



Cohort Profile

Cohort Profile: The European Longitudinal Study of Pregnancy and Childhood (ELSPAC) in the Czech Republic

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Why was the cohort set up?

The Czech ELSPAC study was set up as a part of the European Longitudinal Study of Pregnancy and Childhood (ELSPAC). ELSPAC was designed as a population-based prospective longitudinal birth cohort study to investigate the effects of biological, psychosocial, economic and environmental factors on pregnancy, delivery and subsequent child's development and health.¹ The study was initiated by the World Health Organization (WHO) Regional Office for Europe in 1985, with the aim to enrol 40 000 children across Europe. Seven independent centres—ALSPAC,² Isle of Man,³ the Czech Republic, Slovakia, Ukraine,⁴ Greece and Russia—joined the project, coordinated by Professor Golding at Bristol University, UK. The coordination centre was also responsible for most of the protocol development, including follow-up planning and questionnaire design.

Enrolment of the Czech participants started in 1991. In addition to the primary aims of ELSPAC, the Czech team was interested also in the effects of the profound socio-economic changes related to the societal transformation after the fall of Communism in 1989.

Who is in the Czech cohort?

The birth cohort consists of children born in the Brno and Znojmo regions (South Moravia, Czech Republic) in 1991 and 1992. Some data are also available on their mothers and fathers.

Ethical issues and data protection

A project ethics committee was set up at the beginning of the project by the coordinating team, to promote the international legal and ethics framework of the study design. At national level, the study was approved by local ethics committees. Informed consent was sought from all study participants during each wave of data collection, when using both self-administered questionnaires and transcription of the medical records. The informed consent form and the information leaflet for the study participant were integral parts of each questionnaire. Confidentiality and data protection were important and only anonymous (often aggregated) data are available for the research purposes. Each participant was assigned a unique code by the database system and the participants' names, birth dates and contact details are kept separately.

Study population and study participants

The study population was defined as all pregnancies and births in the two selected regions of the Czech Republic (Brno and Znojmo) in 1991 and 1992. The Brno region, mostly consisting of Brno city and adjacent suburbs, has approximately 400 000 inhabitants. It is a cultural, educational and administrative centre of the South Moravian region. The Znojmo district has over 113 000 inhabitants, and it is a typical rural region with economy based on agriculture and light industry. Over 99% of the residents in both regions consisted of the Czech ethnic group in 1991-92.

Eligibility and enrolment process

The eligibility of pregnant women was defined by their residency in the selected geographical study area (defined by postcodes) and their expected date of delivery between 1 March 1991 and 30 June 1992. Those expected to move from the study areas were not included. Mothers were enrolled between the ultrasound examination at the 20 week of pregnancy and the birth. Eligible mothers received information about the study from their obstetricians who forwarded to the study team contact details of women who were interested in the study. Only these women were subsequently officially invited to participate in the study via mail. Following their enrolment, mothers were given a first set of questionnaires. Participating women also invited their partners to join the study.

Numbers of participants at baseline

Information on 7589 children (5738 children from Brno and 1851 children from Znojmo regions, including 81 twins and one set of triplets) was collected from medical records during the first study wave (96% of all eligible births). From these births, 5151 mothers (4811 enrolled during their pregnancy and 340 during their hospital stay) and 4653 fathers completed a self-reported questionnaire during pregnancy and at least one questionnaire after the child was born. Characteristics of births and mothers who completed the baseline questionnaire, as well as comparison with the overall population, are described in Table 1. The remaining 2438 mothers provided their consent for collection of data on their children using medical records but they did not complete questionnaires.

How often have they been followed up?

The follow-up is described in Figure 1. Data from medical records of pregnant women (including the first-trimester

Table 1. Baseline characteristics of cohort participants at baseline and at age 19 (only participants with informed consent and with data from both medical records and questionnaires), and characteristics of the study population

	Entire study population ^a	Cohort participants, baseline	Cohort participants retained until age 19
Number of births	7895	5151	984
Maternal education (%)			
Primary	45.4%	40.1%	21.2%
Secondary	40.8%	36.5%	37.9%
University	13.7%	16.3%	21.8%
Missing	–	7.1%	19.1%
Maternal marital status (%)			
Married	88.1%	79.5%	72.6%
Single	8.8%	8.9%	6.2%
Divorced/widowed	3.1%	2.5%	2.3%
Missing	–	9.0%	19.0%
Maternal age < 20 years	13.3%	9.9%	6.5%
Birthweight (< 2500g)	5.7%	4.4%	5.0%

^aStudy population: all birth in the Brno and Znojmo region III/1991-VI/1992, data from the national birth register.

medical assessments) were collected retrospectively at the time of the birth. Self-reported questionnaires for mothers and fathers were administered at 6th and 18th months after birth, and subsequently during the 3rd, 5th, 7th, 11th, 15th and 19th years of the child. Questionnaires on the child health, development and behaviour were completed by mothers (or primary carers) in the same time periods [6 months (m), 18 m, 3 years (y), 5 y, 7 y, 11 y, 15 y, 18 y and 19 y]. From the age of 11 y, self-reported questionnaires were also distributed to children (at 11 y, 15 y, 18 y and 19 y). Self-reported data were complemented with information from paediatrician's medical records (for ages 8 m, 18 m, 3 y, 5 y, 7 y, 8 y, 11 y, 13 y, 15 y, 18 y and 19 y). In addition, all children were invited for medical assessments at ages of 8 y, 11 y, 13 y, 15 y, 18 y and 19 y. At the same time, information on participating children was also collected from schools. In addition, a sub-sample of 826 children underwent a detailed psychological assessment at the ages of 8 y, 11 y, 13 y, 15 y, 17 y and 19 y, and another sub-set of 800 participating children was the subject of a detailed dental examination.

Response rates and attrition

Up to the age of 5, the response rate was approximately 70% (Figure 2), which was comparable with other European birth cohort studies such as ALSPAC and Generation R.^{5,6} The first significant drop in participation

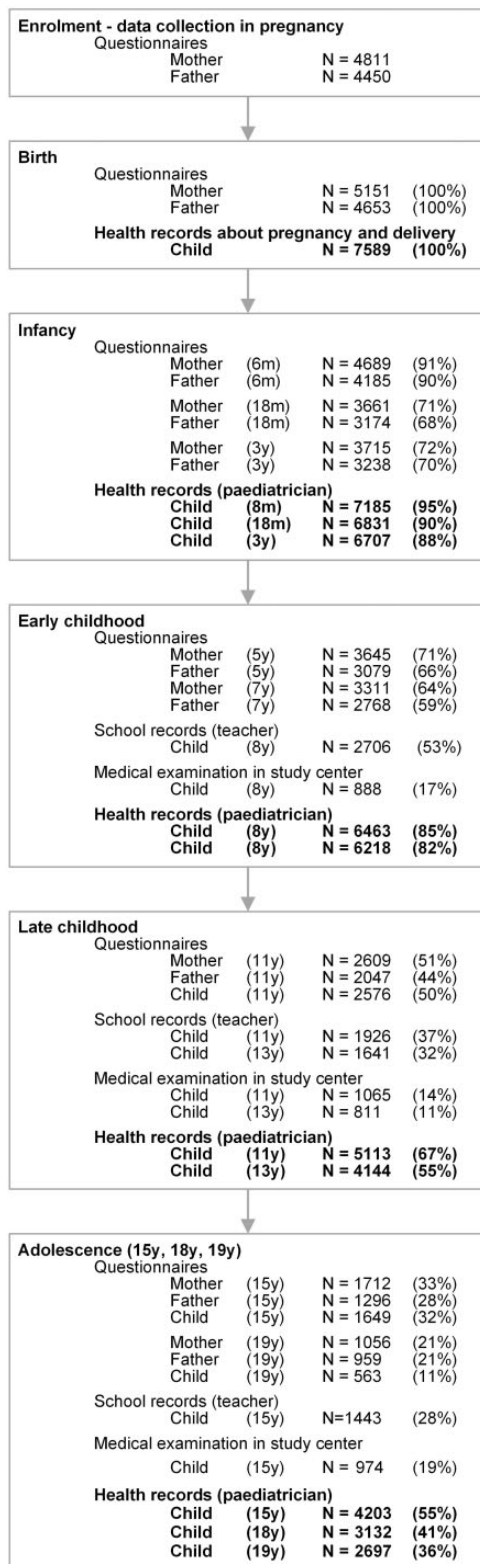


Figure 1 Participant follow-up

was observed during the first 3 years of primary school (when children were aged 7 and 11 years) and the next significant drop was seen at the age of 15, when children left primary school and started secondary education.

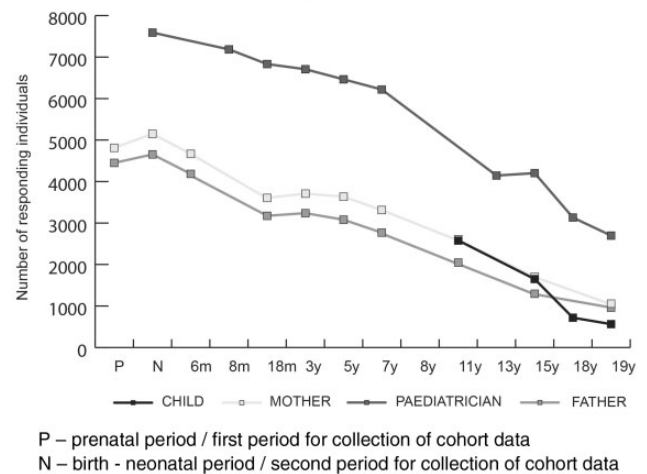


Figure 2 Response rate and attrition

What has been measured?

Three types of data were collected. First, information was collected directly from the gynaecologists providing care to pregnant women, the hospital records for deliveries and the childrens paediatricians. Second, face-to-face examinations of the physical and mental development of participating children were performed by the research team. Finally, questionnaire data were reported by mothers, fathers, children and childrens teachers. Specific *ad hoc* spin-off studies were also allowed.

Medical information was collected from medical records during all phases of the study by trained medical personnel according to the standard operational procedures. The prenatal and perinatal examinations are listed in Box 1. When appropriate, medical data were coded according to the International Classification of Diseases version 9 (ICD-9).

From the age of 6 months, measurements of child's weight, height and blood pressure were taken at intervals defined by the study protocol and described above. In addition, information on breast/formula feeding, diet, vaccination, psychomotor development, hip assessment, injuries, hospitalizations, chronic diseases such as asthma, various types of allergic disorders and medication taken on regular as well as irregular bases was recorded (see Box 2 for details). Repeated data entry checks were carried out to ensure error rates below 1.5 %.

Parent's medical history, including family history, was self-reported at baseline and has been regularly updated. Potential risk factors and covariates were assessed by self-administered questionnaires completed by parents, children (when they were older) and childrens teachers. The questionnaires covered questions on demographic characteristics, socioeconomic status, living and environmental

Box 1. Data collected from obstetrics records

- Repeated measurements of weight, blood pressure, proteinuria, peripheral oedema, haemoglobin
- Gestational age (last menstrual period, ultrasound)
- Blood group
- Pregnancy complications
- Specific medical examinations (amniocentesis, chorionic villus sampling)
- Hospital admissions
- Medication and diets during pregnancy
- Method and place of delivery (including methods of delivery induction)
- Duration of the delivery
- Analgesia, anaesthesia, medication during delivery
- Delivery complications
- Number of children born, placental weight and placental abnormalities
- Sex, APGAR score at 1 and 5 min., weight, length, head circumference, postnatal health
- Neonatal temperature, hip assessment, neonatal bilirubin levels

Box 2. Data collected from paediatrician GP records

- Weight, height, blood pressure,
- Development of child anthropometry
- Growth, development and quality of teeth
- Psychomotor development, posture
- Hearing, vision, development of speech
- Mental health assessment
- Breastfeeding / formula feeding
- Specific diets
- Medication and supplements
- Vaccination
- Cholesterol levels, urine laboratory tests
- Menstrual cycle, contraception
- Skin health
- Injuries, serious acute infections
- Chronic diseases
- Medical imaging (X-ray, ultrasound, CT, MRI, other)
- Visits to hospital/outpatient clinics, sickness rate

conditions, dietary and lifestyle habits and psychosocial and relational factors, as well as overall health and well-being. Psychosocial factors were assessed using standardized validated scales (Table 2).

Data on child health collected between 6th month and 19th year of the child are summarized in Table 3. Health-related data from the child and parent questionnaires were supplemented by data from paediatricians and medical assessments (e.g. sleep patterns, tooth care, exposure to tobacco smoke, pets in the household).

School questionnaires completed by teachers covered their perception of children's development, their behaviour, learning attitudes, academic potential, early signs of attention deficit hyperactivity disorder (ADHD) behaviour and other neurodevelopment pathologies, ability to build standard relationships with their classmates, and relationships between the school and the family. In addition, the psychological sub-study mentioned above specifically focused on factors affecting transition from childhood to adolescence.

What has it found? Key findings and publications

The analysis of prenatal and postnatal tobacco smoke exposure and infant wheezing illnesses of infants²² in two ELSPAC regions (Avon, UK, and South Moravia, Czech Republic) has shown higher prevalence in the UK than in the Czech Republic of: smoking during pregnancy (17.5% v. 7.1%); environmental tobacco smoke exposure of infants during the first 6 months after birth (35.5% vs 9.7%); and prevalence of wheezing in the chest by 6 months of age (21.4% vs 10.3%). Collaborative analyses of prospective cohorts in 12 European countries have found that mother's education was strongly linked with the risk of preterm birth and small for gestational age births across Europe (interestingly, inequalities by maternal education were smaller in the Czech cohort than in the cohorts from the UK, The Netherlands, Sweden and Spain).²³ Also, pre-school children born to mothers with low education were more likely to be overweight and obese.²⁴ Numerous psychological factors were also examined. It was found that even mild levels of distress may influence somatic equivalents and lead to symptoms similar to cognitive and affective disturbances²⁵ or to somatoform dissociative symptoms.²⁶ Clinically significant manifestations of dissociative symptoms were also found in young adult men whose mothers were single and in women whose mothers were re-married.²⁷ The results suggest that dissociative symptoms in young men in fatherless families are linked with conflicting attachment to a father and pathological dependency on mothers, whereas in women, dissociative symptoms appear to be linked to presence of a stepfather in the family. Assessment of dental caries in a subsample of the cohort²⁸ suggested that haplotypes of proinflammatory cytokines are involved in the

Table 2. Questionnaire data reported by parents (antenatal/postnatal)

Main themes	P	N	6 m	18 m	3 y	5 y	7 y	11 y	15 y	18 y	19 y
Health											
Anthropometry/medical history	M/F		M/F	M/F	M/F	M/F	M/F	M/F	M/F	M/F	M/F
Family medical history	M/F										M/F
Medication	M		M								
Reproductive health											
Delivery history	M										
Contraception	M										
Mental health											
Depression 7–9	M/F	M	M/F	M/F	M/F			M/F	M/F	M/F	M/F
Anxiety, feelings, somatization ^{8,9}	M/F	M	M/F	M/F	M/F	M/F	M/F	M/F	M/F	M/F	
Quality of sleep	M		M	M	M						
Demographic											
Age, number of children, religious, marital status, family income, education, employment	M/F		M/F		M/F	M/F	M/F		M/F		M/F
Lifestyle											
Alcohol	M/F		M/F	M/F	M/F	M/F	M/F	M/F	M/F	M/F	M/F
Smoking	M/F		M/F	M/F	M/F	M/F	M/F	M/F	M/F	M/F	M/F
Physical activity	M/F		M/F	M/F	M/F	M/F	M/F	M/F	M/F	M/F	M/F
Diet											
Food frequency questionnaire	M/F		M	M/F			M/F		M/F		
Supplements to diet	M/F			M/F			M/F		M/F		
Marital relationship ^{10–12}	M/F	M/F	M/F	M/F	M/F	M/F	M/F	M/F	M/F	M/F	M/F
Locus of control ¹³	M/F										M/F
Social support ^{14–15}	M/F		M/F		M/F		M/F		M/F		M/F
Life events ¹⁶	M/F	M/F	M/F	M/F	M/F					M/F	
Environmental exposure	M		M	M	M	M	M	M	M	M	M

M, mother; F, father.

pathogenesis of gingivitis in adolescents.^{29,30} Risk of caries was associated with gene variants affecting taste preference (TAS1R2) and glucose transport (GLUT2);³¹ on the other hand, the association between lactotransferrin gene polymorphism and dental caries reported by other studies was not confirmed.³²

What are the main strengths and weaknesses?

The Czech ELSPAC dataset offers great potential for comparative studies due to its choice of study population during a unique period in time. Central and Eastern European populations grew up under specific societal and economic conditions; as a result, the health status and health behaviours in the region in the early 1990s were very different from those in Western Europe.³³ The social and economic environments have changed profoundly during the transformation following the fall of Communism. Therefore, children in the cohort grew under different conditions from their parents, and can be also compared with

their parents who were recruited to the study almost 25 years ago.

There are two major weaknesses to the study. First, there is a substantial attrition in the cohort; almost 50% of participants have health data from paediatrician records available for the whole study duration, but only about 15% of respondents participated in the questionnaire surveys over the whole study period. Second, biological samples are not available on the full cohort; saliva samples for DNA analysis were collected from only 800 children participating in the dental sub-study,³¹ However, the contact with cohort participants was recently re-established in order to explore the feasibility of new data collection with both the original ELSPAC generation of the early 1990s (including collection of biological samples) and their parents.

Can I get hold of the data? Where can I find out more?

A comprehensive electronic database was completed in 2012 when the ELSPAC study became a part of the

Table 3. Questionnaire data completed by mothers about child (6 m-19 y) or child self-report (11 y-19 y)

	N	6 m	18 m	3 y	5 y	7 y	11 y	15 y	18 y	19 y
Health										
Subjective assessment	MC	MC	MC	MC	MC	MC	MC	MC	MC/C	C
Medication	MC	MC	MC	MC	MC	MC	MC	MC	MC/C	C
Vaccination		MC	MC	MC						
Development										
Psychomotor development ¹⁷		MC	MC	MC	MC					
Speech and language development ^{18,19}		MC	MC	MC	MC	MC				
Sleep and crying problems		MC	MC	MC	MC					
Lifestyle										
Activities with child		MC	MC	MC						
Leisure activities					MC	MC	MC	MC/C	C	C
Diet										
Food frequency questionnaire		MC	MC	MC	MC	MC	MC	MC/C	C	C
Breastfeeding	MC	MC	MC							
Dietary supplements	MC	MC	MC							
Feeding problems		MC	MC	MC						
Temperament ²⁰ and behaviour		MC	MC	MC	MC	MC	MC	MC/C	MC/C	C
Abuse										
Alcohol							MC	MC	C	C
Smoking							MC	MC	C	C
Drug abuse							MC	MC	C	C
Attitude										
Self-perception								C	C	C
Life satisfaction								C	C	C
Life events ²¹			MC	MC	MC	MC	MC	MC/C	C	C
Exposure										
Passive smoking	MC	MC	MC	MC	MC	MC	MC	MC	C	C
Exposure to pets	MC	MC	MC	MC	MC	MC	MC	MC	C	C

MC, mother about child; C, child about herself/himself.

RECETOX open-access research infrastructure at Masaryk University. Anonymized datasets in SPSS format are available for data analyses. A new data release policy was created to encourage further collaboration. Collaborations on future follow-up studies are also encouraged. The details as well as the data access application form can be found at [www.elspac.cz].

Profile in a nutshell

- The Czech ELSPAC study was set up as a part of the European Longitudinal Cohort Study of Pregnancy and Childhood (ELSPAC) to investigate effects of biological, psychosocial, economic and environmental factors on pregnancy, delivery and subsequent child development and health. The Czech ELSPAC team was interested also in the effects of the profound socioeconomic changes related to the societal transformation after the fall of Communism in 1989.
- The study collected health information on 7589

children born between 1 March 1991 and 30 June 1992 and questionnaire data on 5151 children that were provided by mothers at baseline.

- Follow-up has included gynaecological and paediatric medical assessments (prenatal, birth, 8 m, 18 m, 3 y, 5 y, 7 y, 8 y, 11 y, 13 y, 15 y, 18 y and 19y), collection of self-reported questionnaires from mothers, their partners and children (6 and 18 months after birth, and subsequently during the 3rd, 5th, 7th, 11th, 15th and 19th year of the child), and specifically focused sub-studies. Response rates during the first 5 years were comparable with European birth cohort studies.
- The Czech ELSPAC study collected health data and information regarding socioeconomic, psychosocial and environmental factors.
- The Czech ELSPAC dataset is unique source of information from Central Europe, available for further research through the study infrastructure [http://www.elspac.cz/index-en.php].

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References

- European Longitudinal Study of Pregnancy and Childhood (ELSPAC). *Paediatr Perinat Epidemiol* 1989;3:460–69.
- Golding J, Pembrey M, Jones R; Team AS. ALSPAC - The Avon Longitudinal Study of Parents and Children - I. Study methodology. *Paediatr Perinat Epidemiol* 2001;15:74–87.
- Goodfellow SA, Rolfe EM, Golding J. Cohort Profile: The Isle of Man Birth Cohort Study. *Int J Epidemiol* 2013;42:1246–52.
- Hryhorczuk D, Dardynskaia I, Lukyanova E *et al.* Risk factors for wheezing in Ukrainian children: Ukraine European Longitudinal Study of Pregnancy and Childhood Group. *Paediatr Perinat Epidemiol* 2009;23:346–51.
- Fraser A, Macdonald-Wallis C, Tilling K *et al.* Cohort Profile: The Avon Longitudinal Study of Parents and Children: ALSPAC mothers cohort. *Int J Epidemiol* 2013;42:97–110.
- Jaddoe VWV, van Duijn CM, Franco OH *et al.* The Generation R Study: design and cohort update 2012. *Eur J Epidemiol* 2012;27:739–56.
- Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. *Br J Psychiatry* 1987;150:782–86.
- Crown S, Crisp A. *Manual of the Crown-Crisp Experimental Index*. London: Hodder and Stoughton, 1979.
- Crisp AH, Ralph PC, McGuinness B, Harris G. Psychoneurotic profiles in the adult population. *Br J Med Psychol* 1978;51:293–301.
- Quinton D, Rutter M. *Parenting Breakdown: the Making and Breaking of Intergenerational Links*. Aldershot, UK: Avebury, 1988.
- Honnor MJ, Zubrick SR, Stanley FJ. The role of life events in different categories of preterm birth in a group of women with previous poor pregnancy outcome. *Eur J Epidemiol* 1994;10:181–88.
- Wilhelm K, Parker G. The development of a measure of intimate bonds. *Psychol Med* 1988;18:225–34.
- Nowicki S, Duke MP. A locus of control scale for noncollege as well as college adults. *J Pers Assess* 1974;38:136–37.
- Barnett BE, Hanna B, Parker G. Life event scales for obstetric groups. *J Psychosom Res* 1983;27:313–20.
- Coddington RD. The significance of life events as etiologic factors in the diseases of children. II. A study of a normal population. *J Psychosom Res* 1972;16:205–13.
- Thomson RM, Allely CS, Purves D *et al.* Predictors of positive and negative parenting behaviours: evidence from the ALSPAC cohort. *BMC Pediatr* 2014;14:10.
- Frankenburg WK, Dodds JB. The Denver developmental screening test. *J Pediatr* 1967;71:181–91.
- Fenson L, Dale P, Reznick S. *Technical Manual for the MacArthur Communicative Development Inventories*. San Diego, CA: Developmental Psychology Laboratory, 1991.
- Reznick JS, Goldsmith L. A multiple form word production checklist for assessing early language. *J Child Lang* 1989;16:91–100.
- Carey WB, McDevitt SC. Revision of the Infant Temperament Questionnaire. *Pediatrics* 1978;61:735–39.
- Enoch MA, Steer CD, Newman TK, Gibson N, Goldman D. Early life stress, MAOA, and gene-environment interactions predict behavioral disinhibition in children. *Genes Brain Behav* 2010;9:65–74.
- Henderson AJ, Sherriff A, Northstone K *et al.*; ALSPAC. Pre- and postnatal parental smoking and wheeze in infancy: cross cultural differences. *Eur Respir J* 2001;18:323–29.
- Ruiz M, Goldblatt P, Morrison J *et al.* Mother's education and the risk of preterm and small for gestational age birth: a DRIVERS meta-analysis of 12 European cohorts. *J Epidemiol Community Health* 2015;69:826–33.
- Ruiz M, Goldblatt P, Morrison J *et al.* Impact of low maternal education on early childhood overweight and obesity in Europe. *Paediatr Perinat Epidemiol* 2016; 3:274–84.
- Bob P, Selesova P, Kukla L. Epileptic-like symptoms and stress conditions in adolescents. *Percept Mot Skills* 2012;115: 790–96.
- Bob P, Selesova P, Raboch J, Kukla L. 'Pseudoneurological' symptoms, dissociation and stress-related psychopathology in healthy young adults. *BMC Psychiatry* 2013;13:149.
- Bob P, Selesova P, Raboch J, Kukla L. Dissociative symptoms and mother's marital status in young adult population. *Medicine (Baltimore)* 2015;94:e408.
- Kukletova M, Holla LI, Musilova K, Broukal Z, Kukla L. Relationship between gingivitis severity, caries experience and orthodontic anomalies in 13-15 year-old adolescents in Brno, Czech Republic. *Community Dent Health* 2012;29: 179–83.
- Holla LI, Musilova K, Vokurka J *et al.* Association of interleukin-6 (IL-6) haplotypes with plaque-induced gingivitis in children. *Acta Odontol Scand* 2008;66:105–12.
- Vokurka J, Klapusova L, Pantuckova P, Kukletova M, Kukla L, Holla LI. The association of MMP-9 and IL-18 gene promoter polymorphisms with gingivitis in adolescents. *Arch Oral Biol* 2009;54:172–78.
- Holla LI, Linhartova PB, Lucanova S *et al.* GLUT2 and TAS1R2 polymorphisms and susceptibility to dental caries. *Caries Res* 2015;49:417–24.
- Volckova M, Linhartova PB, Trefna T *et al.* Lack of association between lactotransferrin polymorphism and dental caries. *Caries Res* 2014;48:39–44.
- Bobak M, Marmot M. East-West mortality divide and its potential explanations: Proposed research agenda. *BMJ* 1996;312: 42125.