Use of Valproate among women of childbearing age has declined in Europe

INTRO:
Valproic acid/valproate-containing medicines (VPA) are first-line treatment for some types of epilepsy and second-line treatment for bipolar disease and migraine. VPA are teratogens that can lead to foetal neurological problems and birth defects. Consequently, its utilization among women of childbearing age is stringently regulated in the European Union to avert VPA exposure during conception and gestation. The objectives of this study were to estimate the incidence and prevalence of VPA use and to characterise patient-level VPA use in young women.

METHODS
We used a population-based cohort as well as a new user cohort. Data was gathered from 5 databases using the OMOP common data model with primary care medical records (IPCI (NL), SIDIAP (ES), CPRD (UK)) and primary and specialist sources (IQVIA DA Germany, IQVIA LPD Belgium). All women present in the databases and aged ≥12 years and ≤55 years in the period 2010-2022 (or latest available), with at least 365 days of data availability before study entry were included in the study. The outcomes were any use of a VPA containing medicine or its alternatives for prevalence, and first use for incidence and patient level utilisation. We calculated period prevalence, as of the 1st January for each year 2010-2022. We estimated initial dose and treatment duration for the first VPA prescription for each person. All analyses were stratified by age. EU PAS register number: EUPAS50789.

RESULTS
Incidence of new VPA prescriptions decreased over 2010-2021 for all analysed databases, from 250 per 100,000 py in 2010 to less than 89 in 2021.

The prevalence decreased for most analysed datasets. Younger age groups (<45) had lower prevalence, which decreased over time.

6,416 (CPRD GOLD), 1,241 (IPCI), 10,398 (SIDIAP), 945 (LPD BE), and 4,002 (DA Germany) eligible women initiated VPA. Anxiety and depressive disorders were frequent comorbidities, with 20%-39% and 16%-44% having a history of these at treatment start. The level of prescription of contraceptives was highest in CPRD GOLD, followed by IQVIA Belgium LPD, IPCI and lowest in SIDIAP and IQVIA Germany DA.

At the date of prescription, most women (66%-95%) had no record of for epilepsy, bipolar disorder or migraine. Among those with a specific indication of use recorded, migraine was the most common indication in CPRD GOLD (5.7%), whereas epilepsy was the most common indication in all other databases.

Initial daily doses for VPA ranged between a median 500 and 875 mg/day. Average treatment duration varied substantially between databases, with a median of 50 days in IQVIA Belgium LPD, 82, 98, and 100 days in CPRD GOLD, IPCI and IQVIA Germany DA, respectively, and 1 year in SIDIAP. Although initial dose did not change over the study period in all databases, cumulative annual dose decreased in SIDIAP (from 2012 onwards), but remained stable for CPRD GOLD, IPCI and IQVIA Belgium LPD.

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