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Twenty-year trends in the use of anti-seizure medication among pregnant women in the Netherlands

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ABSTRACT

Background: Anti-seizure medications (ASMs) are used to treat conditions such as epilepsy and bipolar disorder. Some of these drugs are associated with an increased risk of congenital malformations and adverse developmental outcomes.
Objectives: To examine trends in use of ASMs among pregnant women in the Netherlands according to medication safety profile.
Methods: Using population-based data from the PHARMO Perinatal Research Network, we assessed trends in use of ASMs among pregnant women in the Netherlands between 1999 and 2019, stratified by medication safety profile. Individual treatment patterns were also assessed.
Results: In total, 671,709 pregnancies among 446,169 women were selected, of which 2405 (3.6 per 1000) were ASM-exposed. Over the study period, a significant increase was observed for use of known safest ASMs (0.7–18.0 per 10,000 pregnancies) as well as for those with uncertain risk (5.3–13.4 per 10,000 pregnancies). Use of ASMs with higher risk of congenital malformations decreased significantly (24.8–14.5 per 10,000 pregnancies), except for topiramate (0–6.7 per 10,000 pregnancies). Switches between ASM safety risk categories before and during pregnancy were uncommon; women rather discontinued treatment or switched within the same category. There was no clear change for the proportion using polytherapy during pregnancy (12% overall), however a non-significant trend toward inclusion of known safest ASMs was observed over time (1.9–3.6%).
Conclusions: Over the last two decades, there has been an increase in use of known safest ASMs among pregnant women, together with a trend toward newer ASMs with uncertain risk. Only a small proportion of women switched to a safer alternative before or during pregnancy. Altogether, this highlights the need for an expansion of ASM risk knowledge and communication to healthcare providers and women of reproductive age to improve preconception counseling.

1. Introduction

Anti-seizure medications (ASMs) are used to treat conditions such as epilepsy and bipolar disorder [1]. Some of these drugs are associated with an increased risk of congenital malformations and adverse developmental outcomes [2–4]. However, with the continued need to manage chronic medical conditions, the majority of women remain on ASMs during pregnancy, at times, more than one drug (i.e. polytherapy) [5]. Pharmacotherapeutic management during pregnancy is a subject of concern challenged by many gender-related issues, in which the drug-imposed risks must be weighed against the risks associated with the disorder treated [3,6].

Various new ASMs have entered the market over the last decades. For some, a lower risk of teratogenicity is demonstrated, whereas for others, safety profiles are yet to be fully determined. This challenges prescribers, as recommendations are often still lacking for newer drugs [3,7]. For the first-generation ASMs, the safety risks have been explored in more detail and resulted in a valproate pregnancy prevention program and a recommendation against polytherapy with ASMs [7,8]. Understanding the trends in the use of higher or uncertain risk agents will provide useful information to advise clinical practice guidelines.

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Several international studies have been published assessing ASM exposure among pregnant women over time [9–14] and our study showed that valproic acid use remained common [14]. However, recent long-term population-based data on the full spectrum of ASMs are lacking. The objective of the current study was to examine the trends in use of ASMs among pregnant women in the Netherlands, stratified by medication safety profile. Individual treatment patterns were also assessed, including the extent of changing from one ASM to another and use of polytherapy.

2. Material and methods

2.1. Data sources

This population-based study was performed using the PHARMO Perinatal Research Network (PPRN), which includes linked records from both the Netherlands Perinatal Registry (Perined) and the PHARMO Database Network (PHARMO) [15]. Perined is a nationwide registry that contains validated data from pregnancies with a gestational age (GA) of at least 16 weeks [16]. PHARMO comprises a dynamic cohort of participants and includes, among other information, drug-dispensing records from community pharmacies for more than three million individuals (approximately 25% of the Dutch population) [17,18]. The Out-patient Pharmacy Database (OPD) contains the following information per filled prescription: the Anatomical Therapeutic Chemical (ATC) classification of the drug, dispensing date, dose regimen, prescribing physician, quantity dispensed and estimated duration of use [19]. The OPD represents the Dutch population that has picked up prescription drugs or has registered with a pharmacy. The linkage between PHARMO and Perined has been described in more detail elsewhere, but was generally based on the birth date of the mother and child and their addresses and could be established for about 20% of the pregnancies in Perined [15]. For the current database research with anonymous data, no Institutional Review Board or ethics committee approval was required.

2.2. Study population

Women who gave birth between 1999 and 2019 were selected from the PPRN. No exclusion criteria were applied to increase the generalizability of the results. To allow for women's medication use to be assessed before and during pregnancy, their details needed to be registered in the OPD from 3 months before the conception date (based on ultrasound or first day of the last menstrual period) until the delivery date as recorded in Perined. Women of all ages and women of reproductive age (15–49 years) registered in the OPD were selected as reference populations, excluding pregnant women as recorded in the PPRN from the latter population.

2.3. Maternal and obstetric characteristics

Selected maternal and obstetric characteristics included age at delivery, neighborhood socioeconomic status (SES) [20,21], year of delivery, ethnicity, parity and GA at birth. These characteristics were assessed for all included pregnancies as well as for those exposed to ASMs during pregnancy.

2.4. Exposure

Anti-seizure medications dispensing records, defined by ATC group N03A 'Antiepileptics', were selected from the OPD [22]. ASM use during pregnancy was defined as at least one dispensing from the conception date until the delivery date. ASM use before pregnancy was defined as at least one dispensing in the 3 months before the conception date. In addition to the drug-level analysis, ASMs were grouped according to their safety profile as classified by the Dutch Teratology Information Service Lareb (see Table 1) [7]. According to this classification, we categorized ASMs into 3 levels: known safest, uncertain risk, and higher risk of congenital malformations. This information system was selected as it is deemed applicable to clinical practice in the Netherlands and is being used as the main information body in decision making on medication use during pregnancy by clinicians. It focuses mainly on congenital malformations. Recently, knowledge on adverse developmental outcomes is being incorporated in the recommendations.

Among women who were exposed to an ASM before or during pregnancy, changes in safety category were assessed as well as timing of these medication changes by trimester (first: up to week 12 of amenorrhea; second: 13–27 weeks; third: 28 weeks to delivery). The highest risk category was assigned in case multiple categories were used in the period of interest. For those using medication with higher risk of congenital malformations before pregnancy, the type of ASM used during pregnancy was assessed.

Patient-level switching was defined as discontinuation of one ASM and initiation of another ASM in the period from two years before pregnancy until the end of pregnancy. This was operationalized as at least one dispensing for the first ASM in the 3 months before the introduction of the second ASM (i.e. switch date), no dispensing for the second ASM in the 3 months before the switch date, and no dispensing for the first ASM in the 3 months after the switch date.

The safety profiles of ASMs used during pregnancy were also stratified by prescriber type (general practitioner, neurologist, psychiatrist, other mental health specialist, other specialist or other).

Use of monotherapy vs. polytherapy was assessed before and during pregnancy. It was based on the number of distinct ASMs in the 3 months before pregnancy or in a single pregnancy trimester, respectively. Women using more than one ASM anywhere during the period of interest were classified as being on polytherapy. Similarly, women using an ASM with higher risk of congenital malformations anywhere during the period of interest were classified as using either "monotherapy incl. higher risk" or "polytherapy incl. higher risk".

2.5. Statistical analysis

Trends over time were analyzed for the top 10 most used ASMs per year (1998–2019), separately for women of all ages, women of reproductive age (excluding pregnant women), and pregnant women. Trends were also assessed for the number of exposed

Table 1
Overview of ASM safety profile according to Dutch Teratology Information Service Lareb.

Category	Label in current study	ASMs included
Green	Known safest	lamotrigine ('most safe'), levetiracetam ('probably safe')
Orange	Uncertain risk	brivaracetam, felbamate, gabapentin, lacosamide, oxcarbazepine, perampanel, pregabalin, rufinamide, stiripentol, vigabatrin, zonisamide, clonazepam, ethosuximide and all remaining N03A drugs for which no recommendation is available
Red	Higher risk of congenital malformations	valproic acid, phenytoin, carbamazepine, topiramate, primidone, phenobarbital

Source: Dutch Teratology Information Service Lareb [7].

pregnancies per 10,000 pregnancies per year of delivery (1999–2019), by safety risk category as well as by ASM (for those with at least 100 women exposed during pregnancy overall years). The class-level switches between ASM safety risk categories are presented in a Sankey diagram, showing the proportion of women moving between categories over the selected trimesters. The top 5 most common patient-level ASM switches were determined for the ASM most often switched from, most often switched to and most often switched between, and presented overall and by timing of switch (before pregnancy/during pregnancy). For those with a switch prior to pregnancy, the median time to pregnancy was assessed. Trends in ASM monotherapy and polytherapy were presented before and during pregnancy, categorized by year of delivery. All trends over time were tested by Poisson regression at *P*-value <0.05. Separate categories were created for missing maternal and obstetric characteristics.

2.6. Sensitivity analyses

A sensitivity analysis was performed in which dispensings were converted into treatment episodes of uninterrupted use to define ASM exposure. This method was not chosen for the main analysis as it is known to overestimate exposure, because particularly during pregnancy, drugs may be discontinued [14]. Another sensitivity analysis was performed in which use before pregnancy was defined as at least one dispensing in the year before the conception date. To assess the robustness of the definition of monotherapy vs. polytherapy, two sensitivity analyses were performed in which polytherapy was based on (1) overlapping treatment episodes and (2) same day dispensings.

3. Results

In total, 671,709 pregnancies among 446,169 women were selected from the PPRN of which 2405 (3.6 per 1000) were ASM-exposed, increasing from 3.0 per 1000 in 1999 to 4.2 per 1000 in 2019. Pregnancies were categorized according to the level of risk of the medications used; in 1030 pregnancies (1.5 per 1000) women were exposed to ASMs with higher risk of congenital malformations, 636 (0.9 per 1000) to ASMs with uncertain risk, and 723 (1.1 per 1000) to known safest ASMs. Sensitivity analyses based on treatment episodes of uninterrupted use yielded 2849 pregnancies with maternal ASM exposure (4.2 per 1000; 18% higher). Maternal and obstetric characteristics of included pregnancies are summarized in Table 2.

Fig. 1 shows the trends in use of ASMs among all women, women of reproductive age, and pregnant women. Notable trends over time for all groups include decreased use of carbamazepine and valproic acid, and increased use of pregabalin, gabapentin, levetiracetam, topiramate, and lamotrigine. Lamotrigine shows the highest differences between these three groups with a 24% increase in use over time in pregnant women compared to 3% and 8% in all women and women of reproductive age, respectively. Second highest differences were observed for pregabalin (+36% and +24% in all women and women of reproductive age, respectively, compared to +9% in pregnant women). Third, carbamazepine showed a higher decrease in pregnant women (−37%) compared to all women and women of reproductive age (both −24%). Valproic acid ranked fourth with an approximate 10% higher decrease in pregnant women compared to the other groups, followed by levetiracetam with an approximate 10% higher increase in pregnant women compared to the other groups. Other ASMs not presented in Fig. 1 represented a very small proportion over the years, from approximately 0.5% in 1998 to 1.5% in 2019.

Table 2
Maternal and obstetric characteristics of included pregnancies and those exposed to ASMs.

Characteristic	All pregnancies *N* = 671,709 *n* (%)	ASM-exposed pregnancies *N* = 2405 *n* (%)
Age at delivery (years)		
≤20	9984 (1)	25 (1)
21–30	291,427 (43)	925 (38)
31–40	354,232 (53)	1358 (56)
≥41	16,066 (2)	97 (4)
Mean ± SD	31 ± 5	32 ± 5
SES		
Low	232,761 (35)	937 (39)
Normal	208,996 (31)	708 (29)
High	227,507 (34)	751 (31)
Unknown	2445 (<0.5)	9 (<0.5)
Year of delivery		
1999–2004	104,977 (16)	354 (15)
2005–2009	170,226 (25)	628 (26)
2010–2014	204,186 (30)	683 (28)
2015–2019	192,320 (29)	740 (31)
Ethnicity		
Dutch	527,026 (78)	1837 (76)
Moroccan/Turkish	46,386 (7)	210 (9)
Other European/Western[a]	24,168 (4)	109 (5)
Other[b]	65,701 (10)	220 (9)
Unknown	8428 (1)	29 (1)
Parity		
0	295,352 (44)	1069 (44)
1	242,188 (36)	840 (35)
2	92,755 (14)	330 (14)
≥3	39,451 (6)	160 (7)
Unknown	1963 (<0.5)	6 (<0.5)
GA at birth (weeks)		
≤24	20,327 (3)	79 (3)
25–<28	2532 (<0.5)	11 (<0.5)
28-<33	8904 (1)	31 (1)
33–<37	40,618 (6)	161 (7)
≥37	599,328 (89)	2123 (88)
Mean ± SD	38.8 ± 3.9	38.6 ± 4.0

SD = standard deviation; SES = neighborhood socioeconomic status; GA = gestational age.
[a] Including North American and Canadian.
[b] Creole, Hindu, Asia and other.

The trends in use of ASMs during pregnancy are again presented in Fig. 2, stratified by risk category and individually for selected ASMs. A significant decrease over time was observed for ASMs with higher risk of congenital malformations, whereas use of known safest ASMs as well as ASMs with uncertain risk increased significantly. Of note, a significant increase was observed for topiramate (market entry in 1999), which has a higher risk of congenital malformations. The biggest changes over time were observed for carbamazepine (decreased), followed by levetiracetam (market entry in 2000) and lamotrigine (both increased).

Class-level switches during pregnancy are presented in Fig. 3. The proportion of women on known safest ASMs remains relatively stable throughout pregnancy (about 17% before and during all trimesters). A 10-percent decrease was observed for the proportion using ASMs with uncertain risk. Use of ASMs with higher risk of congenital malformations decreased from 35% before pregnancy to 26% in the third trimester. Overall, switching between safety risk categories was uncommon and the changes observed mostly concerned discontinuation of treatment. Of the women using ASMs with higher risk of congenital malformations before pregnancy, the majority continued their therapy during pregnancy (87%) and those remaining either discontinued treatment (5%), switched to other therapy that includes an ASM with higher risk of congenital malformations (3%) or switched to other ASMs (5%), most often

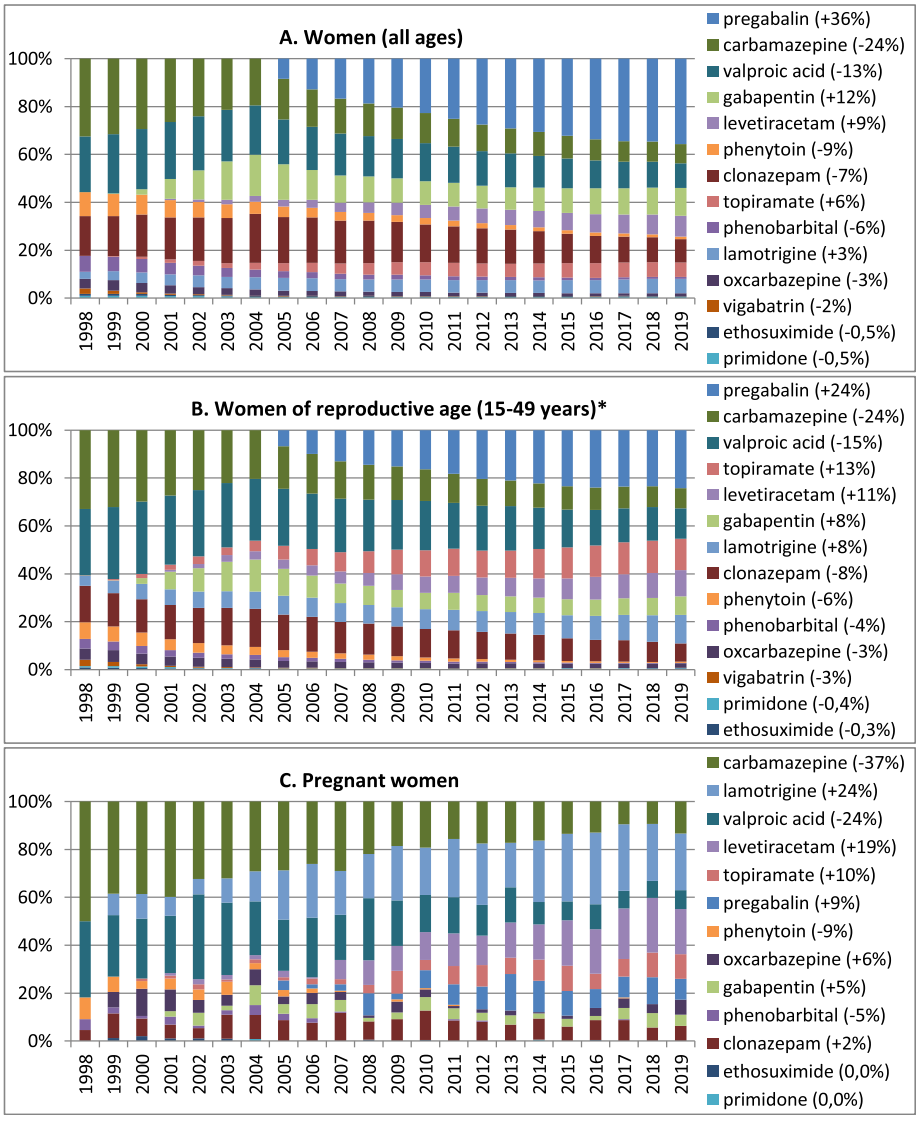

Fig. 1. Trends in use of ASMs among (A) all women; (B) women of reproductive age and (C) pregnant women. * Excluding pregnant women as included in the PPRN.

being lamotrigine and levetiracetam (data not presented). The sensitivity analysis including the year before pregnancy generally shows the same patterns, only increased proportions without treatment during pregnancy, which may indicate that treatment discontinuation generally occurs more than 3 months before pregnancy. The sensitivity analysis on treatment episodes of uninterrupted use also shows similar patterns, but with higher exposure rates for ASM with uncertain risk and with higher risk of congenital malformations. This might indicate that the overestimation of exposure due to unfinished medication fills applies more to the higher risk ASM.

The patient-level switching analysis from two years before pregnancy until the end of pregnancy showed at least one switch in 7% of all ASM users (Supplementary Table S1). Most switches took place before pregnancy (82%), with a median time to pregnancy of 369 days (interquartile range: 186–568 days). Similar to the class-level analysis, this analysis demonstrates that most switches occur within the same safety risk category. Overall, women switched most often from valproic acid (20%) or carbamazepine (16%) and most often to lamotrigine (14%) or levetiracetam (14%).

For all ASMs dispensed during pregnancy, the majority were prescribed by the general practitioner (Supplementary Table S2). This proportion was higher for the ASMs with uncertain risk (65%) and ASMs with higher risk of congenital malformations (61%) compared to known safest ASMs (54%). Similarly, the proportion prescribed by psychiatrists and mental health specialists was higher for ASMs with uncertain risk and ASMs with higher risk of congenital malformations (9% each) compared to known safest ASMs (3%). The proportion of neurologists prescribing known safest ASMs (22%) was higher than for ASMs with uncertain risk (9%) and ASMs with higher risk of congenital malformations (17%).

Overall, 12% of the pregnancies exposed to ASMs included polytherapy and no significant trend over time was observed for the distribution between monotherapy and polytherapy (Fig. 4). A significant trend was observed for the proportion of monotherapy including ASMs with higher risk of congenital malformations (decreased over time) vs. monotherapy excluding ASMs with higher risk of congenital malformations (increased over time). Although non-significant, Fig. 4 shows an increasing proportion of polytherapy excluding ASMs with higher risk of congenital malformations compared to polytherapy including ASMs with higher risk of congenital malformations over time. Comparing before vs. during pregnancy, no clear pattern exists for the distribution between monotherapy and polytherapy.

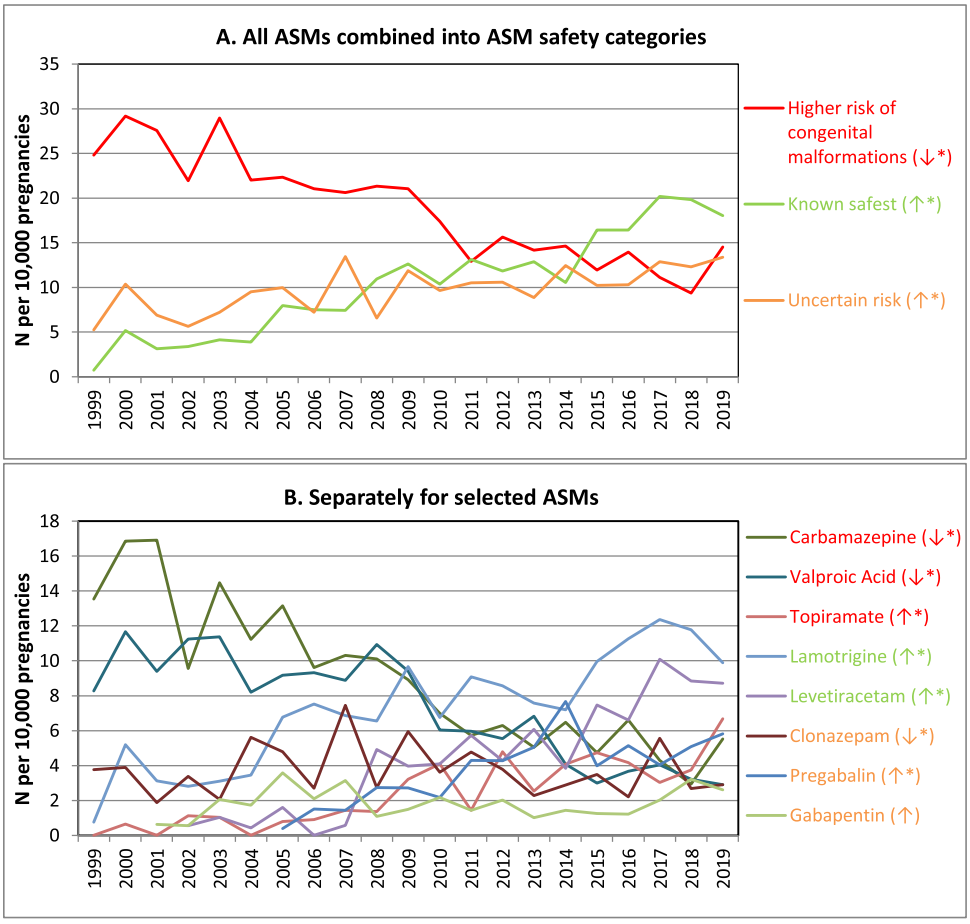

Fig. 2. Trends in use of ASMs during pregnancy, separately for (A) all ASMs combined into ASM safety risk categories and (B) selected ASMs. ↑ Trendline with positive slope; ↓ Trendline with negative slope; * Trend over time was statistically significant at *P*-value <0.05.

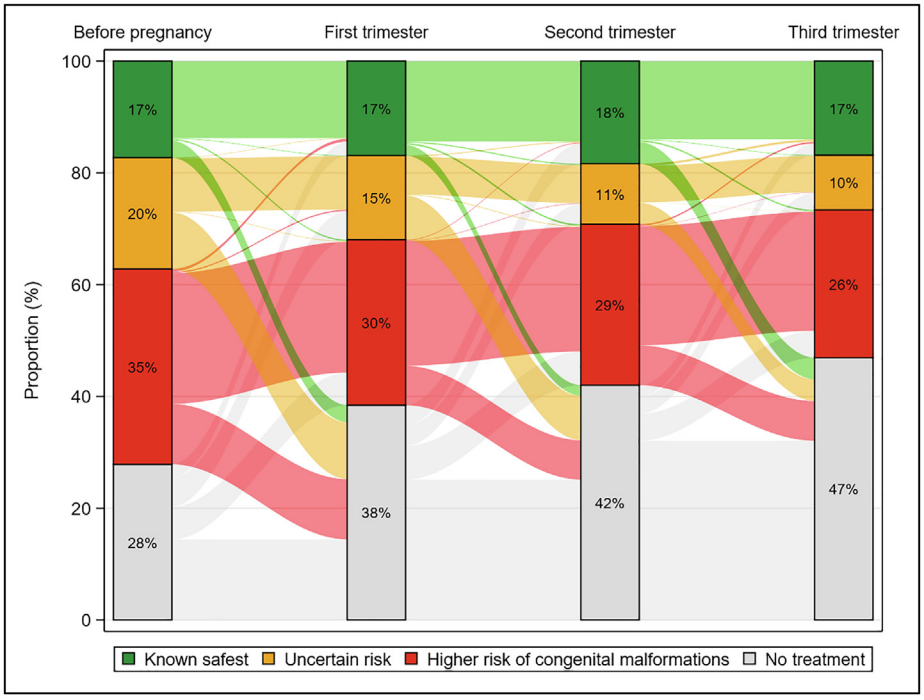

Fig. 3. Switches between ASM safety risk categories before and during pregnancy.

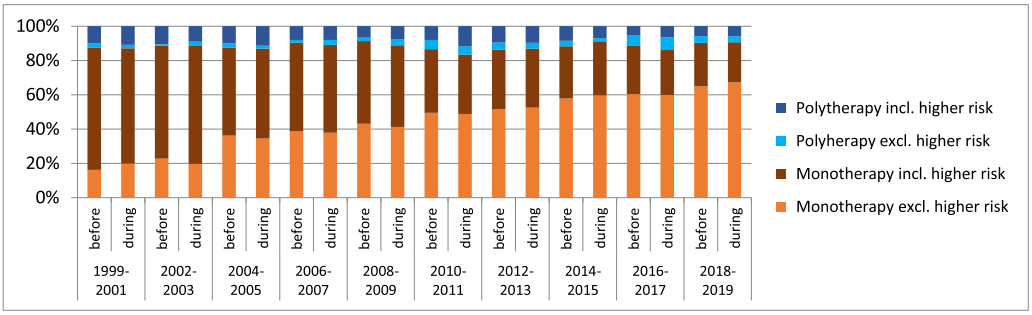

Fig. 4. Trends in ASM monotherapy and polytherapy before and during pregnancy.

The most common polytherapy was a combination of lamotrigine and levetiracetam, followed by lamotrigine and carbamazepine and then by lamotrigine and valproic acid. Numbers did not allow assessment of trends over time; however, when comparing pregnancies from 1999–2009 with those from 2010–2019, there seems a clear decrease in polytherapy including carbamazepine toward the inclusion of levetiracetam. Similar conclusions can be drawn from the sensitivity analyses (data not presented).

4. Discussion

Over the last two decades, a significant increase was observed for use of ASMs with uncertain risk from 5.3 to 13.3 per 10,000 pregnant women. A significant increase was also observed for known safest ASMs, from 0.8 to 18.0 per 10,000 pregnant women. Use of ASMs with higher risk of congenital malformations decreased significantly from 24.8 to 14.5 per 10,000 pregnant women. The decrease in use of carbamazepine and valproic acid was more pronounced in pregnant women compared to all women and women of reproductive age. In pregnant women, lamotrigine use increased over time to a greater degree than all women and women of reproductive age. Pregabalin, which has uncertain risk, showed increased use over time, moreso for all woman and women of reproductive age, compared to pregnant women. There was an increase in use of topiramate over time from 0 to 6.7 per 10,000 pregnant women, which has known higher risk of congenital malformations. Switches between ASM safety risk categories before and during pregnancy were not very common; women rather discontinued treatment or switched within the same category. Results indicate that treatment switches more often occurred longer than 3 months before pregnancy. Before and during pregnancy taken together, women switched most often from valproic acid or carbamazepine and most often to lamotrigine or levetiracetam. About one in ten women used ASM polytherapy rather than monotherapy during pregnancy without a clear change over time, however a non-significant trend toward known safest ASMs was observed.

The current findings are in line with those in previous studies on use of ASMs in pregnancy. Our estimate of overall ASM exposure during pregnancy was somewhat lower than observed in a study published in 2015 (3.6 vs. 4.3 per 1000) in which a broader ASM definition was applied [11]. General trends observed were also very similar to previous multinational studies: increases in the known safest ASMs lamotrigine and levetiracetam [11,13,23,24] as well as in ASMs with uncertain risk, often referred to as the "second-generation" drugs [9,10,13]. Similar declining trends were observed for the higher risk medications, valproic acid and carbamazepine [9,11,24,25], with the exception of the newer topiramate [1,11,13]. In addition to other studies, we compared these trends with female reference populations. Few studies have been published on medication changes around pregnancy; however, a multinational study concluded that patients switched mostly from valproate or topiramate [13]. We observed a higher tendency to switch from carbamazepine than from topiramate, potentially because overall use of topiramate was lower in our study. A previous study in women of childbearing age with epilepsy demonstrated that medication changes should be initiated early prior to conception [26]. This is in line with our observation that most medication changes were made prior to pregnancy. The high rates of ASM discontinuation observed during pregnancy were comparable to those observed in other countries [13,25]. Our study provides additional evidence on ASM switching patterns in relation to their safety profile. The proportion of women on polytherapy during pregnancy was the same as demonstrated in a recent multinational study [13]. A clear trend in polytherapy was also lacking in other studies [23,24,27,28]. Similar to our study, there has been a reported decrease in polytherapy including ASMs with higher risk of congenital malformations, with a larger proportion of polytherapy regimens including lamotrigine and levetiracetam [12,13,24]. These findings are in line with recent beliefs that some polytherapy combinations may not have an elevated risk of malformations [29,30].

A common medication management issue is choosing ASM with lower teratogenic potential in women of reproductive age [30]. Our data show that non-pregnant women of reproductive age are more likely to use medications with higher risk of congenital malformation, compared to pregnant women. Also, we demonstrated that there is a small proportion of women who switch to a preferred agent before or during pregnancy. These findings highlight the need for more preconception counseling to encourage timely and safe treatment adjustments before pregnancy, as many pregnancies are unplanned [31]. Use of ASMs with uncertain risk increased over time, possibly reflecting a shift from drugs with known teratogenicity to those with unknown risk profiles. Treating physicians rely on available evidence when balancing drugs' risks and benefits [32]. Therefore, there is a need for an expansion of research on ASM teratogenicity for these agents. Switches from valproate to topiramate or carbamazepine were relatively common, despite these all having known higher risk of congenital malformations. This might be explained by the awareness that has been specifically raised for valproate over the last decades, for instance by means of a pregnancy prevention program. The switch to topiramate may be in part due to shared indications for seizures as well as migraines. A switch to carbamazepine may relate to a more favorable profile of cognitive and behavioral outcomes, compared with valproate [33,34]. Switching to lamotrigine can be limited by the required slow titration due to risk of Stevens-Johnson Syndrome [35], and switching to levetiracetam can be limited by mood side effects [36]. Outcome research can guide targeted preventive interventions and education programs, and specific recommendations can be made for each ASM [14,37]. There seems to be more need to educate certain groups such as GPs who prescribed the majority

of ASMs. Altogether, this asks for a collaborative, multidisciplinary approach with key roles for neurologists, obstetricians, primary care doctors, clinical pharmacists and nurses in ASM management [30].

Strengths of this study included the use of over 20 years of data from a unique and large population-based cohort, which was shown to be representative of the Dutch population [15]. The timing of drug exposure relative to pregnancy staging could be accurately assessed based on last menstrual period, ultrasound, exact delivery date, drug dispensing dates, and intended duration of use, allowing patient-level analyses of treatment patterns on the full spectrum of ASMs. A common challenge in using administrative data is defining drug exposure or compliance. Treatment episodes of uninterrupted use were not applied in the current study as it is known to overestimate exposure, particularly during pregnancy [14]. Underestimated drug exposure is therefore likely, also because hospital-administered drugs were not captured. Another limitation was the use of a risk classification system for ASMs in pregnancy that did not take into account individualized care, in which weighed treatment decisions are made. The reasons for staying on treatment were unknown; however, for conditions like epilepsy and bipolar disorder treatment adjustments often may not be the safest choice [38,39]. Data on indication were not available in the databases used for this study, which may have demonstrated different patterns per condition treated. However, this study was intended predominantly to characterize medication use according to its safety profile, regardless of the indication. This may have limited the generalizability to the population with epilepsy alone. We recognize that safety profiles have evolved and been revised over time. For example, although the Dutch Teratology Information Service Lareb classifies oxcarbazepine as having uncertain risk, recent international data show oxcarbazepine having low risk for congenital malformations, similar to levetiracetam and lamotrigine [40]. However, we specifically designed our study to use insights linked to current daily practice in the Netherlands (i.e. the Dutch Teratology Information Service Lareb). Although ASM dose adjustments are captured in the PPRN, this was beyond the scope of this paper. The same applies to reporting on similar trends in male patients or on pregnancy outcomes, which would be interesting to study in follow-up research.

5. Conclusions

In conclusion, this study shows an increase in use of known safest ASMs and a decrease for most of the ASMs with higher risk of congenital malformations among pregnant women over the last two decades. However, there also seems to be a trend toward prescribing newer ASMs with uncertain risk. Only a small proportion of women switched to a safer alternative before or during pregnancy. Altogether, this highlights the need for an expansion of ASM risk knowledge and communication to healthcare providers and women of reproductive age and thus improvement of preconception counseling. The observed trends were very similar to those observed in other countries and suggest a collective responsibility at an international level. Future efforts could strive to collaborate or standardize pregnancy registries to maximize data collection and the power of subsequent analyses. Considering the many facets of ASM management and the consequences of untreated underlying conditions, a collaborative, multidisciplinary approach is required for timely, safe, and well-weighed treatment decisions.

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Ethical publication statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Standard protocol approvals, registrations, and patient consents

For the current database research with anonymous data, no Institutional Review Board or ethics committee approval was required.

Data availability

Data are available upon reasonable request. Requests for sharing study data must be made on specific grounds, either (1) with the aim of corroborating the study results in the interest of public health or (2) in the context of an audit by a competent authority. Sufficient information needs to be provided to confirm that the request is made for one of the above-mentioned purposes, including a sound justification and, in case of a request with a view to corroborate study results, a protocol on the research for which the data will be used or a plan for quality control checks, as applicable.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.yebeh.2021.108549.

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