Supplemental Methods

We describe additional details pertaining to the exploratory analysis among the IBD and asthma subcohorts below.

Self-assessed disease severity measures

For asthma, interviewers administered the Pregnancy Asthma Control Test (p-ACT; a validated measure of asthma control; possible range from 5=poor control to 25= complete control),[1,2] and collected information on asthma exacerbations.

Exposure modeling

Medications of interest for the IBD subcohort included OCSs, immunosuppressives, and oral aminosalycilates. Medications of interest for the asthma subcohort included OCSs and other asthma medications excluding short-acting beta-agonists, i.e., inhaled corticosteroids, ipratropium bromide, long-acting beta-agonist/inhaled corticosteroid combinations, leukotriene receptor antagonists, and omalizumab.

For IBD, we allowed for k=2 clusters of cumulative OCS dose during the first 139 days of pregnancy, instead of k=3 clusters as in the RA analysis, given the smaller number of women who used OCSs. For asthma, we did not conduct an OCS dose trajectory analysis during the first 139 days of pregnancy because of the small number with OCS use during this time frame. Instead we considered any OCS use versus none during the first 139 days of pregnancy in the asthma subcohort.

We evaluated high and low OCS daily dose for IBD after gestational day 139, but not for asthma due to the small number of women with OCS use. For IBD, daily doses equivalent to ≥20 mg of prednisone were considered to be high instead of ≥10 mg of prednisone as in the RA analysis, given a higher distribution of doses in this subcohort and few women exposed to daily doses equivalent to <10 mg of prednisone.

Statistical analysis

Using regression adjustment, we modeled the propensity score in tertiles for IBD and asthma instead of quintiles as in the RA analysis, because of the smaller number of women with exposures in these subcohorts. Due to the low number of women exposed to OCS in the IBD subcohort, we did not adjust for potential confounders in analyses of OCS dose.

The following potential confounders were considered for adjustment by propensity score in the IBD analysis: LMP year, gestational age at enrollment, maternal age, race and ethnicity, socio-economic status (Hollingsheds categories[3]), primiparity, multiple gestation, ≥5 servings of alcohol in the first trimester, cigarette smoking in the first trimester, pre-pregnancy overweight or obesity, history of diabetes, history of hypertension, autoimmune disease comorbidities, and rectal aminosalicylate use during the first half of pregnancy. For analyses of exposures after gestational day 139, we also considered for adjustment OCS use (any, none) and use of other medications of interest (any, none) during pregnancy and before the start of the exposure window. We excluded from the IBD propensity score oral aminosalicylates exposure during the first half of pregnancy despite it being associated with both the outcome and the exposure because it predicted oral aminosalicylate exposure later in pregnancy nearly perfectly.

The following potential confounders were considered for adjustment by propensity score in the asthma analysis: LMP year, gestational age at enrollment, maternal age, race and ethnicity, socio-economic status (Hollingsheds categories[3]), primiparity, multiple gestation, ≥5 servings of alcohol in the first trimester, cigarette smoking in the first trimester, pre-pregnancy overweight or obesity, history of diabetes, history of hypertension, autoimmune disease comorbidities, season of the LMP, short-acting beta-agonist use during the first half of pregnancy, p-ACT at the time of enrollment as a continuous variable, and any asthma exacerbation (i.e., hospitalization, emergency room visit, or unplanned clinic

visit for increased asthma symptoms) between the start of pregnancy and enrollment. For analyses of exposures after gestational day 139, we also considered for adjustment OCS use (any, none) and use of other medications of interest (any, none) during pregnancy and before the start of the exposure window.

We imputed missing values with single imputation for p-ACT (n=7) using predictors of p-ACT interest.

1. Schatz M, Sorkness CA, Li JT, Marcus P, Murray JJ, Nathan RA, et al. Asthma Control Test: reliability, validity, and responsiveness in patients not previously followed by asthma specialists. J Allergy Clin Immunol. 2006;117(3):549-556,
2. Palmsten K, Schatz M, Chan PH, Johnson DL, Chambers CD. Validation of the Pregnancy Asthma Control Test. J Allergy Clin Immunol Pract. 2016;4(2):310-315 e311, 4789157.
3. Hollingshead AB. Four factor index of social status, unpublished working paper, 1975. Yale University, New Haven, CT. https://artlesstanzim.files.wordpress.com/2014/05/hollinghead-four-factors-2.pdf, 2 September 2019, date last accessed.

Supplemental Tables

Supplementary Table S1. Characteristics among women in the inflammatory bowel disease subcohort by exposure (not mutually exclusive), n=217.

	Any Exposure After Gestational Day 139 [a]					
	Oral Corticosteroid		Immunosuppressive		Oral Aminosalicylate	
	Yes	No	Yes	No	Yes	No
Characteristic	n=47	n=170	n=184	n=33	n=50	n=167
LMP Year 2009-2014, n (%)	34 (72.3)	137 (80.6)	143 (77.7)	28 (84.8)	36 (72.0)	135 (80.8)
Maternal Age, mean (SD)	31.5 (4.4)	31.1 (4.4)	31.2 (4.5)	31.4 (3.7)	32.1 (4.9)	31.0 (4.2)
Non-Hispanic White, n (%)	42 (89.4)	160 (94.1)	177 (96.2)	25 (75.8)	45 (90.0)	157 (94.0)
Socioeconomic Status, Hollingsheads Categories 1 or 2[b], n (%)	41 (87.2)	133 (78.2)	150 (81.5)	24 (72.7)	46 (92.0)	128 (76.6)
Primiparous, n (%)	28 (59.6)	98 (57.7)	112 (60.9)	14 (42.4)	30 (60.0)	96 (57.5)
Multiple Gestation, n (%)	4 (8.5)	11 (6.5)	14 (7.6)	1 (3.0)	2 (4.0)	13 (7.8)
≥5 Servings of Alcohol in the First Trimester, n (%)	4 (8.5)	28 (16.5)	28 (15.2)	4 (12.1)	9 (18.0)	23 (13.8)
First Trimester Cigarette Smoking, n (%)	5 (10.6)	19 (11.2)	23 (12.5)	1 (3.0)	5 (10.0)	19 (11.4)
Pre-pregnancy Hypertension, n (%)	3 (6.4)	7 (4.1)	9 (4.9)	1 (3.0)	3 (6.0)	7 (4.2)
Oral Corticosteroid Use Before Gestational Day 110, n (%)	17 (36.2)	16 (9.4)	25 (13.6)	8 (24.2)	9 (18.0)	24 (14.4)
Immunosuppressive Use Before Gestational Day 110, n (%)	43 (91.5)	152 (89.4)	184 (100)	11 (33.3)	40 (80.0)	155 (92.8)
Oral Aminosalicylate Use Before Gestational Day 110, n (%)	11 (23.4)	44 (25.9)	42 (22.8)	13 (39.4)	47 (94.0)	8 (4.8)

Abbreviation: LMP, last menstrual period; SD, standard deviation.

[a]An additional 30 days of exposure was added to the reported end date of use.

[b]Calculated using Hollingshead categories based on maternal and paternal education and occupation; Possible Range: 1, highest to 5, lowest. Missing for 1 woman.

Supplementary Table S2. Characteristics among women in the asthma subcohort by exposure (not mutually exclusive), n=234.

	Any Exposure After Gestational Day 139[a]			
	Oral Corticosteroid		Other Asthma Medication[b]	
	Yes	No	Yes	No
Characteristic	n=21	n=213	n=85	n=149
Maternal Age, mean (SD)	34.1 (5.3)	31.8 (5.4)	33.1 (5.1)	31.4 (5.5)
Non-Hispanic White, n (%)	17 (81.0)	177 (83.1)	72 (84.7)	122 (81.9)
Socioeconomic Status, Hollingsheads Categories 1 or 2[c], n (%)	17 (81.0)	165 (77.5)	68 (80.0)	114 (76.5)
Primiparous, n (%)	9 (42.9)	129 (60.6)	53 (62.4)	85 (57.0)
Multiple Gestation, n (%)	0 (0)	9 (4.2)	4 (4.7)	5 (3.4)
≥5 Servings of Alcohol in the First Trimester, n (%)	6 (28.6)	44 (20.7)	16 (18.8)	34 (22.8)
First Trimester Cigarette Smoking, n (%)	1 (4.8)	16 (7.5)	1 (1.2)	16 (10.7)
History of Hypertension, n (%)	1 (4.8)	6 (2.8)	1 (1.2)	6 (4.0)
Inflammatory Bowel Disease, Lupus, or Ankylosing Spondylitis, n (%)	3 (14.3)	18 (8.5)	6 (7.1)	15 (10.1)
Oral Corticosteroid Use Before Gestational Day 110, n (%)	8 (38.1)	16 (7.5)	10 (11.8)	14 (9.4)
Other Asthma Medication Use Excluding Short-Acting Beta Agonists Before Gestational Day 140, n (%)	8 (38.1)	83 (39.0)	77 (90.6)	14 (9.4)
Short-Acting Beta Agonist Use Before Gestational Day 140, n (%)	7 (33.3)	74 (34.7)	41 (48.2)	40 (26.8)
Pregnancy Asthma Control Test, mean (SD)[d]	18.1 (4.7)	20.5 (4.0)	19.7 (4.0)	20.7 (4.1)

Abbreviation: LMP, last menstrual period; OCS, oral corticosteroid; SD, standard deviation.

[a]An additional 30 days of exposure was added to the reported end date of use for oral corticosteroids.

[b]Excludes short-acting beta-agonists.

[c]Calculated using Hollingshead categories based on maternal and paternal education and occupation; possible range: 1, highest to 5, lowest.

[d]Imputed for 7 women; possible range: 5, poor control to 25, complete control.

Supplementary Table S3. Association between exposures and preterm birth adjusted for covariates not related to disease severity.

Time-Dependent Medication Exposure after Gestational Day 139[a]	Adjusted HR[b] (95% CI)	Mutually Adjusted HR[c] (95% CI)
Rheumatoid Arthritis, n=528		
Oral Corticosteroid	2.66 (1.70, 4.18)	2.68 (1.70, 4.23)
No Oral Corticosteroid	Reference	Reference
B-DMARD	0.82 (0.51, 1.33)	0.84 (0.52, 1.37)
No B-DMARD	Reference	Reference
NB-DMARD	0.95 (0.51, 1.76)	0.84 (0.44, 1.58)
No NB-DMARD	Reference	Reference
No Medication of Interest	NA	NA
Rheumatoid Arthritis, n=525		
Oral Corticosteroid High Dose[d]	4.07 (2.46, 6.74)	4.03 (2.43, 6.69)
Oral Corticosteroid Low Dose[d]	1.71 (0.97, 3.04)	1.74 (0.97, 3.11)
No Oral Corticosteroid	Reference	Reference
DMARD	0.90 (0.57, 1.41)	0.91 (0.58, 1.43)
No DMARD	Reference	Reference
No Medication of Interest	NA	NA

Abbreviations: B-DMARD, biologic disease modifying antirheumatic drug; CI, confidence interval; DMARD, disease modifying antirheumatic drug; HR, hazard ratio; NA, not applicable; NB-DMARD, non-biologic disease modifying antirheumatic drug.

[a]An additional 30 days of exposure was added to the reported end date of use.

[b]One model for each medication of interest. HR adjusted for quintiles of the propensity score: Last menstrual period year (<2009, ≤2009), maternal age, race and ethnicity (Non-Hispanic White, Other), multiple gestation, ≥5 servings of alcohol in the first trimester, and autoimmune disease comorbidity (inflammatory bowel disease, lupus, or ankylosing spondylitis).

[c]One model, adjusting for each medication exposure group of interest and each associated propensity score.

Supplementary Table S4. Sensitivity analyses for the association between exposures after day 139 and preterm birth for RA.

Time-Dependent Medication Exposure After Gestational Day 139	n	Preterm Birth	Person-weeks	Rate (per 1000/week)	Crude HR (95% CI)	Adjusted HR[a] (95% CI)	Mutually Adjusted HR[b] (95% CI)
Exposed Person-Time Ending on Reported End Date							
Oral Corticosteroid	237	48	3309	14.5	2.74 (1.76, 4.25)	2.17 (1.22, 3.84)	2.16 (1.22, 3.84)
No Oral Corticosteroid	369	34	6362	5.3	Reference	Reference	Reference
DMARD	250	27	3821	7.1	0.78 (0.50, 1.24)	0.74 (0.47, 1.19)	0.66 (0.41, 1.06)
No DMARD	364	55	5850	9.4	Reference	Reference	Reference
No Medication of Interest	252	23	3844	6.0	NA	NA	NA
Exposed Person-Time Ending on Censoring Date (Intention to Treat)							
Oral Corticosteroid	237	53	3913	13.5	2.47 (1.57, 3.88)	1.92 (1.04, 3.56)	1.89 (1.01, 3.51)
No Oral Corticosteroid	337	29	5796	5.0	Reference	Reference	Reference
DMARD	250	36	4497	8.0	0.84 (0.54, 1.30)	0.79 (0.51, 1.24)	0.75 (0.48, 1.18)
No DMARD	310	46	5211	8.8	Reference	Reference	Reference
No Medication of Interest	252	23	3844	6.0	NA	NA	NA
Exposed Person-Time Ending on Reported End Date							
Oral Corticosteroid							
Oral Corticosteroid ≥10 mg/day[c]	113	30	1222	24.5	4.83 (2.95, 7.89)	2.93 (1.56, 5.48)	2.71 (1.43, 5.12)
Oral Corticosteroid <10 mg/day[c]	157	18	2019	8.9	1.66 (0.94, 2.94)	1.22 (0.64, 2.34)	1.25 (0.65, 2.39)
No Oral Corticosteroid Use	369	34	6377	5.3	Reference	Reference	Reference
DMARD	247	27	3768	7.2	0.80 (0.50, 1.26)	0.75 (0.47, 1.20)	0.71 (0.44, 1.15)
No DMARD	364	55	5850	9.4	Reference	Reference	Reference

Abbreviations: CI, confidence interval; DMARD, disease modifying antirheumatic drug; HR, hazard ratio; NA, not applicable; RA, rheumatoid arthritis.

[a]One model for each medication of interest. HR adjusted for quintiles of the propensity score: Last menstrual period year (<2009, ≤2009), maternal age, race and ethnicity (Non-Hispanic White, Other), multiple gestation, ≥5 servings of alcohol in the first trimester, autoimmune disease comorbidity (inflammatory bowel disease, lupus, or ankylosing spondylitis), cumulative oral corticosteroid dose trajectory before gestational day 140 (high, low, none), non-steroidal anti-inflammatory drug before gestational day 140, and Health Assessment Questionnaire Disability Index, pain score, and global score at enrollment.
[b]One model, adjusting for each medication exposure group of interest and each associated propensity score.
[c]Prednisone dose equivalents.

Supplementary Table S5. OCS exposure between LMP and day 139 by trajectory group for inflammatory bowel disease (n=41).

OCs Trajectory Group		Total Number of Days of OCS Use		Average Daily Prednisone Equivalent Dose[a] (mg)		Total Cumulative Prednisone Equivalent Dose (mg)	
	n	Min, Max	Mean (SD)	Min, Max	Mean (SD)	Min, Max	Mean (SD)
High Dose Trajectory	7	72, 138	104.1 (30.8)	12.9, 37.7	23.6 (8.7)	1570, 5200	2426.8 (1269.4)
Low Dose Trajectory	34	1, 139	50.0 (50.1)	0.7, 41.7	14.4 (13.6)	7, 1473	466.5 (433.2)

Abbreviations: LMP, last menstrual period; max, maximum; min, minimum; OCS, oral corticosteroid; SD, standard deviation.

[a]Average dose on days with oral corticosteroid use.

Supplementary Table S6. Association between exposures before day 140 and preterm birth for inflammatory bowel disease and asthma.

Medication Exposure Before Gestational Day 140[a]	n	Preterm Birth	% Preterm Birth	Crude RR (95% CI)	Adjusted RR[b] (95% CI)	Mutually Adjusted RR[c] (95% CI)
Inflammatory Bowel Disease (n=216)						
Oral Corticosteroid						
High Dose Trajectory	7	2	28.6	2.17 (0.63, 7.45)	NA	NA
Low Dose Trajectory	34	6	17.6	1.34 (0.59, 3.05)	NA	NA
No Oral Corticosteroid	175	23	13.1	Reference	NA	NA
Immunosupressive	193	28	14.5	1.11 (0.37, 3.37)	NA	NA
No Immunosupressive	23	3	13.0	Reference	NA	NA
Oral Aminosalicylate	56	6	10.7	0.69 (0.30, 1.58)	NA	NA
No Oral Aminosalicylate	160	25	15.6	Reference	NA	NA
No Medication of Interest	11	3	27.3	NA	NA	NA
Asthma (n=234)						
Oral Corticosteroid	26	5	19.2	2.55 (1.02, 6.38)	2.15 (0.83, 5.60)	2.28 (0.89, 5.81)
No Oral Corticosteroid	208	15	7.2	Reference	Reference	Reference
Other Asthma Medication[d]	83	8	9.6	0.92 (0.40, 2.13)	0.87 (0.37, 2.03)	0.72 (0.31,1.66)
No Other Asthma Medication[d]	151	12	8.0	Reference	Reference	Reference
No Medication of Interest	75	6	8.0	NA	NA	NA

Abbreviations: CI, confidence interval; NA, not applicable; RR, Risk Ratio.

[a]Mutually exclusive oral corticosteroid trajectory groups and any versus none for other medication exposure groups.

[b]One model for each medication of interest. RR for inflammatory bowel disease subcohort not adjusted given the number of preterm births exposed to high/low dose oral corticosteroids. RR for asthma subcohort adjusted for tertiles of the propensity score: maternal age, race and ethnicity (Non-Hispanic White, Other), socio-economic status (Hollingshead categories 1 or 2, 3 to 5), primiparity, first trimester smoking, and pregnancy Asthma Control Test score at the time of enrollment.

[c]One model for the subcohort, adjusting for each medication exposure group of interest and each associated propensity score.

[d]Excluding short-acting beta-agonists.

Supplementary Table S7. Association between exposures after day 139 and preterm birth for inflammatory bowel disease and asthma.

Time-Dependent Medication Exposure After Gestational Day 139[a]	n	Preterm Birth	Person-weeks	Rate (per 1000/week)	Crude HR (95% CI)	Adjusted HR[b] (95% CI)	Mutually Adjusted HR[c] (95% CI)
Inflammatory Bowel Disease (n=217)							
Oral Corticosteroid	47	7	635	11.0	1.61 (0.69, 3.73)	1.09 (0.45, 2.60)	1.12 (0.45, 2.78)
No Oral Corticosteroid	203	24	4251	5.6	Reference	Reference	Reference
Immunosupressive	186	24	3970	6.0	0.92 (0.40, 2.15)	0.67 (0.28, 1.59)	0.69 (0.28, 1.72)
No Immunosupressive	60	7	915	7.6	Reference	Reference	Reference
Oral Aminosalicylate	175	24	3813	6.3	1.07 (0.46, 2.49)	1.09 (0.46, 2.58)	0.98 (0.40, 2.40)
No Oral Aminosalicylate	52	7	1073	6.5	Reference	Reference	Reference
No Medication of Interest	36	4	410	9.8	NA	NA	NA
Asthma (n=234)							
Oral Corticosteroid	21	2	321	6.2	1.38 (0.32, 5.95)	1.22 (0.27, 5.50)	1.23 (0.27, 5.56)
No Oral Corticosteroid	229	18	5139	3.5	Reference	Reference	Reference
Other Asthma Medication[d]	143	11	3161	3.5	0.83 (0.34, 1.99)	0.72 (0.20, 2.62)	0.75 (0.21, 2.71)
No Other Asthma Medication[d]	112	9	2299	3.9	Reference	Reference	Reference
No Medication of Interest	107	8	2193	3.6	NA	NA	NA

Abbreviations: CI, confidence interval; HR, hazard ratio; NA, not applicable.

[a]An additional 30 days of exposure was added to reported end dates of use for oral corticosteroids, immunosupressives, and oral aminosalicylates.

[b]One model for each medication of interest. HR for inflammatory bowel disease subcohort adjusted for propensity score: maternal age, race and ethnicity (Non-Hispanic White, Other), multiple gestation, primiparity, history of hypertension, and oral corticosteroid use before gestational day 110. HR for asthma subcohort adjusted for tertiles of the propensity score: maternal age, race and ethnicity (Non-Hispanic White, Other), socio-economic status (Hollingshead categories 1 or 2, 3 to 5), primiparity, first trimester smoking, exposure to oral corticosteroids before gestational day 140, exposure to asthma-related medications excluding oral corticosteroids and short-acting beta-agonists before gestational day 140, and pregnancy Asthma Control Test score at the time of enrollment.

[c]One model for each subcohort, adjusting for each medication exposure group of interest and each associated propensity score.

[d]Excluding short-acting beta-agonists.

Supplementary Table S8. Association between exposures after day 139 and preterm birth for inflammatory bowel disease (n=216).

Time-Dependent Medication Exposure after Gestational Day 139[a]	n	Preterm Birth	Person-weeks	Rate (per 1000/week)	Crude HR (95% CI)
Oral Corticosteroid ≥20 mg /day[b]	38	6	425	14.1	2.06 (0.84, 5.04)
Oral Corticosteroid Low Dose <20 mg/day[b]	27	1	209	4.8	0.68 (0.09, 5.04)
No Oral Corticosteroid	202	24	4226	5.7	Reference
Immunosupressive	185	24	3945	6.1	0.93 (0.40, 2.16)
No Immunosupressive	60	7	915	7.6	Reference
Oral Aminosalicylate	51	7	1048	6.7	1.10 (0.47, 2.55)
No Oral Aminosalicylate	175	24	3813	6.3	Reference
No Medication of Interest	36	4	410	9.8	NA

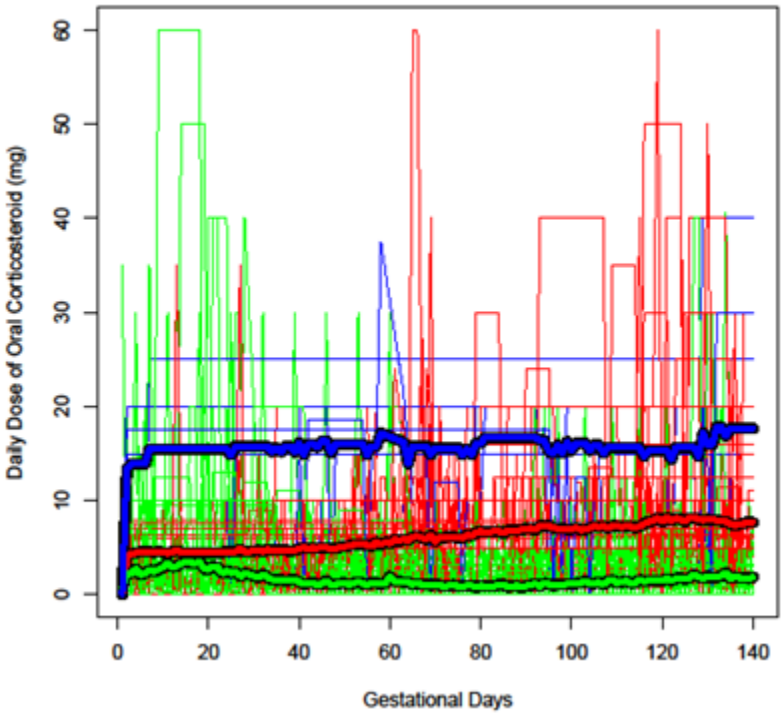
Abbreviations: CI, confidence interval; HR, hazard ratio; NA, not applicable.

[a]An additional 30 days of exposure was added to reported end dates of use.

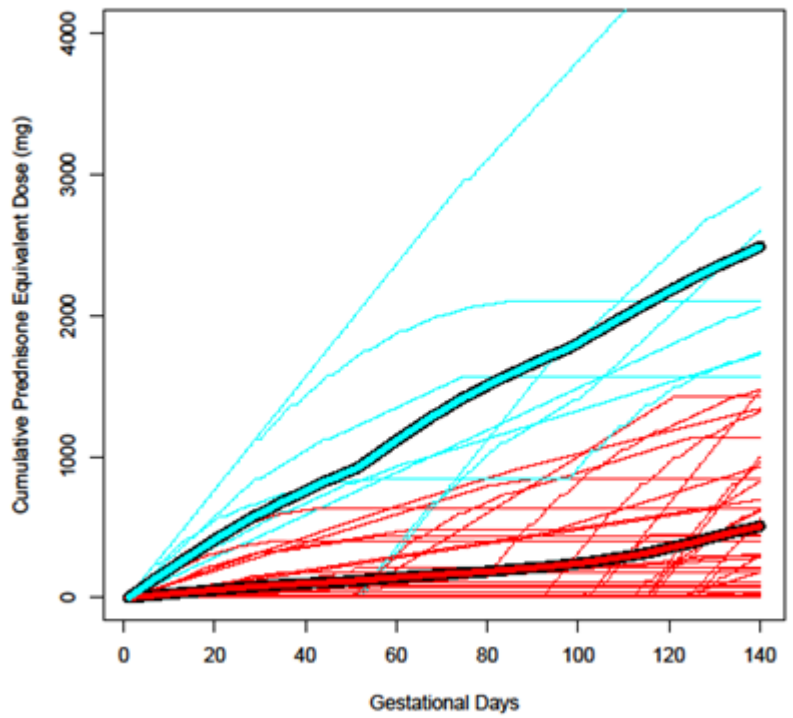
[b]High dose ≥20 mg prednisone equivalent dose per day, low dose <20 mg prednisone equivalent dose per day.

Supplemental Figure Legends

Supplementary Figure S1. OCS daily dose trajectories for RA (n=254). Thick lines are mean daily dose; thin lines are observed trajectories; blue=high, red=medium, green=low.



Supplementary Figure S2. OCS cumulative dose trajectories for inflammatory bowel disease (n=41). Thick lines are mean cumulative dose thin lines are observed trajectories; blue=high, red=low



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