

Article Type: Main Research Article**The implementation of a nationwide anomaly screening programme improves prenatal detection of major cardiac defects: an 11-year national population-based cohort study**

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Short title: Nationwide screening improves prenatal detection of MAJOR CHD

ABSTRACT

Objective

To evaluate whether a nationwide prenatal anomaly screening programme improves detection rates of univentricular heart (UVH) and transposition of great arteries (TGA) and whether maternal risk factors for severe fetal heart disease affect prenatal detection.

Design

Population-based cohort study.

Setting

Nationwide data from Finnish registries 2004 to 2014.

Population

642 456 parturients and 3449 terminated pregnancies due to severe fetal anomaly.

Methods

Prenatal detection rates were calculated in three time periods (prescreening, transition, and screening phase). The effect of maternal risk factors (obesity, in vitro fertilization, pregestational diabetes, and smoking) was evaluated.

Main outcome measures

Change in detection rates and impact of maternal risk factors on screening programme efficacy.

Results

In total 483 cases of UVH and 184 of TGA were detected. The prenatal detection rate of UVH increased from 50.4% to 82.8% and TGA from 12.3% to 41.0% ($P<0.0001$). Maternal risk factors did not affect prenatal detection rate, but detection rate differed substantially by region.

Conclusions

A nationwide screening programme improved overall UVH and TGA detection rates, but regional differences were observed. Obesity or other maternal risk factors did not affect the screening programme efficacy. The establishment of structured guidelines and recommendations are essential when implementing the screening programme. In addition, prospective screening register is highly recommended to ensure high quality of screening.

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Keywords

Prenatal diagnosis, Congenital heart disease, Prenatal screening, Univentricular heart, Transposition of great arteries

Tweetable abstract: Implementation of a nationwide prenatal anomaly screening improved detection rates of UVH and TGA.

INTRODUCTION

Critical congenital heart defects (CHD) are the most common congenital anomalies that may lead to infant death when undiagnosed.¹⁻³ Prenatal detection of severe cardiac defects allows optimal follow up of pregnancy and delivery planning of a critically ill child and reduces mortality and morbidity.⁴⁻⁶ Heart defects such as univentricular heart (UVH) and transposition of the great arteries (TGA) benefit from prenatal diagnosis and should be prioritized in prenatal CHD screening.

Prenatal ultrasound screening of congenital anomalies is recommended and widely implemented.⁷⁻⁹ Screenings are performed in the first (11 to 13 weeks of gestation) and second trimester (detailed structural anomaly screening at 18 to 22 gestational weeks).⁷⁻⁹

National screening programmes of congenital structural anomalies are part of routine prenatal care in developed countries. Previous studies on the impact of anomaly screening programmes have examined regional cohorts;¹⁰⁻¹² and nationwide data are scarce.¹³ Recent obstetrical ultrasound guidelines incorporate screening of cardiac outflow tracks and the four-

chamber view to improve prenatal detection of critical cardiac outflow defects such as TGA.¹⁴⁻¹⁶ There is limited knowledge on whether maternal risk factors that expose offspring to increased risk of critical CHD^{17,18} affect the prenatal detection of fetal CHD.¹⁹

We hypothesise that implementation of a nationwide anomaly screening programme improves prenatal detection rates and may affect the live birth prevalence of UVH and TGA. As a secondary outcome, we evaluated if maternal risk factors for fetal CHD (obesity, in vitro fertilisation [IVF], pregestational diabetes, and smoking) impact prenatal screening programme efficacy.

METHODS

Screening programme. A recommendation on fetal anomaly screening was given by the Finnish Ministry of Social Affairs and Health in 1999. The considerable heterogeneity of examinations raised concern about the quality and reliability of the screening; an expert committee established new official recommendations. The nationwide screening programme for fetal anomalies was introduced in Finland in January 2007. A new decree came into effect in January 2010 that required all municipalities to offer a screening of congenital anomalies for all pregnant women. A transition period from 2007 to 2009 was given to organise the fetal screening in every municipality in Finland. Screening is voluntary and free of charge and includes first-trimester ultrasound, combined screening for chromosomal defects, and second-trimester ultrasound (programme described in detail in Figure S1). The expert committee recommended systematic, ongoing auditing of screening personnel and establishment of a prospective screening register. These recommendations have not been implemented.

Cardiac anatomy assessment is not included in first-trimester ultrasound. The second-trimester ultrasound includes four-chamber view (situs, axis, size and symmetry of the chambers, heart rate, av-valves) and outflow track view (and crossing of the great arteries) as recommended in recent international ultrasound guidelines.¹⁴⁻¹⁶ However, the three-vessel view is not included in the screening requirements. The fetal ultrasound screening protocol is shown in Table S1 and equipment recommendations in Table S2. Examinations are mainly performed by trained midwives. The training programme is shown in Table S3. If an abnormality is suspected, the patient is referred to a perinatologist or a fetal cardiologist for a detailed fetal echocardiogram. Women with an increased risk for a fetal CHD are usually referred directly to a perinatologist or a fetal cardiologist.¹⁶

Comparison of time periods were prescreening phase (2004 to 2006), transition phase (2007 to 2009), and screening phase (2010 to 2014). No reliable data are available on how screening was organized in practice from 2004 to 2006. During the transition period (2007 to 2009), screening personnel were trained as recommended in the guidelines. Combined first-trimester screening was offered to 58% to 87% and second-trimester structural screening to 77% to 88% of all pregnant women in 2007 to 2009. Since 2010, all pregnant women have an equal opportunity to participate in fetal screening performed by trained personnel with high-quality equipment. Since the initial status of prenatal ultrasound screening varied between different regions of Finland, we evaluated the change in prenatal detection rate as the outcome of the effectiveness of implementation of nationwide screening. Regional data suggest that approximately 95% of pregnant women participate in ultrasound screening during pregnancy. In Finland, all pregnancies with antenatally detected critical CHD are referred for delivery and early neonatal surgery exclusively to Helsinki University Hospital.

Classification of heart defects. We selected UVH as an index cardiac anomaly for the four-chamber view and TGA for the outflow track view. From 642 456 parturients, 651 969 children were born of which 649 971 children were born alive (National Medical Birth Register) during the study period from 2004 to 2014; 3449 pregnancies were terminated due to severe fetal anomaly (Finnish Register of Congenital Malformations). UVH classification includes hypoplastic left heart syndrome (HLHS) and other types of UVH; and TGA is classified as simple with or without ventricular septal defect (VSD) and more complex forms. A detailed morphological classification of heart defects is shown in Table S4. Borderline cases of UVH, if operated postnatally following a two-chamber line, were excluded.

Classification of primary outcome; prenatal detection. Data were divided according to prenatal diagnosis (yes/no). We assessed all prenatally detected index cases and considered whether they were detected within or outside (random diagnosis) the screening programme. We further evaluated the number of late prenatal diagnoses (diagnosis after 24+0 gestational weeks; e.g., due to suboptimal imaging of four-chamber or outflow track views of the heart leading to follow-up ultrasound and delayed confirmation of CHD). The cut-off for late diagnosis was set at the latest possible legal pregnancy termination gestational age (24+0 weeks of gestation) allowed for a severe fetal anomaly.

Register data. Study data were collected from national registers containing information on all births, stillbirths, and pregnancy terminations due to fetal anomaly, including all pre- and postnatally diagnosed cases of UVH and TGA. The national registers are comprehensive: 1) the National Register of Paediatric Cardiac Surgery maintained by Children's Hospital at Helsinki University Hospital and the registers at the National Institute for Health and Welfare; 2) the Finnish Register of Congenital Malformations; 3) the Register of Induced

Abortions; 4) the Medical Birth Register; and the 5) Cause-of-Death Register, maintained by Statistics Finland.

The Finnish Register of Congenital Malformations actively collects data on all fetal/congenital malformations in Finland.²⁰ We cross-checked data with the mothers' and live born infants' identification numbers and verified all information from hospital records, including prenatal and postnatal reports, karyotype, and autopsy results. One paediatric and fetal cardiologist (TO) confirmed all cardiac diagnoses and one clinical geneticist (AR) confirmed all extra-cardiac malformations. Major extra-cardiac malformations were included according to EUROCAT guidelines.²¹

Prevalence and maternal risk factors. The total and live birth prevalence was calculated according to EUROCAT guidelines.²² We determined the national and regional total and live birth prevalence of UVH and TGA. Finland is divided into five university hospital districts (city in brackets): southern (Helsinki), central (Tampere), western (Turku), eastern (Kuopio), and northern (Oulu). The mothers' municipality of residence was used to identify the correct region.

Maternal characteristics are shown in Table 1. We analysed the following previously known maternal risk factors for fetal CHD: obesity, pregestational diabetes, multiple pregnancies, IVF, and smoking in the study population (in births). The official national recommendation for folic acid supplementation for all women planning pregnancy was introduced only in 2016; the registers lack this information. BMI was calculated from register data of height and pregestational weight recorded on the first prenatal visit on gestational week 8. $BMI \geq 30$ was considered obese. Data on maternal BMI were accessible in 89% (355/400) of

parturients in our cohort (birth cohort) and in 95% (608 731/642 456) of all parturients. The mother was considered a smoker even if she ceased smoking during the first trimester. These risk factors were compared to the national Medical Birth Register data of all parturients (n=642 456) over the study period. The data on chorionicity in multiple pregnancies were collected from year 2017 and are hence lacking over studied period. IVF data include parturients with IVF, intracytoplasmic sperm injection (ICSI), or frozen embryo transfer (FET) treatment. The incidence of pregestational diabetes was calculated. The Medical Birth Register data of diabetes are collected for all births from the year 2006 onwards (all parturients 2006 to 2014; n=528 618); these years were used to assess pregestational diabetes incidence. The differences in risk factors between mothers with and without a prenatal diagnosis were evaluated.

Statistics. Data analyses were performed with IBM SPSS version 22. A one-sample t-test was used to test if the difference in means was statistically significant between our sample and national data according to the Medical Birth Register. Frequencies and percentages were used to describe categorical variables. The chi-square test, the test for relative proportions, and Fisher's exact test were used for statistical comparisons. We considered $P < 0.05$ as statistically significant. All tests were two-sided.

Core outcome sets were not used and patients were not involved. The funding of this research was only as personal working grants for the corresponding author.

RESULTS

A total of 642 456 births (National Medical Birth Register) were registered and 483 UVH and 184 TGA cases were diagnosed during the study period (2004 to 2014). The majority of cases were singletons, 3.9% (26/667) of all and 5.0% (20/400) of births with CHD were twins, and 0.3% (2/667) and 0.5% (2/400) were triplets, respectively. A flowchart of the data and prenatal diagnosis of UVH and TGA are shown in Figure 1. The assessed maternal demographics are shown in Table 1. Chromosomal anomalies observed in the cohort are listed in Table S5.

Impact of the initiation of the national prenatal screening programme and the prevalence of heart defects

Univentricular heart. Implementation of the nationwide screening programme improved the prenatal detection rates of UVH significantly from 50.4% (63/125; prescreening phase) to 66.7% (84/126; transition phase) and 82.8% (192/232; screening phase) (the total change 32.4%, 95% CI 18.5–49.0; $P < 0.0001$). The changes in regional prenatal detection rates during the study period are shown in Table 2. Random diagnoses (detected outside the screening programme) decreased over the study period (Table 2). These random diagnoses were excluded from the analysis of the screening programme impact. The rate of late diagnoses (after 24+0 gestational weeks) did not change over the study period (Table 2). In 49 cases, UVH was detected before second-trimester structural screening; 77.6% (38/49) of these cases had other major extracardiac anomalies or chromosomal anomalies. Distribution of gestational age at prenatal detection is shown in Figure S2a.

The overall national total prevalence of all UVH was 7.41/10 000 births (over the study period) and 3.74/10 000 births for a subgroup of HLHS. The live birth prevalence of all UVH was 3.39/10 000 and of HLHS 1.87/10 000 live births. While the live birth prevalence of all UVH decreased from 4.48/10 000 (prescreening phase) to 2.90/10 000 (screening phase) ($P=0.005$), the total national prevalence did not change over the study period (7.16/10 000 to 7.79/10 000; $P=0.448$). Differences in the total prevalence of UVH did not vary by region (range 6.80/10 000 to 8.48/10 000, $P=0.405$) (Figure 2a). The pregnancy termination rate in UVH cases increased significantly from 35.2% (44/125; prescreening phase) to 60.8% (141/232; screening phase); total change was 25.6% (95% CI 14.8–35.5; $P<0.0001$).

Transposition of great arteries. Implementation of the nationwide screening programme improved the detection rate of TGA significantly from 12.3% (7/57; prescreening phase) to 20.4% (10/49; transition phase) and to 41.0% (32/78; screening phase) (the total change 28.7%, 95% CI 7.2–74.0; $P<0.0001$). Changes in the regional prenatal detection rates during the study period are shown in Table 2. Random diagnoses decreased significantly over the study period (Table 2). These random diagnoses were excluded from the analysis of the screening programme impact. The rate of late diagnoses (after 24+0 gestational weeks) did not change over the study period (Table 2). Only five cases were found before second-trimester structural screening; all these cases had other major extracardiac anomalies. Distribution of the weeks of gestation at prenatal detection is shown in Figure S2b.

The overall total prevalence of TGA in Finland was 2.82/10 000 births and the live birth prevalence was 2.55/10 000 live births. The national total prevalence (range from 3.26/10 000 to 2.62/10 000; $P=0.201$) and live birth prevalence (range 3.04/10 000 to 2.40/10 000; $P=0.18$) did not change over the study period. However, the total prevalence of TGA varied

significantly between the western (2.07/10 000) and eastern (3.92/10 000) ($P=0.018$) regions (Figure 2b). Pregnancy termination rates in TGA cases did not change significantly (5.3% [5/57], prescreening phase to 9.0% [7/78], screening phase; total change 3.7% [95% CI -6.5–12.8]; $P=0.416$). Most terminated cases had other major extra-cardiac malformations.

Maternal risk factors for heart defects and the impact of risk factors for the screening programme.

No associations between prenatal diagnoses and any of the studied maternal risk factors were observed (obesity, $P=0.61$; pregestational diabetes, $P=0.34$; IVF, $P=0.54$; multiple pregnancy, $P=0.09$; smoking, $P=0.60$). The studied maternal risk factors for heart defects in the CHD birth cohort and comparison with all parturient population are reported in Table 3. There was no difference in the mean BMI (25.5 ± 6.0 versus 25.4 ± 5.2 ; $P=0.850$) between mothers with or without a prenatal diagnosis. Women expecting an infant with UVH or TGA were obese more frequently compared with parturients ($P=0.007$). The results were consistent after excluding mothers with pregestational diabetes or mothers with fetuses with chromosomal defects. Pregestational diabetes was more common among the cohort than in all parturients ($P<0.0001$). No difference in the frequency of IVF treatment was observed between the CHD birth cohort and all parturients. However, after including pregnancy terminations, pregnancies conceived after IVF were significantly more common ($P=0.005$) in the CHD cohort than in the all parturients population. These results were consistent after excluding cases with chromosomal defects ($P=0.03$). The number of twin and triplet pregnancies was significantly higher in CHD cohort than in the all parturient population, although no difference in IVF treatment was observed in these subgroups.

DISCUSSION

Statement of principal findings

The implementation of a nationwide systematic fetal anomaly screening programme significantly improved prenatal detection of UVH and TGA. Ultrasound screening of the fetal heart includes the four-chamber view and the outflow tract areas; UVH and TGA were used as index markers, respectively. The studied maternal factors associated with the risk of fetal CHD did not affect prenatal detection. Importantly, there were still significant variations in detection rates within the country. Previous information on the efficacy of national screening programmes and national prevalence of critical CHDs is limited due to the lack of comprehensive national registers of congenital anomalies and incomplete data on terminations, stillbirths, and live births. Data from a prospective screening register might enable further improvement of the prenatal detection rate in low detection areas. This is essential since prenatal diagnosis decreases perinatal mortality and morbidity in transposition of the great arteries.⁴ Children born with prenatally diagnosed UVH are hemodynamically more stable than those detected postnatally,^{5,6} and detection in screening allows the option of termination as only palliative care is available.

Strengths and limitations

This study has several strengths. First, we controlled and confirmed all diagnoses from patient records by a fetal and paediatric cardiologist and reviewed all potential cases with diagnoses leading to UVH or TGA. Second, Finnish registries are comprehensive as is mandatory to report data on every birth and pregnancy termination. The registers are overlapping; every case in the Finnish Register of Congenital Malformations was also found in the Medical Birth Register or the Register on Induced Abortions. We avoided double-

counting by using the unique identification numbers available in all registers. The Finnish Register of Congenital Malformations is a unique database and receives reports from every pre- or postnatally detected congenital anomalies and actively collects data from all cases found in other registers. This study also has some limitations. Although recommended by the expert committee, a prospective screening register has not been established due to budget restrictions. Due to the lack of a screening register, we do not have data on screening personnel, equipment, or structurally collected data on the findings. Structurally collected data would enable an analysis of the reasons behind regional variation. While exact national numbers are not accessible, approximately 95% of pregnant women participate in ultrasound screening during pregnancy. Finally, terminations did not include data on BMI, smoking, or maternal diagnoses.

Interpretation

In our nationwide study, the prenatal detection rate of UVH increased from 50.4 % to 82.8% after implementing the nationwide screening programme. The results are similar to reports from regional cohorts in the Czech Republic (from 33.6% to 83.2%)¹⁰ and The Netherlands (from 55.3% to 93.6%)¹¹ and from recent nationwide data from Denmark (34.3% to 83.3%).¹³ In our study, prenatal detection rates of TGA increased from 12.3% to 41.0%.

These results were better than those in the Czech cohort (from 5.7% to 25.6%),¹⁰ and similar to those in the Dutch cohort (from 18.6% to 48%)¹¹ and Danish cohort (4.3% to 41.0%).¹³ All these programmes included structural anomaly screening between gestational weeks 18 to 20 to 22. In the Czech Republic, screening is performed by trained local obstetricians/gynaecologists and in The Netherlands mainly by trained ultrasonographers.

Although regional variations were seen, implementing a nationwide screening programme improved the antenatal detection rates of UVH significantly in all parts of the country regardless of initial detection rates before implementation. Similarly, the prenatal detection of TGA increased significantly nationwide. However, there was significant variation within the country. TGA is a rare anomaly and detection rates changed only modestly in the areas where the total prevalence of TGA was low. This minor change may be due to the limited number of cases in these regions and the difficulties in identifying this anomaly.²³ The screening and education criteria for the screening personnel are based on national recommendations. However, every municipality can decide whether to develop the service by training personnel or to obtain the service from private providers. Finally, some effect on the improvement of anomaly detection rates may be due to developments in ultrasound equipment during the study period. The lack of a prospective screening register prevented us from investigating the reasons behind the observed regional variations and how expert committee recommendations were fulfilled.

The total prevalence of UVH was 7.4/10 000 and is higher than previously reported (3.4/10 000 to 5.3/10 000).^{13,24,25} In our study, one fetal cardiologist meticulously evaluated all fetal echocardiograms and autopsy reports. We included every diagnosed case over the study period, even terminated cases with chromosomal anomalies (15.6%) and cases with ultrasound detection but without autopsy confirmation. Previously, these cases or pregnancy terminations were excluded, or reference to inclusion criteria was missing.^{24,26-28}

Interestingly, the live birth rate of UVH was also higher in Finland (2.9/10 000 live births; screening phase), than in Denmark (0.8/10 000)²⁴ and the Paris region (1.5/10 000).²⁵ In our cohort, termination of pregnancy due to UVH occurred in 52% of cases; the corresponding values were 44.8% in Denmark¹³ and 62.7% in Paris.²⁵ These results may indicate that the total prevalence of UVH in Finland may be higher than in Europe overall. A similar

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difference is seen in the total prevalence and live-birth prevalence of severe CHD (34.9/10 000 and 28.1/10 000, respectively, according to the Finnish Register of Congenital Malformations) when compared with The Netherlands (27/10 000 and 20/10 000, respectively). The total and live birth prevalence of TGA (2.82/10 000 and 2.55/10 000, respectively) were consistent with those previously reported (2.0 to 3.5/10 000).^{4,13,29,30}

In our study, obesity or other maternal risk factors did not affect prenatal detection. Previous studies have shown that maternal obesity is a risk factor for fetal congenital heart defects³¹⁻³³ and mothers without a prenatal diagnosis were more obese than mothers with prenatal diagnosis.¹⁹ Suboptimal cardiac views in second-trimester ultrasound are common in obese women.³⁴ In our study, there were no differences in maternal characteristics or risk factors between those with and without a prenatal diagnosis. Late or random diagnoses were not more common in obese women. However, it must be noted that the BMI data of terminated pregnancies are missing and this can affect the results in the UVH cohort due to the high proportion of terminations. However, we did not observe any difference in the TGA cohort in which terminations were few. Pregestational diabetes leads to more thorough follow up and a higher prenatal detection rate of congenital anomalies.³⁵ We did not observe a significant difference in prenatal detection of UVH and TGA among mothers with pregestational diabetes; the numbers were, however, limited. In agreement with previous studies,³⁶ CHD was associated with multiple pregnancies. A recent meta-analysis suggests that IVF treatment increases the risk of CHD.³⁷ Similarly, we observed an association between IVF and CHD when the whole cohort (including pregnancy terminations) was studied. However, no association between IVF and CHD was detected in the birth cohort or the cohort of multiple pregnancies. The latter is probably due to one-embryo transfer that is primarily applied in Finland. Interestingly, multiple pregnancies or IVF treatment did not increase prenatal detection even though these pregnancies are often followed more thoroughly.

CONCLUSIONS

The implementation of nationwide prenatal anomaly screening significantly improves the prenatal detection of UVH and TGA. The establishment of a prospective screening register is strongly recommended to ensure high quality of screening. The total and live birth rates of UVH were higher in Finland than previously reported. The total and live birth rates of TGA were consistent with previous reports. Obesity or other maternal risk factors for severe fetal heart disease did not affect prenatal detection.

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Contribution to authorship: JH, MG, AR, and TO had full access to all data in the study and take full responsibility for the integrity of the data and the accuracy of the data analysis. MG, AR, TO, AT, OP-A, VS, TS, JP, TP, IM, EJ, and JR conceived and designed the study. All authors acquired, analysed, and interpreted the data and critically revised the manuscript for important intellectual content. JH, MG, AR, EH and TO drafted the manuscript. JH, MG, EH and TO performed the statistical analysis. JH and TO obtained funding and provided

administrative, technical, or material support. JH and TO are the guarantors. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Ethical approval: The Ethics Committee of the Helsinki University Hospital approved the study (20th April 2017, HUS/1938/2016). The National Institute for Health and Welfare authorised the use of the health register data in scientific research, as required by the national data protection legislation.

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Figure legends

Figure 1. Prenatal detection rates, extra-cardiac malformations, and chromosomal defects in

a) UVH and b) TGA. (UVH=univentricular heart, HLHS=hypoplastic left heart syndrome, TGA=transposition of great arteries, TOPFA= Termination of Pregnancy due to Fetal Anomaly)

Figure 2. Regional total prevalence (/10 000 births) in five university hospital districts and prenatal detection rates (%) in screening phase 2010 to 2014 of a) UVH and b) TGA

Table legends

Table 1. Clinical characteristics of all mothers.

Table 2. Prenatal detection rates and change after implementation of systematic screening (random prenatal diagnoses excluded) and rates in random and late diagnoses comparing the first and last study periods

Table 3. Comparison of heart anomaly risk factors in birth cohort (mothers of children born with a congenital heart defect) and all parturient population in study period.

Supplementary material legends

Table S1. Screening protocol for first-trimester and second-trimester ultrasound

Table S2. Minimum and preferable ultrasound equipment requirements (The Royal College of Radiologists, 2005)

Table S3. Training modules for fetal screening personnel

Table S4. Distribution of detected heart anomalies

Table S5. Chromosomal anomalies in cases with univentricular heart and transposition of great arteries.

Figure S1. Flowchart of the systematic fetal screening protocol in Finland³⁸.

Figure S2. Timing of total prenatal detection of a) univentricular heart and b) transposition of great arteries over the study period. Cut-off delayed diagnosis marked with a horizontal line and study periods with vertical lines: prescreening phase, transition phase and screening phase.

Table 1. Clinical characteristics of all mothers.

Mothers		Total time period 2004 to 2014
		UVH (n=483)
		TGA (n=184)
		All parturients (n=642 456)
Maternal age ^a (years)	UVH	30.7±5.7
	TGA	30.2±5.2
	All parturients ^c	30.1±5.4
Previous pregnancies (n) ^b	UVH	1(1-2)
	TGA	1(0-2)
	All parturients ^c	1(0-2)
Previous births (n) ^b	UVH	1(0-2)
	TGA	1(0-2)
	All parturients ^c	1(0-1)
BMI ^a	UVH ^c	25.7±5.8*
	TGA ^c	25.1±5.1**
	All	24.3±4.8
	parturients ^c	

a=Mean (SD)

b=Median (IQR range, 25-75%)

c=only births included (UVH n=232, TGA n=168)

* compared to all parturient group, $P=0.0006$

** compared to all parturient group, $P=0.05$

Table 2. Cases and prenatal detection rates and change after implementation of systematic screening (random prenatal diagnoses excluded) and rates in random and late diagnoses comparing the first and last study periods.

Region	Prenatal detection rate prescreening period		Prenatal detection rate screening period		P-value	
	UVH	TGA	UVH	TGA	UVH	TGA
National	50.4% 63/125	12.3% 7/57	82.8% 192/232	41.0% 32/78	<0.0001	<0.0001
Southern	57.4% 27/47	4.8% 1/21	85.1% 57/67	37.0% 10/27	0.001	0.008
Northern	57.1% 12/21	25.0% 2/8	82.1% 32/39	53.3% 8/15	0.04	0.19
Central	47.4% 9/19	10.0% 1/10	81.0% 47/58	18.2% 2/11	0.004	0.59
Western	33.3% 7/21	22.2% 2/9	67.9% 19/28	12.5% 1/8	0.02	0.60
Eastern	47.1% 8/17	11.1% 1/9	92.5% 37/40	64.7% 11/17	0.0001	0.009
Random diagnoses of all diagnoses (national)	8.7% 6/69	22.2% 2/9	3.0% 6/198	3.0% 1/33	0.05	0.048
Late diagnoses of screening diagnoses (national)	1.6% 1/63	14.3% 1/7	6.8% 13/192	12.5% 4/32	0.12	0.90

Table 3. Comparison of heart anomaly risk factors in birth cohort (mothers of children born with a congenital heart defect) and all parturient population in study period.

	Cohort %	All parturients %	P-value
BMI \geq 30	16.6% (59/355)	11.9% (72739/608731)	0.007
Pregestational diabetes*	2.9% (10/340)	0.8% (3996/528618)	<0.0001
Smoking	16.2% (54/333)	15.5% (97241/626811)	0.72
IVF treatment	2.8% (11/400)	2.3% (14579/642456)	0.52
multiple pregnancies	5.5% (22/400)	1.5% (9393/642456)	<0.0001
twins	5.0% (20/400)	1.4% (9272/642456)	<0.0001
triplets	0.5% (2/400)	0.02% (120/642456)	<0.0001
IVF in multiple pregnancies	13.6% (3/22)	14.5% (1363/9393)	0.87

*data from 2006 to 2014



