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Association of Pre-Pregnancy Body Mass Index, Pregnancy-Related Weight Changes, and Parity With the Risk of Developing Degenerative Musculoskeletal Conditions

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Objective. **To examine how pre-pregnancy body mass index (BMI), parity, and pregnancy-related weight changes are associated with long-term risk of degenerative musculoskeletal conditions.**

Methods. **A total of 79,687 mothers with singleton births from the Danish National Birth Cohort were included. Information on height and weight prior to pregnancy and 6 months postpartum as well as gestational weight gain (GWG) was obtained from telephone interviews, while parity was derived from the Danish Medical Birth Registry. Diagnoses of musculoskeletal conditions, including osteoarthritis, disc disorders, low back pain, and soft tissue disorders, were obtained from the Danish National Patient Registry. Hazard ratios (HRs) were estimated using a Cox proportional hazards regression model.**

Results. **The cumulative incidence of musculoskeletal conditions during a median follow-up of 12.4 years was 19.7%. The risk of musculoskeletal conditions increased with both increasing pre-pregnancy BMI and increasing parity. Compared to normal-weight first-time mothers, the highest risk was seen in obese women with >2 births (HR 1.61 [95% confidence interval 1.41–1.83]). GWG of 10–15 kg was associated with the lowest risk of musculoskeletal conditions. Compared to women with no change in weight from preconception to 6 months after childbirth (±1 BMI unit), increasing postpartum weight increased the risk of musculoskeletal conditions in normal-weight and overweight women.**

Conclusion. **Our findings indicate that high pre-pregnancy BMI increases the risk of degenerative musculoskeletal conditions. Low and high GWG, higher postpartum weight retention, and especially higher parity are associated with an increased risk. Prevention of being overweight before, during, and after pregnancy may reduce the risk of development of degenerative musculoskeletal conditions among mothers.**

Degenerative musculoskeletal conditions are serious contributors to poor quality of life and a leading reason for disability pensions (1,2). Obesity is associated with several degenerative musculoskeletal conditions, such as osteoarthritis (OA), soft tissue disorders, and low back pain (3–5). The incidence of degenerative musculoskeletal conditions is higher for women than for men (6), indicating that weight load is not the only important factor.

Pregnancy is characterized by a natural increase in weight, change in hormone status, and physiologic strain on muscles and joints (7). Following pregnancy, many women have difficulty returning to their pre-pregnancy body mass index (BMI), and 21% of new

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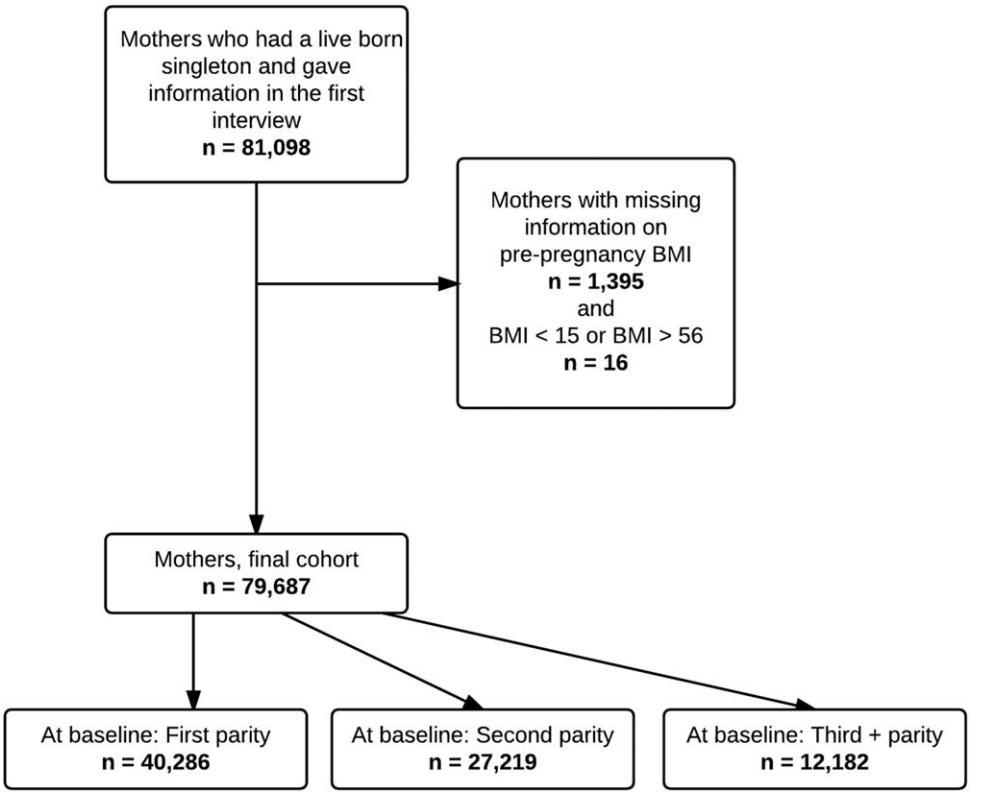

Figure 1. Flow chart showing the disposition of the subjects from the Danish National Birth Cohort. BMI = body mass index.

mothers have postpartum weight retention (PPWR) of ≥5 kg 6 months after childbirth (8). Such weight retention is associated with being overweight or obese later in life (9,10). Furthermore, motherhood is accompanied by increased domestic workload and frequent lifting of a child for several years, and each childbirth may challenge the maternal musculoskeletal system by both weight gain and physical strain. These factors may be an additional burden to women who are already overweight or obese when they become pregnant.

We used a large population-based cohort of mothers to examine how pre-pregnancy BMI and parity were associated with long-term risk of musculoskeletal conditions in the years following pregnancy and childbirth. Also, we compared the risk of musculoskeletal conditions across different permutations of pre-pregnancy BMI with gestational weight gain (GWG) and PPWR, respectively.

SUBJECTS AND METHODS

Study cohort. This study was conducted within the Danish National Birth Cohort (DNBC) (11). The DNBC contains self-reported and register-based information on lifestyle and health during and after pregnancy, including height and weight, for 92,924 pregnant women who were enrolled in early pregnancy by their general practitioner from 1996 to 2002. The women were interviewed twice during pregnancy and twice after delivery. The participation rate was ~60% among invited women. The cohort has been described in detail elsewhere (11,12). In this study, we used information from the first and third interviews, which were carried out at 16 weeks of gestation and at 6 months postpartum, respectively.

Data from these interviews was linked with the Danish National Patient Register (13) and the Danish Civil Registration System (14) by use of the personal identification number assigned to all Danish individuals since 1968 (14).

The Danish National Patient Registry (13) includes information on all inpatient contacts since 1977 and outpatient contacts since 1995 in Danish hospitals. The diagnostic codes used in the patient registry are classified according to the Danish versions of the International Classification of Diseases, Eighth Revision (ICD-8; 1977–1993) and ICD-10 (since 1994). Information on deaths and migration to and from Denmark was retrieved from the Danish Civil Registration System (14).

We included women who had live singleton births and participated in the first interview. We excluded women with missing information on pre-pregnancy weight or height at the first interview (n = 1,395) as well as women with a BMI of <15 or >56 (n = 16). The final study population consisted of 79,687 mothers (Figure 1).

Outcome measures. We used self-reported information on weight prior to conception and height from the first antenatal interview to estimate pre-pregnancy BMI (kg/m^2).

Table 1. Maternal characteristics by body mass index for 79,692 women from the Danish National Birth cohort*

	All	Underweight	Normal weight	Overweight	Obese
Study population	79,687 (100.00)	3,579 (4.49)	54,128 (67.93)	15,455 (19.39)	6,525 (8.19)
Age at conception, mean ± SD years	29.6 ± 4.3	28.9 ± 4.5	29.8 ± 4.3	29.5 ± 4.3	29.2 ± 4.3
Parity					
1	40,286 (50.6)	1,791 (50.0)	28,011 (51.7)	7,398 (47.9)	3,086 (47.3)
2	27,219 (34.2)	1,284 (35.9)	18,095 (33.4)	5,515 (35.7)	2,325 (35.6)
≥3	12,182 (15.3)	504 (14.1)	8,022 (14.8)	2,542 (16.4)	1,114 (17.1)
Socio-occupational status					
Low	6,978 (8.8)	444 (12.4)	4,028 (7.4)	1,537 (9.9)	969 (14.9)
Middle	28,852 (36.2)	1,328 (37.1)	18,293 (33.8)	6,330 (41.0)	2,901 (44.5)
High	40,573 (50.9)	1,601 (44.7)	29,840 (55.1)	6,879 (44.5)	2,253 (34.5)
Smoking in pregnancy					
Nonsmoker	58,474 (73.4)	2,228 (62.3)	39,992 (73.9)	11,415 (73.9)	4,839 (74.2)
Smoking cessation	7,706 (9.7)	351 (9.8)	5,454 (10.1)	1,385 (9.0)	516 (7.9)
Smoker	13,504 (16.9)	1,000 (27.9)	8,680 (16.0)	2,654 (17.2)	1,170 (17.9)
Exercise in pregnancy, minutes/week, no. (%)					
None	49,879 (62.6)	2,424 (67.7)	32,977 (60.9)	10,040 (65.0)	4,438 (68.0)
1–179	23,391 (29.4)	871 (24.3)	16,425 (30.3)	4,378 (28.3)	1,717 (26.3)
≥180	6,324 (7.9)	279 (7.8)	4,672 (8.6)	1,013 (6.6)	360 (5.5)
GWG, kg†					
<10	8,060 (10.1)	235 (6.6)	3,477 (6.4)	2,167 (14.0)	2,181 (33.4)
10–14.99	27,292 (34.2)	1,288 (36.0)	19,013 (35.1)	5,122 (33.1)	1,869 (28.6)
15–19.99	12,562 (15.8)	560 (15.6)	9,490 (17.5)	2,031 (13.1)	481 (7.4)
≥20	13,277 (16.7)	538 (15.0)	9,366 (17.3)	2,716 (17.6)	657 (10.1)
PPWR, BMI units‡					
>1 loss	8,683 (10.9)	99 (2.8)	4,111 (7.6)	2,537 (16.4)	1,936 (29.7)
−1 to <1	30,622 (38.4)	1,561 (43.6)	22,440 (41.5)	4,956 (32.1)	1,665 (25.5)
1 to <2	1,129 (14.2)	548 (15.3)	8,193 (15.1)	2,013 (13.0)	536 (8.2)
2 to <3	5,022 (6.3)	226 (6.3)	3,504 (6.5)	1,023 (6.6)	269 (4.1)
≥3	4,020 (5.0)	157 (4.4)	2,483 (4.6)	1,028 (6.7)	352 (5.4)

* Except where indicated otherwise, values are the number (%) of subjects.
† Gestational weight gain (GWG; n = 61,191) was only used in the analysis of the association between GWG and musculoskeletal conditions.
‡ Postpartum weight retention (PPWR; n = 59,637) was only used in the analysis of the association between PPWR and musculoskeletal conditions.

BMI was categorized according to the World Health Organization (WHO) definitions as underweight (<18.5), normal weight (18.5 to <25), overweight (25 to <30), or obese (≥30) (15). Pre-pregnancy BMI refers to a woman's BMI prior to the index birth. Information on baseline parity was obtained from the Danish Medical Birth Registry (16) and was categorized as 1, 2, or ≥3.

GWG, which was used as a proxy for pregnancy-related weight strain caused by e.g., the fetus, the placenta, and the amniotic fluid as well as increased fat mass, was based on self-reported GWG obtained from the third interview. We categorized GWG as <10 kg, 10–14.99 kg, 15–19.99 kg, or ≥20 kg. PPWR, which was considered a proxy for persistent weight change after pregnancy and hence related to an increase or decrease in fat mass compared to prior to conception, was defined as BMI at 6 months postpartum minus pre-pregnancy BMI. These differences were categorized as a weight loss of >1 BMI unit, no change (±1 BMI unit), a weight gain of 1–1.99 BMI units, a weight gain of 2–2.99 BMI units, or a weight gain of ≥3 BMI units.

The main outcome measure in this study was incident cases of hospital diagnoses of any degenerative musculoskeletal condition (not pregnancy specific) based on ICD-10 codes obtained from the Danish National Patient Registry. To ensure the validity of the diagnosis, we disregarded diagnoses provided by emergency wards. We defined diagnosis of a musculoskeletal condition as the first outpatient or inpatient contact recorded in the Patient Registry with an ICD-10 diagnosis code of 1) OA, 2) other degenerative peripheral joint disorders, 3) spondylosis and spinal stenosis, 4) degenerative disc disorders and low back pain, 5) soft tissue disorders such as bursitis, fasciitis, and enthesitis, and 6) other soft tissue disorders. Finally, we merged the subtypes into one composite end point for musculoskeletal conditions. An experienced rheumatologist (LD) confirmed the ICD-10 codes used to define musculoskeletal conditions as displayed in Appendix A.

In the first interview, women gave information about smoking and leisure time exercise during pregnancy as well as their socio-occupational status. Smoking history was categorized as never smoked, smoking cessation between conception and first interview, or current smoker. Leisure time exercise was categorized as no exercise, 1–180 minutes/week, or >180 minutes/week, and socio-occupational status as high, middle, or low (17). From the Danish Medical Birth Registry, we obtained information on maternal age as well as date of birth and gestational age to calculate estimated day of conception for all pregnancies leading to childbirth during the follow-up period.

Statistical analysis. We used Cox proportional hazards regression models to estimate hazard ratios (HRs) of first diagnosis of each of the 6 degenerative musculoskeletal conditions, as well as a composite end point of all diagnoses, with

Table 2. Hazard ratios (HRs) for degenerative musculoskeletal conditions according to pre-pregnancy BMI in the Danish National Birth Cohort*

	No. of person-years	No. of events	Crude HR	Adjusted HR (95% CI)	Percent
All degenerative disorders, composite end point					18.5
Continuous BMI, per 1 BMI unit	–	–	1.03	1.03 (1.02–1.03)	
Underweight	42,605	556	0.88	0.84 (0.77–0.92)	
Normal weight	635,579	9,409	1.00 (reference)	1.00 (reference)	
Overweight	174,104	3,328	1.30	1.28 (1.22–1.33)	
Obese	72,004	1,418	1.35	1.26 (1.19–1.34)	
Osteoarthritis (excluding spondylosis)					2.1
Continuous BMI, per 1 BMI unit	–	–	1.07	1.07 (1.06–1.08)	
Underweight	47,760	54	0.90	0.87 (0.65–1.16)	
Normal weight	719,358	901	1.00 (reference)	1.00 (reference)	
Overweight	205,169	459	1.80	1.78 (1.59–2.00)	
Obese	86,192	255	2.40	2.32 (2.00–2.69)	
Other degenerative peripheral joint disorders and arthralgia					9.9
Continuous BMI, per 1 BMI unit	–	–	1.03	1.03 (1.02–1.03)	
Underweight	45,835	285	0.87	0.80 (0.71–0.91)	
Normal weight	685,544	4,903	1.00 (reference)	1.00 (reference)	
Overweight	193,166	1,721	1.25	1.22 (1.15–1.29)	
Obese	81,039	792	1.38	1.28 (1.18–1.39)	
Spondylosis and spinal stenosis					0.8
Continuous BMI, per 1 BMI unit	–	–	1.01	1.01 (0.99–1.03)	
Underweight	47,915	27	1.05	0.99 (0.66–1.49)	
Normal weight	723,011	386	1.00 (reference)	1.00 (reference)	
Overweight	207,332	138	1.25	1.28 (1.05–1.56)	
Obese	87,395	49	1.07	0.97 (0.70–1.33)	
Degenerative disc disorders and low back pain					7.0
Continuous BMI, per 1 BMI unit	–	–	1.02	1.01 (1.01–1.02)	
Underweight	45,591	215	0.92	0.86 (0.74–0.99)	
Normal weight	686,820	3,499	1.00 (reference)	1.00 (reference)	
Overweight	194,020	1,190	1.21	1.15 (1.07–1.23)	
Obese	80,732	485	1.18	1.08 (0.97–1.19)	
Soft tissue disorders					3.3
Continuous BMI, per 1 BMI unit	–	–	1.04	1.03 (1.03–1.04)	
Underweight	47,059	91	0.85	0.86 (0.69–1.07)	
Normal weight	707,600	1,602	1.00 (reference)	1.00 (reference)	
Overweight	201,132	660	1.46	1.45 (1.32–1.59)	
Obese	84,457	267	1.41	1.36 (1.18–1.55)	
Other soft tissue disorders, not classified elsewhere					2.5
Continuous BMI, per 1 BMI unit	–	–	1.04	1.03 (1.02–1.04)	
Underweight	47,129	77	1.01	0.93 (0.73-1.18)	
Normal weight	713,782	1,146	1.00 (reference)	1.00 (reference)	
Overweight	203,092	502	1.54	1.47 (1.32–1.64)	
Obese	85,510	227	1.67	1.40 (1.20–1.63)	

* Adjusted for smoking, exercise, and socio-occupational status in pregnancy, and for the time-dependent variables years since start of follow-up, pregnancy, and parity. BMI = body mass index.

95% confidence intervals (95% CIs) according to both BMI as a continuous variable and categories of pre-pregnancy BMI. Normal-weight women were the reference. Women were followed up from the day of conception of the index parity until first outcome event, death, emigration, or end of follow-up on August 1, 2013, whichever came first. In the multivariate analyses, we adjusted for the following covariates, collected at baseline: socio-occupational status, smoking, and leisure time exercise. Further, we adjusted for the following time-varying covariates: maternal age, current pregnancy, parity, and time since start of follow-up (categorical). We defined parity by the reproductive cycle from the day of conception of the actual child until the day before any next conception (18). Potential confounders were chosen according to a directed acyclic graph (19) based on a literature review (results are available from the corresponding author upon request) (20). A restricted cubic spline with 6 knots was generated to visualize the association between continuous variables and musculoskeletal conditions (21).

In the analysis of subtypes of musculoskeletal conditions, women with the respective diagnoses prior to the start of follow-up were excluded. Before the start of follow-up, 4,869 women (6.1%) were diagnosed as having at least one degenerative musculoskeletal condition. In order to estimate the combined association of BMI and index parity, we computed a cross-classification of pre-pregnancy BMI and parity with a normal-weight first-time mother as the reference. We tested for trend by Cox proportional hazards regression on continuous data stratified by subcategories of both pre-pregnancy

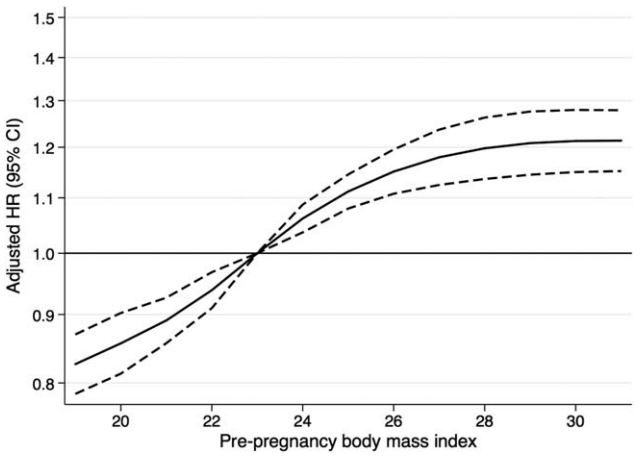

Figure 2. Hazard ratios (HRs; solid line) and 95% confidence intervals (95% CIs; broken lines) for musculoskeletal conditions according to pre-pregnancy body mass index. Associations were assessed using a restricted cubic spline adjusted for smoking, exercise, and socio-occupational status in pregnancy, and for the time-dependent variables years since start of follow-up, age, pregnant (yes/no), and parity.

BMI and parity. To identify interaction on the multiplicative scale, we performed a likelihood ratio test between the 2 variables.

Similarly, we studied the combined association of pre-pregnancy BMI and GWG with a normal-weight woman with a GWG of 10–14.99 kg as a reference and of pre-pregnancy BMI and PPWR with a normal-weight woman with no weight change (±1 BMI unit) at 6 months after delivery as a reference. For these analyses, follow-up started on the day of delivery and on the day of the third interview, respectively. Only women with no prior disease before these points in time were included. Also, we performed the analysis on GWG and musculoskeletal conditions adjusted for PPWR. However, since GWG and PPWR are closely associated, we tested for correlation between the two as continuous variables in kg ($P = 0.46$).

Finally, to examine the validity of the outcome, we performed an analysis of pre-pregnancy BMI and musculoskeletal conditions restricted to diagnoses provided by rheumatology units only. All analyses were performed using Stata 13.0 (StataCorp).

RESULTS

Characteristics of the subjects. The final study cohort consisted of 79,687 women with a mean ± SD age of 29.6 ± 4.3 at the beginning of follow-up. Prior to pregnancy, 4.5% of the mothers were categorized as underweight, 67.9% as having a normal weight, 19.4% as overweight, and 8.2% as obese (Table 1). Median follow-up time for the study population was 12.4 years (interquartile range 11.6–14.5 years).

We identified 14,711 (18.5%) incident cases of degenerative musculoskeletal conditions during follow-up, which ended on August 1, 2013. The incidence rates of any degenerative musculoskeletal condition were 13 per 1,000 person-years for underweight mothers, 15 per 1,000 person-years for normal-weight mothers, 19 per 1,000 person-years for overweight mothers, and 20 per 1,000 person-years for obese mothers.

Pre-pregnancy BMI. The adjusted risk of developing any degenerative musculoskeletal condition increased by 3% for every 1 unit increase in BMI (Table 2). Compared to normal-weight women, the risk of developing any musculoskeletal condition was 16% lower for underweight women, 28% greater for overweight women, and 26% greater for obese women. As indicated by these risk estimates, the excess risk was fairly stable across the overweight and obese categories (Figure 2).

Analyses of the associations between pre-pregnancy BMI and each of the subtypes of musculoskeletal conditions (Table 2) all showed an increased adjusted risk with higher BMI, similar to what was seen for all degenerative musculoskeletal conditions combined. For all subtypes except OA, the increase when moving from the overweight to the obese category was small, if any. In the supplementary analyses, we used a composite end point for all degenerative musculoskeletal conditions. Only 3,431 cases of musculoskeletal conditions (23.3%) received their diagnosis in a rheumatology unit. Hence, the analysis based on these cases only had wide confidence intervals, but estimates remained comparable to the main analysis (data are available from the corresponding author upon request).

Pre-pregnancy BMI and parity. The estimates for the combined effect of pre-pregnancy BMI and parity showed both an increasing risk of developing musculoskeletal conditions in overweight and obese women within each parity strata, as seen for the overall analysis, and a higher risk of developing musculoskeletal conditions with increasing parity in all pre-pregnancy BMI strata (Table 3). Thus, compared to a normal-weight first-time mother, all combinations of both higher parity and higher pre-pregnancy BMI were associated with an elevated risk of developing a musculoskeletal condition, with the highest risk in mothers who were overweight or obese when they became pregnant and had 3 or more children prior to the index birth (HR 1.75 [95% CI 1.60–1.92] and HR 1.61 [95% CI 1.41–1.83], respectively). Tests for trends were statistically significant for all strata of parity and pre-pregnancy BMI. There was no interaction between pre-pregnancy BMI and parity ($P = 0.41$), indicating that the effect of parity on the relative risk of developing musculoskeletal conditions did not differ across categories.

Table 3. Hazard ratios (HRs) for any degenerative musculoskeletal condition according to pre-pregnancy BMI and parity in the Danish National Birth Cohort*

	Pre-pregnancy BMI prior to index birth					
Parity	Underweight, HR (95% CI)	Normal weight, HR (95% CI)	Overweight, HR (95% CI)	Obese, HR (95% CI)	*P* for trend	Parity (95% CI)†
Parity 1 (n = 37,832)	0.85 (0.74–0.97)	1.00 (reference)	1.29 (1.21–1.37)	1.22 (1.11–1.33)	<0.001	1.00 (reference)
Parity 2 (n = 25,651)	0.94 (0.81–1.09)	1.21 (1.16–1.27)	1.49 (1.39–1.59)	1.58 (1.44–1.74)	<0.001	1.27 (1.22–1.33)
Parity ≥3 (n = 11,335)	1.25 (1.02–1.53)	1.33 (1.25–1.42)	1.75 (1.60–1.92)	1.61 (1.41–1.83)	<0.001	1.58 (1.47–1.70)
P for trend	<0.001	<0.001	<0.001	<0.001		<0.001
BMI (n = 74,818)‡	0.83 (0.76–0.91)	1.00 (reference)	1.27 (1.22–1.32)	1.25 (1.18–1.32)	<0.001	–

* Adjusted for smoking, exercise, and socio-occupational status in pregnancy, and for the time-dependent variables years since start of follow-up, age, and pregnancy. The follow-up period was from conception to 14 years postpartum.
† Also adjusted for pre-pregnancy body mass index (BMI).
‡ Adjusted for parity.

Pre-pregnancy BMI and GWG. Compared to a GWG of 10–14.99 kg, all other strata of GWG showed an increased risk of developing musculoskeletal conditions in the years following pregnancy and childbirth, regardless of pre-pregnancy BMI, with 15% (95% CI 8–22%) for GWG of <10 kg, 11% (95% CI 6–17%) for GWG of 15–19.99 kg, and 18% (95% CI 12–24%) for GWG of ≥20 kg (Table 4). No statistically significant

Table 4. Hazard ratios (HRs) for any degenerative musculoskeletal condition according to pre-pregnancy BMI and pregnancy-related weight changes in the Danish National Birth Cohort*

	Pre-pregnancy BMI prior to index birth						
	Underweight, HR (95% CI)	Normal weight, HR (95% CI)	Overweight, HR (95% CI)	Obese, HR (95% CI)	*P* for trend	GWG, HR (95% CI)†	PPWR, HR (95% CI)†
GWG, kg							
<10 (n = 7,396)	1.06 (0.77–1.45)	1.18 (1.08–1.29)	1.5 (1.36–1.65)	1.41 (1.28–1.56)	<0.001	1.15 (1.08–1.22)	–
10–14.99 (n = 25,722)	0.8 (0.68–0.94)	1.00 (reference)	1.32 (1.23–1.42)	1.32 (1.18–1.47)	<0.001	1.0 (reference)	–
15–19.99 (n = 11,886)	0.97 (0.78–1.21)	1.11 (1.05–1.18)	1.48 (1.34–1.64)	1.41 (1.16–1.72)	<0.001	1.11 (1.06–1.17)	–
≥20 (n = 12,452)	0.97 (0.78–1.21)	1.22 (1.15–1.29)	1.44 (1.32–1.58)	1.51 (1.27–1.78)	<0.001	1.18 (1.12–1.24)	–
P for trend	0.93	<0.001	0.45	0.60	–	<0.001	–
BMI (n = 57,456)‡	0.82 (0.74–0.92)	1.00 (reference)	1.28 (1.22–1.34)	1.26 (1.17–1.34)	<0.001	–	–
PPWR, BMI units							
Loss >1 (n = 8,094)	1.16 (0.73–1.84)	1.02 (0.94–1.11)	1.27 (1.16–1.40)	1.35 (1.22–1.50)	<0.001	–	1.03 (0.97–1.09)
−1–0.99 (n = 28,846)	0.86 (0.75–0.99)	1.00 (reference)	1.26 (1.17–1.35)	1.28 (1.14–1.44)	<0.001	–	1.0 (reference)
1–1.99 (n = 10,622)	0.78 (0.61–0.98)	1.05 (0.99–1.12)	1.35 (1.22–1.50)	1.36 (1.12–1.64)	<0.001	–	1.05 (1.00–1.11)
2–2.99 (n = 4,717)	0.78 (0.54–1.14)	1.11 (1.02–1.21)	1.42 (1.24–1.63)	1.09 (0.81–1.48)	0.01	–	1.09 (1.02–1.17)
≥3 (n = 3,752)	1.02 (0.69–1.51)	1.22 (1.11–1.35)	1.58 (1.39–1.81)	1.37 (1.08–1.73)	0.01	–	1.22 (1.13–1.31)
P for trend	0.42	<0.001	<0.001	0.63	–	–	<0.001
BMI (n = 56,031)§	0.83 (0.74–0.92)	1.00 (reference)	1.26 (1.20–1.33)	1.26 (1.18–1.36)	<0.001	–	–

* Adjusted for smoking, exercise, and socio-occupational status in pregnancy, and for the time-dependent variables years since start of follow-up, age, and pregnancy. The follow-up period was from childbirth to 14 years postpartum for pre-pregnancy body mass index (BMI) and from 6 months postpartum to 14 years postpartum for pregnancy-related weight changes.
† Adjusted for smoking, exercise, socio-occupational status in pregnancy, and pre-pregnancy BMI and for the time-dependent variables years since start of follow-up, age, and pregnancy.
‡ Adjusted for smoking, exercise, socio-occupational status in pregnancy, and gestational weight gain (GWG) and for the time-dependent variables years since start of follow-up, age, and pregnancy.
§ Adjusted for smoking, exercise, socio-occupational status in pregnancy, and postpartum weight retention (PPWR) and for the time-dependent variables years since start of follow-up, age, and pregnancy.

interaction was found between pre-pregnancy BMI and GWG ($P = 0.74$) and thus, in all strata of pre-pregnancy BMI, women who gained 10–14.99 kg in pregnancy had the lowest risk of developing musculoskeletal conditions. Adjusting for PPWR in the analysis of GWG and musculoskeletal conditions only changed the estimates marginally (data are available from the corresponding author upon request).

Pre-pregnancy BMI and PPWR. The increase in risk of developing musculoskeletal conditions with high pre-pregnancy BMI was observed in all strata of PPWR (Table 4). Furthermore, for each increase in PPWR category, a clear trend of increasing risk for musculoskeletal conditions was found in the overall analysis and also in normal-weight and overweight women compared to a woman who returned to her pre-pregnancy BMI. However, among obese women, the already increased risk of musculoskeletal conditions compared to normal-weight mothers did not change much with increasing PPWR. No statistically significant interaction was found between pre-pregnancy BMI and PPWR ($P = 0.74$).

DISCUSSION

In this study, the estimated incidence of musculoskeletal conditions increased with both increasing pre-pregnancy BMI and increasing parity. Thus, the largest excess risk was seen in overweight and obese women who had more than 2 children when they entered the study. Pregnancy-related weight changes were also associated with an increased risk of developing a musculoskeletal condition. Women with low or high weight gain in pregnancy had higher risks, and adjusting for PPWR did not change these findings. Weight retention after childbirth also increased the risk, especially in normal-weight and overweight women.

Our finding of a higher risk of musculoskeletal conditions with increased BMI is consistent with the findings of previous studies in the general adult population for multiple musculoskeletal conditions (3–5,22,23). Notably, trends in each of the individual subtypes of musculoskeletal conditions showed an increased risk with increasing pre-pregnancy BMI, which leveled off when reaching overweight. The only exception was the subtype of OA, where risk continued to increase. Based on this finding, we decided to combine the subtypes of diseases. This may indicate that weight is associated with all of these heterogeneous musculoskeletal conditions despite their different etiopathologies, which is consistent with studies of major musculoskeletal diseases such as low back pain (24), lumbar disc disorders (25), spinal stenosis (26), fibromyalgia (27), and tendinopathy (28,29). A meta-analysis of knee OA (30) found a dose-response association between continuous BMI and risk of disease, corroborating our finding of a continuing increase in risk of OA with increasing BMI beyond overweight. We are well aware that the composite end point of all degenerative musculoskeletal conditions consists of very heterogeneous conditions, but by combining these musculoskeletal conditions, we illustrate the total burden of these diagnoses in a population of mothers in midlife.

Multiparity displayed an increased risk of musculoskeletal conditions, which may be due to the repeated weight strain and hormonal changes that occur across several pregnancies. Multiparity has been associated with musculoskeletal pain and discomfort in pregnancy (31), and it is likely that this also has a long-term effect on the musculoskeletal system. Additionally, each new child in a family increases the workload in early motherhood, e.g., with repeated lifting. For women with excessive weight, this may be more of a challenge. Our finding for OA is consistent with previous studies on parity in relation to OA and joint replacement which conclude that parity affects the incidence of hip and especially knee replacement in women older than 50 years of age (32,33).

GWG represents a sudden increase in weight that is directly related to pregnancy, including the fetus, amniotic fluid, and possible edema, on top of fat gain. We found that women with a GWG of ≥15 kg had an increased risk of developing musculoskeletal conditions compared to women with a GWG of 10–14.99 kg, both independently and in combination with pre-pregnancy BMI. This indicates that moderate weight gain in pregnancy, regardless of pre-pregnancy BMI, holds the lowest risk for development of musculoskeletal conditions. Notably, our results also suggest that even a short period of increased weight, which is lost again after pregnancy, affects the musculoskeletal system in the following years.

Since high BMI is a risk factor for musculoskeletal conditions and PPWR is an indicator for long-term increased weight and obesity (9,10), PPWR might be an independent risk factor for musculoskeletal conditions in mothers. We found that women who were of normal weight or overweight prior to pregnancy had an increased risk of musculoskeletal conditions with increasing PPWR. This is consistent with the findings of studies in the general population (34–36). Manninen et al found that weight change from normal weight to overweight carried a higher risk of developing OA than constant overweight over a 30-year period

(37). We did not observe the same trend of higher risk of musculoskeletal conditions with increasing PPWR in women who were already obese prior to pregnancy. Mechanisms linking obesity and musculoskeletal conditions are not purely biomechanical due to the increased weight load. Release of proinflammatory mediators from joint tissue due to excessive fat accumulation might also affect joint degeneration, increase pain, and decrease joint function (22). High pre-pregnancy BMI may indicate long-term obesity and hence a constant stress on the metabolic system as well as a long-term burden on the musculoskeletal system. Thus, weight gain in already-obese mothers may not add much to an already elevated risk.

The DNBC is a large well-documented birth cohort with almost complete baseline information on weight and height as well as on important potential confounders. Another strength of this study is the inclusion of information from the Danish registers, which, by linkage to each individual in the DNBC, allowed us to follow up each woman for up to 16 years postpartum.

Our data are based on observations; hence, we cannot rule out unmeasured or residual confounding. There is a risk of misclassification of exposure since data on weight was self-reported. However, self-reported data on pre-pregnancy BMI have previously been validated in a subcohort of 5,033 women in the DBNC, and there was a strong agreement on BMI category as defined by the WHO (~90%) (38). Misclassification of PPWR may be limited by the fact that a similar underreport of weight 6 months postpartum as seen for pre-pregnancy weight may be anticipated.

Incidence of musculoskeletal conditions was based on ICD-10 codes and represent therefore mainly severe cases, since milder cases may remain undiagnosed or may be treated by general practitioners. We performed a sensitivity analysis on outcome defined by diagnoses from rheumatology departments, since these have previously been found to enhance the validity of another musculoskeletal condition, rheumatoid arthritis (39). Despite wide confidence intervals, the results were consistent with our findings in the main analysis.

The women in the DNBC represent ~30% of the pregnant women of that time in Denmark and have been found to be healthier with regard to weight and smoking and to have a higher socioeconomic status than the source population (40). However, selected odd ratios for 3 different exposure–risk associations were not biased by nonparticipation in this cohort (40), which is reassuring. Of the 79,687 women initially included in this study, 75.8% gave information on PPWR. Women who did report weight at 6 months postpartum were more likely to have a healthy BMI prior to pregnancy, were less likely to smoke, and had higher socio-occupational status than the initial study cohort. We minimized the risk of bias by controlling for these factors, which may potentially be related to women's choice to participate (41). Last, our study population primarily consisted of white women, and our results may not be valid for other ethnic groups.

The DNBC includes very few women who never gave birth, which makes it impossible to establish a never-childbearing comparison group. It would be of considerable interest to compare the risk of midlife musculoskeletal conditions according to pre-pregnancy BMI in childbearing women with women who never gave birth to investigate whether the association between preconception BMI and later musculoskeletal conditions is driven by BMI alone or in conjunction with parity as well as pregnancy-related weight changes. However, it should be noted that such a comparison group of never-childbearing women will differ substantially in other ways than parity and childbirth. For instance, they may have a higher prevalence of chronic diseases. In Denmark, the majority of pregnancies and childbirth indicate a healthy process in a healthy woman.

To conclude, we corroborated that high pre-pregnancy BMI increased the occurrence of degenerative musculoskeletal conditions in the years following pregnancy and childbirth. Both low and high GWG, higher PPWR, and especially higher parity led to an increased risk. Our findings suggest that prevention of being overweight before, during, and after pregnancy may reduce the risk of development of degenerative musculoskeletal conditions among mothers. Clinicians should recommend that mothers, especially those with musculoskeletal problems, avoid high GWG and postpartum weight retention in possible future pregnancies.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Bliddal had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Acquisition of data. Bliddal, Pottegård, Olsen, Sørensen, Nohr.

Analysis and interpretation of data. Bliddal, Pottegård, Olsen, Sørensen, Nohr.

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