

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed.
We post it as supplied by the authors.

Supplement to: Perucca P, Malpas CB, Berry-Noronha A, et al. Antiseizure medication use in pregnancy and the risk of poor fetal growth in the EURAP international registry: a prospective cohort study. *Lancet Neurol* 2026; **25**: 840–51.

Supplementary Appendix

Piero Perucca, Charles B. Malpas, Alexander Berry-Noronha, Susan P. Walker, Tomas Kalincik, Bibiane Moche Kanga, Silje Alvestad, John Craig, Anne Sabers, Frank, J.E. Vajda, Dina Battino, Emilio Perucca, Torbjorn Tomson; EURAP Collaborators. Antiseizure medication use in pregnancy and the risk of poor fetal growth: a prospective cohort study of the EURAP international registry

Table of Contents

EURAP Collaborators.....	3
Table S1. List of factors known to be associated with fetal growth, selected a priori from the literature for consideration in the study	11
Table S2. Top 10 most common antiseizure medication (ASM) polytherapies in the study population	12
Table S3. Characteristics of the study subset consisting of a single offspring (first recorded in EURAP in case of multiple offspring) for each mother	13
Table S4. Relationship of ASM regimen (monotherapy vs polytherapy) and different indicators of fetal growth, with addition of maternal and paternal educational levels to model adjustments	16
Table S5. Relationship of ASM regimen (monotherapy vs polytherapy) and different indicators of fetal growth, with greater stratification of maternal folate intake among model adjustments.	18
Table S6. Relationship of ASM regimen (monotherapy vs polytherapy) and different indicators of fetal growth, with addition of total seizure burden to model adjustments.....	20
Table S7. Relationship of ASM regimen (monotherapy vs polytherapy) and different indicators of fetal growth in offspring born to mothers who were seizure-free during pregnancy.....	22
Table S8. Strength of association between individual ASM monotherapy daily doses and different indicators of fetal growth	24
Table S9. Comparative risk of small-for-gestational age (SGA) associated with different dose ranges for oxcarbazepine	25
Table S10. Relationship of ASM regimen (monotherapy vs polytherapy) and different indicators of fetal growth in offspring exposed only to carbamazepine, lamotrigine, levetiracetam, phenytoin and/or valproic acid.	26
Table S11. Strength of association of the most common ASM polytherapies with different indicators of fetal growth, relative to lamotrigine monotherapy	28

Figure S1. Relationship between number of concomitantly used ASMs and different indicators of poor fetal growth.....	29
Figure S2. Relationship between individual ASM monotherapies and different indicators of fetal growth	30
References.....	31

EURAP Collaborators.

Investigator	Site	Country
Janet E. Graham	Australian Pregnancy Register, The Royal Melbourne Hospital, Melbourne, Australia	Australia
Alison A. Hitchcock	Australian Pregnancy Register, The Royal Melbourne Hospital, Melbourne, Australia	Australia
Gudrun Kalss	Department of Neurology, Christian Doppler University Hospital, Centre for Cognitive Neuroscience, Member of the ERN EpiCARE, Paracelsus Medical University of Salzburg, Salzburg, Austria	Austria
Halina Navumava	Center of paroxysmal conditions, Vitebsk Regional Clinical Diagnostic Center, Vitebsk, Republic of Belarus	Republic of Belarus
Stephanie Hödl	University Hospital Ghent, Ghent, Belgium	Belgium
Bregje D'haeze	University Hospital Ghent, Ghent, Belgium	Belgium
Stefanie Gadeyne	University Hospital Ghent, Ghent, Belgium	Belgium
Alejandro De Marinis	Liga Chilena contra la Epilepsia, Santiago, Chile	Chile
Paul Mardones Escobar	Liga Chilena contra la Epilepsia, Santiago, Chile	Chile
Lei Chen	West China Hospital, Sichuan University, Chengdu, Sichuan, China	China
Yutong Fu	West China Hospital, Sichuan University, Chengdu, Sichuan, China	China
Jana Zarubova	Department of Neurology, Charles University, Second Faculty of Medicine and Motol University Hospital - Full Member of the ERN EpiCAR, Prague, Czech Republic	Czech Republic
Jana Amlerová	Department of Neurology, Charles University, Second Faculty of Medicine and Motol University Hospital - Full Member of the ERN EpiCAR, Prague, Czech Republic	Czech Republic
Michaela Kalinova	Department of Neurology, Charles University, Second Faculty of Medicine and Motol University Hospital - Full Member of the ERN EpiCAR, Prague, Czech Republic	Czech Republic
Hana Krijtová	Department of Neurology, Charles University, Second Faculty of Medicine and Motol University Hospital - Full Member of the ERN EpiCAR, Prague, Czech Republic	Czech Republic
Renata Listonova	Department of Neurology Clinic, Falta s.r.o., Náchod, Czech Republic	Czech Republic
David Franc	Department of Neurology, Faculty of Medicine and Dentistry, Palacky University Olomouc and University Hospital Olomouc, Olomouc, Czech Republic	Czech Republic

Petr Busek	Department of Neurology, Charles Univesity, First Faculty of Medicine and General University Hospital, Prague, Czech Republic	Czech Republic
Michael Nielsen	University Hospital Aalborg, Aalborg, Denmark	Denmark
Karina Als	University Hospital Aalborg, Aalborg, Denmark	Denmark
Jakob Christensen	Aarhus Universitetshospital, Palle Juul-Jensens Boulevard 165, Aarhus N, Denmark	Denmark
Tine M. Christiansen	Aarhus Universitetshospital, Palle Juul-Jensens Boulevard 165, Aarhus N, Denmark	Denmark
Amalia Larsen	Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark	Denmark
Hanne Moerk Christensen	Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark	Denmark
Noemi Andersen	Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark	Denmark
Annette Sidaros	Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark	Denmark
Per Jensen	Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark	Denmark
Anna Stefansdottir	Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark	Denmark
Ioannis Tsiropoulos	Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark	Denmark
Lars Pinborg	Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark	Denmark
Gita Femhøj Lauritsen	Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark	Denmark
Rannva Gammelgård	Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark	Denmark
Josefine Skytte Jensen	Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark	Denmark
Katarzyna Cebula	The Danish Epilepsy Center, Filadelfia, Dianalund, Denmark	Denmark
Stefan Juhl	The Danish Epilepsy Center, Filadelfia, Dianalund, Denmark	Denmark
Katarzyna Mieszczanek	The Danish Epilepsy Center, Filadelfia, Dianalund, Denmark	Denmark
Lone Olsen	The Danish Epilepsy Center, Filadelfia, Dianalund, Denmark	Denmark
Mette Nielsen	The Danish Epilepsy Center, Filadelfia, Dianalund, Denmark	Denmark
Birgitte Forsom Sodal	Gødstrup Regional Hospital, Holstebro, Denmark	Denmark
Karen Nielsen	Gødstrup Regional Hospital, Holstebro, Denmark	Denmark
Aleksei Rakitin	Neurology Clinic, Tartu University Hospital, Tartu, Estonia	Estonia
Anne Kirss	Women's Clinic of Tartu University Hospital, Tartu, Estonia	Estonia
Reetta Kälviäinen	Kuopio University Hospital, Kuopio, Finland	Finland

Pirjo Lavi	Kuopio University Hospital, Kuopio, Finland	Finland
Anna M. Saukkonen	Pohjois-Karjala Central Hospital, Joensuu, Finland	Finland
Minna Niskanen	Mikkeli Central Hospital, Mikkeli, Finland	Finland
Marion Quirins	Hôpital Fondation Adolphe de Rothschild, Paris, France	France
Sofia Kasradze	Caucasus International University, Tbilisi, Georgia	Georgia
Nino Gogatishvili	Caucasus International University, Tbilisi, Georgia	Georgia
Bettina Schmitz	Vivantes Humboldt Hospital, Department of Neurology, Berlin, Germany	Germany
Florian Losch	Vivantes Humboldt Hospital, Department of Neurology, Berlin, Germany	Germany
Kirsten Krämer	Vivantes Humboldt Hospital, Department of Neurology, Berlin, Germany	Germany
Rebekka Lehmann	Center for Epilepsy Berlin-Brandenburg: Königin Elisabeth Herzberge Hospital, Bernau, Berlin - Brandenburg, Germany	Germany
Hans-Beatus Straub	Center for Epilepsy Berlin-Brandenburg: Königin Elisabeth Herzberge Hospital, Bernau, Berlin - Brandenburg, Germany	Germany
David Steinbart	Charité - Universitätsmedizin Berlin, Berlin, Germany	Germany
Ge Yu	Private Practice, Neurology, Berlin, Germany	Germany
Sabine Nehler	Private Practice, Neurology, Berlin, Germany	Germany
Wenke Grönheit	Centre for Neurology and Epilepsy, Knappschaft-Hospital, Bochum-Langendreer, Bochum, Germany	Germany
Susanne Hallmeyer-Elgner	Private Practice, Neurology, Dresden, Germany	Germany
Hajo Hamer	University Friedrich-Alexander of Erlangen, University hospital, Department of Neurology and Epileptology, Erlangen, Germany	Germany
Catrin Mann	University of Frankfurt, Department of Neurology, Frankfurt, Germany	Germany
Felix Rosenow	University of Frankfurt, Department of Neurology, Frankfurt, Germany	Germany
Elisa K. El-Allawy-Zielke	Centre of Neurology & Epilepsy Alsterdorf, Hamburg, Germany	Germany
Nele Gao	Centre of Neurology & Epilepsy Alsterdorf, Hamburg, Germany	Germany
Jan S. Gerdes	Centre of Neurology & Epilepsy Alsterdorf, Hamburg, Germany	Germany
Anja Herzer	Centre of Neurology & Epilepsy Alsterdorf, Hamburg, Germany	Germany
Eva-Katharina Kliewer	Centre of Neurology & Epilepsy Alsterdorf, Hamburg, Germany	Germany

Iryna Schamim	Centre of Neurology & Epilepsy Alsterdorf, Hamburg, Germany	Germany
Matthias Lindenau	Centre for Neurology, Private Practice "Neurologie Neuer Wall, Dr. Bredow & Partner", Hamburg, Germany	Germany
Nicole Beindorff	Private Practice, Hannover, Germany	Germany
Bernhard Steinhoff	Centre of Epilepsy, Kehl Kork, Germany	Germany
Miriam Wienecke	Centre of epilepsy Kleinwachau, Kleinwachau, Germany	Germany
Brigitte Scheid	Private Practice, Leipzig, Germany	Germany
Ilka Immisch	University of Marburg, Marburg, Germany	Germany
Katja Menzler	University of Marburg, Marburg, Germany	Germany
Lisa M. Langenbruch	University of Münster, Department of Neurology, Münster, Germany	Germany
Christine Strippel	University of Münster, Department of Neurology, Münster, Germany	Germany
Dieter Dennig	Neurological community practice "Am Seelberg", Stuttgart, Germany	Germany
Christian Dippon	Neurological community practice "Am Seelberg", Stuttgart, Germany	Germany
Kerstin Erdmann	Neurological community practice "Am Seelberg", Stuttgart, Germany	Germany
Christiane Asenbauer	Centre of Neurology, Private Practice, Dr. Christiane Asenbauer, Tübingen, Germany	Germany
Ramshekhhar N. Menon	Sree Chitra Tirunal Institute for Medical Sciences & Technology, Trivandrum, India	India
Kiren G. Koshy	Sree Chitra Tirunal Institute for Medical Sciences & Technology, Trivandrum, India	India
Nasim Tabrizi	Mazandaran University of medical sciences, Sari, Iran	Iran
Jafar Mehvari Habibabadi	Isfahan University of medical sciences, Isfahan, Iran	Iran
Lilach Goldstein	Tel Aviv Medical Center, Tel Aviv, Israel	Israel
Stefano D'Arrigo	Department of Pediatric Neurosciences, Fondazione Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS) Istituto Neurologico Carlo Besta, Milano, Italy	Italy
Chiara Pantaleoni	Department of Pediatric Neurosciences, Fondazione Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS) Istituto Neurologico Carlo Besta, Milano, Italy	Italy
Claudia Ciaccio	Department of Pediatric Neurosciences, Fondazione Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS) Istituto Neurologico Carlo Besta, Milano, Italy	Italy
Barbara Mostacci	IRCCS Istituto delle Scienze Neurologiche di Bologna - Full Member of the ERN EpiCARE, Bologna, Italy	Italy

Francesca Bisulli	IRCCS Istituto delle Scienze Neurologiche di Bologna - Full Member of the ERN EpiCARE & Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy	Italy
Lorenzo Muccioli	IRCCS Istituto delle Scienze Neurologiche di Bologna - Full Member of the ERN EpiCARE, Bologna, Italy	Italy
Aldo Paggi	Private Neurologist, Ancona, Italy	Italy
Andrea Ortenzi	Private Neurologist, Ancona, Italy	Italy
Nicoletta Foschi	Ospedale Regionale Torrette, Ancona, Italy	Italy
Sara Zagaglia	Ospedale Regionale Torrette, Ancona, Italy	Italy
Antonio Gambardella	University Magna Graecia, Catanzaro, Italy	Italy
Alessandra Pistelli	Centro di Riferimento Regionale di Tossicologia Perinatale, S.O.D.c Tossicologia Medica, Azienda Ospedaliero Universitaria Careggi, Firenze, Italy	Italy
Maria P. Canevini	Childhood and Adolescence Neuropsychiatry Unit, ASST Santi Paolo e Carlo, San Paolo Hospital, Milano, Italy; Università degli Studi di Milano, Milano, Italy	Italy
Katherine Turner	Childhood and Adolescence Neuropsychiatry Unit, ASST Santi Paolo e Carlo, San Paolo Hospital, Milano, Italy	Italy
Elena Zambrelli	Childhood and Adolescence Neuropsychiatry Unit, ASST Santi Paolo e Carlo, San Paolo Hospital, Milano, Italy	Italy
Laura Gargantini	Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano, Italy	Italy
Cristina M. Bonato	Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano, Italy	Italy
Stefania Falchi	Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano, Italy	Italy
Simone Beretta	Fondazione IRCCS San Gerardo Monza, University of Milano-Bicocca, Monza, Italy	Italy
Simona D'Andrea	Fondazione IRCCS San Gerardo Monza, University of Milano-Bicocca, Monza, Italy	Italy
Giulia Pederzoli	Fondazione IRCCS San Gerardo Monza, University of Milano-Bicocca, Monza, Italy	Italy
Michela Cecconi	Simple Departmental Unit of Neurophysiopathology, Azienda Ospedaliera di Perugia, Perugia, Italy	Italy
Francesca Muzzi	Centro Epilessia LICE I Livello Medico Adulti ASL ROMA 3, Roma, Italy	Italy
Marta Piccioli	ASL Roma 1 - P.O. San Filippo Neri, Dipartimento delle Specialità Mediche, UOC Neurologia, Roma, Italy	Italy
Pietro Pignatta	Humanitas Gradenigo, Torino, Italy	Italy

Hideyuki Ohtani	Shizuoka Institute of Epilepsy and Neurological Disorders, Shizuoka, Japan	Japan
Takuji Nishida	Shizuoka Institute of Epilepsy and Neurological Disorders, Shizuoka, Japan	Japan
Etsuko Yamazaki	Shizuoka Institute of Epilepsy and Neurological Disorders, Shizuoka, Japan	Japan
Katsuyuki Fukushima	Fukushima Neurology Clinic, Hokkaido, Japan	Japan
Yoshio Omote	Okayama Medical Center, Okayama, Japan	Japan
Misa Nakano	Suita Municipal Hospital, Osaka, Japan	Japan
Takahiro Mitsueda	Osaka City General Hospital, Osaka, Japan	Japan
Masahiro Mizobuchi	Nakamura-Kinen Hospital, Sapporo, Japan	Japan
Masaaki Kato	MusashinoKokubunni Clinic, Tokyo, Japan	Japan
Hidemoto Kubota	Nihonbashi Neuro Clinic, Tokyo, Japan	Japan
Gordana Kiteva-Trenchevska	Medical Faculty, University "Ss Cyril and Methodius", Skopje, Macedonia	Macedonia
Eline Dahl-Hansen	Department of Neurology, Drammen Hospital, Vestre Viken HF, Drammen, Norway	Norway
Torleiv Svendsen	Department of Neurology, Innlandet Hospital Trust, Lillehammer, Norway	Norway
Torill B. Jensen de Martinez	The National Center for Epilepsy, Member of the ERN EpiCARE, Oslo University Hospital, Oslo, Norway	Norway
Katrine Haggag	Department of Neurohabilitation, Oslo University Hospital, Oslo, Norway	Norway
Alma Sikiric	Department of Neurohabilitation, Oslo University Hospital, Oslo, Norway	Norway
Erik Taubøll	Department of Neurology, Oslo University Hospital, Oslo, Institute of Clinical Medicine, University of Oslo, Oslo, Norway	Norway
Gudveig Toverud Lunde	Department of Neurology, University Hospital of North Norway, Troms, Norway	Norway
Eylert Brodtkorb	Department of Neurology and Clinical Neurophysiology, St.Olav University Hospital, Trondheim; Department of Neuromedicine and Movement Science, Norwegian University of Science and Technology, Trondheim, Norway	Norway
Carla Bentes	Centro de Referência Epilepsias Refratárias (EpiCARE member), Centro Hospitalar Universitário Lisboa Norte & Centro de Estudos Egas Moniz, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal	Portugal
Ana C. Gonçalves Franco	Centro de Referência Epilepsias Refratárias (EpiCARE member), Centro Hospitalar Universitário Lisboa Norte & Centro de Estudos Egas Moniz, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal	Portugal

Sara Parreira	Centro de Referência Epilepsias Refratárias (EpiCARE member), Centro Hospitalar Universitário Lisboa Norte & Centro de Estudos Egas Moniz, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal	Portugal
Yakunina Albina Viktorovna	Samara State Medical University of the Ministry of Health of the Russian Federation, Samara, Russia	Russia
Maja Milovanović	Institute of mental health & Faculty for Special Education and Rehabilitation, University of Belgrade, Belgrade, Serbia	Serbia
Vladimír Šafčák	Department of Neurology, Air Force Military Hospital, Kosice, Slovakia	Slovakia
Meritxell Martinez Ferri	Hospital Universitari MútuaTerrassa, Barcelona, Spain	Spain
Belén Díaz Fernandez	Hospital Universitari MútuaTerrassa, Barcelona, Spain	Spain
Alvaro Sanchez Larsen	Hospital General Universitario de Albacete, Albacete, Spain	Spain
David Sopelana Garay	Hospital General Universitario de Albacete, Albacete, Spain	Spain
Fernando Ortega Valín	Hospital Universitario Marques de Valdecilla, Santander, Spain	Spain
Clara Cabeza Alvarez	Hospital Universitario de Toledo, Toledo, Spain	Spain
Mercedes Garces Sanchez	Hospital Universitari i Politèctic la Fe, Valencia, Spain	Spain
Maria D. Castro Vilanova	Alvaro Cunqueiro University Hospital, Vigo, Spain	Spain
Kristina Lisovska	Sahlgren Academy, University of Gotheburg, Gothenburg, Sweden	Sweden
Anders Lundgren	Neurology Clinic, Helsingborg Hospital, Helsingborg, Sweden	Sweden
Anna Wendelin	Neurology Clinic, Helsingborg Hospital, Helsingborg, Sweden	Sweden
Irene Hakansson	Department of Neurology, and Department of Biomedical and Clinical Sciences, Linköping University, Linköping, Sweden	Sweden
Avan S. Rashid	Department of Neurology, and Department of Biomedical and Clinical Sciences, Linköping University, Linköping, Sweden	Sweden
Petra Brooks	Department of Neurology, and Department of Biomedical and Clinical Sciences, Linköping University, Linköping, Sweden	Sweden
C-G Ahlin	Neurology Clinic, Motala Hospital, Motala, Sweden	Sweden
Zarouhi Hertz	Neurology Clinic, Motala Hospital, Motala, Sweden	Sweden
Kim Leerbeck	Neurology Clinic, Motala Hospital, Motala, Sweden	Sweden
Birgitta Magnusson	Department of Neurology, University Hospital, Örebro, Sweden	Sweden

Benno Mahler	Neurology Clinic, Karolinska University Hospital, Solna, Sweden	Sweden
Eva Kumlien	Department of Medical Sciences, Neurology, Uppsala, Sweden	Sweden
Peter Mattsson	Department of Medical Sciences, Neurology, Uppsala, Sweden	Sweden
Johan Vahlgren	Department of Medical Sciences, Neurology, Uppsala, Sweden	Sweden
Elisabeth Sellitto	Swiss Epilepsy Center - Klinik Lengg, Zurich, Switzerland	Switzerland
Stephan Rüegg	Department of Neurology, University Hospital Basel, Basel, Switzerland	Switzerland
Dominique Flügel	Department of Neurology, Cantonal Hospital St Gallen, St Gallen, Switzerland	Switzerland
Michaela Gegusch	Department of Neurology, Cantonal Hospital St Gallen, St Gallen, Switzerland	Switzerland
Hsiang-Yu Yu	Neurology Department, Taipei Veterans General Hospital & National Yang Ming Chiao Tung University, Taipei, Taiwan	Taiwan

Table S1. List of factors known to be associated with fetal growth, selected a priori from the literature for consideration in the study.

Factors	Excluded from analysis	Included in multivariable models
Offspring-related factors		
MCM or genetic/chromosomal abnormality ¹	X	
Multiple pregnancy ²	X	
Maternal factors		
Age ³		X
Alcohol consumption ⁴		X
Infection ⁵⁻⁸	X	
Ethnicity ^{9,a}		X
Exposure to potentially teratogenic drugs ¹⁰	X	
Folic acid supplementation ^{11,12,b}		X
Gestational diabetes mellitus ¹³	X	
Hyperhomocysteinemia ¹⁴	X	
Occurrence of seizures during pregnancy ¹⁵		X
Parity ¹⁶		X
Pre-gestational diabetes mellitus ¹⁷	X	
Region of origin ¹⁸		X
Tobacco smoking ¹⁹		X
Other factors		
Calendar year ²⁰		X

(a) Maternal ethnicity was initially included in all models, but subsequently excluded due to significant collinearity mainly resulting from its strong association with another variable, region of enrolment; (b) evidence suggests that folic acid supplementation may be protective against poor fetal growth when taken pre- and post-conception or post-conception only, but not when taken pre-conception only.¹²

MCM=major congenital malformation

Table S2. Top 10 most common antiseizure medication (ASM) polytherapies in the study population.

ASM combinations	N (% of all 2,982 ASM polytherapies)
Lamotrigine + levetiracetam	470 (15.8%)
Lamotrigine + valproic acid	258 (8.6%)
Carbamazepine + levetiracetam	173 (5.8%)
Carbamazepine + lamotrigine	133 (4.5%)
Carbamazepine + clobazam	119 (4.0%)
Lamotrigine + topiramate	86 (2.9%)
Carbamazepine + phenobarbital	75 (2.5%)
Carbamazepine + valproic acid	65 (2.2%)
Levetiracetam + oxcarbazepine	61 (2.0%)
Lacosamide + levetiracetam	53 (1.8%)

ASM=antiseizure medication

Table S3. Characteristics of the study subset consisting of a single offspring (first recorded in EURAP in case of multiple offspring) for each mother. Reported values are means $\pm$ SD or number of cases (%), as appropriate. The category ‘unknown’ refers to missing data.

Variable	Overall (n=13,728)	ASM monotherapy (n=11,142)	ASM polytherapy (n=2,586)
<i>Offspring characteristics</i>			
Sex			
Female	6,642 (48.4%)	5,421 (48.6%)	1,221 (47.2%)
Male	7,075 (51.5%)	5,712 (51.3%)	1,363 (52.7%)
Unknown	11 (0.1%)	9 (0.1%)	2 (0.1%)
Year of birth			
1999 to 2003	2,113 (15.4%)	1,720 (15.4%)	393 (15.2%)
2004 to 2008	3,895 (28.4%)	3,212 (28.8%)	683 (26.4%)
2009 to 2013	3,349 (24.4%)	2,763 (24.8%)	586 (22.7%)
2014 to 2018	2,712 (19.7%)	2,181 (19.6%)	531 (20.5%)
2019 to 2023	1,659 (12.1%)	1,266 (11.4%)	393 (15.2%)
Gestational age (weeks)	39.5 $\pm$ 1.9	39.5 $\pm$ 1.8	39.4 $\pm$ 2.0
Birthweight (grams)	3,293.7 $\pm$ 554.1	3,314.7 $\pm$ 545.2	3,203.4 $\pm$ 582.3
Birthweight centile	36.3 $\pm$ 28.1	37.1 $\pm$ 28.0	32.9 $\pm$ 28.3
Birthweight categories			
SGA (<10 th centile)	2,945 (21.4%)	2,215 (19.9%)	730 (28.2%)
Severe SGA (<3 rd centile)	1,129 (8.2%)	823 (7.4%)	306 (11.8%)
LBW (<2500 grams)	890 (6.5%)	638 (5.7%)	252 (9.7%)
<i>Mothers' characteristics</i>			
Maternal age at conception (years)	29.7 $\pm$ 5.0	29.7 $\pm$ 5.0	29.6 $\pm$ 5.1
Maternal ethnicity			
Caucasian	11,612 (84.6%)	9,567 (85.9%)	2,045 (79.1%)
African	34 (0.2%)	27 (0.2%)	7 (0.3%)
Asian	1,553 (11.3%)	1,137 (10.2%)	416 (16.1%)
Mixed	249 (1.8%)	174 (1.6%)	75 (2.9%)
North African	84 (0.6%)	63 (0.6%)	21 (0.8%)
Other	170 (1.2%)	151 (1.4%)	19 (0.7%)
Unknown	25 (0.2%)	22 (0.2%)	3 (0.1%)
Region of enrolment			
Western Europe	3,368 (24.5%)	2,818 (25.3%)	550 (21.3%)
Australia and New Zealand	1,010 (7.4%)	764 (6.9%)	246 (9.5%)
Eastern Europe	759 (5.5%)	598 (5.4%)	161 (6.2%)
Northern Europe	3,761 (27.4%)	3,126 (28.1%)	635 (24.5%)
South and Central America	233 (1.7%)	159 (1.4%)	74 (2.9%)
South and East Asia	1,402 (10.2%)	1,011 (9.1%)	391 (15.1%)

Southern Europe	2,863 (20.8%)	2,394 (21.5%)	469 (18.1%)
Western Asia and North Africa	332 (2.4%)	272 (2.4%)	60 (2.3%)
Maternal education level			
Low ^a	1,923 (14.0%)	1,481 (13.3%)	442 (17.1%)
Medium or high ^b	10,742 (78.2%)	8,850 (79.4%)	1,892 (73.2%)
Unknown	1,063 (7.7%)	811 (7.3%)	252 (9.7%)
Type of maternal epilepsy			
Generalised	5,915 (43.1%)	4,987 (44.8%)	928 (35.9%)
Focal	7,046 (51.3%)	5,485 (49.2%)	1,561 (60.4%)
Undetermined	451 (3.3%)	396 (3.5%)	55 (2.1%)
Occurrence of seizures during pregnancy			
Any seizure type	5,011 (36.5%)	3,483 (31.3%)	1,528 (59.1%)
Tonic-clonic seizures ^c	2,301 (16.8%)	1,571 (14.1%)	730 (28.2%)
Other seizure types ^c	3,818 (27.8%)	2,598 (23.3%)	1,220 (47.2%)
Total seizure burden			
No seizures	8,717 (63.5%)	7,659 (68.7%)	1,058 (40.9%)
1-9 seizures	2,954 (21.5%)	2,159 (19.4%)	795 (30.7%)
10 or more seizures	1,709 (12.4%)	1,053 (9.5%)	656 (25.4%)
Unknown	348 (2.5%)	271 (2.4%)	77 (3.0%)
Primigravida			
Yes	7,167 (52.2%)	5,800 (52.9%)	1,367 (52.9%)
No	6,543 (47.7%)	5,326 (47.8%)	1,217 (47.1%)
Unknown	18 (0.1%)	16 (0.1%)	2 (0.1%)
Maternal tobacco smoking			
Yes	1,628 (11.9%)	1,267 (11.4%)	361 (14.0%)
No	12,046 (87.7%)	9,829 (88.2%)	2,217 (85.7%)
Unknown	54 (0.4%)	46 (0.4%)	8 (0.3%)
Maternal alcohol consumption			
Yes	1,340 (9.8%)	1,135 (10.2%)	205 (7.9%)
No	12,325 (89.8%)	9,952 (89.3%)	2,373 (91.8%)
Unknown	63 (0.5%)	55 (0.5%)	8 (0.3%)
Folic acid intake			
Pre- and post-conception ^d	4,579 (33.4%)	3,776 (33.9%)	803 (31.0%)
Post-conception only ^e	4,627 (33.7%)	3,699 (33.2%)	928 (35.9%)
No intake or underdosed ^f	3,142 (22.9%)	2,573 (23.1%)	569 (22.0%)
Unknown	1,380 (10.0%)	1,094 (9.8%)	286 (11.1%)
<i>Additional information</i>			
Parental history of MCMs			
Positive	136 (1.0%)	108 (1.0%)	28 (1.1%)
Negative	12,821 (93.4%)	10,442 (93.7%)	2,379 (92.0%)
Unknown	771 (5.6%)	592 (5.3%)	179 (6.9%)

Paternal education level			
Low ^a	2,044 (14.9%)	1,615 (14.5%)	429 (16.6%)
Medium or high ^b	10,279 (74.9%)	8,440 (75.7%)	1,839 (71.1%)
Unknown	1,405 (10.2%)	1,087 (9.8%)	318 (12.3%)

(a) ≤ 9 years of education; (b) > 9 years of education; (c) Some mothers had both ‘tonic-clonic seizures’ and ‘other seizure types’ during pregnancy, explaining why the sum of the counts for the two seizure categories exceed those for ‘any seizure type’; (d) folic acid supplementation of a dose ≥ 0.4 mg/day, initiated at least 3 months before conception and maintained throughout the first trimester at least; (e) folic acid supplementation of a dose ≥ 0.4 mg/day, initiated any time after conception; (f) no folic acid supplementation or any other supplementation.

ASM=antiseizure medication; LBW=low birthweight; MCM=major congenital malformations; SGA=small-for-gestational age.

Table S4. Relationship of ASM regimen (monotherapy vs polytherapy) and different indicators of fetal growth, with addition of maternal and paternal educational levels to model adjustments. Findings were obtained from four separate models, one for each indicator of fetal growth. A generalised linear mixed model was used for birthweight centile and applied to the entire study cohort except for offspring from Australia and New Zealand for whom parental educational level data were not available (N=14,701). Logistic regression models were used for small-for-gestational age (SGA), severe SGA, and low birthweight (LBW); due to failure of model convergence, logistic regression models were run on a subset comprising a single offspring (the first recorded in EURAP in case of multiple offspring) for each mother (n=12,718). Values are point estimates with 95% confidence intervals (95% CI). The widths of 95% CI have been adjusted for family-wise multiplicity with a false discovery rate of $q=5\%$. Bolded values indicate estimates with 95% CI not capturing the null hypothesis value.

Predictor	<i>b</i> [95% CI]	OR [95% CI]		
	Birthweight centile	SGA	Severe SGA	LBW
ASM polytherapy	-2.81 [-4.37 to -1.24]	1.51 [1.30 to 1.75]	1.54 [1.24 to 1.91]	1.52 [1.15 to 2.00]
Year of pregnancy	0.04 [-0.06 to 0.13]	0.99 [0.98 to 1.00]	0.99 [0.97 to 1.00]	1.00 [0.98 to 1.02]
Male offspring	8.84 [7.58 to 10.11]	0.58 [0.51 to 0.66]	0.59 [0.49 to 0.71]	0.64 [0.51 to 0.82]
Region of enrolment (ref: Western Europe)				
Eastern Europe	0.07 [-2.07 to 2.21]	0.86 [0.67 to 1.10]	0.61 [0.38 to 0.97]	0.67 [0.39 to 1.16]
Northern Europe	4.42 [2.78 to 6.06]	0.82 [0.69 to 0.96]	0.75 [0.58 to 0.96]	0.82 [0.60 to 1.12]
South and Central America	0.26 [-3.46 to 3.98]	0.72 [0.46 to 1.13]	0.71 [0.36 to 1.39]	0.96 [0.52 to 1.74]
South and East Asia	-19.22 [-21.94 to -16.51]	4.19 [3.37 to 5.22]	3.90 [2.90 to 5.26]	3.34 [2.29 to 4.87]
Southern Europe	-7.18 [-9.08 to -5.27]	1.45 [1.23 to 1.72]	1.39 [1.08 to 1.79]	1.13 [0.83 to 1.53]
Western Asia and North Africa	-6.91 [-10.76 to -3.05]	1.18 [0.86 to 1.61]	1.23 [0.77 to 1.96]	1.26 [0.69 to 2.28]
Maternal age at conception (years)	0.08 [-0.03 to 0.19]	1.01 [1.00 to 1.02]	1.01 [0.99 to 1.02]	1.01 [0.99 to 1.03]
Low maternal education level	-2.06 [-3.89 to -0.22]	1.07 [0.92 to 1.24]	1.14 [0.91 to 1.43]	1.03 [0.77 to 1.36]
Low paternal education level	-0.31 [-1.86 to 1.25]	1.08 [0.93 to 1.26]	1.14 [0.91 to 1.43]	1.21 [0.89 to 1.65]
Parental history of MCMs	-3.06 [-8.16 to 2.04]	1.57 [0.97 to 2.56]	2.00 [1.04 to 3.84]	1.96 [0.89 to 4.32]
Type of maternal epilepsy (ref: generalised)				
Focal	-1.35 [-2.55 to -0.15]	1.16 [1.03 to 1.30]	1.24 [1.03 to 1.48]	1.31 [1.04 to 1.66]
Undetermined	0.68 [-2.09 to 3.46]	1.20 [0.91 to 1.60]	1.38 [0.90 to 2.11]	0.89 [0.49 to 1.62]
Tonic-clonic seizures during pregnancy	-1.32 [-2.78 to 0.14]	1.15 [1.00 to 1.33]	1.17 [0.95 to 1.43]	1.31 [1.00 to 1.71]
Other seizure types during pregnancy	-0.28 [-1.42 to 0.87]	0.92 [0.81 to 1.04]	0.97 [0.83 to 1.13]	1.01 [0.83 to 1.23]
Primigravida	-5.60 [-6.87 to -4.33]	1.44 [1.27 to 1.65]	1.37 [1.14 to 1.64]	1.51 [1.18 to 1.94]
Maternal tobacco smoking	-6.05 [-8.00 to -4.10]	1.66 [1.39 to 1.99]	1.63 [1.26 to 2.11]	1.57 [1.10 to 2.23]

Maternal alcohol consumption	0.37 [-1.30 to 2.03]	0.90 [0.75 to 1.08]	1.04 [0.82 to 1.33]	0.92 [0.62 to 1.35]
Folate (ref: no intake or underdosed)				
Pre- and post-conception	-1.22 [-2.61 to 0.16]	1.04 [0.91 to 1.18]	0.94 [0.78 to 1.14]	1.00 [0.79 to 1.25]
Post-conception only	-0.47 [-1.78 to 0.84]	0.98 [0.87 to 1.12]	0.86 [0.70 to 1.05]	0.72 [0.54 to 0.97]

(a) Model for LBW was also adjusted for gestational age (weeks): OR=0.45 [95% CI: 0.42 to 0.48].

ASM=antiseizure medication; *b*=unstandardised model coefficient; LBW=low birthweight;

MCM=major congenital malformations; OR=odds ratio; ref=reference; SGA=small-for-gestational age.

Table S5. Relationship of ASM regimen (monotherapy vs polytherapy) and different indicators of fetal growth, with greater stratification of maternal folate intake among model adjustments. Findings were obtained from four separate models, one for each indicator of fetal growth. A generalised linear mixed model was used for birthweight centile and applied to the entire study cohort (N=15,893). Logistic regression models were used for SGA, severe SGA, and LBW; due to failure of model convergence, logistic regression models were run on a subset comprising a single offspring (the first recorded in EURAP in case of multiple offspring) for each mother (n=13,728). These models were adjusted for all variables used in other models (see legend of **Table 2**), except for maternal folate intake which was stratified into four categories instead of three, as follows: pre- and post-conception; post-conception only; underdosed; and no intake. Values are point estimates with 95% confidence intervals (95% CI). The widths of 95% CI have been adjusted for family-wise multiplicity with a false discovery rate of $q=5\%$. Bolded values indicate estimates with 95% CI not capturing the null hypothesis value.

Predictor	<i>b</i> [95% CI]	OR [95% CI]		
	Birthweight centile	SGA	Severe SGA	LBW ^a
ASM polytherapy	-2.78 [-4.27 to -1.30]	1.48 [1.29 to 1.71]	1.50 [1.23 to 1.83]	1.50 [1.15 to 1.95]
Year of pregnancy	0.05 [-0.04 to 0.14]	0.99 [0.98 to 1.00]	0.98 [0.97 to 1.00]	1.00 [0.98 to 1.01]
Male offspring	8.65 [7.42 to 9.85]	0.59 [0.52 to 0.66]	0.60 [0.50 to 0.72]	0.66 [0.52 to 0.83]
Region of enrolment (ref: Western Europe)				
Australia and New Zealand	4.00 [1.64 to 6.36]	0.76 [0.60 to 0.97]	0.81 [0.58 to 1.13]	0.86 [0.56 to 1.32]
Eastern Europe	-0.10 [-2.24 to 2.04]	0.87 [0.69 to 1.11]	0.63 [0.40 to 0.99]	0.68 [0.40 to 1.17]
Northern Europe	4.32 [2.68 to 5.95]	0.82 [0.70 to 0.97]	0.76 [0.59 to 0.97]	0.82 [0.60 to 1.12]
South and Central America	-0.06 [-3.68 to 3.56]	0.74 [0.48 to 1.14]	0.74 [0.38 to 1.43]	0.97 [0.54 to 1.77]
South and East Asia	-19.33 [-22.04 to -16.63]	4.24 [3.37 to 5.35]	4.03 [3.00 to 5.40]	3.43 [2.33 to 4.99]
Southern Europe	-7.47 [-9.35 to -5.59]	1.48 [1.26 to 1.75]	1.45 [1.13 to 1.85]	1.17 [0.86 to 1.58]
Western Asia and North Africa	-7.16 [-11.01 to -3.31]	1.19 [0.87 to 1.62]	1.25 [0.77 to 2.02]	1.26 [0.69 to 2.28]
Maternal age at conception (years)	0.08 [-0.03 to 0.19]	1.01 [1.00 to 1.02]	1.00 [0.99 to 1.02]	1.00 [0.99 to 1.02]
Parental history of MCMs	-2.01 [-6.85 to 2.82]	1.56 [0.99 to 2.47]	1.98 [1.06 to 3.72]	1.84 [0.85 to 3.97]
Type of maternal epilepsy (ref: generalised)				
Focal	-1.14 [-2.29 to 0.01]	1.14 [1.01 to 1.27]	1.23 [1.04 to 1.46]	1.31 [1.04 to 1.64]
Undetermined	0.60 [-2.11 to 3.31]	1.23 [0.93 to 1.63]	1.39 [0.91 to 2.12]	0.86 [0.47 to 1.59]
Tonic-clonic seizures during pregnancy	-1.36 [-2.77 to 0.05]	1.15 [1.00 to 1.32]	1.19 [0.98 to 1.45]	1.27 [0.98 to 1.66]
Other seizure types during pregnancy	-0.17 [-1.21 to 0.87]	0.93 [0.83 to 1.04]	0.97 [0.83 to 1.13]	1.02 [0.84 to 1.24]
Primigravida	-5.55 [-6.77 to -4.34]	1.40 [1.24 to 1.59]	1.32 [1.11 to 1.57]	1.43 [1.13 to 1.82]
Maternal tobacco smoking	-6.28 [-8.15 to -4.42]	1.70 [1.43 to 2.02]	1.77 [1.38 to 2.27]	1.65 [1.18 to 2.29]

Maternal alcohol consumption	0.39 [-1.19 to 1.97]	0.93 [0.79 to 1.09]	1.04 [0.83 to 1.32]	0.96 [0.69 to 1.35]
Folate (ref: no intake)				
Pre- and post-conception ^b	-1.45 [-4.30 to 1.41]	1.02 [0.79 to 1.30]	1.13 [0.77 to 1.66]	0.97 [0.76 to 1.22]
Post-conception only ^c	-0.99 [-3.75 to 1.78]	0.97 [0.76 to 1.24]	1.02 [0.71 to 1.46]	0.72 [0.54 to 0.95]
Underdosed ^d	-0.58 [-3.34 to 2.17]	1.00 [0.78 to 1.27]	1.19 [0.80 to 1.76]	1.74 [0.93 to 3.23]

(a) Model for LBW was also adjusted for gestational age (weeks): OR=0.44 [95% CI: 0.41 to 0.47];
 (b) folic acid supplementation of a dose ≥ 0.4 mg/day, initiated at least 3 months before conception and maintained throughout the first trimester at least; (c) folic acid supplementation of a dose ≥ 0.4 mg/day, initiated any time after conception; (d) any other folic acid supplementation.

ASM=antiseizure medication; *b*=unstandardised model coefficient; LBW=low birthweight; MCM=major congenital malformations; OR=odds ratio; ref=reference; SGA=small-for-gestational age.

Table S6. Relationship of ASM regimen (monotherapy vs polytherapy) and different indicators of fetal growth, with addition of total seizure burden to model adjustments.

Findings were obtained from four separate models, one for each indicator of fetal growth. A generalised linear mixed model was used for birthweight centile and applied to the entire study cohort (N=15,893). Logistic regression models were used for SGA, severe SGA, and LBW; due to failure of model convergence, logistic regression models were run on a subset comprising a single offspring (the first recorded in EURAP in case of multiple offspring) for each mother (n=13,728). Values are point estimates with 95% confidence intervals (95% CI). The widths of 95% CI have been adjusted for family-wise multiplicity with a false discovery rate of $q=5\%$. Bolded values indicate estimates with 95% CI not capturing the null hypothesis value.

Predictor	<i>b</i> [95% CI]	OR [95% CI]		
	Birthweight centile	SGA	Severe SGA	LBW
ASM polytherapy	-2.71 [-4.19 to -1.23]	1.49 [1.29 to 1.71]	1.51 [1.23 to 1.86]	1.47 [1.13 to 1.91]
Year of pregnancy	0.05 [-0.04 to 0.14]	0.99 [0.98 to 1.00]	0.98 [0.97 to 1.00]	1.00 [0.98 to 1.01]
Male offspring	8.63 [7.41 to 9.86]	0.59 [0.52 to 0.66]	0.60 [0.50 to 0.72]	0.65 [0.52 to 0.83]
Region of enrolment (ref: Western Europe)				
Australia and New Zealand	4.04 [1.65 to 6.42]	0.76 [0.60 to 0.97]	0.81 [0.58 to 1.15]	0.84 [0.55 to 1.30]
Eastern Europe	-0.10 [-2.23 to 2.04]	0.87 [0.68 to 1.11]	0.63 [0.40 to 1.00]	0.69 [0.40 to 1.19]
Northern Europe	4.35 [2.70 to 6.00]	0.82 [0.70 to 0.97]	0.76 [0.59 to 0.98]	0.83 [0.60 to 1.14]
South and Central America	-0.04 [-3.66 to 3.58]	0.74 [0.48 to 1.14]	0.73 [0.38 to 1.43]	1.01 [0.56 to 1.83]
South and East Asia	-19.39 [-22.12 to -16.66]	4.25 [3.42 to 5.28]	4.01 [2.98 to 5.40]	3.52 [2.41 to 5.14]
Southern Europe	-7.47 [-9.37 to -5.57]	1.48 [1.26 to 1.75]	1.45 [1.13 to 1.85]	1.18 [0.87 to 1.60]
Western Asia and North Africa	-7.15 [-11.10 to -3.20]	1.19 [0.87 to 1.63]	1.24 [0.77 to 1.99]	1.28 [0.71 to 2.33]
Maternal age at conception (years)	0.08 [-0.03 to 0.19]	1.01 [1.00 to 1.02]	1.00 [0.99 to 1.02]	1.00 [0.99 to 1.02]
Parental history of MCMs	-1.97 [-6.76 to 2.83]	1.57 [0.99 to 2.48]	1.99 [1.06 to 3.75]	1.80 [0.82 to 3.92]
Type of maternal epilepsy (ref: generalised)				
Focal	-1.11 [-2.23 to 0.02]	1.14 [1.01 to 1.27]	1.23 [1.03 to 1.46]	1.30 [1.04 to 1.62]
Undetermined	0.58 [-2.09 to 3.25]	1.23 [0.92 to 1.63]	1.38 [0.90 to 2.13]	0.87 [0.48 to 1.58]
Tonic-clonic seizures during pregnancy	-2.19 [-4.38 to -0.01]	1.23 [1.00 to 1.51]	1.17 [0.88 to 1.56]	1.12 [0.79 to 1.59]
Other seizure types during pregnancy	-0.91 [-3.34 to 1.51]	1.01 [0.81 to 1.26]	0.97 [0.71 to 1.33]	0.78 [0.50 to 1.22]
Frequency of any seizure type (ref: no seizures)				
1 to 9 seizures	1.45 [-1.18 to 4.08]	0.90 [0.70 to 1.15]	1.02 [0.73 to 1.43]	1.23 [0.76 to 1.98]
10 or more seizures	0.23 [-2.67 to 3.13]	0.90 [0.67 to 1.22]	0.93 [0.61 to 1.42]	1.63 [0.87 to 3.06]
Primigravida	-5.56 [-6.78 to -4.34]	1.40 [1.24 to 1.59]	1.32 [1.11 to 1.58]	1.43 [1.12 to 1.82]
Maternal tobacco smoking	-6.27 [-8.15 to -4.39]	1.70 [1.43 to 2.03]	1.77 [1.37 to 2.27]	1.64 [1.16 to 2.31]

Maternal alcohol consumption	0.40 [-1.15 to 1.96]	0.93 [0.79 to 1.09]	1.05 [0.83 to 1.32]	0.96 [0.69 to 1.34]
Folate (ref: no intake or underdosed)				
Pre- and post-conception	-0.86 [-2.16 to 0.45]	1.02 [0.90 to 1.15]	0.95 [0.79 to 1.14]	0.96 [0.76 to 1.22]
Post-conception only	-0.40 [-1.64 to 0.85]	0.98 [0.86 to 1.10]	0.86 [0.70 to 1.05]	0.71 [0.53 to 0.94]

(a) Model for LBW was also adjusted for gestational age (weeks): OR=0.44 [95% CI: 0.41 to 0.47].

ASM=antiseizure medication; *b*=unstandardised model coefficient; LBW=low birthweight;

MCM=major congenital malformations; OR=odds ratio; ref=reference; SGA=small-for-gestational age.

Table S7. Relationship of ASM regimen (monotherapy vs polytherapy) and different indicators of fetal growth in offspring born to mothers who were seizure-free during pregnancy. Findings were obtained from four separate models, one for each indicator of fetal growth. A generalised linear mixed model was used for birthweight centile and applied to all offspring born to mothers who were seizure-free during pregnancy (N=10,229). Logistic regression models were used for SGA, severe SGA, and LBW; due to failure of model convergence, logistic regression models were run on a subset comprising a single offspring (the first recorded in EURAP in case of multiple offspring) for each mother (n=8,717). Given that the models were applied to offspring of mothers who did not experience seizures during pregnancy, no adjustment for occurrence of tonic-clonic seizures or other seizure types during pregnancy was made. Values are point estimates with 95% confidence intervals (95% CI). The widths of 95% CI have been adjusted for family-wise multiplicity with a false discovery rate of $q=5\%$. Bolded values indicate estimates with 95% CI not capturing the null hypothesis value.

Predictor	<i>b</i> [95% CI]	OR [95% CI]		
	Birthweight centile	SGA	Severe SGA	LBW ^a
ASM polytherapy	-3.24 [-5.35 to -1.13]	1.55 [1.26 to 1.90]	1.65 [1.23 to 2.21]	1.61 [1.07 to 2.43]
Year of pregnancy	0.07 [-0.05 to 0.18]	0.99 [0.98 to 1.00]	0.98 [0.97 to 1.00]	1.00 [0.97 to 1.02]
Male offspring	8.67 [7.17 to 10.17]	0.60 [0.52 to 0.70]	0.61 [0.49 to 0.77]	0.68 [0.50 to 0.92]
Region of enrolment (ref: Western Europe)				
Australia and New Zealand	4.47 [1.47 to 7.48]	0.70 [0.50 to 0.97]	0.78 [0.48 to 1.26]	1.02 [0.58 to 1.81]
Eastern Europe	0.68 [-1.97 to 3.33]	0.84 [0.62 to 1.14]	0.63 [0.35 to 1.12]	0.92 [0.50 to 1.70]
Northern Europe	5.46 [3.40 to 7.53]	0.79 [0.65 to 0.98]	0.75 [0.54 to 1.04]	0.93 [0.61 to 1.42]
South and Central America	-2.11 [-7.69 to 3.46]	0.89 [0.51 to 1.55]	0.90 [0.37 to 2.20]	1.32 [0.50 to 3.49]
South and East Asia	-19.62 [-22.97 to -16.27]	4.55 [3.47 to 5.98]	4.88 [3.32 to 7.15]	4.85 [2.90 to 8.09]
Southern Europe	-6.54 [-8.83 to -4.25]	1.54 [1.25 to 1.89]	1.62 [1.18 to 2.22]	1.40 [0.90 to 2.16]
Western Asia and North Africa	-7.34 [-12.27 to -2.41]	1.34 [0.88 to 2.04]	1.46 [0.76 to 2.80]	2.04 [0.86 to 4.81]
Maternal age at conception (years)	0.08 [-0.06 to 0.21]	1.00 [0.99 to 1.02]	1.00 [0.98 to 1.02]	1.00 [0.97 to 1.02]
Parental history of MCMs	-2.51 [-8.42 to 3.41]	1.54 [0.85 to 2.78]	2.28 [1.00 to 5.19]	1.84 [0.60 to 5.66]
Type of maternal epilepsy (ref: generalised)				
Focal	-1.52 [-2.89 to -0.16]	1.16 [1.01 to 1.32]	1.21 [0.99 to 1.49]	1.28 [0.96 to 1.70]
Undetermined	0.12 [-2.91 to 3.14]	1.20 [0.86 to 1.67]	1.16 [0.68 to 1.99]	0.71 [0.29 to 1.73]
Primigravida	-5.64 [-7.15 to -4.13]	1.34 [1.16 to 1.55]	1.44 [1.14 to 1.82]	1.45 [1.06 to 1.98]
Maternal tobacco smoking	-5.01 [-7.31 to -2.71]	1.64 [1.31 to 2.06]	1.63 [1.18 to 2.24]	1.57 [0.99 to 2.50]
Maternal alcohol consumption	-0.88 [-2.89 to 1.13]	0.99 [0.82 to 1.21]	1.16 [0.84 to 1.59]	1.08 [0.67 to 1.74]
Folate (ref: no intake or underdosed)				

Pre- and post-conception	-1.39 [-3.04 to 0.25]	1.14 [0.96 to 1.35]	1.06 [0.83 to 1.36]	1.06 [0.76 to 1.48]
Post-conception only	-1.00 [-2.66 to 0.65]	1.01 [0.86 to 1.17]	0.97 [0.77 to 1.23]	0.67 [0.45 to 1.00]

(a) Model for LBW was also adjusted for gestational age (weeks): OR=0.42 [95% CI: 0.38 to 0.47].

ASM=antiseizure medication; *b*=unstandardised model coefficient; LBW=low birthweight; MCM=major congenital malformations; OR=odds ratio; ref=reference; SGA=small-for-gestational age.

Table S8. Strength of association between individual ASM monotherapy daily doses and different indicators of fetal growth. For each of the eight common monotherapies, separate models were used to assess the relationship between maternal daily doses at conception, expressed as prescribed daily dose/defined daily dose (PDD/DDD), and each fetal growth indicator. The generalised linear mixed model was used for birthweight centile and applied to the entirety of offspring exposed to a specific monotherapy. Logistic regression models were used for SGA, severe SGA, and LBW; due to failure of model convergence, these models were run on a subset comprising only a single offspring (the first recorded in EURAP in case of multiple offspring) for each mother. Values are point estimates with 95% confidence intervals (95% CI), adjusted for clinicodemographic confounders. Bolded values indicate estimates with 95% CI that do not capture the null hypothesis value.

ASM	Birthweight centile Adjusted <i>b</i> [95% CI]	SGA Adjusted OR [95% CI]*	Severe SGA Adjusted OR [95% CI]*	LBW Adjusted OR [95% CI]*
Lamotrigine	0.08 [0.02 to 0.13]	0.79 [0.62 to 1.01]	0.99 [0.97 to 1.01]	1.00 [0.98 to 1.03]
Carbamazepine	-1.24 [-4.61 to 2.77]	1.40 [0.93 to 2.12]	1.82 [0.98 to 3.35]	1.86 [0.79 to 4.39]
Levetiracetam	1.13 [-1.67 to 3.92]	0.94 [0.71 to 1.25]	0.95 [0.60 to 1.51]	0.56 [0.25 to 1.29]
Oxcarbazepine	-5.59 [-12.14 to 0.97]	2.20 [1.16 to 4.19]	1.58 [0.72 to 3.44]	1.15 [0.45 to 2.94]
Phenobarbital	-2.47 [-7.84 to 2.80]	1.03 [0.68 to 1.57]	0.96 [0.43 to 2.11]	1.43 [0.42 to 4.93]
Phenytoin	4.97 [-11.26 to 21.20]	0.84 [0.08 to 8.49]	0.41 [0.01 to 18.69]	1.23 [0.03 to 45.99]
Topiramate	-2.65 [-13.97 to 8.68]	0.68 [0.20 to 2.32]	3.73 [0.52 to 26.86]	0.77 [0.08 to 7.23]
Valproic acid	-3.68 [-10.06 to 2.69]	1.86 [0.93 to 3.73]	2.49 [0.84 to 7.38]	3.80 [0.86 to 16.73]

*The estimates represent the change in odds for a 1 unit change in prescribed daily dose/defined daily dose (PDD/DDD) for each ASM.

ASM=antiseizure medication; *b*=unstandardised model coefficient; LBW=low birthweight; OR=odds ratio; ref=reference; SGA=small-for-gestational age.

Table S9. Comparative risk of small-for-gestational age (SGA) associated with different dose ranges for oxcarbazepine. Dose ranges (low, mid, high) were established using a cutoff-optimisation algorithm.²¹ Bolded values indicate estimates with 95% CI that do not capture the null hypothesis value.

ASM	Dose range (mg/day)			SGA, n (%)			OR [95% CI]	
	Low	Mid	High	Low	Mid	High	Mid vs Low	High vs Low
Oxcarbazepine	<1100	>1100 to <1700	>1700	62 (22.1%)	39 (26.2%)	24 (38.1%)	1.60 [0.80 to 3.19]	3.47 [1.27 to 9.50]

OR=odds ratio; SGA=small-for-gestational age.

Table S10. Relationship of ASM regimen (monotherapy vs polytherapy) and different indicators of fetal growth in offspring exposed only to carbamazepine, lamotrigine, levetiracetam, phenytoin and/or valproic acid. Findings were obtained from four separate models, one for each indicator of fetal growth. A generalised linear mixed model was used for birthweight centile and applied to offspring exposed only to any of the above-listed ASMs (N=12,517). Logistic regression models were used for SGA, severe SGA, and LBW; due to failure of model convergence, logistic regression models were run on a subset comprising a single offspring (the first recorded in EURAP in case of multiple offspring) for each mother (n=10,788). Values are point estimates with 95% confidence intervals (95% CI). The widths of 95% CI have been adjusted for family-wise multiplicity with a false discovery rate of $q=5\%$. Bolded values indicate estimates with 95% CI not capturing the null hypothesis value.

Predictor	<i>b</i> [95% CI]	OR [95% CI]		
	Birthweight centile	SGA	Severe SGA	LBW
ASM polytherapy	0.22 [-1.51 to 1.95]	1.22 [0.99 to 1.49]	1.12 [0.86 to 1.48]	1.10 [0.76 to 1.59]
Year of pregnancy	0.02 [-0.08 to 0.12]	1.00 [0.99 to 1.01]	0.99 [0.97 to 1.00]	1.00 [0.98 to 1.02]
Male offspring	8.97 [7.50 to 10.44]	0.57 [0.50 to 0.66]	0.60 [0.48 to 0.75]	0.68 [0.51 to 0.91]
Region of enrolment (ref: Western Europe)				
Australia and New Zealand	3.93 [1.28 to 6.58]	0.73 [0.55 to 0.97]	0.79 [0.52 to 1.20]	0.92 [0.57 to 1.51]
Eastern Europe	-0.80 [-3.34 to 1.75]	0.85 [0.64 to 1.12]	0.77 [0.47 to 1.24]	0.86 [0.48 to 1.57]
Northern Europe	4.68 [2.89 to 6.47]	0.80 [0.66 to 0.96]	0.82 [0.62 to 1.08]	0.92 [0.65 to 1.30]
South and Central America	-0.61 [-5.15 to 3.94]	0.77 [0.46 to 1.30]	0.68 [0.28 to 1.68]	1.51 [0.67 to 3.41]
South and East Asia	-19.80 [-22.85 to -16.75]	4.34 [3.35 to 5.62]	4.43 [3.08 to 6.39]	4.17 [2.61 to 6.68]
Southern Europe	-6.94 [-9.07 to -4.81]	1.46 [1.20 to 1.77]	1.58 [1.17 to 2.15]	1.20 [0.83 to 1.76]
Western Asia and North Africa	-7.59 [-11.89 to -3.29]	1.27 [0.88 to 1.83]	1.59 [0.90 to 2.82]	1.57 [0.77 to 3.23]
Maternal age at conception (years)	0.09 [-0.04 to 0.22]	1.01 [0.99 to 1.02]	1.01 [0.99 to 1.02]	1.01 [0.98 to 1.03]
Parental history of MCMs	-2.60 [-8.12 to 2.92]	1.42 [0.83 to 2.44]	1.64 [0.76 to 3.52]	1.37 [0.53 to 3.53]
Type of maternal epilepsy (ref: generalised)				
Focal	-0.70 [-1.91 to 0.52]	1.11 [0.98 to 1.25]	1.28 [1.04 to 1.57]	1.30 [0.99 to 1.72]
Undetermined	0.89 [-2.08 to 3.86]	1.24 [0.90 to 1.71]	1.64 [1.00 to 2.69]	1.02 [0.55 to 1.89]
Tonic-clonic seizures during pregnancy	-1.45 [-3.12 to 0.23]	1.16 [0.98 to 1.38]	1.37 [1.06 to 1.78]	1.35 [0.96 to 1.88]
Other seizure types during pregnancy	-0.21 [-1.43 to 1.00]	0.94 [0.82 to 1.07]	0.99 [0.82 to 1.19]	1.06 [0.82 to 1.38]
Primigravida	-5.80 [-7.18 to -4.43]	1.41 [1.23 to 1.63]	1.37 [1.11 to 1.69]	1.47 [1.09 to 1.96]
Maternal tobacco smoking	-5.98 [-8.11 to -3.86]	1.74 [1.42 to 2.13]	1.75 [1.30 to 2.37]	1.60 [1.06 to 2.41]
Maternal alcohol consumption	0.11 [-1.53 to 1.75]	0.93 [0.77 to 1.11]	1.13 [0.86 to 1.50]	1.08 [0.73 to 1.60]
Folate (ref: no intake or underdosed)				
Pre- and post-conception	-1.34 [-2.91 to 0.22]	1.10 [0.94 to 1.28]	1.12 [0.89 to 1.42]	1.06 [0.79 to 1.43]

Post-conception only	-1.05 [-2.56 to 0.47]	1.06 [0.91 to 1.22]	0.97 [0.77 to 1.21]	0.83 [0.59 to 1.17]
----------------------	-----------------------	---------------------	---------------------	---------------------

(a) Model for LBW was also adjusted for gestational age (weeks): OR=0.42 [95% CI: 0.39 to 0.46].

ASM=antiseizure medication; *b*=unstandardized model coefficient; LBW=low birthweight; MCM=major congenital malformations; OR=odds ratio; ref=reference; SGA=small-for-gestational age.

Table S11. Strength of association of the most common ASM polytherapies with different indicators of fetal growth, relative to

lamotrigine monotherapy. The generalised linear mixed model used to model birthweight centile was applied to offspring exposed to either the most common ASM polytherapies in the study population (lamotrigine and levetiracetam; lamotrigine and valproic acid; and carbamazepine and levetiracetam) or lamotrigine monotherapy (n=5,573). Due to failure of model convergence, the logistic regression models used for SGA, severe SGA, and LBW were run on a subset comprising only a single offspring (the first recorded in EURAP in case of multiple offspring) for each mother (n=4,771). Values are point estimates with 95% confidence intervals (95% CI), adjusted for clinicodemographic confounders. Bolded values indicate estimates with 95% CI that do not capture the null hypothesis value.

ASM exposure	Birthweight centile		SGA		Severe SGA		LBW	
	Mean $\pm$ SD	Adjusted <i>b</i> [95% CI]	n (%)	Adjusted OR [95% CI]	n (%)	Adjusted OR [95% CI]	n (%)	Adjusted OR [95% CI]
Lamotrigine	42.3 $\pm$ 28.6	ref	583 (14.6%)	ref	204 (5.1%)	ref	177 (4.4%)	ref
Lamotrigine + levetiracetam	41.9 $\pm$ 28.9	0.19 [-2.67 to 3.06]	75 (18.6%)	1.32 [0.94 to 1.87]	25 (6.2%)	1.24 [0.73 to 2.10]	27 (6.7%)	1.41 [0.73 to 2.72]
Lamotrigine + valproic acid	41.4 $\pm$ 29.7	0.11 [-3.59 to 3.82]	49 (21.5%)	1.51 [0.97 to 2.37]	17 (7.5%)	1.33 [0.70 to 2.52]	12 (5.3%)	1.20 [0.54 to 2.66]
Carbamazepine + levetiracetam	37.1 $\pm$ 27.8	-6.27 [-12.03 to -0.50]	33 (22.3%)	1.86 [1.06 to 3.25]	10 (6.8%)	1.31 [0.62 to 2.75]	10 (6.8%)	2.10 [0.77 to 5.74]

ASM=antiseizure medication; *b*=unstandardised model coefficient; LBW=low birthweight; OR=odds ratio; ref=reference; SGA=small-for-gestational age

Figure S1. Relationship between number of concomitantly used ASMs and different indicators of poor fetal growth. (A) Mean birthweight centiles in offspring exposed to 1 through ≥ 4 ASMs, with monotherapy exposure as reference. (B-D) Prevalence of SGA (B), severe SGA (C) and LBW (D) in offspring exposed to 1 through ≥ 4 ASMs, with monotherapy exposure as reference. Aligned with the models run in the study, mean birthweight centiles were obtained from the entire study cohort ($n=15,893$), whereas prevalence estimates for SGA, severe SGA and LBW were computed on the study subset comprising only a single offspring (the first recorded in EURAP in case of multiple offspring) for each mother ($n=13,728$). ASM=antiseizure medication; LBW=low birthweight; SGA=small-for-gestational age.

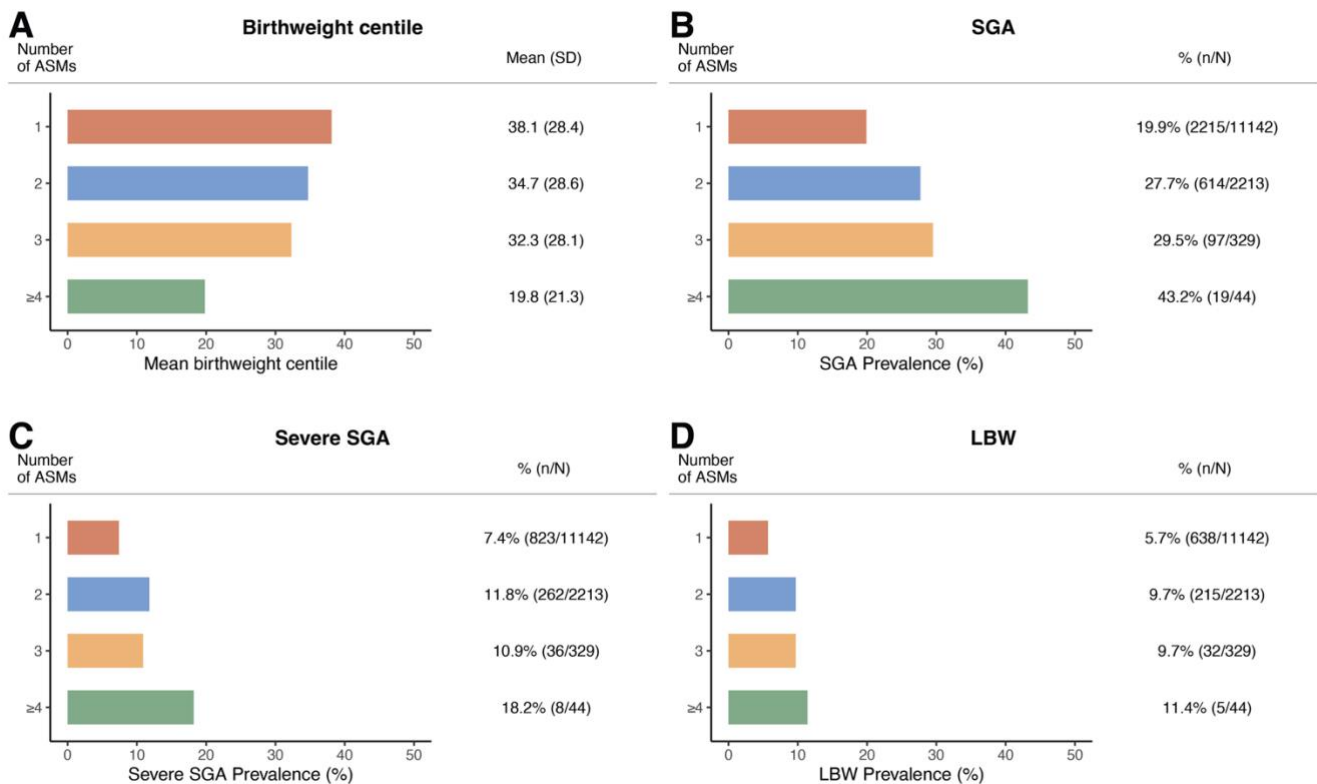
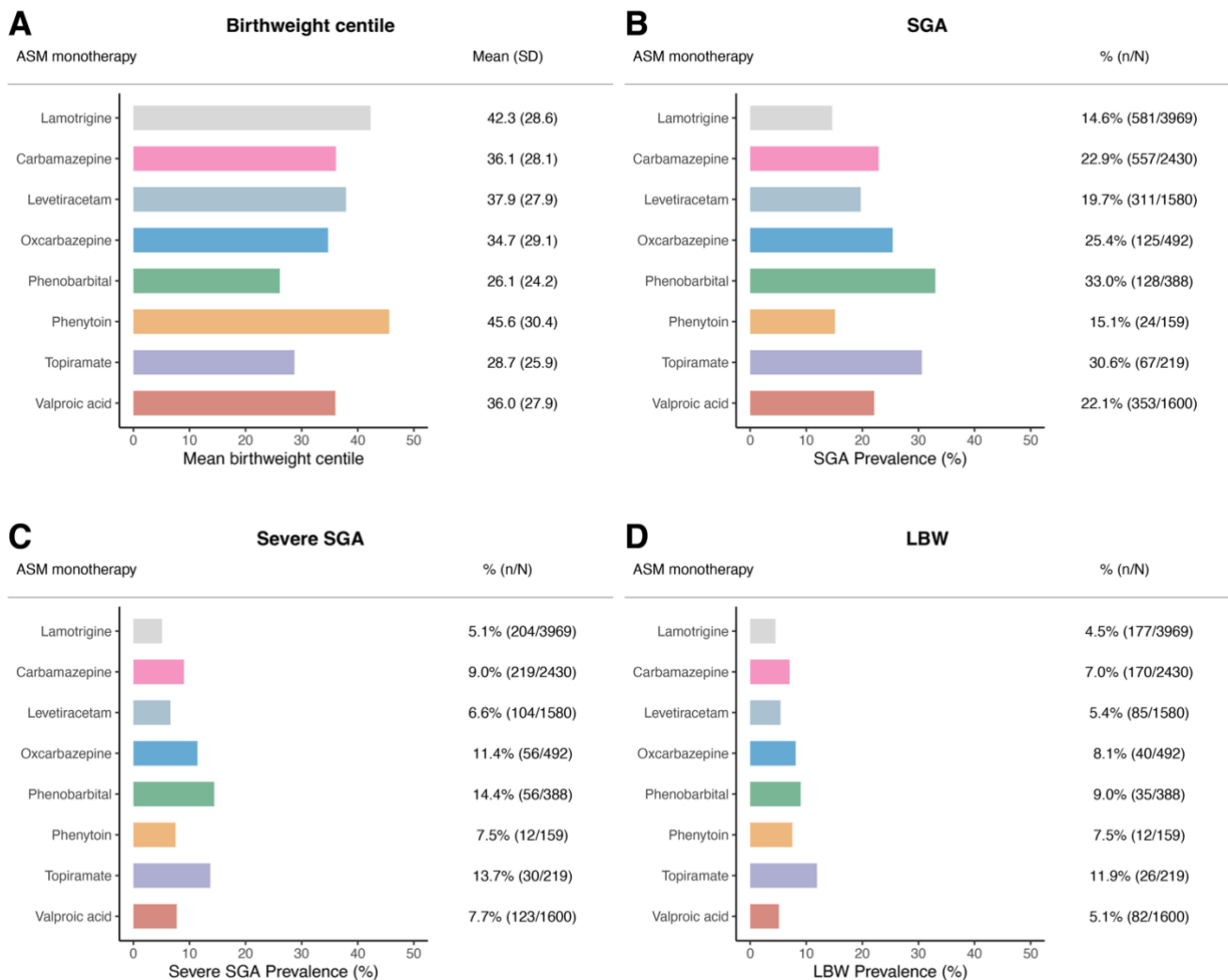


Figure S2. Relationship between individual ASM monotherapies and different indicators of fetal growth. (A) Mean birthweight centiles in offspring exposed to individual ASM monotherapies, with lamotrigine as reference. (B-D) Prevalence of SGA (B), severe SGA (C) and LBW (D) in offspring exposed to individual ASM monotherapies, with lamotrigine as reference. Aligned with the models run in the study, mean birthweight centiles were obtained from offspring exposed to any of eight common monotherapies (n=12,523), whereas prevalence estimates for SGA, severe SGA and LBW were computed on the study subset comprising only a single offspring (the first recorded in EURAP in case of multiple offspring) for each mother (n=10,837). ASM=antiseizure medication; LBW=low birthweight; SGA=small-for-gestational age.



References

1. Corsello G, Giuffre M. Congenital malformations. *J Matern Fetal Neonatal Med* 2012; **25 Suppl 1**: 25-9.
2. Townsend R, Khalil A. Fetal growth restriction in twins. *Best Pract Res Clin Obstet Gynaecol* 2018; **49**: 79-88.
3. Wang S, Yang L, Shang L, et al. Changing trends of birth weight with maternal age: a cross-sectional study in Xi'an city of Northwestern China. *BMC Pregnancy Childbirth* 2020; **20**(1): 744.
4. Mills JL, Graubard BI, Harley EE, Rhoads GG, Berendes HW. Maternal alcohol consumption and birth weight. How much drinking during pregnancy is safe? *JAMA* 1984; **252**(14): 1875-9.
5. Chung MH, Shin CO, Lee J. TORCH (toxoplasmosis, rubella, cytomegalovirus, and herpes simplex virus) screening of small for gestational age and intrauterine growth restricted neonates: efficacy study in a single institute in Korea. *Korean J Pediatr* 2018; **61**(4): 114-20.
6. Wedi CO, Kirtley S, Hopewell S, Corrigan R, Kennedy SH, Hemelaar J. Perinatal outcomes associated with maternal HIV infection: a systematic review and meta-analysis. *Lancet HIV* 2016; **3**(1): e33-48.
7. Huang QT, Hang LL, Zhong M, Gao YF, Luo ML, Yu YH. Maternal HCV infection is associated with intrauterine fetal growth disturbance: A meta-analysis of observational studies. *Medicine (Baltimore)* 2016; **95**(35): e4777.
8. Lamont RF, Sobel JD, Carrington D, et al. Varicella-zoster virus (chickenpox) infection in pregnancy. *BJOG* 2011; **118**(10): 1155-62.
9. Sheikh J, Allotey J, Kew T, et al. Effects of race and ethnicity on perinatal outcomes in high-income and upper-middle-income countries: an individual participant data meta-analysis of 2 198 655 pregnancies. *Lancet* 2022; **400**(10368): 2049-62.
10. Battino D, Tomson T, Bonizzoni E, et al. Risk of Major Congenital Malformations and Exposure to Antiseizure Medication Monotherapy. *JAMA Neurol* 2024; **81**(5): 481-9.
11. Hodgetts VA, Morris RK, Francis A, Gardosi J, Ismail KM. Effectiveness of folic acid supplementation in pregnancy on reducing the risk of small-for-gestational age neonates: a population study, systematic review and meta-analysis. *BJOG* 2015; **122**(4): 478-90.
12. Guo H, Mao B, Wang M, et al. Folic acid supplementation, dietary folate intake and risk of small for gestational age in China. *Public Health Nutr* 2020; **23**(11): 1965-73.
13. Drever HJ, Davidson SJ, Callaway LK, Sekar R, SJ DEJ. Factors associated with higher risk of small-for-gestational-age infants in women treated for gestational diabetes. *Aust N Z J Obstet Gynaecol* 2023; **63**(5): 714-20.
14. Hogeveen M, Blom HJ, den Heijer M. Maternal homocysteine and small-for-gestational-age offspring: systematic review and meta-analysis. *Am J Clin Nutr* 2012; **95**(1): 130-6.
15. Chen YH, Chiou HY, Lin HC, Lin HL. Affect of seizures during gestation on pregnancy outcomes in women with epilepsy. *Arch Neurol* 2009; **66**(8): 979-84.
16. Hinkle SN, Albert PS, Mendola P, et al. The association between parity and birthweight in a longitudinal consecutive pregnancy cohort. *Paediatr Perinat Epidemiol* 2014; **28**(2): 106-15.
17. Kong L, Nilsson IAK, Gissler M, Lavebratt C. Associations of Maternal Diabetes and Body Mass Index With Offspring Birth Weight and Prematurity. *JAMA Pediatr* 2019; **173**(4): 371-8.
18. Grundy S, Lee P, Small K, Ahmed F. Maternal region of origin and Small for gestational age: a cross-sectional analysis of Victorian perinatal data. *BMC Pregnancy Childbirth* 2021; **21**(1): 409.

19. Zheng W, Suzuki K, Tanaka T, Kohama M, Yamagata Z, Okinawa Child Health Study G. Association between Maternal Smoking during Pregnancy and Low Birthweight: Effects by Maternal Age. *PLoS One* 2016; **11**(1): e0146241.
20. Agay-Shay K, Rudolf M, Rubin L, Haklai Z, Grotto I. Trends in Fetal Growth Between 2000 to 2014 in Singleton Live Births from Israel. *Sci Rep* 2018; **8**(1): 1089.
21. Tomson T, Battino D, Bonizzoni E, et al. Comparative risk of major congenital malformations with eight different antiepileptic drugs: a prospective cohort study of the EURAP registry. *Lancet Neurol* 2018; **17**(6): 530-8.