

Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods.

Data Sources.

We linked individual-level data between the various data sources using the unique person identification number assigned to all inhabitants in Denmark. All registries utilized for this study have nationwide coverage in Denmark. Information on study medication were obtained through the Registry of Medicinal Product Statistics. Ever since 1995 data on all filled prescriptions (including anatomical therapeutic chemical [ATC] code and date of filled prescriptions) at Danish pharmacies have been registered in the Registry of Medicinal Product Statistics.¹ From the Medical Birth Registry, we obtained information on live births and stillbirths, while information on pregnancies with abortive outcomes was attained from the National Patient Registry. Ever since 1968 the Medical Birth Registry has contained records of all births and data on birth-related and maternal-related variables, including information on gestational age, which is estimated based on maternal report of the first day of last menstrual period.² The gestational age is subsequently ultrasonographical confirmed at the antenatal screening. For pregnancies with abortive outcomes, information on gestational age was obtained from the National Patient Registry. Ever since 1977, the National Patient Registry has contained information on records of inpatient admissions, outpatient- and emergency department contacts; all with physician-assigned diagnoses coded according to International Classification of Diseases version 10 (ICD-10) since 1994.³ From this registry, we attained information on previous pregnancy history of birth defects and abortive outcomes. For demographic data, we used the Central Person Registry (established in 1968) and socio-economic data was attained from Statistics Denmark.⁴ All registries are continuously updated.

Excluded birth defects.

Information on birth defects was obtained from the National Patient Registry. Based on the physician-assigned diagnoses recorded during the infants first year of life we excluded minor defects according EUROCAT exclusion list and defects of known causes: chromosomal aberrations (ICD-10: Q90-99), genetic syndromes (ICD-10: Q447B, Q619A, Q751, Q754, Q771, Q772, Q780, Q796, Q85, Q87), malformation syndromes with known causes (ICD-10: Q86).⁵

eTable 1. Covariates definition included in propensity score and data sources.

Variable	Categories	Data source
Pregnancy characteristics		
Age at pregnancy onset	≤19, 20-24, 25-29, 30-34, ≥35	Central Person Registry
Marital status or living with partner	yes/no	Central Person Registry
Place of birth	Denmark, Europe, Outside of Europe	Central Person Registry
Region of residence	The Capital Region of Denmark, Region Zealand, The Region of Southern Denmark, Central Denmark Region, The North Denmark Region	Central Person Registry
Gross household income	Quartiles	Statistic Denmark
Education level, years	<12, 12-13, 14-15, >15	Statistic Denmark
Parity ^a	1,2, ≥3	Medical Birth Registry
Multiple birth pregnancy ^a	yes/no	Medical Birth Registry
Season of conception	Winter, Spring, Summer, Autumn	Medical Birth Registry and National Patient Registry
Smoking during pregnancy ^a	yes/no	Medical Birth Registry
Previous pregnancy with the same fetal outcome ^b	yes/no	Medical Birth Registry and National Patient Registry
Prescription drug use in past year prior to pregnancy onset		
	<i>ATC codes</i>	
Antacids, H ₂ -blockers, and PPIs	A02A, A02BA, A02BC	Registry of Medicinal Product Statistics
Insulin	A10A	Registry of Medicinal Product Statistics
Oral antidiabetic drugs	A10B	Registry of Medicinal Product Statistics
Antihypertensives	C03A, C03C, C03D, C03E, C07, C08C, C08D, C09A-C09D	Registry of Medicinal Product Statistics
Topical corticosteroids group II ^c	D07AB, D07BB, D07CB, D07XB	Registry of Medicinal Product Statistics
Topical corticosteroids group III ^c	D07AC, D07BC, D07CC, D07XC	Registry of Medicinal Product Statistics
Topical corticosteroids group IV ^c	D07AD	Registry of Medicinal Product Statistics
Oral corticosteroids	H02AB	Registry of Medicinal Product Statistics
Thyroid drugs	H03A, H03B	Registry of Medicinal Product Statistics
NSAIDs	M01A except M01AX	Registry of Medicinal Product Statistics
Opiates	N02A	Registry of Medicinal Product Statistics
Antimigraine drugs	N02C	Registry of Medicinal Product Statistics
Antidepressants	N06A	Registry of Medicinal Product Statistics
Nasal corticosteroids	R01AD	Registry of Medicinal Product Statistics

(eTable 1. Continued)

Variable	Categories	Data source
Pulmonary inhalants	R03AC, R03AK, R03AL, R03BA, R03BB	Registry of Medicinal Product Statistics
Leukotriene receptor antagonists	R03DC	Registry of Medicinal Product Statistics
Other second-generation antihistamines ^d	R06AE09, R06AX13, R06AX18, R06AX22, R06AX27, R06AX29	Registry of Medicinal Product Statistics
Ophthalmological antiallergics	S01G	Registry of Medicinal Product Statistics
No. of drugs used	0, 1-2, 3-4, ≥5	Registry of Medicinal Product Statistics
Hospital care utilization in past year prior to pregnancy onset		
No. of hospitalization	0, 1-2, ≥3	National Patient Registry
No. of outpatient contacts	0, 1-2, ≥3	National Patient Registry

ATC: anatomic therapeutic chemical; NSAID: non-steroid anti-inflammatory drug; PPIs: proton pump inhibitors. ^aCovariate was available for analyses on live births only. ^bThe individual previous adverse fetal outcome variable was included for the specific outcome analysis. ^cGroup II-IV denotes the strength of the respective topical corticosteroid preparations. ^dLoratadine (ATC code: R06AX13) was removed from this variable in sensitivity analyses of fexofenadine compared with loratadine exposed pregnancies.

eTable 2. Number of missing values (percentages) for the unmatched study cohorts.

Variable	For analysis of major birth defects (n=9203)	For analysis of spontaneous abortion (n=16,236)	For analysis of preterm birth (n=18,565)	For analysis of small size for gestational age (n=19,321)	For analysis of stillbirth (n=22,331)
Pregnancy characteristics					
Age at pregnancy onset	0	0	0	0	0
Marital status or living with partner	18 (0.2)	64 (0.4)	73 (0.4)	78 (0.4)	102 (0.5)
Place of birth	0	0	1 (0.0)	1 (0.0)	1 (0.0)
Region of residence	0	0	0	0	0
Gross household income	0	0	0	0	0
Education level	263 (2.9)	493 (3.0)	576 (3.1)	609 (3.2)	708 (3.2)
Parity	71 (0.8)	NA	149 (0.8)	153 (0.8)	NA
Multiple birth pregnancy	0	NA	0	0	NA
Season of conception	0	0	0	0	0
Smoking during pregnancy	149 (1.6)	NA	342 (1.8)	352 (1.8)	NA
Previous pregnancy with the same fetal outcome	0	0	0	0	0
Prescription drug use in past year prior to pregnancy onset^a	0	0	0	0	0
Hospital care utilization in past year prior to pregnancy onset^b	0	0	0	0	0

NA: not available. ^aNo missing values for any drug use in the past year. ^bNo missing values for any health care utilization in past year.

eTable 3. Baseline characteristics of unmatched pregnancy cohorts of fexofenadine and cetirizine users for analyses of primary outcomes. Values are numbers (percentages).

Pregnancy characteristics	Unmatched cohort for analysis of major birth defects		Unmatched cohort for analysis of spontaneous abortion	
	Fexofenadine users (n=3011)	Cetirizine users (n=6192)	Fexofenadine users (n=4928)	Cetirizine users (n=11,308)
Gestational age at first filled prescription, median (IQR)	7 (-12-34)	22 (-6-51)	17 (-9-62)	41 (3-95)
Age at pregnancy onset				
≤19	21 (0.7)	64 (1.0)	119 (2.4)	279 (2.5)
20-24	297 (9.9)	597 (9.6)	567 (11.5)	1255 (11.1)
25-29	981 (32.6)	1998 (32.3)	1491 (30.3)	3359 (29.7)
30-34	1088 (36.1)	2263 (36.5)	1607 (32.6)	3910 (34.6)
≥35	624 (20.7)	1270 (20.5)	1144 (23.2)	2505 (22.2)
Married or living with partner	2611 (86.7)	5423 (87.6)	4025 (81.7)	9409 (83.2)
Place of birth				
Denmark	2619 (87.0)	5259 (84.9)	4261 (86.5)	9544 (84.4)
Europe	144 (4.8)	293 (4.7)	237 (4.8)	534 (4.7)
Outside of Europe	248 (8.2)	640 (10.3)	430 (8.7)	1230 (10.9)
Region of residence				
The Capital Region of Denmark	928 (30.8)	1848 (29.8)	2257 (45.8)	4659 (41.2)
Region Zealand	321 (10.7)	829 (13.4)	406 (8.2)	1277 (11.3)
The Region of Southern Denmark	608 (20.2)	1273 (20.6)	751 (15.2)	1975 (17.5)
Central Denmark Region	825 (27.4)	1623 (26.2)	1063 (21.6)	2505 (22.2)
The North Denmark Region	329 (10.9)	619 (10.0)	451 (9.2)	892 (7.9)
Gross household income, quartile				
1	746 (24.8)	1555 (25.1)	1261 (25.6)	2798 (24.7)
2	772 (25.6)	1529 (24.7)	1242 (25.2)	2817 (24.9)
3	736 (24.4)	1565 (25.3)	1200 (24.4)	2859 (25.3)
4	757 (25.1)	1543 (24.9)	1225 (24.9)	2834 (25.1)
Education level, years				
<12	594 (19.7)	1352 (21.8)	1172 (23.8)	2843 (25.1)
12-13	437 (14.5)	905 (14.6)	729 (14.8)	1684 (14.9)
14-15	744 (24.7)	1539 (24.9)	1134 (23.0)	2711 (24.0)
>15	1237 (41.1)	2396 (38.7)	1893 (38.4)	4070 (36.0)
Parity				
1	1454 (48.3)	2984 (48.2)	NA	NA
2	1020 (33.9)	2107 (33.9)	NA	NA
≥3	537 (17.8)	1101 (17.8)	NA	NA
Multiple birth pregnancy	111 (3.7)	272 (4.4)	NA	NA
Season of conception				
Winter	521 (17.3)	1135 (18.3)	1133 (23.0)	3143 (27.8)
Spring	1054 (35.0)	2528 (40.8)	1610 (32.7)	3937 (34.8)
Summer	979 (32.5)	1630 (26.3)	1404 (28.5)	2481 (21.9)
Autumn	457 (15.2)	899 (14.5)	781 (15.9)	1747 (15.5)
Smoking during pregnancy	343 (11.4)	781 (12.6)	NA	NA
Previous pregnancy with the same fetal outcome	67 (2.2)	116 (1.9)	759 (15.4)	1847 (16.3)

(eTable 3. Continued)

	Unmatched cohort for analysis of major birth defects		Unmatched cohort for analysis of spontaneous abortion	
	Fexofenadine users (n=3011)	Cetirizine users (n=6192)	Fexofenadine users (n=4928)	Cetirizine users (n=11,308)
Prescription drug use in past year prior to pregnancy onset				
Antacids, H ₂ -blockers, and PPIs	271 (9.0)	530 (8.6)	470 (9.5)	935 (8.3)
Insulin	11 (0.4)	40 (0.7)	22 (0.5)	69 (0.6)
Oral antidiabetic drugs	61 (2.0)	132 (2.1)	88 (1.8)	217 (1.9)
Antihypertensives	80 (2.7)	174 (2.8)	140 (2.8)	327 (2.9)
Topical corticosteroids group II	309 (10.3)	563 (9.1)	471 (9.6)	981 (8.7)
Topical corticosteroids group III	374 (12.4)	693 (11.2)	578 (11.7)	1153 (10.2)
Topical corticosteroids group IV	94 (3.1)	125 (2.0)	139 (2.8)	213 (1.9)
Oral corticosteroids	387 (12.9)	548 (8.9)	610 (12.4)	999 (8.8)
Thyroid drugs	65 (2.2)	128 (2.1)	103 (2.1)	234 (2.1)
NSAIDs	663 (22.0)	1325 (21.4)	1091 (22.1)	2390 (21.1)
Opiates	169 (5.6)	348 (5.6)	302 (6.1)	664 (5.9)
Antimigraine drugs	110 (3.7)	230 (3.7)	181 (3.7)	399 (3.5)
Antidepressants	282 (9.4)	500 (8.1)	518 (10.5)	1020 (9.0)
Nasal corticosteroids	743 (24.7)	1570 (25.4)	1158 (23.5)	2643 (23.4)
Pulmonary inhalants	623 (20.7)	1282 (20.7)	961 (19.5)	2230 (19.7)
Leukotriene receptor antagonists	81 (2.7)	90 (1.5)	128 (2.6)	158 (1.4)
Other second-generation antihistamines	319 (10.6)	746 (12.1)	501 (10.2)	1288 (11.4)
Ophthalmological antiallergics	654 (21.7)	1275 (20.6)	1014 (20.6)	2171 (19.2)
No. of drugs used				
1-2	1466 (48.6)	2974 (47.9)	2313 (46.9)	5376 (47.5)
3-4	645 (21.4)	1270 (20.5)	1050 (21.3)	2175 (19.2)
≥5	175 (5.8)	313 (5.0)	285 (5.8)	551 (4.9)
Hospital care utilization in past year prior to pregnancy onset				
No. of hospitalization				
1	329 (11.0)	685 (11.1)	560 (11.4)	1361 (12.0)
2	63 (2.1)	153 (2.5)	120 (2.4)	282 (2.5)
≥3	22 (0.7)	57 (0.9)	44 (0.9)	107 (1.0)
No. of outpatient contacts				
1	500 (16.6)	946 (15.3)	817 (16.6)	1756 (15.5)
2	203 (6.7)	380 (6.1)	341 (6.9)	721 (6.4)
≥3	110 (3.7)	194 (3.1)	177 (3.6)	384 (3.4)

IQR: Interquartile range; NA: not available; NSAID: non-steroid anti-inflammatory drug; PPIs: proton pump inhibitors.

eTable 4. Baseline characteristics of unmatched pregnancy cohorts of fexofenadine and cetirizine users for analyses of secondary outcomes. Values are numbers (percentages).

Pregnancy characteristics	Unmatched cohort for analysis of preterm birth		Unmatched cohort for analysis of small size for gestational age		Unmatched cohort for analysis of stillbirth	
	Fexofenadine users (n=4957)	Cetirizine users (n=13,608)	Fexofenadine users (n=5138)	Cetirizine users (n=14,183)	Fexofenadine users (n=6195)	Cetirizine users (n=16,136)
Gestational age at first filled prescription, median (IQR)	50 (0-144)	99 (27-174)	56 (2-156)	106 (31-185)	36 (-3-133)	86 (19-174)
Age at pregnancy onset						
≤19	36 (0.7)	158 (1.2)	40 (0.8)	167 (1.2)	130 (2.1)	346 (2.1)
20-24	486 (9.8)	1364 (10.0)	510 (9.9)	1460 (10.3)	694 (11.2)	1794 (11.1)
25-29	1578 (31.8)	4260 (31.3)	1646 (32.0)	4446 (31.4)	1877 (30.3)	4856 (30.1)
30-34	1800 (36.3)	4953 (36.4)	1855 (36.1)	5150 (36.3)	2077 (33.5)	5663 (35.1)
≥35	1057 (21.3)	2873 (21.1)	1087 (21.2)	2960 (20.9)	1417 (22.9)	3477 (21.6)
Married or living with partner	4279 (86.3)	11774 (86.5)	4437 (86.4)	12290 (86.7)	5108 (82.5)	13581 (84.2)
Place of birth						
Denmark	4305 (86.9)	11573 (85.1)	4453 (86.7)	12059 (85.0)	5345 (86.3)	13668 (84.7)
Europe	241 (4.9)	657 (4.8)	256 (5.0)	685 (4.8)	307 (5.0)	770 (4.8)
Outside of Europe	410 (8.3)	1378 (10.1)	429 (8.4)	1439 (10.2)	543 (8.8)	1698 (10.5)
Region of residence						
The Capital Region of Denmark	1543 (31.1)	4036 (29.7)	1589 (30.9)	4158 (29.3)	2622 (42.3)	6038 (37.4)
Region Zealand	516 (10.4)	1847 (13.6)	530 (10.3)	1920 (13.5)	534 (8.6)	1932 (12.0)
The Region of Southern Denmark	932 (18.8)	2911 (21.4)	971 (18.9)	3067 (21.6)	979 (15.8)	3092 (19.2)
Central Denmark Region	1332 (26.9)	3569 (26.2)	1379 (26.8)	3734 (26.3)	1384 (22.3)	3757 (23.3)
The North Denmark Region	634 (12.8)	1245 (9.2)	669 (13.0)	1304 (9.2)	676 (10.9)	1317 (8.2)
Gross household income, quartile						
1	1208 (24.4)	3434 (25.2)	1252 (24.4)	3580 (25.2)	1585 (25.6)	3998 (24.8)
2	1259 (25.4)	3382 (24.9)	1307 (25.4)	3522 (24.8)	1563 (25.2)	4020 (24.9)
3	1243 (25.1)	3398 (25.0)	1280 (24.9)	3550 (25.0)	1509 (24.4)	4074 (25.3)
4	1247 (25.2)	3394 (24.9)	1299 (25.3)	3531 (24.9)	1538 (24.8)	4044 (25.1)
Education level, years						
<12	979 (19.8)	2998 (22.0)	1021 (19.9)	3120 (22.0)	1419 (22.9)	3892 (24.1)
12-13	694 (14.0)	1997 (14.7)	715 (13.9)	2083 (14.7)	893 (14.4)	2394 (14.8)
14-15	1208 (24.4)	3338 (24.5)	1248 (24.3)	3490 (24.6)	1439 (23.2)	3878 (24.0)
>15	2076 (41.9)	5275 (38.8)	2154 (41.9)	5490 (38.7)	2444 (39.5)	5972 (37.0)
Parity						
1	2367 (47.8)	6350 (46.7)	2463 (47.9)	6663 (47.0)	NA	NA
2	1724 (34.8)	4718 (34.7)	1778 (34.6)	4898 (34.5)	NA	NA
≥3	866 (17.5)	2540 (18.7)	897 (17.5)	2622 (18.5)	NA	NA
Multiple birth pregnancy	205 (4.1)	661 (4.9)	204 (4.0)	668 (4.7)	NA	NA
Season of conception						
Winter	1294 (26.1)	3967 (29.2)	1332 (25.9)	4050 (28.6)	1510 (24.4)	4397 (27.3)
Spring	1381 (27.9)	3694 (27.2)	1408 (27.4)	3787 (26.7)	1779 (28.7)	4504 (27.9)
Summer	1264 (25.5)	2554 (18.8)	1298 (25.3)	2739 (19.3)	1630 (26.3)	3303 (20.5)
Autumn	1018 (20.5)	3393 (24.9)	1100 (21.4)	3607 (25.4)	1276 (20.6)	3932 (24.4)
Smoking during pregnancy	579 (11.7)	1662 (12.2)	606 (11.8)	1722 (12.1)	NA	NA
Previous pregnancy with the same fetal outcome	191 (3.9)	533 (3.9)	299 (5.8)	713 (5.0)	17 (0.3)	60 (0.4)

(eTable 4. Continued)

	Unmatched cohort for analysis of preterm birth		Unmatched cohort for analysis of small size for gestational age		Unmatched cohort for analysis of stillbirth	
	Fexofenadine users (n=4957)	Cetirizine users (n=13,608)	Fexofenadine users (n=5138)	Cetirizine users (n=14,183)	Fexofenadine users (n=6195)	Cetirizine users (n=16,136)
Prescription drug use in past year prior to pregnancy onset						
Antacids, H ₂ -blockers, and PPIs	421 (8.5)	1069 (7.9)	428 (8.3)	1095 (7.7)	559 (9.0)	1278 (7.9)
Insulin	26 (0.5)	76 (0.6)	26 (0.5)	76 (0.5)	31 (0.5)	88 (0.6)
Oral antidiabetic drugs	104 (2.1)	286 (2.1)	105 (2.0)	297 (2.1)	114 (1.8)	312 (1.9)
Antihypertensives	129 (2.6)	355 (2.6)	134 (2.6)	363 (2.6)	175 (2.8)	434 (2.7)
Topical corticosteroids group II	412 (8.3)	1061 (7.8)	422 (8.2)	1087 (7.7)	532 (8.6)	1277 (7.9)
Topical corticosteroids group III	558 (11.3)	1280 (9.4)	575 (11.2)	1306 (9.2)	694 (11.2)	1512 (9.4)
Topical corticosteroids group IV	127 (2.6)	243 (1.8)	129 (2.5)	250 (1.8)	161 (2.6)	290 (1.8)
Oral corticosteroids	574 (11.6)	1177 (8.7)	581 (11.3)	1213 (8.6)	709 (11.4)	1378 (8.5)
Thyroid drugs	105 (2.1)	265 (2.0)	107 (2.1)	273 (1.9)	130 (2.1)	314 (2.0)
NSAIDs	1048 (21.1)	2795 (20.5)	1082 (21.1)	2904 (20.5)	1327 (21.4)	3333 (20.7)
Opiates	272 (5.5)	744 (5.5)	279 (5.4)	759 (5.4)	370 (6.0)	910 (5.6)
Antimigraine drugs	172 (3.5)	467 (3.4)	175 (3.4)	476 (3.4)	218 (3.5)	551 (3.4)
Antidepressants	422 (8.5)	1077 (7.9)	431 (8.4)	1112 (7.8)	597 (9.6)	1366 (8.5)
Nasal corticosteroids	1126 (22.7)	2941 (21.6)	1144 (22.3)	3004 (21.2)	1368 (22.1)	3428 (21.2)
Pulmonary inhalants	940 (19.0)	2412 (17.7)	951 (18.5)	2471 (17.4)	1141 (18.4)	2881 (17.9)
Leukotriene receptor antagonists	104 (2.1)	156 (1.2)	104 (2.0)	158 (1.1)	136 (2.2)	190 (1.2)
Other second-generation antihistamines	465 (9.4)	1550 (11.4)	470 (9.2)	1583 (11.2)	582 (9.4)	1746 (10.8)
Ophthalmological antiallergics	982 (19.8)	2446 (18.0)	997 (19.4)	2509 (17.7)	1196 (19.3)	2869 (17.8)
No. of drugs used						
1-2	2320 (46.8)	6411 (47.1)	2403 (46.8)	6664 (47.0)	2881 (46.5)	7592 (47.1)
3-4	990 (20.0)	2438 (17.9)	1000 (19.5)	2489 (17.6)	1230 (19.9)	2864 (17.8)
≥5	235 (4.7)	569 (4.2)	236 (4.6)	576 (4.1)	313 (5.1)	684 (4.2)
Hospital care utilization in past year prior to pregnancy onset						
No. of hospitalization						
1	551 (11.1)	1568 (11.5)	567 (11.0)	1642 (11.6)	691 (11.2)	1909 (11.8)
2	108 (2.2)	318 (2.3)	114 (2.2)	333 (2.4)	148 (2.4)	390 (2.4)
≥3	40 (0.8)	112 (0.8)	40 (0.8)	116 (0.8)	53 (0.9)	138 (0.9)
No. of outpatient contacts						
1	803 (16.2)	2098 (15.4)	831 (16.2)	2176 (15.3)	1013 (16.4)	2487 (15.4)
2	335 (6.8)	816 (6.0)	344 (6.7)	850 (6.0)	416 (6.7)	986 (6.1)
≥3	166 (3.4)	447 (3.3)	172 (3.4)	464 (3.3)	214 (3.5)	531 (3.3)

IQR: Interquartile range; NA: not available; NSAID: non-steroid anti-inflammatory drug; PPIs: proton pump inhibitors.

eTable 5. Baseline characteristics of propensity-score matched pregnancy cohorts of fexofenadine and cetirizine users in 1:1 ratio for analyses of secondary outcomes. Values are numbers (percentages).

Pregnancy characteristics	Matched cohort for analysis of preterm birth		Matched cohort for analysis of small size for gestational age		Matched cohort for analysis of stillbirth	
	Fexofenadine users (n=4933)	Cetirizine users (n=4933)	Fexofenadine users (n=5110)	Cetirizine users (n=5110)	Fexofenadine users (n=6153)	Cetirizine users (n=6153)
Gestational age at first filled prescription, median (IQR)	51 (1-144)	52 (1-146)	57 (2-157)	60 (4-157)	37 (-2-134)	36 (-2-130)
Age at pregnancy onset						
≤19	36 (0.7)	31 (0.6)	40 (0.8)	44 (0.9)	130 (2.1)	134 (2.2)
20-24	482 (9.8)	470 (9.5)	506 (9.9)	504 (9.9)	689 (11.2)	692 (11.3)
25-29	1574 (31.9)	1573 (31.9)	1636 (32.0)	1653 (32.4)	1863 (30.3)	1822 (29.6)
30-34	1792 (36.3)	1808 (36.7)	1849 (36.2)	1808 (35.4)	2066 (33.6)	2054 (33.4)
≥35	1049 (21.3)	1051 (21.3)	1079 (21.1)	1101 (21.6)	1405 (22.8)	1451 (23.6)
Married or living with partner	4257 (86.3)	4278 (86.7)	4411 (86.3)	4421 (86.5)	5074 (82.5)	5095 (82.8)
Place of birth						
Denmark	4282 (86.8)	4274 (86.6)	4427 (86.6)	4427 (86.6)	5304 (86.2)	5317 (86.4)
Europe	241 (4.9)	237 (4.8)	254 (5.0)	253 (5.0)	306 (5.0)	295 (4.8)
Outside of Europe	410 (8.3)	422 (8.6)	429 (8.4)	430 (8.4)	543 (8.8)	541 (8.8)
Region of residence						
The Capital Region of Denmark	1538 (31.2)	1579 (32.0)	1582 (31.0)	1585 (31.0)	2602 (42.3)	2583 (42.0)
Region Zealand	516 (10.5)	490 (9.9)	530 (10.4)	476 (9.3)	534 (8.7)	515 (8.4)
The Region of Southern Denmark	931 (18.9)	920 (18.7)	970 (19.0)	965 (18.9)	976 (15.9)	1008 (16.4)
Central Denmark Region	1330 (27.0)	1302 (26.4)	1375 (26.9)	1383 (27.1)	1377 (22.4)	1392 (22.6)
The North Denmark Region	618 (12.5)	642 (13.0)	653 (12.8)	701 (13.7)	664 (10.8)	655 (10.7)
Gross household income, quartile						
1	1205 (24.4)	1206 (24.5)	1246 (24.4)	1251 (24.5)	1574 (25.6)	1586 (25.8)
2	1252 (25.4)	1262 (25.6)	1300 (25.4)	1276 (25.0)	1554 (25.3)	1553 (25.2)
3	1239 (25.1)	1231 (25.0)	1275 (25.0)	1278 (25.0)	1497 (24.3)	1485 (24.1)
4	1237 (25.1)	1234 (25.0)	1289 (25.2)	1305 (25.5)	1528 (24.8)	1529 (24.9)
Education level, years						
<12	974 (19.7)	988 (20.0)	1017 (19.9)	1005 (19.7)	1412 (23.0)	1440 (23.4)
12-13	692 (14.0)	682 (13.8)	714 (14.0)	684 (13.4)	886 (14.4)	889 (14.4)
14-15	1203 (24.4)	1192 (24.2)	1240 (24.3)	1233 (24.1)	1432 (23.3)	1421 (23.1)
>15	2064 (41.8)	2071 (42.0)	2139 (41.9)	2188 (42.8)	2423 (39.4)	2403 (39.1)
Parity						
1	2356 (47.8)	2337 (47.4)	2450 (48.0)	2448 (47.9)	NA	NA
2	1713 (34.7)	1711 (34.7)	1767 (34.6)	1807 (35.4)	NA	NA
≥3	864 (17.5)	885 (17.9)	893 (17.5)	855 (16.7)	NA	NA
Multiple birth pregnancy	204 (4.1)	155 (3.1)	204 (4.0)	160 (3.1)	NA	NA
Season of conception						
Winter	1291 (26.2)	1308 (26.5)	1327 (26.0)	1339 (26.2)	1505 (24.5)	1495 (24.3)
Spring	1379 (28.0)	1377 (27.9)	1403 (27.5)	1404 (27.5)	1768 (28.7)	1769 (28.8)
Summer	1246 (25.3)	1240 (25.1)	1281 (25.1)	1255 (24.6)	1610 (26.2)	1630 (26.5)
Autumn	1017 (20.6)	1008 (20.4)	1099 (21.5)	1112 (21.8)	1270 (20.6)	1259 (20.5)
Smoking during pregnancy	577 (11.7)	571 (11.6)	604 (11.8)	602 (11.8)	NA	NA
Previous pregnancy with the same fetal outcome	190 (3.9)	184 (3.7)	297 (5.8)	300 (5.9)	17 (0.3)	15 (0.2)

(eTable 5. Continued)

	Matched cohort for analysis of preterm birth		Matched cohort for analysis of small size for gestational age		Matched cohort for analysis of stillbirth	
	Fexofenadine users (n=4933)	Cetirizine users (n=4933)	Fexofenadine users (n=5110)	Cetirizine users (n=5110)	Fexofenadine users (n=6153)	Cetirizine users (n=6153)
Prescription drug use in past year prior to pregnancy onset						
Antacids, H ₂ -blockers, and PPIs	416 (8.4)	388 (7.9)	424 (8.4)	430 (8.4)	546 (8.9)	530 (8.6)
Insulin	26 (0.5)	32 (0.7)	26 (0.5)	29 (0.6)	31 (0.5)	30 (0.5)
Oral antidiabetic drugs	104 (2.1)	99 (2.0)	105 (2.1)	120 (2.4)	114 (1.9)	120 (2.0)
Antihypertensives	127 (2.6)	125 (2.5)	131 (2.6)	124 (2.4)	170 (2.8)	165 (2.7)
Topical corticosteroids group II	411 (8.3)	406 (8.2)	418 (8.2)	418 (8.2)	527 (8.6)	531 (8.6)
Topical corticosteroids group III	555 (11.3)	552 (11.2)	568 (11.1)	565 (11.1)	676 (11.0)	658 (10.7)
Topical corticosteroids group IV	123 (2.5)	115 (2.3)	123 (2.4)	134 (2.4)	151 (2.5)	159 (2.6)
Oral corticosteroids	562 (11.4)	529 (10.7)	568 (11.1)	530 (10.4)	684 (11.1)	674 (11.0)
Thyroid drugs	103 (2.1)	99 (2.0)	106 (2.1)	103 (2.0)	128 (2.1)	128 (2.1)
NSAIDs	1044 (21.2)	1016 (20.6)	1075 (21.0)	1064 (20.8)	1315 (21.4)	1311 (21.3)
Opiates	271 (5.5)	255 (5.2)	276 (5.4)	278 (5.4)	366 (6.0)	349 (5.7)
Antimigraine drugs	171 (3.5)	178 (3.6)	175 (3.4)	177 (3.5)	217 (3.5)	219 (3.6)
Antidepressants	419 (8.5)	381 (7.7)	430 (8.4)	403 (7.9)	591 (9.6)	588 (9.6)
Nasal corticosteroids	1120 (22.7)	1099 (22.3)	1136 (22.2)	1110 (21.7)	1353 (22.0)	1328 (21.6)
Pulmonary inhalants	930 (18.9)	948 (19.2)	940 (18.4)	942 (18.4)	1123 (18.3)	1148 (18.7)
Leukotriene receptor antagonists	99 (2.0)	102 (2.1)	95 (1.9)	82 (1.6)	119 (1.9)	107 (1.7)
Other second-generation antihistamines	463 (9.4)	460 (9.3)	466 (9.1)	421 (8.2)	577 (9.4)	555 (9.0)
Ophthalmological antiallergics	972 (19.7)	962 (19.5)	989 (19.4)	959 (18.8)	1181 (19.2)	1181 (19.2)
No. of drugs used						
1-2	2314 (46.9)	2306 (46.8)	2391 (46.8)	2362 (46.2)	2870 (46.6)	2871 (46.7)
3-4	982 (19.9)	948 (19.2)	991 (19.4)	970 (19.0)	1213 (19.7)	1196 (19.4)
≥5	230 (4.7)	227 (4.6)	231 (4.5)	227 (4.4)	299 (4.9)	297 (4.8)
Hospital care utilization in past year prior to pregnancy onset						
No. of hospitalization						
1	549 (11.1)	543 (11.0)	565 (11.1)	535 (10.5)	684 (11.1)	686 (11.2)
2	107 (2.2)	98 (2.0)	114 (2.2)	109 (2.1)	146 (2.4)	136 (2.2)
≥3	40 (0.8)	40 (0.8)	40 (0.8)	33 (0.7)	51 (0.8)	56 (0.9)
No. of outpatient contacts						
1	802 (16.3)	780 (15.8)	825 (16.1)	846 (16.6)	1001 (16.3)	980 (15.9)
2	330 (6.7)	328 (6.7)	340 (6.7)	323 (6.3)	407 (6.6)	395 (6.4)
≥3	164 (3.3)	159 (3.2)	171 (3.4)	157 (3.1)	210 (3.4)	227 (3.7)

IQR: Interquartile range; NA: not available; NSAID: non-steroid anti-inflammatory drug; PPIs: proton pump inhibitors.

eTable 6. Standardized differences for comparison of fexofenadine and cetirizine use during pregnancy before propensity score matching. Values are percentages (%).

	For analysis of major birth defects	For analysis of spontaneous abortion	For analysis of preterm birth	For analysis of SGA	For analysis of stillbirth
Pregnancy characteristics					
Age at pregnancy onset					
≤19	3.6	0.3	4.5	4.1	0.3
20-24	0.8	1.3	0.7	1.2	0.3
25-29	0.7	1.2	1.1	1.5	0.5
30-34	0.9	4.2	0.2	0.4	3.3
≥35	0.5	2.5	0.5	0.7	3.2
Married or living with partner	2.6	4.0	0.6	0.9	4.6
Place of birth					
Denmark	5.9	5.9	5.2	4.7	4.5
Europe	0.2	0.4	0.2	0.7	0.9
Outside of Europe	7.2	7.2	6.4	6.2	6.0
Region of residence					
The Capital Region of Denmark	2.1	9.3	3.2	3.5	10.0
Region Zealand	8.4	10.3	9.8	10.0	11.1
The Region of Southern Denmark	0.9	6.0	6.5	6.8	8.9
Central Denmark Region	2.7	1.4	1.5	1.2	2.3
The North Denmark Region	3.0	4.5	11.7	12.2	9.4
Gross household income, quartile					
1	0.8	2.0	2.0	2.0	1.9
2	2.2	0.7	1.3	1.4	0.7
3	1.9	2.2	0.2	0.3	2.1
4	0.5	0.5	0.5	0.9	0.5
Education level, years					
<12	5.2	3.2	5.6	5.2	2.9
12-13	0.3	0.3	1.9	2.2	1.2
14-15	0.4	2.3	0.4	0.7	1.9
>15	4.9	5.0	6.4	6.6	5.0
Parity					
1	0.2	NA	2.2	1.9	NA
2	0.3	NA	0.2	0.2	NA
≥3	0.1	NA	3.1	2.7	NA
Multiple birth pregnancy	3.6	NA	3.5	3.6	NA
Season of conception					
Winter	2.7	11.1	6.8	5.9	6.6
Spring	12.0	4.5	1.6	1.6	1.8
Summer	13.6	15.1	16.3	14.3	13.8
Autumn	1.9	1.1	10.5	9.5	9.0
Smoking during pregnancy	3.8	NA	1.6	1.1	NA
Previous pregnancy with the same fetal outcome	3.0	2.6	0.3	3.5	1.7

(eTable 6. Continued)

	For analysis of major birth defects	For analysis of spontaneous abortion	For analysis of preterm birth	For analysis of SGA	For analysis of stillbirth
Prescription drug use in past year prior to pregnancy onset					
Antacids, H ₂ -blockers, and PPIs	1.6	4.5	2.3	2.2	4.0
Insulin	4.0	2.3	0.5	0.4	0.7
Oral antidiabetic drugs	0.7	1.0	0.0	0.4	1.4
Antihypertensives	0.9	0.3	0.0	0.3	0.6
Topical corticosteroids group II	4.0	3.1	1.9	2.0	2.5
Topical corticosteroids group III	3.8	4.9	6.1	6.6	6.0
Topical corticosteroids group IV	7.0	6.2	5.3	5.2	5.5
Oral corticosteroids	12.9	11.5	9.7	9.2	9.7
Thyroid drugs	0.6	0.2	1.2	1.1	0.8
NSAIDs	1.5	2.4	1.5	1.4	1.1
Opiates	0.0	1.1	0.1	0.4	1.4
Antimigraine drugs	0.3	0.8	0.2	0.3	4.1
Antidepressants	4.6	5.0	2.2	2.0	4.0
Nasal corticosteroids	1.6	0.3	2.7	2.6	2.0
Pulmonary inhalants	0.0	0.6	3.2	2.8	1.5
Leukotriene receptor antagonists	8.7	8.6	7.5	7.3	7.9
Other second-generation antihistamines	4.6	4.0	6.7	6.7	4.7
Ophthalmological antiallergics	2.8	3.5	4.7	4.4	3.9
No. of drugs used					
1-2	1.4	1.2	0.6	0.4	1.1
3-4	2.2	5.2	5.3	4.9	5.4
≥5	3.3	4.1	2.7	2.6	3.9
Hospital care utilization in past year prior to pregnancy onset					
No. of hospitalization					
1	0.4	2.1	1.7	1.7	2.1
2	2.5	0.4	1.3	0.9	0.2
≥3	2.1	0.6	1.1	0.4	0.0
No. of outpatient contacts					
1	3.6	4.1	3.7	2.3	2.6
2	2.5	2.9	2.1	2.9	2.5
≥3	2.9	1.1	3.1	0.4	0.9

NA: not available; NSAID: non-steroid anti-inflammatory drug; PPIs: proton pump inhibitors.

eTable 7. Standardized differences for comparison of fexofenadine and cetirizine use during pregnancy after propensity score matching. Values are percentages (%).

	For analysis of major birth defects	For analysis of spontaneous abortion	For analysis of preterm birth	For analysis of SGA	For analysis of stillbirth
Pregnancy characteristics					
Age at pregnancy onset					
≤19	1.5	1.6	1.2	0.9	0.5
20-24	0.6	0.5	0.8	0.1	0.2
25-29	1.9	0.6	0.0	0.7	1.5
30-34	1.8	0.9	0.7	1.7	0.4
≥35	0.0	0.1	0.1	1.1	1.8
Married or living with partner	0.2	0.2	1.3	0.6	0.9
Place of birth					
Denmark	1.9	0.0	0.5	0.0	0.6
Europe	1.6	0.8	0.4	0.1	0.8
Outside of Europe	1.1	0.6	0.9	0.1	0.1
Region of residence					
The Capital Region of Denmark	0.9	2.0	1.8	0.1	0.6
Region Zealand	1.0	1.6	1.7	3.6	1.1
The Region of Southern Denmark	0.0	1.9	0.6	0.3	1.4
Central Denmark Region	1.4	0.1	1.3	0.4	0.6
The North Denmark Region	0.2	0.6	1.5	2.8	0.5
Gross household income, quartile					
1	0.6	0.9	0.1	0.2	0.5
2	1.9	0.9	0.5	1.1	0.0
3	3.3	1.1	0.4	0.1	0.5
4	0.9	1.1	0.1	0.7	0.0
Education level, years					
<12	0.6	1.9	0.7	0.6	1.1
12-13	1.6	1.8	0.6	1.7	0.1
14-15	1.5	1.1	0.5	0.3	0.4
>15	1.9	0.6	0.3	1.9	0.7
Parity					
1	0.9	NA	0.8	0.1	NA
2	1.1	NA	0.1	1.6	NA
≥3	0.2	NA	1.1	2.0	NA
Multiple birth pregnancy	6.2	NA	5.3	4.7	NA
Season of conception					
Winter	0.2	1.8	0.8	0.5	0.4
Spring	2.3	0.6	0.1	0.0	0.0
Summer	2.7	1.0	0.3	1.2	0.7
Autumn	0.2	0.1	0.5	0.6	0.4
Smoking during pregnancy	2.0	NA	0.4	0.1	NA
Previous pregnancy with the same fetal outcome	1.4	0.1	0.6	0.3	0.6

(eTable 7. Continued)

	For analysis of major birth defects	For analysis of spontaneous abortion	For analysis of preterm birth	For analysis of SGA	For analysis of stillbirth
Prescription drug use in past year prior to pregnancy onset					
Antacids, H ₂ -blockers, and PPIs	0.9	0.3	2.1	0.4	0.9
Insulin	2.0	0.6	1.6	0.8	0.2
Oral antidiabetic drugs	1.2	2.3	0.7	2.0	0.7
Antihypertensives	2.0	1.0	0.3	0.9	0.5
Topical corticosteroids group II	0.5	0.8	0.4	0.0	0.2
Topical corticosteroids group III	3.4	0.3	0.2	0.2	0.9
Topical corticosteroids group IV	2.6	0.1	1.1	0.1	0.8
Oral corticosteroids	1.3	1.5	2.1	2.4	0.5
Thyroid drugs	1.9	1.1	0.6	0.4	0.0
NSAIDs	0.4	0.5	1.4	0.5	0.2
Opiates	1.5	1.2	1.4	0.2	1.2
Antimigraine drugs	1.8	0.3	0.8	0.2	0.2
Antidepressants	0.6	1.5	2.8	1.9	0.2
Nasal corticosteroids	0.7	0.5	1.0	1.2	1.0
Pulmonary inhalants	2.2	1.3	0.9	0.1	1.1
Leukotriene receptor antagonists	2.0	0.4	0.4	2.0	1.5
Other second-generation antihistamines	1.8	0.9	0.2	3.1	1.2
Ophthalmological antiallergics	0.3	0.2	0.5	1.5	0.0
No. of drugs used					
1-2	2.0	0.4	0.3	1.5	0.0
3-4	0.6	0.1	1.7	2.6	0.7
≥5	1.2	1.4	0.3	0.9	0.2
Hospital care utilization in past year prior to pregnancy onset					
No. of hospitalization					
1	1.0	0.3	0.4	1.9	0.1
2	1.4	0.1	1.3	0.7	1.1
≥3	1.5	0.2	0.0	1.6	0.9
No. of outpatient contacts					
1	0.9	0.4	1.2	1.1	0.9
2	0.1	1.4	0.2	1.4	0.8
≥3	1.8	0.8	0.6	1.6	1.5

NA: not available; NSAID: non-steroid anti-inflammatory drug; PPIs: proton pump inhibitors.

eTable 8. Sensitivity analyses of the association between fexofenadine use during pregnancy and primary outcomes according to restriction of exposure time intervals, singleton pregnancies and induced abortions.

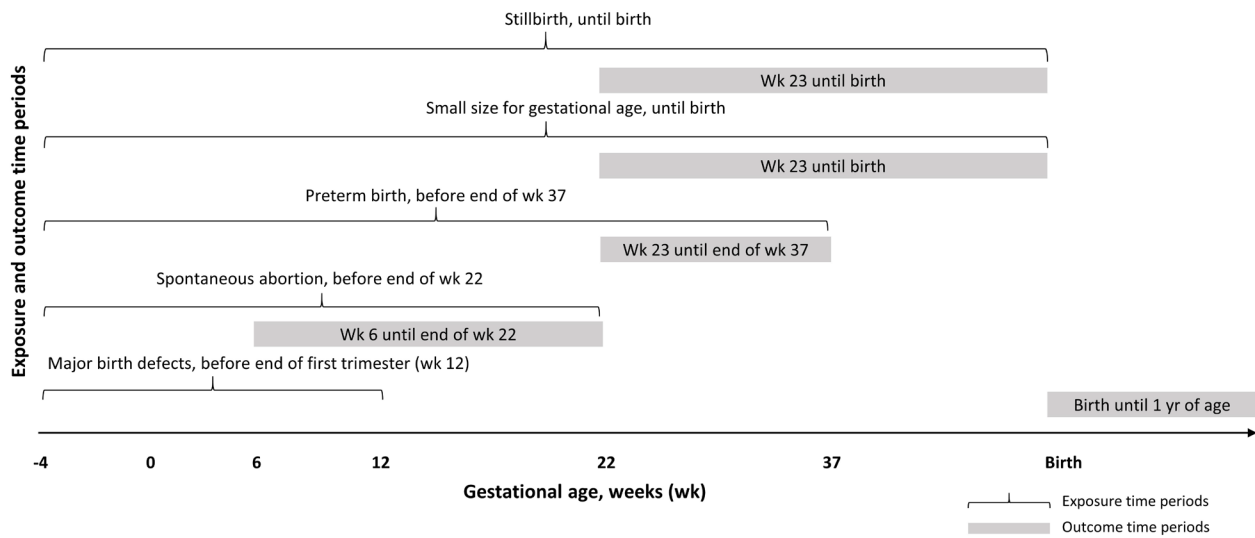
Major birth defects	No. with outcome/total no. (%)	Prevalence Odds Ratio (95% CI)
Exposure interval limited to day 0-84		
Fexofenadine	67/1751 (3.8%)	1.01 (0.72-1.43)
Cetirizine	67/1773 (3.8%)	1.00 (reference)
Singleton pregnancies only		
Fexofenadine	112/2853 (3.9%)	1.09 (0.83-1.43)
Cetirizine	104/2885 (3.6%)	1.00 (reference)
Spontaneous abortion	No. with outcome/total no. (%)	Hazard Ratio (95% CI)
Exposure interval limited to day 0-154		
Fexofenadine	214/3227 (6.6%)	0.87 (0.72-1.04)
Cetirizine	248/3255 (7.6%)	1.00 (reference)
Induced abortions		
Fexofenadine	605/4901 (12.3%)	0.98 (0.88-1.10)
Cetirizine	610/4901 (12.5%)	1.00 (reference)

eTable 9. Post-hoc analyses of the association between fexofenadine use during pregnancy and spontaneous abortion, preterm birth, small size for gestational age, and stillbirth according to ending exposure time interval prior to start of follow-up.

Primary outcome	No. with outcome/total no. (%)	Hazard Ratio or Prevalence Odds Ratio (95% CI)^a
Spontaneous abortion^b		
Fexofenadine	341/3082 (11.1%)	0.94 (0.81-1.09)
Cetirizine	357/3055 (11.7%)	1.00 (reference)
Secondary outcomes^c		
Preterm birth		
Fexofenadine	279/3829 (7.3%)	1.01 (0.85-1.20)
Cetirizine	275/3807 (7.2%)	1.00 (reference)
Small size for gestational age		
Fexofenadine	382/3808 (10.0%)	0.94 (0.81-1.08)
Cetirizine	406/3810 (10.7%)	1.00 (reference)
Stillbirth		
Fexofenadine	13/4842 (0.3%)	0.60 (0.30-1.19)
Cetirizine	22/4894 (0.5%)	1.00 (reference)

^aHazard ratio was estimated for the association with spontaneous abortion and stillbirth. Prevalence Odds Ratio was estimated for the association with preterm birth and small size for gestational age. ^bExposure time interval was restricted to filled prescriptions before end of gestational week five. ^cExposure time intervals were restricted to filled prescriptions before end of gestational week 22, which is the defined viability threshold in Denmark.

eFigure. Overview of the exposure and outcome time periods for the specific outcome analyses.



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