## Article

# Epidemiology of cardiovascular malformations among newborns in Monchegorsk (north-west Russia): a register-based study

**Vitaly A. Postoev,[1] Ljudmila V. Talykova,[2] Arild Vaktskjold[3,4]**

*[1]International School of Public Health, Arkhangelsk, Russia; [2]Kola Research Laboratory for Occupational Health, Kirovsk, Russia; [3]Department of Public Health, Norwegian University of Life Sciences, Ås, Norway; [4]Faculty of Public Health, Hedmark University College, Elverum, Norway*

**Significance for public health**

Cardiovascular malformation is one of the most common groups of birth defects. It is considered an important public health issue, as these malformations are the main cause of infant deaths in developed countries. Precise estimates about the prevalence and perinatal survival are needed to organise and plan health care for such newborns. Our study is the first report from the Russian Federation based on data from population-based birth registers.

## Abstract

*Background*. Cardiovascular malformations (CVM) are one of the most prevalent groups of birth defects. Knowledge about the prevalence, distribution and survival in Russia has been limited. The aim of our study was to assess the perinatal prevalence, structure and risk factors for CVM among newborns in Monchegorsk (Murmansk Oblast, Russia) and the mortality among the affected newborns in the period 1973-2008.

*Design and methods*. A register-based study on data from the Kola and Murmansk County Birth Registers. The study included 28,511 births.

*Results*. The registered perinatal prevalence was 3.0 per 1000 newborns, with septal defects as the most prevalent. CVM was twenty times more prevalent among stillborn than live born, and one-third of the live born with a CVM died during the first week of life. The perinatal mortality rate with CVM was 442 per 1000 newborns. This indicator decreased over time. The mothers of newborns with a CVM were ten times more likely to have stillbirth in their anamnesis. The adjusted odds ratio between maternal smoking during pregnancy and CVM was 4.09 [95% confidence interval: 1.75-9.53].

*Conclusions*. The diagnosed perinatal prevalence was relatively low. A previous stillbirth by the mother was highly associated with being born with a CVM. An adjusted elevated risk was also observed among smoking mothers. Perinatal survival increased over time, but varied to a large extent between the different types of CVM.

## Introduction

Cardiovascular malformations (CVM) are one of the most prevalent groups of birth defects and include congenital heart defects and vessels anomalies. In the populations covered by the European Surveillance of Congenital Anomalies (EUROCAT), the total prevalence of CVM in 2000-2005 was 7.97 per 1000 births (including stillborn and terminations of pregnancy due to fetal anomaly).[1] The reported prevalence in other countries has varied from 3 to 12 per 1000 births.[2-7]

Cardiovascular malformations are considered an important public health issue, being the main cause of infant deaths in developed countries. In the United States, CVM represented about 1/3 of all infant deaths, which were due to congenital anomalies. On the other hand, recent advances in medical care for this group of patients result in increased survival into adulthood. It has been estimated that the worldwide adult population with a CVM is growing by 5% per year.[8]

Little is known about CVM prevalence in the Russian Federation (RF). No administrative units are members of EUROCAT, and only a register in the Moscow Oblast is a member of International Clearinghouse for Birth Defects Surveillance and Research. According to federal methodology, systematic registration is obligatory for only two forms of CVM: transposition of great vessels and hypoplasia of left heart.[9] As far as northern territories of RF are concerned, sources of information about CVM prevalence are limited, and no studies are yet available. The Russian Institute of Public Health estimated the prevalence in North-West Russia to be in the range 2.7-3.8 per 1000 children (0-13 years) in 2006-2008.[10] In the population-based birth register in Monchegorsk, which was the first of its kind in the RF, all anomalies diagnosed prenatally were systematically registered – in contrary to the national norm. These data provide a possibility to quantify and analyse the perinatal prevalence and survival of newborns with CVM in a population of northern Russia, which we have made use of in this study.

The mortality rate in the RF from cardiovascular diseases and CVM among children 0-14 years was 14.4 per 100,000 children in year 2000. According to official figures of the RF, about 50% of children with CVM die neonatally without receiving specialised medical aid, and an additional 25% die later in infancy.[11]

The aetiology of most CVM is not well defined. Gene mutations and chromosomal aberrations are evident in a portion of the cases. The heart develops in the period 3-11 weeks of gestation, and hence the critical period for exposure to teratogens.[12] Among the birth defects observed to co-occur with chromosomal anomalies, neural tube defects are more common than malformations of the heart. An increased risk of CVM has been observed when maternal age is above 41 or under 16 years,[13,14] and when the mother smokes, drinks alcohol or uses drugs in early pregnancy.[13,15-17] Maternal diseases, such as diabetes mellitus, obesity and overweight, and viral infections during pregnancy (rubella, Coxsackie virus, respiratory viruses) are also reported to be risk factors.[15,18,19] In addition some occupational exposures (*e.g.* dyes, lacquers or paints) appear to increase the risk.[20] The aetiology of a CVM usually involves combinations of several factors.[12,13]

The aim of our study was to investigate the perinatal prevalence and structure of CVM among newborns in Monchegorsk, and the mortality among the affected newborns. The associations between potential risk factors during pregnancy and CVM were also assessed.

## Design and methods

### Context and study population

Monchegorsk had 47,975 inhabitants in 2010 and is one of the largest cities in Murmansk Oblast (MO) in north-west Russia (Census-2010 official results). The main employer is the local nickel refinery complex. The study population was all newborns in the township in the period 1973-2008, a total of 28,650 live and stillborn. Obligatory ultrasound screening for fetal anomalies was established in the RF from year 2000. The maternal care and maternal benefits in Russia, as well as the study population, have been described earlier in some detail.[21,22]

### Data sources and inclusion in the study

The study was register-based using data from the Kola Birth Register (KBR) and Murmansk County Birth Register.

### The Kola (Monchegorsk) birth register

Information about all births in Monchegorsk from March 1973 through 2005 was compiled in a population-based birth register, a total of 26,841 births. The register was set up to study the association between occupational exposures and reproductive health and pregnancy outcome. Data about all live births and stillbirths from 28 weeks of pregnancy were collected from general medical journals, the hospital gynaecology records and delivery records.[21] The validity of these medical sources has been recognised as satisfactory for epidemiological investigations.[23] We included all registered newborns in the study, except those for whom the source chart containing diagnoses at birth was missing or the interpretation of the recorded diagnosis was uncertain. The total number of excluded newborns was 130 (0.5%). Hence, 26,711 newborns from the years 1973-2005 were included in the study.

### The Murmansk County birth register

The Murmansk County Birth Register (MCBR) includes all births in MO since January 1st, 2006. The registered data have been systematically collected in all 15 obstetrics departments in MO from five sources: the mother's medical history, obstetric journal and delivery record, the newborn's birth record, and through an interview with the mother conducted by a physician or midwife.[24] In the period 2006-2008, the registered births included 1809 births in Monchegorsk. Of these, nine records were missing data about birth defects and excluded from the study. The population coverage of the register was estimated to 98.9% in 2006.[24] In both registries, the diagnoses of congenital malformations were registered based on the International Classification of Disease (ICD) coding system. According to the tenth version (ICD-10), all CVM were coded in the range Q 20-Q 28. The diagnoses were made before the newborns left the birth clinic. From the late 1990s the use of echocardiography supplemented routine examinations and prenatal indications of CVM needed confirmation by examination after birth. In case of fetal deaths, the diagnosis was based on autopsy results.

In total the study included 28,511 newborns.

### Data analysis

To analyse the structure of CVM, the prevalence and proportional distribution of the different forms were estimated based on the registered two- and three-digit level ICD-10 code. Newborns with more than one CVM-diagnosis were included in the numerator for each diagnosis. Newborns with multiple malformations were included in the numerator, if CVM was present among the diagnoses. These analyses were also carried out for stillbirths and for early neonatal deaths separately. In addition, the stillbirth, early neonatal and perinatal mortality rates among newborns with CVM were estimated. The time trends of the prevalence and mortality were estimated using six 6-year time intervals from 1973 to 2008, and tested using chi-square for trend (MedCalc 12.0 software). All prevalence estimates are presented with 95% confidence intervals (CI). The prevalence of selected, possible risk factors was estimated for newborns with and without CVM, respectively, and statistically compared using the chi-square or t-test. The comparison between the two groups was carried out for the following potential risk factors: mean maternal age, parity, TORCH infections (i.e., toxoplasmosis, rubella, cytomegalovirus, herpes simplex, syphilis) during pregnancy, alcohol abuse during pregnancy, tobacco smoking during pregnancy, endocrine disease during pregnancy, paternal or maternal employment in the production departments of the nickel factory at the onset of the pregnancy, maternal occupation with exposure to organic solvents, and maternal body mass index (BMI) at the first antenatal visit. The adjusted risk of a CVM associated with the studied risk factors was analysed by multiple logistic regression, with CVM as a binary outcome (IBM SPSS 17.0 software package). The significance level in all analyses was set at five per cent.

### Ethical considerations

The data in the birth registers have been approved for research purposes by the Murmansk Regional Health Administration and the Committee for Research Ethics at the University in Tromsø. Permission to use the register data was obtained from the KBR and MCBR. The data files obtained for this study contained no personal identifiers.

## Results

Of the 28,511 newborns, 436 were from multiple-birth deliveries, 274 were stillborn (1.0%), and 555 (1.9%) died during the first 7 days after birth. The total number of newborns with one or more anomalies was 1029 (36.1 per 1000 newborns), of these 86 had one or more CVM [3.0 (95% CI: 2.1, 3.9) per 1000 newborns]. One newborn had three CVM, three newborns had two and the rest had one CVM; one in this last group was born as a twin. The mean gestational age for newborns with CVM was significantly lower in comparison with the reference group. The women who delivered a baby with a CVM were ten times more likely to have had a previous stillbirth than the mothers of the newborns without a diagnosed CVM. Maternal smoking was more prevalent in the CVM group (P=0.03). Additional characteristics of mothers, pregnancies and newborns in the study groups are presented in Table 1.

The prevalence of CVM among stillborn was 51/1000 (95% CI: 25/1000, 78/1000), compared to 2.5/1000 (95% CI: 1.4/1000, 3.1/1000) among live born. Sixteen per cent of the newborns with CVM were stillborn. The prevalence of CVM among term and preterm stillbirths did not differ: 54.5/1000 (95%CI: 11.4/1000, 97.7/1000) and 49.4/1000 (95%CI: 15.7/1000, 83.1/1000). The prevalence of newborns with CVM, and among live- and stillborn, in the different time periods is presented in Table 2. The total prevalence did not change over time ($\chi^2$=0.12, P=0.7). Of the 72 live newborns with CVM, 25 were delivered preterm and 24 died during the first seven days (333 per 1000 live births). All newborns with chamber defects and 86% of newborns with anomalies in arteries and veins died perinatally. The perinatal mortality rate with isolated CVM or combined with other congenital malformations was 442 per 1000 newborns with CVM. This indicator decreased over time ($\chi^2$=602.01, P<0.0001).

Table 3 shows the structure of CVM among all newborns and those who died perinatally. Septal defects constituted 27% of all CVM and were the most prevalent of the verified diagnoses, while among stillborn and perinatal deaths, chamber defects were the most prevalent (24.1%). In total, 46.1% of the CVM diagnoses were unspecified, but

this percentage was smaller among those who died perinatally. Of the two types of CVM that have been obligatory to register in the federal system in the RF, there was one diagnosed case (Q 20.3).

The adjusted odds ratio (OR) for smoking during pregnancy was 4.09 (95% CI: 1.75, 9.53). None of the other risk factors we studied were associated with the risk of CVM (Table 4).

## Discussion

A relatively high average stillbirth rate (10/1000 births) with a slight decline in the last decade was observed in Monchegorsk. In most European countries, it was less than 6 per 1000 newborns in the same period.[25] In a similar study period in Hungary (1971-2010), the average rate was 6.5 per 1000.[26] The prevalence, observed in our study, was

also higher than the officially reported average rate from Russia as a whole, which declined from 6.8 to 4.7 during 2000-2010.[27]

We found no difference in prevalence of CVM between preterm and term stillbirths. According to the data of the Russian State Statistics Service, the most common cause of stillbirth has been intrauterine hypoxia and birth asphyxia,[27] which suggests that the main explanation of the higher stillbirth rate in the RF was insufficient health care service during delivery. At the same time, live births before 28 weeks in the RF were until 2011 defined as stillborn unless they survived the first seven days, which inflates the stillbirth rate compared to most other European countries.

Interestingly, the mothers who delivered a child with CVM were ten times more likely to have experienced a previous stillbirth. Another study reported the same picture for Ebstein's anomaly, and suggested that genetic risk factors lead to defects that are non-compatible with

**Table 1. Univariate comparisons of maternal and newborn characteristics between newborns with and without a cardiovascular malformation in Monchegorsk.**

| Characteristics (records missing information) | Newborns with CVM* | Newborns without CVM* | P |
|---|---|---|---|
| Mean maternal age (0.2%) | 25.8 (24.4, 27.1) | 25.2 (25.1, 25.2) | 0.66° |
| Male proportion at birth (4.9%) | 55% (44.2, 64.8) | 51% (49.9, 52.0) | 0.44# |
| Mean number of previous live births (6.4%) | 1.4 (1.2, 1.6) | 1.6 (1.6, 1.6) | 0.36° |
| Mean number of previous stillborn (6.4%) | 0.23 (0.21, 0.25) | 0.02 (0.02, 0.02) | <0.0001° |
| Mean gestational age (4.9%) | 37.8 (37.4, 38.1) | 39.4 (39.3, 39.5) | <0.001° |
| Mean maternal body mass index (8.4%) | 26.4 (25.7, 27.2) | 27.2 (27.1, 27.2) | 0.11° |
| Proportion with hyperglycaemia during pregnancy (6.6%) | 2.4% (0.2, 8.9) | 3.2% (3.0, 3.4) | 0.73# |
| Proportion with TORCH infection during pregnancy (7.4%) | 6.1% (2.3, 13.8) | 3.1% (2.9, 3.3) | 0.12# |
| Proportion observed with alcohol abuse during pregnancy (0.3%) | 1.2% (0.0, 6.9) | 0.5% (0.4, 0.6) | 0.36# |
| Proportion observed as smokers during pregnancy (0.3%) | 7.0% (3.0, 14.7) | 2.1% (1.9, 2.2) | 0.009# |
| Proportion of mothers suffered from endocrine disease during pregnancy (7.2%) | 16.0% (9.4, 25.4) | 11.7% (11.3, 12.1) | 0.23# |
| Proportion of fathers employed at the nickel factory§ (3.5%) | 49.2% (39.0, 61.0) | 43.2% (42.7, 43.9) | 0.10# |
| Proportion of mothers employed at the nickel factory§ (3.1%) | 20.7% (13.3, 30.7) | 20.4% (20.0, 20.9) | 0.94# |
| Proportion of maternal occupations involving organic solvent exposure (3.1%) | 3.5% (0.8, 10.2) | 2.6% (2.4, 2.8) | 0.59° |

CVM, cardiovascular malformation. *95% wald confidence intervals are presented in brackets; °T-test for independent samples; #Chi-square test; §the numerators include only workers in the production departments.

**Table 2. The total frequency (n) and prevalence of newborns with cardiovascular malformations among live and stillborn infants in Monchegorsk in 6-year intervals in the period 1973-2008.**

| Time period | N. | Total CVM | Prevalence | N. | Live births CVM | Prevalence | N. | Stillborn CVM | Prevalence |
|---|---|---|---|---|---|---|---|---|---|
| 1973-1978 | 5021 | 14 | 2.8 (1.3, 4.2) | 4963 | 10 | 2.0 (0.8, 3.3) | 58 | 4 | 69.0 (1.8, 136.2) |
| 1979-1984 | 6511 | 26 | 4.0 (2.5, 5.5) | 6443 | 22 | 3.4 (2.0, 4.8) | 68 | 4 | 58.8 (1.4, 116.0) |
| 1985-1990 | 6508 | 17 | 2.6 (1.4, 3.8) | 6443 | 14 | 2.1 (1.0, 3.3) | 65 | 3 | 46.2 (0, 98.5) |
| 1991-1996 | 3637 | 14 | 3.8 (1.8, 5.8) | 3607 | 13 | 3.6 (1.6, 5.6) | 30 | 1 | 33.3 (0, 101.5) |
| 1997-2002 | 3362 | 9 | 2.7 (0.9, 4.4) | 3336 | 7 | 2.1 (0.5, 3.7) | 26 | 2 | 76.9 (0, 186.7) |
| 2003-2008 | 3472 | 6 | 1.7 (0, 3.1) | 3445 | 6 | 1.7 (0, 3.1) | 27 | 0 | 0.0 |
| Total | 28,511 | 86 | 3.0 (2.1, 3.9) | 28,237 | 72 | 2.5 (1.9, 3.1) | 274 | 14 | 51.1 (25.0, 77.6) |

CVM, cardiovascular malformations; N, total number of newborns registered in the time period. Prevalence is indented per 1000 births, with 95% confidence intervals.

life.[28] This hypothesis is supported by the data in our study. When we excluded stillbirths from the analysis, the relative likelihood of previous stillbirth among the mothers who delivered a child with CVM fell from factor ten to factor three.

The overall prevalence was lower than that reported in EUROCAT and from studies in two populations in other parts of the RF.[1,29] Compared to the EUROCAT averages, the prevalence was lower for all 16 forms of CVM that the EUROCAT monitors.[1] The most prevalent group of CVM was septal defects, but almost one-half of all registered cases were recorded with an unspecified CVM diagnosis. There were no registered cases of the severe defects: hypoplastic left heart and coarctation of aorta. Also the prevalence of transposition of great vessels (the other diagnosis that is obligatory to report in the Russian system of surveillance) was lower than that reported from neighbouring regions of MO and from Moscow.[10,30,31] In the RF, a prenatal diagnosis of severe CVM in regional districts may prompt a transfer of the delivery to regional centres or to Moscow for early surgical correction. According to the data obtained from the paediatric polyclinic in Monchegorsk, two deliveries of newborns with hypoplastic left heart were transferred to Moscow in 2002-03. Records of births which took place elsewhere were not filed at the local hospital and were not registered in either the KBR or the MCBR. The absence of obligatory ultrasound screening for fetal anomalies until 2000 could be another possible explanation low prevalence rate.

In any birth surveillance system, both inside and outside the RF, the true prevalence of CVM among delivered newborns is underestimated.

The estimated rates are a function of the degree of prenatal screening and of early neonatal diagnostic measures, while the true rates also include children who have CVM that reveals itself later in life. A study in Bosnia-Herzegovina found that the average age for CVM diagnosis was between the first and the second year of life, and that most of the late diagnoses were minor CVM.[2] Thus, the prevalence of small septal and valves defects without haemodynamic problems in our study was likely an underestimation, but the registered number of chamber defects can be assumed to be close to the true frequency. In provincial clinics in the RF, the lack of diagnostic tools, such as echocardiography, at the neonatal stage of care also suggests that some forms of CVM were under-diagnosed perinatally in most of the studied period. To achieve a better assessment of the prevalence among newborns in Monchegorsk we did a chart review at the local paediatric polyclinic. The findings revealed 16 children born in 2006-2008 who had a diagnosis of CVM at the age of one year, while our perinatal figures based on the MCBR included four of these (25%). Thus, the true perinatal prevalence was likely at least four times higher than the perinatal diagnostic procedures, recording, reporting and registration in the MCBR revealed.

Although birth-registers data provide gross underestimations of the true prevalence of CVM and are not very comparable between systems, the data may reveal interesting trends over time within a system, especially in terms of mortality. We observed no increase in prevalence over time, despite the technological improvements for perinatal diagnostics that have taken place in the RF during the last twenty years. This find-

**Table 3. The diagnosis-specific frequency, prevalence (per 1000 newborns) and distribution (%) of cardiovascular malformations among all births, and among newborns that died perinatally in Monchegorsk (1973-2008).**

| Birth defect (ICD-10 code) | All births* | | Among stillborn* | | Among perinatal deaths*° | |
|---|---|---|---|---|---|---|
| | N.# | % | N. | % | N. | % |
| Congenital malformations of cardiac chambers and connections (Q20) | 10 (0.35) | 11.0 | 4 | 26.7 | 10 | 23.3 |
| Septal defects (Q 21) | 25 (0.87) | 27.4 | 3 | 20.0 | 14 | 32.6 |
| Valves defects (Q 22-23) | 4 (0.14) | 4.4 | 0 | 0.0 | 1 | 2.3 |
| Other congenital malformations of heart (Q24) | 45 (1.57) | 49.5 | 6 | 40.0 | 12 | 27.9 |
| Unspecified, Q 24.9 | 42 (1.47) | | | | | |
| Arteries and veins anomalies (Q 25-Q27) | 7 (0.25) | 7.7 | 2 | 13.3 | 6 | 13.9 |
| Other congenital malformations of circulatory system (Q28) | 0 | 0 | 0 | 0.0 | 0 | 0.0 |
| Total | 91 (3.18)§ | 100 | 15 | 100 | 43 | 100 |

*The figures include more than one CVM per newborn. Among stillborn one fetus had two CVM (Q 21.1, Q 25.2); among early neonatal deaths one newborn had 3 CVM (Q 21.1, Q 25.0, Q25.3) and two 2 CVM (21.0, 21.1 and 20.0, 24.8). °Includes CVM among stillborn and newborns who died during the first seven days. #Prevalence per 1000 newborns is presented in brackets. §The prevalence with a CVM only was 2.2 (95% C.I.: 1.6-2.7).

**Table 4. Odds ratios of cardiovascular malformations for selected risk factors in Monchegorsk.**

| Risk factors* | Unadjusted OR° (95% CI) | Adjusted OR# (95% CI) |
|---|---|---|
| Maternal age less than 18 years | 2.33 (0.84, 6.44) | 2.11 (0.77, 5.78) |
| Maternal age more than 39 years | 1.57 (0.22, 11.37) | 1.48 (0.20, 10.69) |
| Alcohol abuse during pregnancy | 0.83 (0.10, 6.80) | 0.98 (0.12, 7.90) |
| Smoking during pregnancy | 4.34 (1.75, 10.59) | 4.09 (1.75, 9.53) |
| Maternal occupation involving organic solvent exposure | 1.41 (0.45, 4.52) | 1.44 (0.44, 4.45) |
| TORCH infection during pregnancy | 1.96 (0.79, 4.77) | Not included |
| Endocrine disease during pregnancy | 1.41 (0.78, 4.87) | Not included |
| Father employed at the nickel factory | 1.40 (0.90, 2.16) | Not included |

OR, odds ratios; CI, confidence intervals. *The models were tested for multi-collinearity (tolerance was about 1 for all factors); body mass index was not included in the analysis due to the number of missing values for the newborns with CVM [12 newborns (14%)]. °We omitted in the analysis 1747 newborns (6.6%) due to missing data for one or more of the included factors, whereof 4 (4.7%) of the newborns that had CVM. #The model included only factors without missing data for newborns with CVM. Among newborns without CVM, 1465 (5.1%) were excluded from the analysis due to missing data for one or more of the included factors.

ing may suggest that the true prevalence has decreased, or that the improved detection also led to more pregnancies being terminated in the second trimester. Our study revealed that the perinatal mortality among newborns with CVM has decreased in Monchegorsk (from 23 per 1000 newborns in the 1970s to 9.3 per 1000 in 2003-06), and that the reduction mainly occurred in the early neonatal period. This finding suggests that the capability of the neonatal care has improved, or that a larger proportion of severe cases are transferred. The absence of perinatal mortality observed among newborns with CVM in Monchegorsk in the last time period may be explained by the small number of newborns in that period (only half as many per year as in the 1970-80s) and transfer of women with a severe pathology of the fetus to another clinic (one such newborn with CVM died in Moscow in 2002).

Based on data from the Monchegorsk paediatric polyclinic, five cases of CVM were eliminated by induced abortion after 20-25 weeks of gestation in the period 2000-2006 (there were six newborns with CVM in this time period). Data concerning miscarriages and abortions before 28 weeks are not logged in the birth registers, and therefore pregnancies are not included in our prevalence estimates.

There was a tendency towards an elevated risk of CVM associated with all the factors studied except alcohol abuse, but only an association with smoking during pregnancy was statistically significant [OR: 4.09 (95%CI:1.75, 9.53)]. A similar adjusted OR has also been reported by other studies.[16,18] One of the studies investigated the association between smoking and 22 different categories of congenital malformations, and found a causal association only with CVM.[16]

Birth registers have limitations when it comes to assessment of outcomes that are not readily diagnosed in the perinatal period. Our findings suggest that most cases of CVM were not revealed in the perinatal period, and that some were transferred prenatally, and thereby not registered in the birth register on which our study population was based, which constitutes a weakness. In addition, the small numbers due to the rarity of CVM and the size of the study population lowered the precision of the estimates. Nevertheless, the limitations we have found concerning monitoring and studies of CVM are important findings in themselves. The study also revealed new knowledge about the distribution of different CVM diagnoses, the degree of diagnostic specification, and the distribution and level of perinatal mortality associated with CVM in a population in the RF.

## Conclusions

Our study was the first in the RF that estimated the perinatal prevalence of CVM through the use of data from population-based birth registers. The diagnosed perinatal prevalence in Monchegorsk was relatively low and we did not observe a change over time (1973-2008). Septal defects were the most prevalent of the CVM that were specified perinatally. Mothers of newborns with CVM were ten times more likely to have a history of previous stillbirth. One out of three infants born alive with CVM died during the first week of life, but the perinatal survival increased over time. All newborns with chamber defects and 86% of newborns with anomalies in arteries and veins died perinatally. The adjusted risk of giving birth to an infant with CVM was higher among smoking mothers than among non-smoking.

## References

1. Dolk H, Loane M, Garne E, EUROCAT Working Group (2011). Congenital heart defects in Europe: prevalence and perinatal mortality, 2000 to 2005. Circulation 2011;123:841-9.
2. Begic H, Tahirovich H. Epidemiological and clinical aspects of congenital heart disease in children in Tuzla Canton, Bosnia-Herzegovina. Eur J Pediatr 2003;162:191-3.
3. Dadvand P, Rankin J, Shirly M, et al. Descriptive epidemiology of congenital heart disease in Northern England. Paediatr Perinatal Epidemiol 2008;23:58-65.
4. Başpinar O, Karaaslan S, Oran B, et al. Prevalence and distribution of children with congenital heart diseases in the central Anatolian region, Turkey. Turk J Pediatr 2006;48:237-43.
5. Pedra AC, Haddad J. Pediatrics and congenital heart diseases in South America: an overview. Heart 2009;95:1385-92.
6. Hoffman JI, Kaplan S. The incidence of congenital heart disease. J Am Coll Cardiol 2002;39:1890-900.
7. Loffredo CA. Epidemiology of cardiovascular malformations: prevalence and risk factors. Am J Med Genet 2000;97:319-25.
8. Marelli A, Mackie AS, Ionescu-Ittu K. Congenital heart disease in general population: changing prevalence and age distribution. Circulation 2007;115:163-72.
9. Kirillova EA, Nikiforova OK, Ghuchenko NA, et al. [Monitoring vrogdennih porokov razvitija u novorogdennih]. Russ Bull Perinatol Pediatr 2000;1:18-21. [Article in Russian].
10. Russian Institute of Public Health. Report of federal informational center of gene registering and birth defects' monitoring. (in Russian). Moscow, 2011.
11. Schkolnikova MA, Osokona GG, Abdullatipova IV. Sovremennye tendencii serdechno-sosudistoj zabolevaemosti i smertnosti u detej v RF; struktura serdechnoj patologii detskogo vozrasta. Kardiologiya 2003;8:4-8.
12. Pierpont ME, Basson CT, Benson DW, Gelb BD. Genetic basis for congenital heart defects: current knowledge: a scientific statement from the American heart association congenital cardiac defects committee, council on cardiovascular disease in the young: endorsed by the American academy of pediatrics. Circulation 2007;115:3015-38.
13. Pejtsik B, Pinter J, Horvath M, Hadnagy J. Relationship between

congenital heart disease and various factors affecting pregnancy. Orvosi Hetilap 1992;133:155-8.

14. Reefhuis J, Honein M. Maternal age and non-chromosomal birth defects, Atlanta 1968-2000: teenager or thirty-something, who is at risk? Birth Defects Res (Part A) 2004;70:572-9.

15. Kuciene R, Dulskiene V. Selected environmental risk factors and congenital heart defects. Medicina (Kaunas) 2008;44:827-32.

16. Woods SE, Raju U. Maternal smoking and the risk of congenital birth defects: a cohort study. J Am Board Fam Pract 2001;14:330-4.

17. Malik S, Cleves MA, Honein MA, et al. National birth defects prevention study. Maternal smoking and congenital heart defects. Pediatrics 2008;121:810-6.

18. Neilsen G, Norgard B, Puho E. Risk of specific congenital abnormalities in off-spring of women with diabetes. Diabet Med 2005;22:693-6.

19. Ohotnikova IM, Agejkin VA, Lozovskaya LS. Znachenie vnutriutrobnoj virusnoj infekcii v organnoj patologii detej grudnogo vozrasta. Med Sci Educ J 2001;5:81-7.

20. Tikkanen J, Heinonen OP. Risk factors for cardiovascular malformations in Finland. Eur J Epidemiol 1990;6:348-56.

21. Vaktskjold A, Talykova L, Chashcin V, et al. The Kola Birth Registry and perinatal mortality in Moncegorsk, Russia. Acta Obstet Gynecol Scand 2004;83:58-69.

22. Vaktskjold A, Paulsen EE, Talykova L, et al. The prevalence of selected pregnancy outcomes risk factors in the life-style and medical history of the delivering population in north-western Russia. Int J Circumpolar Health 2004;63:39-60.

23. Odland J, Tchachtchine VP, Bykov V. Critical evaluation of medical, statistical, and occupational data sources in the Kola Peninsula of Russia pertinent to reproductive health studies. Int Arch Occup Environ Health 1999;72:151-60.

24. Anda EE, Nieboer E, Voitov AV, et al. Implementation, quality control and selected pregnancy outcomes of the Murmansk County Birth Registry in Russia. Int J Circumpolar Health 2008;67:318-34.

25. Cousens S, Blencowe H, Stanton C, et al. National, regional, and worldwide estimates of stillbirth rates in 2009 with trends since 1995: a systematic analysis. Lancet 2011;377:1319-30.

26. Nyari TA. Risk factors and trends in the rate of stillbirth in Hungary between 1971 and 2010. J Matern Fetal Neonatal Med 2014;27: 1195-8.

27. Shchegolev AI, Pavlov KA, Dubova EA, Frolova OG. Uroven mertvorozhdaemosti v subjektah Rossijskoy Federacii v 2010. Arkhiv Patologii 2013;75:20-4.

28. Correa-Villasenor A, Ferencz C, Neill CA, et al. Ebstein's malformation ofhe tricuspid valve: genetic and environmental factors. The Baltimore-Washington infants study group. Teratology 1994;50: 137-47.

29. Fokina VV, Udalova OB, Chernova OV. Epidemiologicheskaja kharakteristika vrozdennich porokov serdca po dannim monitoring vrozdennich porokov serdca. Collected theses of All-Russian seminar in commemoration of Professor Belokon N.A.: Arkhangelsk, 2003.

30. International clearinghouse for birth defects surveillance and research. Annual report 2006. Rome, 2006, p. 226. Available from: http://www.icbdsr.org/filebank/documents/Report2006.pdf

31. International clearinghouse for birth defects surveillance and research. Annual report 2007. Rome, 2007, p. 230. Available from: http://www.icbdsr.org/filebank/documents/Report2007.pdf