Pregnancy outcome after first trimester exposure to fluoroquinolones: an observational cohort study

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Supplementary material

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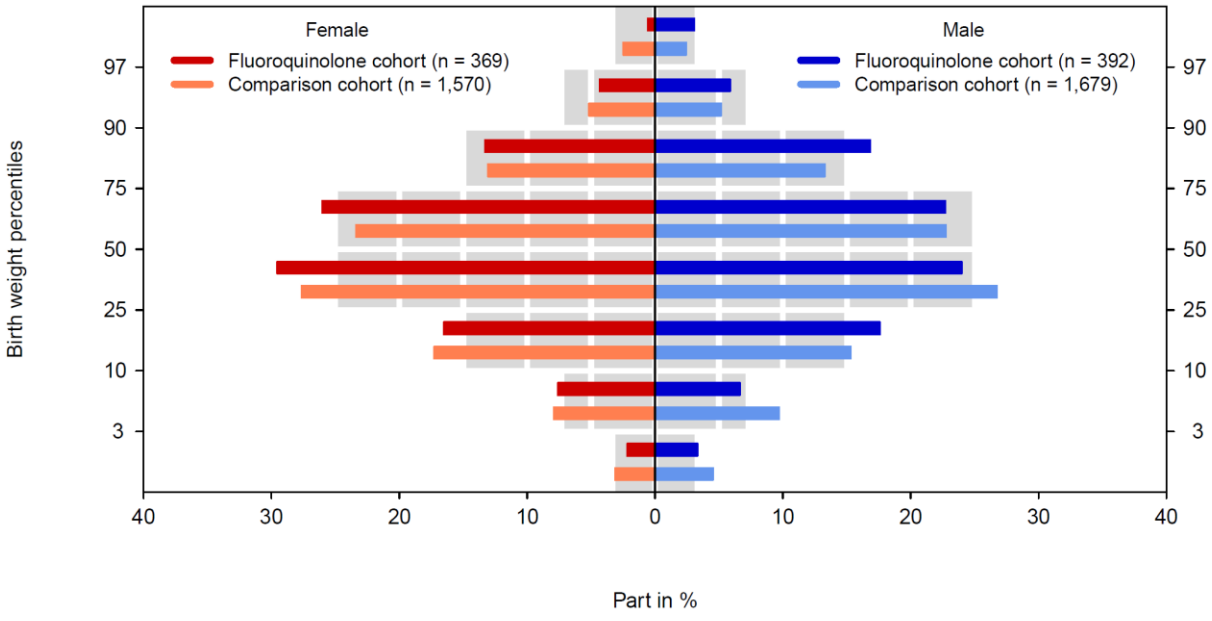

FIG S1 Percentiles of birth weights. Colored bars give the distribution of fluoroquinolone exposed and comparison infants. Gray bars represent the German perinatal survey.

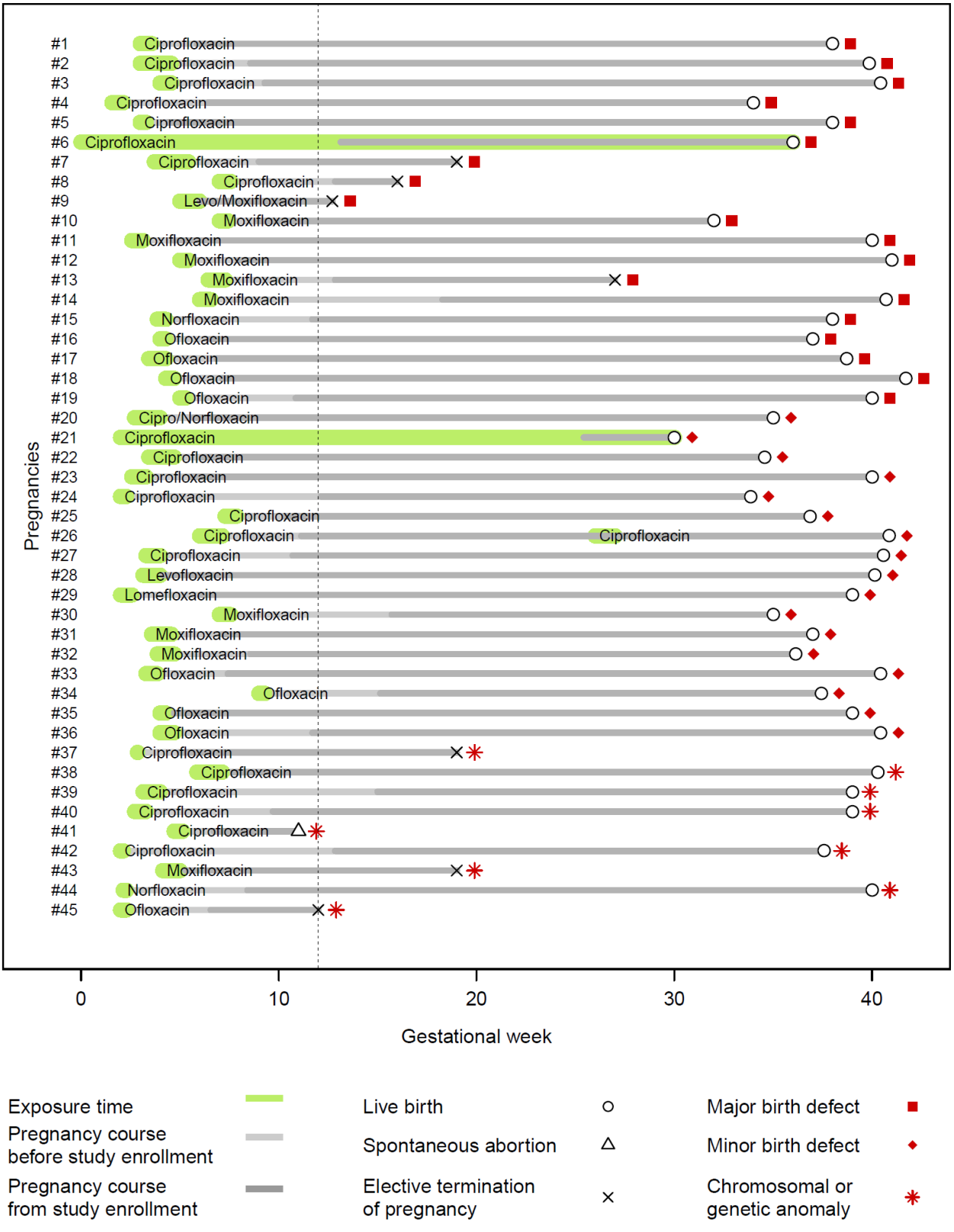

FIG S2 Birth defects and exposure time window of the fluoroquinolone cohort.

TABLE S1 Treatment indication for fluoroquinolone therapy; multiple indications per pregnant women are possible

Treatment indication	**951 (100)**
Kidney and urinary tract infections	479 (50.4)
Respiratory tract infections	175 (18.4)
Ear, nose, throat infections	80 (8.4)
Genital infections	37 (3.9)
Gastrointestinal infections	27 (2.8)
Not otherwise specified bacterial infections	89 (9.4)
Other indication	49 (3.7)
Unknown indication	15 (1.6)

Data presented as number (%).

TABLE S2 Gestational week at elective termination of pregnancy (ETOP) and reason for ETOP

	Study cohort	**Comparison cohort**
ETOPs	94	233
Gestational week at ETOP	68	170
Gestational week at ETOP	10[a] (8–12)[b]	10[a] (8–12)[b]
Reason for ETOP	94	233
Social reason	82 (87.2)	196 (84.1)
Embryopathology	7 (7.4)	21 (9.0)
Maternal reason	4 (4.3)	12 (5.2)
Unknown reason	1 (1.1)	4 (1.7)

Data presented as number (%) unless otherwise stated.
[a]Median.
[b]Interquartile range.

TABLE S3 Minor birth defects in the fluoroquinolone cohort

GW at birth	Birth defect	Substance	Dosage (mg/day)	GW at exposure
35	Pyloric stenosis, inguinal hernia	Ciprofloxacin Norfloxacin	500 500	3 – 4 2 – 3
30	Macrocephaly	Ciprofloxacin	1250	0 – 30
34	Pyloric stenosis	Ciprofloxacin	2 x 500	3 – 4
40	Inguinal hernia (operated 8 weeks after births)	Ciprofloxacin	250	2 – 3
33	Small hemangioma (right upper abdomen, 3x5 mm)	Ciprofloxacin	3 x 250	Before 6
36	Macrocephaly	Ciprofloxacin	250	7
40	Microcephaly	Ciprofloxacin Ciprofloxacin	Unknown Unknown	6 – 7 26
40	Microcephaly	Ciprofloxacin	250	3 – 4
40	Macrocephaly	Levofloxacin	1000	3 – 4
39	Macrocephaly	Lomefloxacin	400	2 – 3
35	Pes adductus on both sides, inguinal testis left side	Moxifloxacin	400	7 – 8
37	Osseous protrusion on the left lateral orbital margin	Moxifloxacin	400	3 – 4
36	Hydrocele testis, false posture of both little toes	Moxifloxacin	400	3 – 4
40	Preauricular appendage, simian crease left side	Ofloxacin	100	3
37	Pes calcaneus on both sides (redressing therapy)	Ofloxacin	Unknown	9 – 11
39	Slight pes calcaneus on both sides (4 weeks after birth normalized)	Ofloxacin	200	4
40	Microcephaly	Ofloxacin	400	4

GW, gestational week.

TABLE S4 Congenital anomalies with chromosomal or genetic background in the fluoroquinolone cohort

GW at birth/ ETOP / SAB	Birth defect	Substance	Dosage (mg/day)	GW at exposure
19 (ETOP)	Trisomy 21	Ciprofloxacin	500	2
40	Medium-chain acyl-CoA dehydrogenase deficiency	Ciprofloxacin	2 x 750	5 – 7
39	Trisomy 21, patent foramen ovale	Ciprofloxacin	250	3 – 4
39	Trisomy 2 (mosaic, infant unsuspicious)	Ciprofloxacin	2 x 250	2 – 3
11 (SAB)	Trisomy 18	Ciprofloxacin	200	Before 5
37	Trisomy 21	Ciprofloxacin	Unknown	1 – 2
19 (ETOP)	Triple X syndrome	Moxifloxacin	400	4 – 5
40	Phenylketonuria	Norfloxacin	800	2 – 6
12 (ETOP)	Turner syndrome	Ofloxacin	Unknown	2 – 3

ETOP, elective termination of pregnancy; GW, gestational week; SAB, spontaneous abortion.

TABLE S5 Major birth defects ordered by organ system. Several birth defects of the same organ are counted once. Two or more unrelated major structural malformations not classified as a syndrome are classified as multiple malformations.

Organ system	**Study cohort** (779[a])	**Comparison cohort** (3,329[b])
Major birth defects	19 (2.4)	93 (2.8)
Malformations of the nervous system	2 (0.3)	4 (0.1)
Eye malformations	–	1 (0.03)
Ear, face and neck malformations	–	–
Heart defects	9 (1.2)	28 (0.8)
Respiratory defects	–	1 (0.03)
Oro-facial clefts	1 (0.1)	6 (0.2)
Malformation of the digestive system	–	6 (0.2)
Abdominal wall defects	1 (0.1)	2 (0.06)
Renal and urinary tract malformations	–	12 (0.4)
Malformations of the genital tract	1 (0.1)	1 (0.03)
Limb defects	2 (0.3)	9 (0.3)
Other malformations and syndromes	2 (0.3)	9 (0.3)
Multiple malformations	1 (0.1)	14 (0.4)

Data presented as number (%); reference for each group is the total number of all live-born infants plus the number of pregnancy losses with major birth defects.
[a]775 live born infants + 4 elective terminations of pregnancy with major birth defects.
[b]3318 live born infants + 9 elective terminations of pregnancy and 2 spontaneous abortions with major defects.