Triptans

Study details	Patients	Prognostic factors	Outcome measures	Effect size	Comments
Author & Year Shuhaiber et al, 1998[721] **Study design:** Prospective cohort **Setting:** Motherisk (Toronto), Pregnancy healthline (USA), Fetal risk assessment programme (UK), Pregnancy exposure information service (USA). **Duration of**	**Patient group:** Women using sumatriptan during pregnancy. **Inclusion criteria:** Pregnant women using sumatriptan who contacted a teratogen information service (TIS) requesting counselling on potential teratogenicity of drugs for migraine. **Exclusion criteria:** NR **All patients** **N:** 288 **Drop outs:** NR **Group 1- Women taking triptans** **N:** 96 **Age (mean):** 32.3 (4.9) **Exposed in 1st trimester:** 95/96 (98.9%) **Number of maternal doses:** 5.5 (0.5 -100) Used drug once: 57/96 (59.4%), Used drug >1: 38/96 (39.6%) **Smokers:** 15/96 (15.6%) **Group 2 Disease-matched controls.** **N:** 96	**Group 1** All patients contacted by telephone within 2 years of the expected date of confinement and asked details about the outcomes of pregnancy, birth weight, presence or absence of birth defects and perinatal and post natal complications. One centre (Motherisk) confirmed the data obtained from the follow ups by requesting written documentation from the child's physician. **Group 2 Disease-matched controls.** Pregnant women contacting motherisk who had migraine headache and used other drugs such as acetaminophen, NSAIDs, narcotic analgesics). **Group 3 Non teratogen**	**Live born infants** N (%)	**Group1:** 82/96 (85.4%) **Group 2:** 90/96 (93.7%) **Group 3:** 91/96 (94.8%) **p value:** NR	**Funding:** NR **Limitations:** Modest sample size. Limited ability to determine migraine case status. All outcomes apart from major birth defects (MBD) analysed on ITT basis; MBD analysed on ACA basis. No confounding factors identified. Adjusted OR not reported. Drug use self reported, therefore may be underestimated. **Additional outcomes**: Individual MBDs reported. **Notes:** Major birth defects defined as those being potentially life threatening, resulting in major cosmetic defects or having a major impact on social
			Spontaneous abortion N (%)	**Group1:** 11/96 (11.5%) **Group 2:** 6/96 (6.3%) **Group 3:** 4/96 (4.2%) **p value:** NR	
			Therapeutic abortion N (%)	**Group1:** 4/96 (4.2%) **Group 2:** 2/96 (2.1%) **Group 3:** 1/96 (1.1%) **p value:** NR	
			Gestational age <37weeks N (%)	**Group1:** 8/96 (8.4%) **Group 2:** 16/96 (16.8%) **Group 3:** 5/96 (5.2%)	

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follow-up: Up to 2 years	**Age (mean):** 31.7 (4.5) **Smokers:** 21/96 (21.9%) **Group 3 Non teratogen controls.** **N:** 96 **Age (mean):** 31.2 (4.8) **Smokers:** 12/96 (12.5%)	**controls.** Pregnant women who contacted motherisk requesting counselling about medications known to be safe in the human fetus.		**p value:** NR	acceptability of the child. No Odds Ratios stated in study. Study states that there was no significant difference in any outcome. Continuous outcomes analysed using ANOVA.
			Major birth defects N (%)	**Group1:** 1/82 (1.2%) **Group 2:** 1/90 (1%) **Group 3:** 1/91 (1%) **p value:** NR	

Abbreviations: NR=not reported, NA=not applicable, M/F=male/female, N=total number of patients randomised, SD=Standard deviation, SE=Standard error, ITT=Intention to treat analysis, NSAID= non steroidal anti-inflammatory drugs, MBD= major birth defects; s.c= subcutaneous, OR=odds ratio

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Author & Year: Nezvalova-Henriksen el al, 2010[588] **Study design:** Prospective cohort **Setting:** Norway (Mother and child cohort study and medical birth registry) 1999-2007 **Duration of follow-up:** Follow up to birth of infant	**Patient group:** Data collected from the Medical birth registry of Norway between 1999- 2007. **Inclusion criteria:** Pregnant women living in Norway between 1999- 2006. **Exclusion criteria:** NR **All patients** **N:** 69,929 pregnant women **Age (mean):** NR **Drop outs:** NR **Group 1** **N:** 1535 **Age (mean):** NR **Drop outs:** NR **Maternal age:** <20: 1/1535 (0.07%), 20-29: 166/1535 (10.8%), 30-39: 202/1535 (13.2%), >40: 4/1535 (0.3%) **Parity:**-0: 190/1535 (12.4%), >1: 183/1535 (0.3%) **Plurality:** 1: 366/1535 (23.8%), >1: 7/1535 (0.5%) **Married/ cohabiting:** 364/1535 (23.7%) **BMI prior to pregnancy:** <18.5: 18/1535 (1.2%), 18.5- 25:	**Group 1 - triptan exposure in 1st trimester** Women who used triptans during the 1st trimester of pregnancy **Group 2 - triptan exposure during the 2nd or 3rd trimesters** **Group 1 and 2 – triptan exposure any time during pregnancy** **Group 3 - migraine control** Triptan use in the 6 months prior to pregnancy **Group 4 - non-migraine control** Women with migraine who had not reported any triptan use during pregnancy **All groups:** Two self administered questionnaires. Pregnant women live in Norway between 1999 – 2006 received a postal invitation prior to first ultrasound	**Any congenital malformation** N (%) Crude odds ratio presented unless **	**Group1:** 69/1387 (5%) **Group 2:** 49/1000 (4.9%) **Group 1 and 2:** 75/1535 (4.9%) **Group 3:** 22/373 (5.9%) **Group 4:** 3405/68021 (5%) **Odds ratios & CI** **Group 1 vs 4:** 1 [0.7-1.2] **Group 2 vs 4:** 0.9 [0.7-1.3] **Group 1 &2 vs 4:** 0.9 [0.7-1.2] **Group 3 vs 4:** 1.1 [0.7-1.8] **p value:** NR	**Funding:** Norwegian Ministry of health NIH/NIEHS grant and Norwegian research council/FUGE grant **Limitations:** Low exposure numbers. Based on self reported migraine pharmacotherapy with possible under-reporting of drug use. 2nd questionnaire only covered triptan use up to gestational age 30 weeks, may be loss of data on triptan use after this point. Migraine diagnosis not validated. Categorisation of the three study groups dependent on the accuracy of the women's reporting. Only 42% of invited months agreed to participate in this study. **Additional outcomes:** Concomitant drug use during pregnancy. Individual triptans used by women. Maternal health during
			Major congenital malformation N (%) Crude odds ratio presented unless **	**Group1:** 43/1387 (3.1%) **Group 2:** 30/1000 (3%) **Group 1 and 2:** 46/1535 (3%) **Group 3:** 11/373 (2.9%) **Group 4:** 2003/68021 (2.9%) **Odds ratios & CI** **Group 1 vs 4:** 1 [0.7-1.4] **Group 2 vs 4:** 1 [0.7-1.4] **Group 1 &2 vs 4:** 1 [0.7-1.3] **Group 3 vs 4:** 0.9 [0.5-1.7] **p value:** NR	
			Live birth N (%) Crude odds ratio presented unless **	**Group1:** 1376/1387 (99.2%) **Group 2:** 995/1000 (99.5%) **Group 1 and 2:**1524/1535 (99.2%) **Group 3:**368/373 (98.7%) **Group 4:** 67480/68021 (99.2%)* **Odds ratios & CI** **Group 1 vs 4:** 1 [0.6-1.9]	

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	227/1535 (14.8%), >25: 116/1535 (7.6%) **Smoking at gestational week 30**: 37/1535 (2.4%) **Caffeine consumption during pregnancy:** 342/1535 (22.3%) **Alcohol intake during pregnancy:** 174/1535 (11.3%) **Group 2** **N:** 1897 **Age (mean):** NR **Drop outs:** NR **Maternal age:** -<20: 12/1897 (0.6%), 20-29: 625/1897 (32.9%), 30-39: 872/1897 (46%), >40: 26/1897 (1.4%) **Parity:** 0: 723/1897 (38.1%), >1: 812/1897 (42.8%) **Plurality:** 1: 1513/1897 (79.8%), >1: 22/1897 (1.2%) **Married/ cohabiting:** 1496/1897 (78.9%) **BMI prior to pregnancy:** <18.5: 40/1897 (2.1%), 18.5- 25: 886/1897 (46.7%), >25: 580/1897 (30.6%) **Smoking at gestational week 30:** 142/1897 (7.5%) **Caffeine consumption during pregnancy:** 1405/1897 (74.1%) **Alcohol intake during pregnancy:**	scan between gestational weeks 17 – 18. The invitation contained the fist questionnaire which covered sociodemographic data, maternal medical history, drug exposure other exposures in the 6 months prior to pregnancy and during the 1st 18 weeks of the current pregnancy. 2nd questionnaire given out at gestational week 30- covered lifestyle and medical data during the 2nd and 3rd trimesters. Information from the medical birth registry of Norway was obtained from mandatory standardised forms containing information about the mother and the newborn. These forms are filled out by midwives, obstetricians and/or paediatricians at each delivery, information on the mother is obtained from the mother's pregnancy medial records.		**Group 2 vs 4:**1.6 [0.6-3.8] **Group 1 &2 vs 4**:1.1 [0.6-2.0] **Group 3 vs 4:** 0.7 [0.3-1.7] **p value:** NR	pregnancy. Obstetric complications. Chronic conditions. **Notes:** Multiple pregnancies were included, but only data on the first born infant were used. *paper states 6748, but 99.2%, assumed a type error. **adjusted for possible confounding factors- maternal socio-demographic data, medical characteristics (including concomitant drug use), maternal health, pregnancy complications. Provides OR- adjusted for variable including: parity, plurality, maternal BMI prior to pregnancy, caffeine and alcohol intake during pregnancy , paracetamol and or codeine in combination with paracetamol use during pregnancy, pre eclampsia, eclampsia, polyhydramnios, placenta previa, abruption placentae and caesarean section by birth weight >4500g and vaginal bleeding during pregnancy).
			Still birth (intrauterine death after gestational week 20) N (%) Crude odds ratio presented unless **	**Group1:** 0/1387 **Group 2:** 0/1000 **Group 1 and 2:** 0/1535 **Group 3:** 2/373** (0.5%) **Group 4:** 19/68021 (0.03%) **Odds ratios & CI** **Group 1 vs 4:** NA **Group 2 vs 4:** NA **Group 1 & 2 vs 4:** NA **Group 3 vs 4:** 11.7 [2.8-49.5] **p value:** NR	
			Perinatal death (death during labour or within 20 hours of delivery) N (%) Crude odds ratio presented unless **	**Group1:** 6/1387 (0.4%) **Group 2:** 3/1000 (0.3%) **Group 1 and 2:** 6/1535 (0.4%) **Group 3:**3/373 (0.8%) **Group 4:** 314/68021 (0.4%) **Odds ratios & CI** **Group 1 vs 4:** 0.9 [0.4-2.0] **Group 2 vs 4:** 0.7 [0.2-2.1] **Group 1 &2 vs 4:** 0.8 [0.4-1.8] **Group 3 vs 4:** 1.5 [0.5-4.8] **p value:** NR	
			Death during the 1st 12 months of life N (%)	**Group1:** 5/1387 (0.3%) **Group 2:** 2/1000 (0.2%) **Group 1 and 2:** 5/1535 (0.3) **Group 3:** 0/373	

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	819/1897 (43.1%) **Group 3** **N:** 68,021 **Age (mean):** NR **Drop outs:** NR **Maternal age**: <20: 742/68,021 (1.1%), 20-29: 30007/68,021 (44.1%), 30-39: 35973/68,021 (52.9%), >40: 1299/68,021 (1.9%) **Parity:** 0: 29508/68,021 (43.4%), >1: 38507/68,021 (0.05%) **Plurality:** 1: 66760/68,021 (98.1%), >1: 1261/68,021 (1.9%) **Married/ cohabiting:** 66072/68,021 (97.1%) **BMI prior to pregnancy:** <18.5: 2073/68,021 (3.0%), 18.5-25: 43431/68,021 (63.8%), >25: 20551/68,021 (30.2%) **Smoking at gestational week 30:** 6156/68,021 (9.1%) **Caffeine consumption during pregnancy:** 59581/68,021 (87.6%) **Alcohol intake during pregnancy:** 35058/68,021 (51.5%)		Crude odds ratio presented unless **	**Group 4:** 192/68021 (0.3%) **Odds ratios & CI** **Group 1 vs 4:** 1.3 [0.5-3.1] **Group 2 vs 4:** 0.7 [0.2-2.9] **Group 1 &2 vs 4:** 1.2 [0.5-2.8] **Group 3 vs 4:** NA **p value:** NR	
			Birth weight <2500g N (%) Crude odds ratio presented unless **	**Group1:** 63/1387 (4.5%) **Group 2:** 40/1000 (4%) **Group 1 and 2**:65/1535 (4.2%) **Group 3:** 19/373 (5.1%) **Group 4:** 2663/68021 (3.9%) **Odds ratios & CI** **Group 1 vs 4:** 1.2 [0.8-1.7] **Group 2 vs 4:** 1.1 [0.7-1.8] **Group 1 &2 vs 4:** 1.1 [0.8-1.6] **Group 3 vs 4:** 1 [0.5-1.8] **p value:** NR	
			Gestational age <37 weeks N (%) Crude odds ratio presented unless **	**Group1:** 82/1387 (5.9%) **Group 2:** 55/1000 (5.5%) **Group 1 and 2:**86/1535 (5.6%) **Group 3:** 30/373 (8.0%) **Group 4:** 4148/68021 (6.1%) **Odds ratios & CI** **Group 1 vs 4:** 0.8 [0.6-1.0] **Group 2 vs 4:** 0.8 [0.6-1.0] **Group 1 &2 vs 4:** 0.8 [0.6-1.0] **Group 3 vs 4:**1.2 [0.8-1.8] **p value:** NR	
			Apgar score <7 at 1	**Group1:** 81/1387 (5.8%)	

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			minute N (%) Crude odds ratio presented unless **	**Group 2:** 55/1000 (5.5%) **Group 1 and 2**:88/1535 (5.7%) **Group 3:**18/373 (4.8%) **Group 4:** 3708/68021 (5.5%) **Odds ratios & CI** **Group 1 vs 4: 1 [0.8-1.2]** **Group 2 vs 4:** 0.9 [0.7-1.2] **Group 1 &2 vs 4:** 1 [0.8-1.2] **Group 3 vs 4:** 0.8 [0.5-1.2] **p value:** NR	
			Apgar score <7 at 5 minutes N (%) Crude odds ratio presented unless **	**Group1:** 20/1387 (1.4%) **Group 2:** 11/1000 (1.1%) **Group 1 and 2:**22/1535 (1.4%) **Group 3:** 4/373 (1.1%) **Group 4:** 925/68021 (1.4%) **Odds ratios & CI** **Group 1 vs 4:** 1 [0.6-1.6] **Group 2 vs 4:** 0.8 [0.4-1.4] **Group 1 &2 vs 4:** 1 [0.7-1.6] **Group 3 vs 4:** 0.6 [0.2-1.7] **p value:** NR	

Abbreviations: NR=not reported, NA=not applicable, M/F=male/female, N=total number of patients randomised, SD=Standard deviation, SE=Standard error, ITT=Intention to treat analysis, OR=odds ratio

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Author & Year: Oleson et al, 2000[597] **Study design:** Prospective cohort **Setting:** Denmark **Duration of follow-up**: To birth of infant	**Patient group:** Pregnant women who redeemed a prescription for sumatriptan from 1991 – 1996 **Inclusion criteria:** Women redeeming a prescription for sumatriptan identified through the prescription database. Healthy controls identified through the Danish national birth registry Exclusion criteria: **All patients** **N:** 35950 (total number of births) **Age (mean):** NR **Drop outs:** NR in any group **Group 1** **N:** 34 **Age (mean):** 29.6 **Smoking:** 11/34 (32.4%) **Marital status (women living with child's father):** 23/34 (64.6%) **Parity (proportion of primiparous women):**10/34 (29.4%) **Group 2** **N:** 89 **Age (mean):** 28.4 **Smoking:** 33/89 (37.0%) **Marital status (women living with child's father):** 59/89 (66.3%)	**Group 1- women exposed to sumatriptan** Women exposed to Sumatriptan during their pregnancy were identified. **Group 2- migraine control group** Women who redeemed at least one prescription for sumatriptan or ergotamine 52 – 12 weeks prior to conception, but not during pregnancy. **Group 3 -Healthy women** Women who did not redeem any prescriptions during pregnancy **All groups** All prescriptions redeemed in North Jutland county, Denmark from January 1991 – 1996, using the countries prescription database. Using the prescription database, identified all prescriptions for women who had given birth in the county of North Jutland from 1991- 1996. Prescription data was linked to the national birth registry.	**Low birth weight (<2500g)** N (%) *Adjusted OR	**Group1:** 1/34 (2.4%) **Group 2:** 5/89 (5.6%) **Group 3:** 291/15,995 (1.8%) **Odds ratios & CI** **Group 1 vs 2:** 2.3 [0.3-17.6] **Group 1 vs 3:** 0.9 [0.1-11.8] **Group 2 vs 3:** 3.2 [1.3-8.1] **p value:** NR	**Funding:** EU BIOMED programme, Danish medical research council, 1991 pharmacy foundation, North Jutland Research council. **Limitations:** Exposure to sumatriptan may be underestimated because the use of drugs during hospital admission is not included and prescriptions redeemed prior to pregnancy may have been used during pregnancy. Severity of illness that led to the prescriptions could have been a confounding variable. **Additional outcomes:** NR **Notes:** *All OR reported were adjusted for parity, smoking, maternal age and marital status. Logistic regression used to estimate association between sumatriptan use and preterm delivery and low
			Preterm (<37 weeks) N (%) Adjusted OR	**Group1:** 5/34 (14.7%) **Group 2:** 3/89 (3.4%) **Group 3**: 950/15,995 (5.9%) **Odds ratios & CI** **Group 1 vs 2:** 3.3 [1.3-8.5] **Group 1 vs 3:** 6.3 [1.2-32.0] **Group 2 vs 3:** 0.6 [0.2-1.9] **p value:** NR	
			Still births N (%) Adjusted OR	**Group 1**:0 **Group 2:** NR **Group 3:** NR	
			Birth defects N (%) Adjusted OR	**Group 1**:0 **Group 2:** NR **Group 3:** NR	

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	Parity (proportion of primiparous women): 37/89 (41.6%) **Group 3** **N:** 15,995 **Age (mean):** 27.9 **Smoking:** 4846/15,995 (30.3%) **Marital status (women living with child's father):** 13,116/15,995 (82%) **Parity (proportion of primiparous women):** 8717/15,995 (54.5%)	Data obtained from official reports filled in by midwives attending deliveries.			birth weight. Association with low birth weight assessed in pregnancies that reached full term only.

Abbreviations: NR=not reported, NA=not applicable, M/F=male/female, N=total number of patients randomised, SD=Standard deviation, SE=Standard error, ITT=Intention to treat analysis