction of labour (yes/no) and gestational weight gain (GWG). GWG categories (recommended GWG/less than recommended GWG/more than recommended GWG) were set by BMI category (Rasmussen and Yaktine, 2009).

We examined two primary composite outcomes: (i) uncomplicated pregnancy and birth (defined as no diabetes, no hypertension in pregnancy, a term, singleton vaginal birth with no induction of labour, no congenital malformations, no NICU admission, not large for gestational age (LGA), not small for gestational age (SGA), no neonatal mortality); and (ii) healthy baby (defined as the absence of preterm birth, stillbirth, neonatal death and congenital malformation). The outcome 'uncomplicated pregnancy and birth' was based on the WHO's definition of normal birth (World Health Organization TWG, 1997).

We examined the following secondary outcomes: caesarean section (yes, no); pre-term birth (<37 weeks gestation); LGA (birth weight above the 90th percentile); SGA (birth weight below the 10th percentile); and multiple pregnancies (yes, no). We examined low birth weight (LBW) (birth weight <2500 g) and macrosomia (birth weight >4000 g) as well. SGA and LGA include an infant's weight in relation to gestational age and are by definition more robust outcomes, but LBW and macrosomia have been commonly used in the past and were included to facilitate comparison/meta-analysis.

Statistical analysis

We conducted complete-case analysis except for the variables smoking and a previous caesarean section since they are associated with the outcomes studied. Imputation was not appropriate due to an absence of relevant variables. We included cases with missing smoking data or previous caesarean section data and added a category 'missing data' (Supplementary Table SI). We conducted data analysis using Stata 15 software. We applied the following cut-offs for excluding cases: a birth weight of <500 or >6000 g, a gestation of <22 or >44 weeks, maternal length of <120 or >200 cm, maternal weight before pregnancy of <30 or >190 kg, weight at the end of pregnancy of <35 or >200 kg, a BMI of <12.5 or >52.5 kg/m^2, GWG outside of the range of −25 to +50 kg.

The risk of the adverse perinatal outcomes in women who did or did not receive ART for different BMI categories was estimated using Poisson regression. We adjusted for maternal age, parity, GWG, smoking and previous caesarean section. We have reported unadjusted risk ratios (RRs) and adjusted RRs (ARRs) with 95% CIs. For the primary outcomes, we first calculated the adjusted predicted probabilities by BMI categories. To investigate in depth how BMI and MAR impact the primary outcomes and to facilitate clinical decision making, we examined BMI as a continuous variable and differentiate between different types of MAR (spontaneous, hormonal, IVF/ICSI). During univariate exploratory analysis of BMI and age in relation to the primary outcomes, we identified a breakpoint at a BMI of ≥20 kg/m^2 and an age of ≥33 years. We subsequently conducted multivariable piecewise regression to assess the adjusted predicted probabilities in relation to BMI for primiparous, non-smoking woman of average age with no previous caesarian section and optimal GWG.

The scientific committee of the Study Centre for Perinatal Epidemiology granted approval for the analysis of the anonymous data. This study was exempt from approval by an institutional review board.

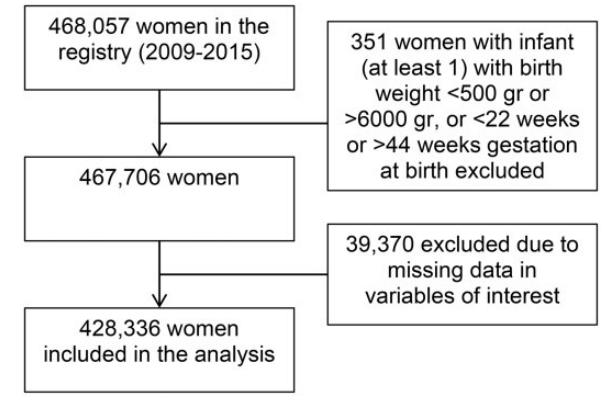

Figure 1. This flowchart shows the number of participants of the original sample that were included in the analysis.

Results

Of 468 057 women in the database, we included 428 336 (91.5%) in the analysis (Fig. 1). We examined the BMI of the 351 women excluded because they had an infant with a birth weight <500 or >6000 g, or had a gestation of <22 or >44 weeks at birth. Of these 351 women, 23.64% were overweight and 9.45% were obese, compared to 22.04% and 10.96% in the sample included in the analysis (Table I). The average age of the included women was 30.0 ± 4.78 years, 194 061 (45.31%) women were nulliparous, and 6.3% (n = 26 971) of women conceived with MAR. Seven thousand four hundred and eighty-nine (1.75%) women had a multiple pregnancy, 29 456 (6.88%) women gave birth prematurely (<37 weeks gestation) and the overall caesarean section rate was 19.52% (n = 83 615). The rate of stillbirth was 0.13% (n = 576), and 14.89% (n = 63 765) of women had their baby(ies) transferred to the NICU (Table I).

Uncomplicated pregnancy and birth

Overall, 36.80% (n = 157 623) had an uncomplicated pregnancy and birth. For all methods of conception (spontaneous, hormonal, IVF, ICSI), women who were overweight and obese were less likely to experience an uncomplicated pregnancy and birth. Compared to an optimal BMI, women who were overweight/obese and conceived spontaneously were less likely have an uncomplicated pregnancy and birth, and for women who used MAR the probability of having an uncomplicated pregnancy and birth was further reduced. Results stratified by the specified type of MAR used (hormonal stimulation, IVF and ICSI) were similar (Table II and Supplementary Table SII and Supplementary Fig. S1).

The predicted probability of an uncomplicated pregnancy and birth decreases with increasing BMI (above optimal level) for all methods of conception (Fig. 2). For a BMI of 25 kg/m^2, women who conceived

Table I Description of the study population by BMI.

Participant characteristics	Total	BMI (kg/m^2)						*P*-value[a]
		<18.5	18.5–24.99	25–29.99	30–34.99	35–39.99	≥40	
Number (%)	428 336	22 397 (5.23)	264 603 (61.77)	94 389 (22.04)	33 757 (7.88)	9954 (2.32)	3236 (0.76)	<0.001
Age (mean, SD)	29.99 ± 4.78	28.70 ± 5.05	29.94 ± 4.66	30.24 ± 4.86	30.37 ± 5.02	30.41 ± 5.07	30.54 ± 5.11	<0.001
Parity								
Primiparous	194 061 (45.31)	11 390 (50.85)	127 296 (48.11)	38 183 (40.45)	12 387 (36.69)	3638 (36.55)	1167 (36.06)	<0.001
Multiparous	234 275 (54.69)	11 007 (49.15)	137 307 (51.89)	56 206 (59.55)	21 370 (63.31)	6316 (63.45)	2069 (63.94)	
ART								
Spontaneous conception	401 365 (93.70)	21 113 (94.27)	248 081 (93.76)	88 658 (93.93)	31 348 (92.86)	9161 (92.03)	3004 (93.83)	<0.001
ART hormonal	10 160 (2.37)	533 (2.38)	6080 (2.30)	2144 (2.27)	904 (2.68)	368 (3.70)	131 (4.05)	
ART IVF	9672 (2.26)	448 (2.00)	6053 (2.29)	2062 (2.18)	841 (2.49)	214 (2.15)	55 (1.70)	
ART ICSI	7139 (1.67)	303 (1.35)	4389 (1.66)	1526 (1.62)	664 (1.97)	211 (2.12)	46 (1.42)	
Multiple pregnancy	7489 (1.75)	336 (1.50)	4387 (1.66)	1754 (1.86)	719 (2.13)	230 (2.31)	63 (1.95)	<0.001
Smoking								
Yes	17 224 (4.02)	1556 (6.95)	9765 (3.69)	3684 (3.90)	1589 (4.71)	461 (4.63)	169 (5.22)	<0.001
No	178 991 (41.79)	8659 (38.66)	110 364 (41.71)	40 076 (42.46)	14 410 (42.69)	4161 (41.80)	1321 (40.82)	
Stopped	4676 (1.09)	244 (1.09)	2855 (1.08)	1019 (1.08)	393 (1.16)	121 (1.22)	44 (1.36)	
Missing	227 445 (53.10)	11 938 (53.30)	141 619 (53.52)	49 610 (52.56)	17 365 (51.44)	5211 (52.35)	1702 (52.60)	
Hypertension in current pregnancy	19 867 (4.64)	493 (2.20)	8726 (3.30)	5491 (5.82)	3134 (9.28)	1394 (14.00)	629 (19.44)	<0.001
Diabetes in current pregnancy	13 044 (3.05)	300 (1.34)	5404 (2.04)	3768 (3.99)	2206 (6.53)	931 (9.35)	435 (13.44)	<0.001
GWG[b]								
Recommended	161 376 (37.68)	8896 (39.72)	109 973 (41.56)	29 032 (30.76)	9514 (28.18)	3015 (30.29)	946 (29.23)	<0.001
Less than recommended	126 191 (29.46)	10 631 (47.47)	92 655 (35.02)	13 521 (14.32)	5610 (16.62)	2586 (25.98)	1188 (36.71)	
More than recommended	140 769 (32.86)	2870 (12.81)	61 975 (23.42)	51 836 (54.92)	18 633 (55.20)	4353 (43.73)	1102 (34.05)	
Preterm birth	29 456 (6.88)	2059 (9.19)	17 848 (6.75)	6170 (6.54)	2345 (6.95)	789 (7.93)	245 (7.57)	0.006
Induced	102 573 (23.95)	4397 (19.63)	58 254 (22.02)	25 101 (26.59)	10 336 (30.62)	3340 (33.55)	1145 (35.38)	<0.001
Caesarean section	83 615 (19.52)	3313 (14.79)	45 522 (17.20)	21 009 (22.26)	9286 (27.51)	3243 (32.58)	1242 (38.38)	<0.001
SGA[c]	40 560 (9.47)	3796 (16.95)	25 672 (9.70)	7573 (8.02)	2546 (7.54)	756 (7.59)	217 (6.71)	<0.001
LGA[d]	45 386 (10.60)	955 (4.26)	23 989 (9.07)	12 423 (13.16)	5471 (16.21)	1821 (18.29)	727 (22.47)	<0.001
Low birth weight	19 324 (4.51)	1910 (8.53)	11 994 (4.53)	3569 (3.78)	1311 (3.88)	408 (4.10)	132 (4.08)	<0.001
Macrosomia	45 548 (10.63)	1040 (4.64)	24 542 (9.28)	12 447 (13.19)	5236 (15.51)	1676 (16.84)	607 (18.76)	<0.001
Major congenital malformation	3803 (0.89)	227 (1.01)	2206 (0.83)	873 (0.92)	341 (1.01)	113 (1.14)	43 (1.33)	<0.001
Neonatal death	576 (0.13)	41 (0.18)	321 (0.12)	145 (0.15)	48 (0.14)	15 (0.15)	6 (0.19)	0.247
Stillbirth	1559 (0.36)	74 (0.33)	928 (0.35)	349 (0.37)	133 (0.39)	58 (0.58)	17 (0.53)	<0.001
Transfer to NICU[e]	63 765 (14.89)	3632 (16.22)	36 558 (13.82)	14 694 (15.57)	6121 (18.13)	2004 (20.13)	756 (23.36)	<0.001
Composite outcome: uncomplicated pregnancy and birth	157 623 (36.80)	9003 (40.20)	105 663 (39.93)	31 240 (33.10)	9003 (26.67)	2176 (21.86)	538 (16.63)	<0.001
Composite outcome: healthy baby	395 793 (92.40)	20 176 (90.08)	244 989 (92.59)	87 468 (92.67)	31 127 (92.21)	9075 (91.17)	2958 (91.41)	<0.001

[a]Non-parametric test for trend across ordered groups (except for age, we used one-way ANOVA).
[b]Gestational weight gain.
[c]Small for gestational age.
[d]Large for gestational age.
[e]Neonatal intensive care unit. LGA, large for gestational age; SGA, small for gestational age.

spontaneously, by hormonal stimulation or by IVF/ICSI, had a probability of 33% (32–35%), 28% (24–32%) and 26% (22–29%), respectively of having an uncomplicated pregnancy and birth. This was only 28% (26–30%), 22% (16–29%) and 20% (14–26%) for a BMI of 30 kg/m^2 and decreased further to 24% (21–26%), 18% (7–28%) and 17% (7–26%) for a BMI of 35 kg/m^2.

Table II Univariable and multivariable regression—primary outcomes.

Method of conception	N	Uncomplicated pregnancy and birth			Healthy baby		
		Cases (%)	Unadjusted RR[a]	Adjusted RR[b]	Cases (%)	Unadjusted RR[a]	Adjusted RR[b]
no ART[c]							
BMI < 18.5 kg/m^2	21 113	40.73	1.00 (0.98–1.02)	0.99 (0.97–1.00)	90.43	0.97 (0.97–0.98)	0.98 (0.97–1.00)
BMI 18.5–25 kg/m^2	248 081	40.57	Reference	Reference	92.97	Reference	Reference
BMI 25–30 kg/m^2	88 658	33.77	0.83 (0.82–0.84)	0.86 (0.85–0.87)	93.05	1.00 (1.00–1.00)	0.98 (0.97–0.99)
BMI 30–35 kg/m^2	31 348	27.38	0.67 (0.66–0.69)	0.71 (0.69–0.72)	92.67	1.00 (0.99–1.00)	0.98 (0.97–0.99)
BMI 35–40 kg/m^2	9161	22.40	0.55 (0.53–0.57)	0.59 (0.57–0.61)	91.73	0.99 (0.98–0.99)	0.98 (0.96–1.00)
BMI ≥ 40 kg/m^2	3004	16.74	0.41 (0.38–0.45)	0.45 (0.42–0.49)	91.58	0.99 (0.97–0.99)	0.98 (0.95–1.02)
ART—any							
BMI < 18.5 kg/m^2	1284	31.46	1.04 (0.96–1.13)	1.02 (0.94–1.11)	84.35	0.97 (0.95–0.99)	1.00 (0.94–1.06)
BMI 18.5–25 kg/m^2	16 522	30.24	Reference	Reference	86.88	Reference	Reference
BMI 25–30 kg/m^2	5731	22.74	0.75 (0.71–0.79)	0.76 (0.72–0.80)	86.79	1.00 (0.99–1.01)	0.95 (0.92–0.99)
BMI 30–35 kg/m^2	2409	17.43	0.58 (0.53–0.63)	0.58 (0.53–0.64)	86.22	0.99 (0.96–1.01)	0.95 (0.90–0.99)
BMI 35–40 kg/m^2	793	15.64	0.52 (0.44–0.61)	0.54 (0.46–0.63)	84.74	0.98 (0.95–1.01)	0.95 (0.88–1.03)
BMI ≥ 40 kg/m^2	232	15.09	0.50 (0.37–0.68)	0.51 (0.38–0.68)	89.22	1.03 (0.98–1.07)	1.01 (0.88–1.16)
ART—hormonal							
BMI < 18.5 kg/m^2	533	34.33	1.03 (0.91–1.16)	0.99 (0.85–1.16)	87.05	0.95 (0.91–1.00)	0.99 (0.90–1.09)
BMI 18.5–25 kg/m^2	6080	33.44	Reference	Reference	89.38	Reference	Reference
BMI 25–30 kg/m^2	2144	23.97	0.72 (0.66–0.78)	0.73 (0.66–0.81)	89.09	1.00 (0.98–1.02)	0.96 (0.91–1.02)
BMI 30–35 kg/m^2	904	19.03	0.57 (0.50–0.65)	0.58 (0.49–0.68)	89.27	1.00 (0.97–1.02)	0.96 (0.89–1.04)
BMI 35–40 kg/m^2	368	17.39	0.52 (0.42–0.65)	0.53 (0.41–0.69)	87.50	0.99 (0.93–1.05)	0.96 (0.86–1.07)
BMI ≥ 40 kg/m^2	131	16.79	0.50 (0.34–0.74)	0.51 (0.33–0.77)	92.37	1.05 (0.95–1.14)	1.02 (0.85–1.22)
ART—IVF							
BMI < 18.5 kg/m^2	448	29.69	1.07 (0.92–1.24)	1.09 (0.92–1.31)	81.03	0.95 (0.91–1.00)	0.98 (0.88–1.09)
BMI 18.5–25 kg/m^2	6053	27.69	Reference	Reference	85.13	Reference	Reference
BMI 25–30 kg/m^2	2061	21.93	0.79 (0.72–0.87)	0.78 (0.70–0.87)	85.15	1.00 (0.98–1.02)	0.95 (0.90–1.00)
BMI 30–35 kg/m^2	841	16.53	0.60 (0.51–0.70)	0.59 (0.50–0.70)	85.02	1.00 (0.97–1.03)	0.95 (0.88–1.03)
BMI 35–40 kg/m^2	214	12.15	0.44 (0.31–0.63)	0.47 (0.32–0.70)	84.11	0.99 (0.93–1.05)	0.96 (0.83–1.11)
BMI ≥ 40 kg/m^2	55	10.91	0.39 (0.18–0.83)	0.38 (0.17–0.86)	89.09	1.04 (0.95–1.14)	1.02 (0.77–1.35)
ART—ICSI							
BMI < 18.5 kg/m^2	303	29.04	0.99 (0.83–1.19)	1.01 (0.81–1.25)	84.49	0.98 (0.94–1.03)	1.02 (0.90–1.16)
BMI 18.5–25 kg/m^2	4389	29.32	Reference	Reference	85.85	Reference	Reference
BMI 25–30 kg/m^2	1526	22.08	0.75 (0.68–0.84)	0.75 (0.66–0.85)	85.78	1.00 (0.98–1.02)	0.95 (0.89–1.01)
BMI 30–35 kg/m^2	664	16.42	0.55 (0.47–0.67)	0.55 (0.45–0.67)	83.58	0.97 (0.94–1.01)	0.92 (0.84–1.01)
BMI 35–40 kg/m^2	211	16.11	0.54 (0.40–0.75)	0.56 (0.40–0.79)	80.57	0.94 (0.88–1.00)	0.91 (0.78–1.06)
BMI ≥ 40 kg/m^2	46	15.22	0.29 (0.26–1.02)	0.49 (0.23–1.04)	80.43	0.94 (0.81–1.08)	0.91 (0.66–1.26)

[a]Risk ratio.
[b]Adjusted for maternal age, parity, gestational weight gain, smoking and previous caesarean section. RR, risk ratio.

Healthy baby

Most women (92.40%; n = 395 793) gave birth to a healthy baby overall. Of women with normal BMI who conceived spontaneously 92.97% (n = 230 634) gave birth to a healthy baby. This was 86.88% (n = 14 355) in women who used MAR. Overweight or obese women were only slightly less likely to give birth to a healthy baby. The probability of having a healthy baby only varied little by BMI category but was influenced by the method of conception (Table II and Supplementary Table SIII and Fig. S2).

The predicted probability of having a healthy baby decreases with increasing BMI above optimal level for all methods of conception, although for women who undergo hormonal conception the impact of increasing BMI seems less (Fig. 3). For a BMI of 25 kg/m^2, women who conceived spontaneously, by hormonal conception or by IVF/ICSI, had a probability of 92% (91–93%), 89% (87–92%) and 85%

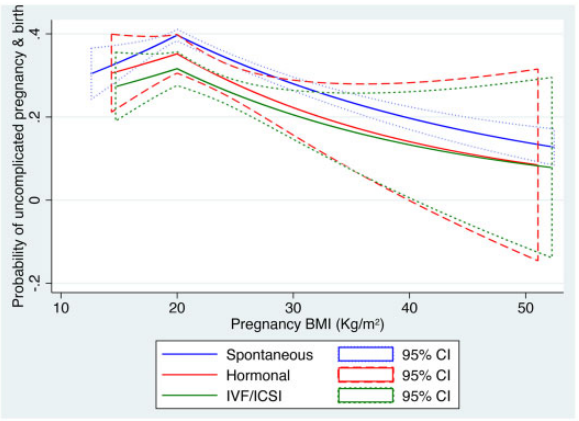

Figure 2. This graph shows the predicted probabilities with 95% confidence intervals of an uncomplicated pregnancy and birth by BMI. This analysis was stratified by method of conception.

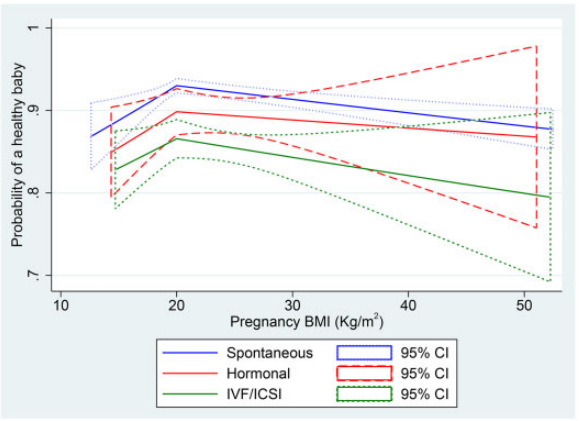

Figure 3. This graph shows the predicted probabilities with 95% confidence intervals of having a healthy baby by BMI. This analysis was stratified by method of conception.

(84–87%), respectively of having a healthy baby. This was only 91% (90–92%), 89% (86–92%) and 84% (81–87%) for a BMI of 30 kg/m^2 and was 91% (89–92%), 88% (84–93%) and 83% (79–86%) for a BMI of 35 kg/m^2.

Secondary outcomes

We have presented the results for the secondary outcomes in Tables III and IV. One in five women (19.52%; n = 83 615) gave birth by caesarean section and the caesarean section rate varied across the different BMI categories with higher rates with increasing BMI category (Table I). The caesarean section rate in obese women who conceived spontaneously was 28.58% (n = 12 437) and in obese women who underwent MAR it was 38.85% (n = 1334). Women who conceived spontaneously and women using MAR were more likely to give birth by caesarean section if they were overweight or obese (Table III).

The proportion of women with a multiple pregnancy was 1.22% (n = 4889) in women who conceived spontaneously, 7.14% (n = 725) in women who had hormonal stimulation, 10.65% (n = 1030) in women who had IVF and 11.84% (n = 845) in the ICSI group. However, for women who had the same method of conception, BMI category was not associated with multiple pregnancy after adjusting for confounders (Table III).

Twenty-nine thousand four hundred and fifty-six (6.88%) women gave birth before 37 weeks gestation. Preterm birth was associated with BMI, with higher proportions of preterm births observed in women who were underweight and women who were obese (Table I). Women who used MAR and were overweight (ARR 1.41, 1.29 to 1.54) or obese (Class I obesity: ARR 1.45, 1.28 to 1.64; Class II: ARR 1.32, 1.09 to 1.60; Class III: ARR 0.95, 0.63 to 1.42) were particularly at risk of preterm birth (Table III).

A total of 9.47% of newborns (n = 40 560) were SGA and 10.60% (n = 45 386) LGA (Table I). Women who were underweight were more likely to give birth to a newborn who was SGA whether she conceived spontaneously (ARR 1.54, 1.49 to 1.59) or using ART (ARR 1.46, 1.26 to 1.69). Overweight and obese women were more likely to give birth to a newborn LGA compared to women with an optimal BMI in both women who conceived spontaneously (overweight ARR 1.15, 1.12 to 1.18; obesity Class I: ARR 1.43, 1.39 to 1.48; Class II: ARR 1.76, 1.67 to 1.85; Class III: ARR 2.41, 2.23 to 2.60) or by MAR (overweight ARR 1.14, 1.04 to 1.24; obesity Class I: ARR 1.35, 1.21 to 1.51; Class II: ARR 1.65, 1.40 to 1.95; Class III: ARR 1.78, 1.33 to 2.38). In the group of women who conceived spontaneously, being obese was associated with a decreased risk of a newborn who was SGA (Class I obesity: ARR 0.92, 0.89 to 0.96; Class II: ARR 0.82, 0.76 to 0.89; Class III: ARR 0.68, 0.59 to 0.78), but this was not the case in women who conceived by MAR (Table IV).

Women who were underweight were less likely to have a LGA newborn whether they conceived spontaneously (ARR 0.55, 0.51 to 0.59) or by ART (ARR 0.55, 0.43 to 0.70) (Table IV). Being underweight was associated with LBW for all methods of conception expect hormonal stimulation. Being overweight was associated with macrosomia for all methods of conception although obese women who had ICSI were not more likely to have a baby with macrosomia compared to women of optimal weight who had ICSI (Supplementary Table SIV).

Discussion

This large registry study examined the association of MAR and BMI with perinatal outcomes. For a given BMI category, women who used MAR had poorer outcomes, and overweight and obese women were more at risk of adverse outcomes than women of optimal weight. Obese women who use MAR are at the highest risk of pregnancy and birth complications. The rate of MAR use in our study was high compared to overall numbers in Europe. Just under 7 in 100 women in this Flemish registry (years 2009–2015) used MAR compared to 2 in 100 in 2014 in Europe (De Geyter *et al.*, 2018).

Predictions based on this dataset show that 35% (34–35%) of women with optimal BMI would have an uncomplicated pregnancy

Table III Univariable and multivariable regression—secondary outcomes: part 1.

Method of conception	n	Caesarean section			Multiple pregnancy			Preterm		
		Cases (%)	Unadjusted RR[a]	Adjusted RR[b]	Cases (%)	Unadjusted RR[a]	Adjusted RR[c]	Cases (%)	Unadjusted RR[a]	Adjusted RR[b] (95% CI)
No ART										
BMI < 18.5 kg/m^2	21 113	14.30	0.86 (0.83–0.89)	0.92 (0.88–0.95)	0.99	0.87 (0.76–1.01)	0.91 (0.79–1.04)	8.87	1.39 (1.33–1.46)	1.22 (1.17–1.28)
BMI 18.5–25 kg/m^2	248 081	16.66	Reference	Reference	1.13	Reference	Reference	6.37	Reference	Reference
BMI 25–30 kg/m^2	88 658	21.72	1.30 (1.28–1.32)	1.20 (1.18–1.22)	1.36	1.21 (1.13–1.29)	1.19 (1.11–1.27)	6.15	0.97 (0.94–1.00)	1.30 (1.26–1.34)
BMI 30–35 kg/m^2	31 348	26.67	1.60 (1.57–1.63)	1.38 (1.34–1.41)	1.51	1.34 (1.21–1.47)	1.31 (1.18–0.44)	6.50	1.02 (0.98–1.07)	1.34 (1.28–1.41)
BMI 35–40 kg/m^2	9161	32.08	1.93 (1.87–1.99)	1.55 (1.49–1.61)	1.66	1.47 (1.25–1.73)	1.44 (1.22–1.70)	7.43	1.17 (1.08–1.26)	1.35 (1.25–1.46)
BMI ≥ 40 kg/m^2	3004	37.92	2.28 (2.17–2.39)	1.73 (1.64–1.84)	1.63	1.44 (1.09–1.91)	1.41 (1.06–1.87)	7.36	1.16 (1.02–1.31)	1.18 (1.03–1.34)
ART—any										
BMI < 18.5 kg/m^2	1284	22.82	0.90 (0.81–1.00)	0.94 (0.83–1.05)	9.97	1.04 (0.87–1.22)	1.04 (0.87–1.25)	14.56	1.17 (1.02–1.35)	1.00 (0.86–1.16)
BMI 18.5–25 kg/m^2	16 522	25.43	Reference	Reference	9.62	Reference	Reference	12.40	Reference	Reference
BMI 25–30 kg/m^2	5731	30.64	1.20 (1.15–1.26)	1.16 (1.10–1.23)	9.49	0.99 (0.90–1.08)	0.99 (0.89–1.09)	12.46	1.00 (0.93–1.09)	1.41 (1.29–1.54)
BMI 30–35 kg/m^2	2409	38.48	1.51 (1.43–1.60)	1.47 (1.36–1.58)	10.21	1.06 (0.93–1.21)	1.06 (0.93–1.21)	12.74	1.03 (0.92–1.15)	1.45 (1.28–1.64)
BMI 35–40 kg/m^2	793	38.34	1.51 (1.37–1.65)	1.36 (1.21–1.53)	9.84	1.02 (0.82–1.27)	1.03 (0.82–1.29)	13.62	1.10 (0.92–1.31)	1.32 (1.09–1.60)
BMI ≥ 40 kg/m^2	232	44.40	1.75 (1.51–2.02)	1.71 (1.41–2.08)	6.03	0.63 (0.38–1.04)	0.63 (0.37–1.07)	10.34	0.83 (0.57–1.22)	0.95 (0.63–1.42)
ART—Hormonal										
BMI < 18.5 kg/m^2	533	17.26	0.84 (0.69–1.03)	0.90 (0.73–1.11)	9.19	1.29 (0.98–1.72)	1.27 (0.95–1.71)	12.02	1.19 (0.94–1.52)	1.22 (1.17—1.28)
BMI 18.5–25 kg/m^2	6080	20.66	Reference	Reference	7.11	Reference	Reference	10.05	Reference	Reference
BMI 25–30 kg/m^2	2144	26.49	1.28 (1.18–1.40)	1.22 (1.10–1.36)	6.81	0.96 (0.80–1.15)	0.96 (0.79–1.16)	10.26	1.02 (0.88–1.18)	1.30 (1.26–1.34)
BMI 30–35 kg/m^2	904	35.95	1.74 (1.57–1.92)	1.63 (1.44–1.85)	7.30	1.03 (0.80–1.32)	1.02 (0.78–1.32)	9.73	0.97 (0.78–1.20)	1.35 (1.28–1.41)
BMI 35–40 kg/m^2	368	32.07	1.55 (1.33–1.82)	1.37 (1.13–1.66)	7.34	1.03 (0.71–1.50)	1.03 (0.70–1.52)	10.87	1.08 (0.80–1.46)	1.35 (1.25–1.46)
BMI ≥ 40 kg/m^2	131	44.27	2.14 (1.76–2.61)	2.02 (1.55–2.63)	3.82	0.53 (0.23–1.27)	0.53 (0.22–1.28)	7.63	0.76 (0.42–1.38)	1.18 (1.03–1.34)
ART—IVF										
BMI < 18.5 kg/m^2	448	27.23	0.95 (0.81–1.11)	0.96 (0.80–1.16)	11.83	1.12 (0.86–1.46)	1.13 (0.86–1.50)	17.63	1.26 (1.02–1.55)	1.02 (0.79–1.32)
BMI 18.5–25 kg/m^2	6053	28.73	Reference	Reference	10.54	Reference	Reference	14.01	Reference	Reference
BMI 25–30 kg/m^2	2061	33.58	1.17 (1.09–1.26)	1.13 (1.03–1.24)	10.72	1.02 (0.88–1.18)	1.01 (0.87–1.18)	13.97	1.00 (0.88–1.13)	1.43 (1.22–1.68)
BMI 30–35 kg/m^2	841	40.43	1.41 (1.28–1.54)	1.36 (1.20–1.53)	11.18	1.06 (0.86–1.30)	1.04 (0.84–1.30)	14.27	1.01 (0.85–1.22)	1.38 (1.03–1.73)
BMI 35–40 kg/m^2	214	45.79	1.59 (1.37–1.85)	1.36 (1.11–1.67)	8.88	0.84 (0.54–1.30)	0.82 (0.52–1.29)	13.55	0.97 (0.69–1.36)	1.27 (1.00–1.75)
BMI ≥ 40 kg/m^2	55	47.27	1.65 (1.24–2.18)	1.53 (1.04–2.26)	9.09	0.86 (0.37–2.00)	0.84 (0.35–2.03)	9.09	0.65 (0.28–1.50)	0.84 (0.45–1.60)
ART—ICSI										
BMI < 18.5 kg/m^2	303	26.07	0.95 (0.78–1.15)	0.95 (0.76–1.20)	8.58	0.72 (0.50–1.06)	0.72 (0.49–1.07)	14.52	1.08 (0.81–1.43)	1.08 (0.85–1.36)
BMI 18.5–25 kg/m^2	4389	27.50	Reference	Reference	11.85	Reference	Reference	13.44	Reference	Reference
BMI 25–30 kg/m^2	1526	32.50	1.18 (1.08–1.29)	1.15 (1.03—1.29)	11.60	0.97 (0.83–1.15)	0.98 (0.82–1.16)	13.50	1.00 (0.87–1.16)	1.39 (1.21–1.60)

(continued)

Table III Continued

Method of conception	n	Caesarean section			Multiple pregnancy			Preterm		
		Cases (%)	Unadjusted RR[a]	Adjusted RR[b]	Cases (%)	Unadjusted RR[a]	Adjusted RR[c]	Cases (%)	Unadjusted RR[a]	Adjusted RR[b] (95% CI)
BMI 30–35 kg/m^2	664	39.46	1.43 (1.29–1.59)	1.44 (1.26–1.66)	12.95	1.09 (0.88–1.35)	1.09 (0.87–1.38)	14.91	1.11 (0.91–1.35)	1.37 (1.13–1.66)
BMI 35–40 kg/m^2	211	41.71	1.52 (1.28–1.79)	1.44 (1.16–1.80)	15.17	1.28 (0.92–1.78)	1.28 (0.90–1.84)	18.48	1.37 (1.03–1.84)	1.17 (0.81–1.70)
BMI $\geq$ 40 kg/m^2	46	41.30	1.51 (1.06–2.13)	1.49 (0.95–2.34)	8.70	0.73 (0.29–1.88)	0.74 (0.28–1.99)	19.57	1.46 (0.81–2.63)	0.75 (0.31–1.80)

[a]Risk ratio.
[b]Adjusted for maternal age, parity, gestational weight gain, smoking and previous caesarean section.
[c]Adjusted for maternal age, parity, smoking, and previous caesarean section. RR, risk ratio.

Table IV Univariable and multivariable regression—secondary outcomes: part 2.

Method of conception	n	SGA			LGA		
		Cases (%)	Unadjusted RR[a]	Adjusted RR[b]	Cases (%)	Unadjusted RR[a]	Adjusted RR[b]
No ART							
BMI < 18.5 kg/m^2	21 113	17.02	1.75 (1.70–1.81)	1.54 (1.49–1.59)	4.21	0.47 (0.44–0.50)	0.55 (0.51–0.59)
BMI 18.5–25 kg/m^2	248 081	9.70	Reference	Reference	8.96	Reference	Reference
BMI 25–30 kg/m^2	88 658	7.99	0.82 (0.80–0.84)	1.01 (0.98–1.04)	13.05	1.46 (1.42–1.49)	1.15 (1.12–1.18)
BMI 30–35 kg/m^2	31 348	7.50	0.77 (0.74–0.81)	0.92 (0.89–0.96)	16.09	1.80 (1.75–1.84)	1.43 (1.39–1.48)
BMI 35—40 kg/m^2	9161	7.37	0.76 (0.71–0.82)	0.82 (0.76–0.89)	18.15	2.02 (1.94–2.12)	1.76 (1.67–1.85)
BMI ≥ 40 kg/m^2	3004	6.72	0.69 (0.61–0.79)	0.68 (0.59–0.78)	22.64	2.53 (2.36–2.70)	2.41 (2.23–2.60)
ART—any							
BMI < 18.5 kg/m^2	1284	15.81	1.62 (1.42–1.86)	1.46 (1.26–1.69)	5.14	0.48 (0.38–0.61)	0.55 (0.43–0.70)
BMI 18.5–25 kg/m^2	16 522	9.70	Reference	Reference	10.72	Reference	Reference
BMI 25–30 kg/m^2	5731	8.46	0.87 (0.79–0.96)	1.06 (0.96–1.18)	14.92	1.39 (1.29–1.50)	1.14 (1.04–1.24)
BMI 30–35 kg/m^2	2409	8.09	0.83 (0.72–0.96)	1.00 (0.86–1.17)	17.68	1.65 (1.50–1.82)	1.35 (1.21–1.51)
BMI 35–40 kg/m^2	793	10.21	1.05 (0.85–1.30)	1.15 (0.92–1.45)	19.92	1.86 (1.61–2.15)	1.65 (1.40–1.95)
BMI ≥ 40 kg/m^2	232	6.47	0.67 (0.41–1.09)	0.71 (0.43–1.18)	20.26	1.89 (1.46–2.45)	1.78 (1.33–2.38)
ART—hormonal							
BMI < 18.5 kg/m^2	533	16.14	1.70 (1.38–2.10)	1.53 (1.22–1.93)	4.50	0.46 (0.31–0.68)	0.54 (0.36–0.81)
BMI 18.5–25 kg/m^2	6080	9.47	Reference	Reference	9.85	Reference	Reference
BMI 25–30 kg/m^2	2144	8.82	0.93 (0.80–1.09)	1.15 (0.97–1.37)	14.74	1.50 (1.32–1.70)	1.15 (1.00–1.33)
BMI 30–35 kg/m^2	904	7.96	0.84 (0.66–1.06)	1.03 (0.80–1.32)	18.03	1.83 (1.56–2.14)	1.40 (1.17–1.68)
BMI 35–40 kg/m^2	368	11.68	1.23 (0.92–1.65)	1.37 (1.00–1.87)	19.29	1.96 (1.57–2.45)	1.67 (1.30–2.14)
BMI ≥ 40 kg/m^2	131	6.87	0.72 (0.38–1.37)	0.76 (0.39–1.47)	16.79	1.70 (1.16–2.51)	1.58 (1.03–2.42)
ART—IVF							
BMI < 18.5 kg/m^2	448	15.63	1.63 (1.30–2.05)	1.44 (1.12–1.85)	5.80	0.51 (0.35–0.75)	0.57 (0.39–0.85)
BMI 18.5–25 kg/m^2	6053	9.60	Reference	Reference	11.33	Reference	Reference
BMI 25–30 kg/m^2	2061	8.93	0.93 (0.79–1.09)	1.14 (0.96–1.35)	14.94	1.32 (1.16–1.49)	1.10 (0.96–1.27)
BMI 30–35 kg/m^2	841	7.49	0.78 (0.61–1.00)	0.94 (0.72–1.22)	17.60	1.55 (1.32–1.83)	1.31 (1.09–1.58)
BMI 35–40 kg/m^2	214	9.35	0.97 (0.63–1.48)	1.09 (0.70–1.71)	19.16	1.69 (1.27–2.25)	1.50 (1.09–2.06)
BMI ≥ 40 kg/m^2	55	9.09	0.94 (0.41–2.19)	1.03 (0.42–2.48)	20.00	1.76 (1.04–3.01)	1.67 (0.92–3.04)
ART—ICSI							
BMI < 18.5 kg/m^2	303	15.51	1.52 (1.16–2.01)	1.37 (1.02–1.86)	5.28	0.48 (0.29–0.77)	0.54 (0.33–0.88)
BMI 18.5–25 kg/m^2	4389	10.16	Reference	Reference	11.07	Reference	Reference
BMI 25–30 kg/m^2	1526	7.34	0.72 (0.59–0.88)	0.85 (0.70–1.07)	15.14	1.37 (1.18–1.58)	1.16 (0.99–1.37)
BMI 30–35 kg/m^2	664	9.04	0.89 (0.69–1.15)	1.05 (0.80–1.38)	17.32	1.56 (1.30–1.88)	1.32 (1.07- 1.63)
BMI 35–40 kg/m^2	211	8.53	0.84 (0.54–1.32)	0.88 (0.55–1.42)	21.00	1.97 (1.50–2.58)	1.80 (1.32–2.43)
BMI ≥ 40 kg/m^2	46	2.17	0.21 (0.03–1.49)	0.24 (0.03–1.73)	30.43	2.75 (1.76–4.29)	2.52 (1.48–4.29)

[a]Risk ratio.
[b]Adjusted for maternal age, parity, gestational weight gain, smoking and previous caesarean section. LGA, large for gestational age; SGA, small for gestational age; RR, risk ratio.

and birth if they conceived spontaneously, but only 28% (27–29%) of women with optimal BMI using MAR. These findings are influenced by the definition of 'uncomplicated pregnancy and birth' we used in this study. The low number could question the scope of our definition. However, it was based on existing definitions and our figures compare to findings of other studies examining the rate of normal childbirth (World Health Organization TWG, 1997). Prosser *et al.* (2018) in a survey of 5840 women in Australia found a normal childbirth rate of 28.7%. In a survey across 32 maternity units in the UK published by the Royal College of Midwives, the overall rate of normal labour and birth was 22% (Downe and Finlayson, 2016). Both these studies excluded the use of epidural from their definition of normal birth which explain why the rate is even lower than in our study.

In our study, BMI had less impact on having a healthy baby in women with hormonal conception. Aubry *et al.* (2019) found that obese women had an increased risk of preterm birth only if they were diagnosed with the co-morbidities diabetes or hypertension but we did not stratify by these co-morbidities as well as types of conception. Scott-Pillai *et al.*

(2013) found that only obesity class III was associated with an increased risk of preterm birth, stillbirth and admission to the neonatal unit. The number of women in our study with a BMI over 40 kg/m^2 was relatively small, hence smaller effects might have been missed and confidence intervals are wide. Also, our definition of the outcome healthy baby did not include variables such as SGA and LGA which were influenced by BMI.

Clinically, increased complications and thus interventions can be expected when obese women use MAR. Based on our data, women can be informed that when undergoing MAR at optimal BMI, the probability of an uncomplicated pregnancy and birth is 28% for hormonal stimulation and 26% for IVF/ICSI but this decreases further for obese women, reducing with increasing BMI. Evidently, how much risk someone is willing to take will vary from family to family, doctor to doctor and from health service to health service. It will also be dependent on the outcomes that are considered most important to individuals and services, and on the resources available. For some women, the desire to have a child might override the potential risks leading to different priorities and expectations. For example, having a caesarean section might not be important for some women if it gives them the opportunity to becoming a mother while it can be a crucial barrier for others. Both short-term outcomes and potential long-term implications for mother and child should be considered (O'Reilly and Reynolds, 2013; Godfrey *et al.*, 2017).

Public funding for MAR is limited and varies across clinics and across countries (Calhaz-Jorge *et al.*, 2020). In some countries/clinics, BMI is already a criterion taken into consideration due to its impact on pregnancy and birth outcomes. Policy makers should also consider the additional risk of adverse perinatal outcomes in women who are obese and use MAR when designing funding policies for MAR taking into consideration the higher healthcare costs during and after pregnancy due to increased intervention rates. This strengthens the argument to restrict MAR public funding based on women's BMI. Which cut-off individual countries/policies choose will depend on multiple factors including available resources and expertise to manage adverse outcomes as well as providing MAR. It is important that decision makers engage in multistakeholder discussions that include patients' perspectives to discuss the ethics and consequences of any policy decision.

While there is clear evidence of the impact of BMI on direct MAR outcomes such as live birth rate, miscarriage rate, pregnancy rate (Supramaniam *et al.*, 2018), this is, to our knowledge, the first study that examines the risk of adverse pregnancy and birth outcomes when using MAR stratified by BMI categories. While being overweight or obese poses additional risks for women using MAR, it is important to explore if weight loss prior to MAR would eliminate such risks. Weight loss interventions before using MAR seem a plausible step to improve outcomes, but the effectiveness and cost-effectiveness is yet to be examined in randomized controlled trials. Optimal body weight could not only improve MAR and pregnancy outcomes but also has multiple life-long health benefits thus reducing healthcare costs (Arroyo-Johnson and Mincey, 2016). In further examining the potential effectiveness and feasibility of such interventions, it will be important to consider other co-morbidities and socio-demographic factors in this population to understand all factors involved for successful prevention of complications. Our study provides evidence to stimulate and inform discussion concerning the use of MAR in subgroups of women with an elevated pregnancy and birth risks, and subsequently more interventions, due to an increased BMI.

Study strengths and limitations

The WHO recommends a different BMI categorization for Asian women (WHO Expert Consultation, 2004), but the ethnicity of women was not recorded in the dataset. However, a previous study that used the same SPE dataset linked women's data to their ethnicity (collected from civil registry and municipalities datasets) and found a very low prevalence of Asian women giving birth in Flanders (Bogaerts *et al.*, 2012). The database did not include data on socio-economic status. In Europe, lower socio-economic status has been linked with higher rates of obesity (Stam-Moraga *et al.*, 1999; Jaacks *et al.*, 2019) and women of lower socio-economic status will also access pre-natal care less (Beeckman *et al.*, 2010; Chiavarini *et al.*, 2014), which leads to poorer pregnancy outcomes (Boudet-Berquier *et al.*, 2017). We did not have data on pre-pregnancy morbidities that could confound the association between higher BMI and pregnancy and birth outcomes and could therefore not adjust for such factors.

We examined the impact of BMI but recent evidence suggests that body fat distribution particularly waist circumference could be more relevant in predicting ART outcomes (Christofolini *et al.*, 2020). The SPE database does not specify the indication for the use of MAR, if it was a cryopreserved/thawed embryo, fresh or mixed embryo transfer, nor does it include data on whether sperm and/or eggs were from a donor or not. These parameters can influence perinatal outcomes especially for birth weight. Different studies have shown that macrosomia and LGA are significantly increased for infants born after frozen embryo transfer compared with fresh embryo transfer cycles (Gonzalez-Comadran *et al.*, 2014; Berntsen and Pinborg, 2018; Terho *et al.*, 2021). We did not have data on paternal BMI, which has previously been linked to poorer sperm quality (Raad *et al.*, 2017).

Supplementary data

Supplementary data are available at *Human Reproduction* online.

Data availability

Data cannot be shared publicly because of restrictions of the 'eBirth Medical' and 'eBirth City' portals. Data can be made available for researchers after fulfilling strict criteria by an authorization request (servicedesk.DTO@bosa.fgov.be; https://dt.bosa.be/nl/gegevensuitwisseling/combinatie_van_gegevens/ebirth). Summaries and highlights of perinatal activities are published yearly on governmental websites (https://www.zorg-en-gezondheid.be/sites/default/files/atoms/files/EMBARGO_SPE_Perinatale%20activiteiten%20in%20Vlaanderen%202018.pdf; https://www.cepip.be/pdf/rapport_CEPIP_wallonie2016_tma.pdf).

Authors' roles

All authors were involved in the design of the study. F.W. and L.A. conducted the analysis, with support of A.B., P.C. and A.P.F., F.W. drafted the manuscript. All authors reviewed the manuscript and had input in the discussion.

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Conflict of interest

None to declare.

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