

Children born in Denmark (N=2 701 408) from January 1973 to March 2016 from the Danish Medical Birth Register (MBR)

Excluded of children with missing birth date (N=1 929) and children with missing information on parents in the Danish Civil Registration System (CRS), (N=26 771)

Full MBR period 1973-2016 N=2 672 708 available for discrimination between vaginal delivery N= 2 271 913, Cesarian sectio N= 400 795

Not available for further discrimination of sectio type born before 1991 N= 1 067 922 unknown sectio type N=5 952

New MBR period 1991-2016, N=1 598 834 births available for discrimination between Vaginal delivery N= 1 312 522 Elective CS N= 122 419 Acute CS N= 163 893

Record linkage to National Patient Registry(NPR)

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Supplemental Table 1. ICD diagnoses codes

Disease	ICD-8 codes	ICD-10 codes
DM	249* Diabetes mellitus	DE1* Diabetes mellitus
	250* Diabetes mellitus	
RA	712* Rheumatoid arthritis and allied conditions	DM05* Rheumatoid arthritis
	715* Arthritis, unspecified UD	DM06* Rheumatoid arthritis DM08* Juvenile rheumatoid arthritis
CD	269* Other nutritional deficiency	DK900* Celiac disease
Crohn's disease	563.00; 563.01; 563.02; 563.08; 563.09 Mb. Crohn	K50* Crohn's sygdom
Ulcerative colitis	563.19 Ulcerosa, proctocolitis, haemorrhagica	K51* Colitis Ulcerosa
	569.04 Proctitis haemorrhagica	

Abbreviations: CD: Coeliac disease; DM: Diabetes mellitus; IBD; Inflammatory bowel disease; RA: Rheumatoid arthritis. * signifies that all subgroups are included.

Supplemental Table 2. Counts and proportions for delivery method with respect to outcome diseases

	Full period 1973-2016 (N=2 672 708 births)		New MFR period 1991-2016 (N=1 598 834 births, excluding 5 952 births with unkown type of sectio)		
	Vaginal delivery	CS	Vaginal delivery	Elective CS	Acute CS
Total	2 271 913 (85.0%)	400 795 (15.0%)	1 312 522 (82.1%)	122 419 (7.7%)	163 893 (10.3%)
DM	20 936 (87.7%)	2 932 (12.3%)	5 159 (82.9%)	477 (7.7%)	590 (9.5%)
RA	9 075 (86.7%)	1 395 (13.3%)	3 776 (82.6%)	353 (7.7%)	444 (9.7%)
CD	6 085 (85.3%)	1 047 (14.7%)	2 677 (81.7%)	248 (7.6%)	350 (10.7%)
Crohn's disease	8 051 (87.9%)	1 104 (12.1%)	2 075 (84.1%)	175 (7.1%)	218 (8.8%)
Ulcerative colitis	11 436 (88.9%)	1 428 (11.1%)	2 103 (84.9%)	179 (7.2%)	196 (7.9%)
IBD	17 293 (88.5%)	2 240 (11.5%)	3 735 (84.5%)	316 (7.2%)	368 (8.3%)
Combined (at least one)	51 926 (87.5%)	7 405 (12.5%)	14 896 (82.9%)	1 363 (7.6%)	1 703 (9.5%)
DM & RA	225 (89.6%)	26 (10.4%)	36 (0.0%)	<5 (0.0%)	<5 (0.0%)
DM & CD	400 (83.2%)	81 (16.8%)	237 (0.0%)	22 (0.0%)	32 (0.0%)
DM & IBD	383 (89.1%)	47 (10.9%)	45 (0.0%)	0 (0.0%)	<5 (0.0%)
RA & CD	58 (87.9%)	8 (12.1%)	22 (0.0%)	<5 (0.0%)	<5 (0.0%)
RA & IBD	227 (91.5%)	21 (8.5%)	61 (0.0%)	<5 (0.0%)	5 (0.0%)
CD & IBD	202 (86.7%)	31 (13.3%)	60(0.0%)	<5 (0.0%)	<5 (0.0%)
Dead	25 067 (79.7%)	6 392 (20.3%)	6 590 (69.1%)	1 021 (10.7%)	1 930 (20.2%)
Emigrated	73 661 (87.4%)	10 661 (12.6%)	31 802 (84.0%)	2 471 (6.5%)	3 581 (9.5%)

Count below 5 are presented as “<5” due to confidentiality issues. The disease combinations do not sum up to the “Combined” count, as 35 persons in the full cohort, respectively, 11 persons in the new MFR cohort experienced more than two of the diseases.

Abbreviations: CD: Coeliac disease; CS: Caesarean section; DM: Diabetes mellitus; IBD; Inflammatory bowel disease; RA: Rheumatoid arthritis

Supplemental Table 3. Cox regressions for the association between caesarean section and disease incidence with sequential adjustment for potential confounding variables for the full period (1973-2016)

Disease	Birth method	Undadjusted		Partly adjusted ^A		Fully adjusted ^B	
		(HR 95% CI)	P-value	(HR 95% CI)	P-value	(HR 95% CI)	P-value
DM	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	CS (1973-2016)	1.17 (1.12; 1.21)	<0.001	1.15 (1.10; 1.19)	<0.001	1.08 (1.04; 1.12)	<0.001
RA	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	CS (1973-2016)	1.15 (1.08; 1.21)	<0.001	1.09 (1.03; 1.15)	0.005	1.07 (1.02; 1.14)	0.013
CD	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	CS (1973-2016)	1.17 (1.10; 1.25)	<0.001	1.13 (1.06; 1.21)	<0.001	1.10 (1.03; 1.18)	0.005
IBD	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	CS (1973-2016)	1.12 (1.08; 1.17)	<0.001	1.07 (1.03; 1.12)	0.002	1.07 (1.02; 1.12)	0.003
Combined	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	CS (1973-2016)	1.15 (1.12; 1.18)	<0.001	1.11 (1.08; 1.14)	<0.001	1.08 (1.05; 1.10)	<0.001

A) Adjusted for decade of birth, child's sex, mother's and father's age

B) Adjusted for decade of birth, child's sex, mother's and father's age and mother's and father's diabetes, arthritis, coeliac disease and IBD

Abbreviations: CD: Coeliac disease; CS: Caesarean section; DM: Diabetes mellitus; IBD; Inflammatory bowel disease; RA: Rheumatoid arthritis

Supplemental Table 4. Cox regression for girls only for the association between caesarean section and disease incidence with sequential adjustment for potential confounding variables for the full period (1973-2016)

Disease	Birth method	Undadjusted		Partly adjusted ^A		Fully adjusted ^B	
		(HR 95% CI)	P-value	(HR 95% CI)	P-value	(HR 95% CI)	P-value
DM	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	CS (1973-2016)	1.17 (1.11; 1.24)	<0.001	1.16 (1.10; 1.22)	<0.001	1.09 (1.03; 1.15)	0.002
RA	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	CS (1973-2016)	1.18 (1.10; 1.27)	<0.001	1.11 (1.03; 1.19)	0.005	1.10 (1.02; 1.18)	0.013
CD	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	CS (1973-2016)	1.29 (1.19; 1.41)	<0.001	1.18 (1.08; 1.28)	<0.001	1.15 (1.05; 1.25)	0.002
IBD	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	CS (1973-2016)	1.10 (1.03; 1.17)	0.003	1.05 (0.99; 1.12)	0.093	1.05 (0.99; 1.12)	0.125
Combined	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	CS (1973-2016)	1.17 (1.13; 1.20)	<0.001	1.12 (1.08; 1.16)	<0.001	1.08 (1.05; 1.12)	<0.001

A) Adjusted for decade of birth, child's sex, mother's and father's age

B) Adjusted for decade of birth, child's sex, mother's and father's age and mother's and father's diabetes, arthritis, coeliac disease and IBD

Abbreviations: CD: Coeliac disease; CS: Caesarean section; DM: Diabetes mellitus; IBD: Inflammatory bowel disease; RA: Rheumatoid arthritis

Supplemental Table 5. Cox regression for boys for the association between caesarean section and disease incidence with sequential adjustment for potential confounding variables for the full period (1973-2016)

Disease	Undadjusted		Partly adjusted ^A		Fully adjusted ^B		P-value
	Birth method	(HR 95% CI)	P-value	(HR 95% CI)	P-value	(HR 95% CI)	
DM	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	CS (1973-2016)	1.17 (1.10; 1.24)	<0.001	1.14 (1.07; 1.20)	<0.001	1.07 (1.01; 1.13)	0.019
RA	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	CS (1973-2016)	1.13 (1.03; 1.23)	0.011	1.05 (0.96; 1.15)	0.317	1.04 (0.95; 1.14)	0.414
CD	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	CS (1973-2016)	1.04 (0.94; 1.15)	0.478	1.07 (0.96; 1.19)	0.214	1.04 (0.94; 1.16)	0.438
IBD	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	CS (1973-2016)	1.16 (1.09; 1.24)	<0.001	1.09 (1.03; 1.17)	0.006	1.09 (1.02; 1.16)	0.007
Combined	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	CS (1973-2016)	1.14 (1.10; 1.19)	<0.001	1.10 (1.06; 1.14)	<0.001	1.07 (1.03; 1.11)	<0.001

A) Adjusted for decade of birth, child's sex, mother's and father's age

B) Adjusted for decade of birth, child's sex, mother's and father's age and mother's and father's diabetes, arthritis, coeliac disease and IBD

Abbreviations: CD: Coeliac disease; CS: Caesarean section; DM: Diabetes mellitus; IBD; Inflammatory bowel disease; RA: Rheumatoid arthritis

Supplemental Table 6. Cox regressions for the association between caesarean section and disease incidence with sequential adjustment for potential confounding for the new MFR period (1991-2016)

Disease	Birth method	Undadjusted		Partly adjusted ^A		Fully adjusted ^B	
		(HR 95% CI)	P-value	(HR 95% CI)	P-value	(HR 95% CI)	P-value
DM	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	Acute CS	1.10 (1.01; 1.20)	0.033	1.09 (1.00; 1.19)	0.054	1.05 (0.96; 1.14)	0.274
	Elective CS	1.20 (1.09; 1.31)	<0.001	1.19 (1.08; 1.31)	<0.001	1.14 (1.03; 1.25)	0.009
RA	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	Acute CS	1.09 (0.99; 1.21)	0.078	1.10 (0.99; 1.21)	0.069	1.09 (0.99; 1.20)	0.094
	Elective CS	1.17 (1.05; 1.31)	0.004	1.15 (1.03; 1.29)	0.011	1.14 (1.02; 1.27)	0.019
CD	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	Acute CS	1.22 (1.09; 1.36)	0.001	1.17 (1.05; 1.31)	0.005	1.15 (1.03; 1.29)	0.014
	Elective CS	1.15 (1.01; 1.31)	0.041	1.09 (0.95; 1.24)	0.206	1.04 (0.92; 1.19)	0.513
IBD	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	Acute CS	1.08 (0.97; 1.20)	0.174	1.07 (0.96; 1.19)	0.243	1.06 (0.95; 1.18)	0.282
	Elective CS	1.20 (1.07; 1.34)	0.002	1.18 (1.05; 1.33)	0.004	1.16 (1.03; 1.30)	0.011
Combined	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	Acute CS	1.12 (1.06; 1.17)	<0.001	1.10 (1.05; 1.16)	<0.001	1.08 (1.03; 1.14)	0.002
	Elective CS	1.19 (1.13; 1.26)	<0.001	1.17 (1.11; 1.24)	<0.001	1.13 (1.07; 1.20)	<0.001

A) Adjusted for decade of birth, child's sex, mother's and father's age

B) Adjusted for decade of birth, child's sex, mother's and father's age and mother's and father's diabetes, arthritis, coeliac disease and IBD

Abbreviations: CD: Coeliac disease; CS: Caesarean section; DM: Diabetes mellitus; IBD; Inflammatory bowel disease; RA: Rheumatoid arthritis

Supplemental Table 7. Cox regression for girls for the association between caesarean section and disease incidence with sequential adjustment for potential confounding for the new MFR period (1991-2016)

Disease	Birth method	Undadjusted		Partly adjusted ^A		Fully adjusted ^B	
		(HR 95% CI)	P-value	(HR 95% CI)	P-value	(HR 95% CI)	P-value
DM	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	Acute CS	1.20 (1.06; 1.35)	0.004	1.19 (1.05; 1.34)	0.006	1.14 (1.01; 1.29)	0.033
	Elective CS	1.22 (1.07; 1.39)	0.003	1.22 (1.07; 1.40)	0.003	1.16 (1.02; 1.32)	0.028
RA	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	Acute CS	1.16 (1.02; 1.32)	0.029	1.14 (1.00; 1.30)	0.047	1.13 (0.99; 1.29)	0.065
	Elective CS	1.15 (0.99; 1.32)	0.060	1.14 (0.99; 1.31)	0.079	1.12 (0.97; 1.30)	0.109
CD	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	Acute CS	1.37 (1.19; 1.58)	<0.001	1.29 (1.12; 1.48)	<0.001	1.26 (1.09; 1.45)	0.001
	Elective CS	1.17 (0.99; 1.37)	0.064	1.11 (0.95; 1.31)	0.197	1.07 (0.91; 1.27)	0.392
IBD	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	Acute CS	0.99 (0.84; 1.16)	0.871	0.97 (0.83; 1.15)	0.738	0.97 (0.82; 1.14)	0.693
	Elective CS	1.28 (1.10; 1.49)	0.002	1.28 (1.09; 1.49)	0.002	1.25 (1.07; 1.46)	0.006
Combined	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	Acute CS	1.18 (1.10; 1.27)	<0.001	1.16 (1.08; 1.24)	<0.001	1.13 (1.06; 1.22)	<0.001
	Elective CS	1.21 (1.12; 1.30)	<0.001	1.19 (1.11; 1.28)	<0.001	1.15 (1.07; 1.24)	<0.001

A) Adjusted for decade of birth, child's sex, mother's and father's age

B) Adjusted for decade of birth, child's sex, mother's and father's age and mother's and father's diabetes, arthritis, coeliac disease and IBD

Abbreviations: CD: Coeliac disease; CS: Caesarean section; DM: Diabetes mellitus; IBD; Inflammatory bowel disease; RA: Rheumatoid arthritis

Supplemental Table 8. Cox regression for boys for the association between caesarean section and disease incidence with sequential adjustment for potential confounding for the new MFR period (1991-2016)

Disease	Birth method	Undadjusted		Partly adjusted ^A		Fully adjusted ^B	
		(HR 95% CI)	P-value	(HR 95% CI)	P-value	(HR 95% CI)	P-value
DM	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	Acute CS	1.02 (0.90; 1.15)	0.773	1.00 (0.89; 1.13)	0.953	0.97 (0.86; 1.10)	0.637
	Elective CS	1.17 (1.02; 1.34)	0.023	1.16 (1.01; 1.33)	0.036	1.11 (0.97; 1.27)	0.132
RA	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	Acute CS	1.06 (0.91; 1.23)	0.441	1.04 (0.89; 1.21)	0.616	1.03 (0.89; 1.20)	0.663
	Elective CS	1.20 (1.01; 1.42)	0.037	1.18 (0.99; 1.40)	0.059	1.17 (0.98; 1.39)	0.075
CD	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	Acute CS	1.08 (0.90; 1.29)	0.431	1.02 (0.85; 1.23)	0.824	1.00 (0.83; 1.20)	0.997
	Elective CS	1.10 (0.88; 1.36)	0.405	1.05 (0.84; 1.30)	0.688	1.01 (0.81; 1.25)	0.960
IBD	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	Acute CS	1.16 (1.01; 1.34)	0.036	1.15 (0.99; 1.32)	0.059	1.14 (0.99; 1.32)	0.067
	Elective CS	1.11 (0.93; 1.31)	0.254	1.08 (0.91; 1.29)	0.378	1.07 (0.90; 1.27)	0.449
Combined	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	Acute CS	1.07 (0.99; 1.15)	0.071	1.05 (0.97; 1.13)	0.220	1.03 (0.96; 1.11)	0.455
	Elective CS	1.16 (1.07; 1.27)	<0.001	1.14 (1.05; 1.24)	0.002	1.11 (1.02; 1.21)	0.016

A) Adjusted for decade of birth, child's sex, mother's and father's age

B) Adjusted for decade of birth, child's sex, mother's and father's age and mother's and father's diabetes, arthritis, coeliac disease and IBD

Abbreviations: CD: Coeliac disease; CS: Caesarean section; DM: Diabetes mellitus; IBD; Inflammatory bowel disease; RA: Rheumatoid arthritis

Supplemental Table 9. Cox regression for the association between caesarean section and disease incidence with sequential adjustment for potential confounding variables for the full period (1973-2016) including only those children born with gestational age at least 37 weeks.

Disease	Birth method	Undadjusted		Partly adjusted ^A		Fully adjusted ^B	
		(HR 95% CI)	P-value	(HR 95% CI)	P-value	(HR 95% CI)	P-value
DM	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	CS (1973-2016)	1.17 (1.08; 1.26)	<0.001	1.16 (1.08; 1.26)	<0.001	1.13 (1.04; 1.22)	0.002
RA	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	CS (1973-2016)	1.11 (1.02; 1.22)	0.023	1.11 (1.01; 1.22)	0.033	1.10 (1.00; 1.21)	0.055
CD	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	CS (1973-2016)	1.10 (0.99; 1.22)	0.079	1.08 (0.97; 1.21)	0.137	1.07 (0.96; 1.19)	0.236
IBD	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	CS (1973-2016)	1.11 (1.00; 1.23)	0.059	1.09 (0.98; 1.22)	0.098	1.08 (0.97; 1.20)	0.172
Combined	Vaginal	1 (Reference)		1 (Reference)		1 (Reference)	
	CS (1973-2016)	1.13 (1.08; 1.18)	<0.001	1.12 (1.07; 1.17)	<0.001	1.10 (1.05; 1.15)	<0.001

A) Adjusted for decade of birth, child's sex, mother's and father's age

B) Adjusted for decade of birth, child's sex, mother's and father's age and mother's and father's diabetes, arthritis, coeliac disease and IBD

Abbreviations: CD: Coeliac disease; CS: Caesarean section; DM: Diabetes mellitus; IBD: Inflammatory bowel disease; RA: Rheumatoid arthritis

