PROSPERITAS VESTRA FINIS NOSTRA!

Medical University - Varna
Prof. Dr. Paraskev Stoyanov

Faculty of Medicine
Department of Pediatrics

Tanya Lyubomirova Zlateva, MD

Organisation and results of a programme for early detection and follow-up of children born small for their gestational age

Thesis summary

OF DISSERTATION ABSTRACT FOR AWARDING EDUCATIONAL AND SCIENTIFIC DEGREE "PhD"

Scientific supervisor:

prof. Violeta Mihova Iotova, MD, PhD, DSc

Scientific jury:

prof. Dimitrichka Bliznakova, MD, PhD

assoc. prof. Natalya Usheva, MD, PhD

prof. Maya Krasteva-Vilmosh. MD, PhD

assoc. prof. Ralitsa Georgieva, MD, PhD

assoc. prof. Chayka Petrova, MD, PhD

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The dissertation work is presented on 180 pages and contains 11 tables, 29 figures and 16 annexes. 238 sources were cited, of which 11 in Bulgarian and 227 in English.

The dissertation is developed in:

• Department of Pediatrics, Medical University – Varna

• 21 neonatological units in Bulgaria

The dissertation was discussed and directed for public defense at a meeting of the Department of Pediatrics Department, Medical University – Varna. The materials of the dissertation are available in the scientific department of the Medical University – Varna.

The public defense will take place on 30.05.2024. in the Department of Pediatrics, University Hospital "St. Marina" – Varna, Hall 501 and in the Webex platform..

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ABBREVIATIONS:

AAP – American Academy of Pediatrics

AGA – adequate for gestational age

BPA – Bulgarian pediatric association

BNA – Bulgarian neonatology association

VAPES – Varna Pediatric Endocrine Society

LGA – large for gestational age

PE – pediatric endocrinologist

IC – informed consent

BMI – body mass index

BG – blood glucose

PDD – probable due date

SGA – small for gestational age

SAR – scientific and applied research

HC – head circumference

GP – general practitioner(s)

WC – waist circumference

reg. - regarding

a/t – against

HG – hypoglycemia

I. 1. INTRODUCTION

Growth is an important indicator of child health. Growth deviations are constantly in the focus of scientists from different branches of pediatrics. Growth hormone (GH) treatment is currently being carried out worldwide for children who are lagging behind in growth due to various diseases. Most often, these are children with a deficiency of GH, with proven syndromes and abnormalities, or those born of small size for their gestational age (SGA) and a lack of postnatal growth catch-up. The present work is aimed at the latter group, given its special characteristics, the need for treatment with GH in childhood and distant complications, especially in the absence of appropriate behavior in childhood. Children born SGA have a significant number of early (hypoglycemia, hypothermia, mortality, etc.) and late complications (early puberty, disability, cardiovascular disease, non-invasive growth).

The age of diagnosis requiring treatment with GH is decreasing worldwide. Our country does not lag significantly behind this trend, but despite the available information about the many and various conditions associated with impaired growth, children with delayed diagnosis are often observed in practice.

Two programmes related to early diagnosis and treatment of children with growth abnormalities have been planned and conducted in Bulgaria so far. Both are primarily aimed at conditions associated with GH deficiency or syndromic short stature. At the time of writing the dissertation, we know only one population study on full-term SGA children from single pregnancies, carried out by Iotova in 1999. Despite the availability of many data on the frequency of the condition worldwide, in our country epidemiological data are extremely scarce and difficult to access.

I. 2. Preconditions

1. The diagnosis of SGA children in our country and globally is still late.

2. Inadequate awareness of doctors and the public about the condition.

3. Lack of recent data on the frequency in Bulgaria, as well as publications with an assessment of the SGA sizes at birth according to the modernly accepted standards for classification of Fenton.

4. Lack of information on the number of SGA children in need of follow-up in the health system.

5. The need to prepare neonatologists and pediatricians for timely evaluation of syndromes associated with the birth of a child with small size.

6. The need for timely treatment with GH (10% of SGA children by literature do not catch up in their growth), prevention of obesity and treatment at early onset of puberty development.

7. Urgent need to reduce age in diagnosis and increase coverage and success in the treatment of various diseases.

8. The lack of a structured approach to diagnosis and follow-up of children born SGA, although it is not a rare condition.

9. Sufficiently accumulated data on the beneficial impact of scientific and applied programmes on the awareness of the society, the target groups in it and the medical specialists.

I. 3. Aim

By creating, implementing and evaluating a pilot study (Programme) for identification, tracking and prevention of the health consequences for full-term and preterm born SGA children in Bulgaria, to build a basis for its introduction into routine neonatological and pediatric practice in Bulgaria.

I. 4. Tasks

1. To analyze the literature data on the frequency and complications of SGA birth in Bulgaria for the period 1990-2020.

2. To assess the knowledge of practicing neonatologists on the frequency and complications associated with SGA birth.
3. To design a timely detection and follow-up programme for full-term and preterm infants born SGA, to be implemented in interested neonatal care facilities (First stage, neonatal) and to continue with the follow-up of enrolled SGA children in paediatric endocrinologists (Second stage, endocrinological).
4. To assess the frequency of full-term and premature SGA children born in the participating neonatological structures the period of the Programme (01.04.2021 – 31.03.2022), as well as detection of syndrome patients already in maternity hospitals.
5. To evaluate the results of the first phase of the Programme (neonatological).
6. To assess the potential impact of the Programme on society (media coverage).
7. To assess on an ongoing basis and at the end of the Programme the expected and unexpected barriers and facilitators, registered during the Programme.
8. To offer an advanced approach for early diagnosis and coverage of children born IBS, in order to avoid the early and late consequences of the condition and related syndromes and other diseases.

I. MATHERIALS AND METHODS:

II. 1. Methods:

1. Search in multiple medical databases.

The following approaches have been used to accomplish task. First there was a search in PubMed by keywords SGA, Bulgaria (SGA, Bulgaria) for a 30-year period (1990 – 2020). A bibliographic reference has also been made to the national library, as well as an own study of the epidemiological data on the high incidence of SGA childbirth and the complications associated with it in our country for the above period.

2. Questionnaire method.

Two surveys were used in the study. Task 2 was carried out using the online MonkeySurvey questionnaire. The survey consists of 11 questions, 8 of them with answers. The aim is to determine the material security of neonatal structures, as well as to assess the knowledge of the participants neonatologists on the definition of full-term and premature SGA child and the complications related to the condition. The survey examined the number of

newborns for 2020 in neonatal units and how many of them are full-term, respectively premature. Questions were included on routine blood glucose (BG) measurement, as well as their experience of referral to a paediatric endocrinologist (PE).

The second author's survey was conducted after the analysis of the data for the first 6 months of the pilot Programme. The purpose of the author's questionnaire is to assess the degree of application (implementation) in the participating neonatological structures. The online Monkey Survey software was used again. Ten questions have been used about the difficulties that the working neonatologists on the Programme face on a daily basis, whether they have support from their colleagues, the time that neonatologists devote to the Programme, as well as whether there is an interest in the parents and the medical community in the project.

3. Organizational methods.

The pilot Programme was created through the joint efforts of the Bulgarian Neonatology Association (BNA, www.neonatologyabg.com) and the Varna Society of Pediatric Endocrinology (VAPES, www.vapesbg.eu). After the Conference on Neonatology in Burgas and the Congress of BNA in Hisarya in 2019, the idea for organizing a project was born, which not only to acquaint the general public with the mentioned problem, but also to update the data on the frequency of SGA births, as well as to avoid late complications in the same.

After the conference, active preparation for the project began. The Programme was designed as a scientific and applied research and was presented for funding to the international independent financing instrument Global Medical Grants (Pfizer). Permission and funding under project number 64919053 was obtained. Due to the beginning of the pandemic and the announced in March 2020 total lockdown in the country and the subsequent very difficult times for the health and public systems, the beginning of the Programme was postponed. In January 2021, reconnection with the requested neonatological structures began and on 01.03.2021 was announced the beginning of the pilot Programme. In the process of preparation, a visualization (branding) of the Programme was created and the plan for its dissemination and media coverage was specified, with the main purpose of increasing the knowledge of the SGA status among health professionals and in society.

4. Clinical methods

Each newborn was measured in height and weight in the delivery room, as follows from the birth protocol. The height was measured by a standardized Seca baby height meter by two

people, with the external auditory passage and mandible in a plane parallel to the horizontal board of the meter, and the head crown is touched to the height meter. The legs should be stretched and lean to the other end of the height meter in an angle of 90 degrees. Measurement shall be carried out with an accuracy of 0,1 cm.

The weight of the newborn shall be measured on an appropriate scale after birth without a diaper and before wearing it, with an accuracy of 0,01 kg. The head circumference (HC) in the birth hall was measured with an unstretchable band.

At the first convenient time, the child is assessed whether he is an SGA for the respective gestational age relative to the length at birth, weight and/or both together. This occurs by placing the measured length and weight at birth on the Fenton curves for the respective sex and gestational age. When considering one of the two or both points below the 10th percentile, the newborn is defined as SGA relative to height (length), weight, or height and weight at the same time.

At the age of 2 years, each child participating in the Programme is subject to examination by a pediatric endocrinologist (PE). All participants who have requested PE are promptly provided with a folder with materials under the Programme. All materials prepared for the Programme were available on its website for free use.

At a meeting of the project team, an algorithm for re-evaluation and follow-up of SGA children by a pediatric endocrinologist was developed at the Second (endocrinological) stage of the Project. It is based on the steps needed to evaluate each child. The training of parents and doctors is in the direction of children to consult initially at 2 years of age or soon after. Initially, a detailed history of pregnancy and childbirth is taken, as well as data on nutrition, past and present diseases of the child by the time of the examination. Of importance are hereditary diseases and the presence of short stature/growth deviations on both lines. Then a full examination is performed – examined and all body systems, dysmorphic stigmas, if any, are described, pulse, heart rate and respiratory rate are measured. The child's neuropsychological development is assessed. The data on the growth of the child (most often the GP measurements, but can also be used by a tracking pediatrician and/or neonatologist, including those regularly measured in the home), which the family is warned to wear.

In the office of PE is carried out the entire physical examination, including actual measurement of height, weight, head circumference and abdomen. The height was measured to an accuracy of 0.1 cm by means of standardised height meters, which equipped the office of

each PE. The weight was measured to an accuracy of 0.1 kg on a standardised weighing instrument, with children measured without shoes and dressed in light clothing. Head (HC) and waist (WC) circumferences are carried out according to generally accepted rules and are measured to an accuracy of 0.1 cm.

On the basis of the review and the recorded auxological data of the measurements in the GP and/or the pediatrician, a growth assessment is performed. The data on height and weight are applied to the curves of the Center for Disease Control (CDC, Centers for Disease Control and Prevention), available on the site https://www.cdc.gov/growthcharts/clinical_charts.htm. CDC curves are widely used worldwide and in particular, in Europe and in our country.

When performing the growth assessment, the growth of the mother (Hm) and that of the father (Hf) in centimeters are taken into account. They are important for determining the prognosis of the child's final height - target height (TH) and target range (TR). Or in other words – to what it strives for and where the normal height is expected to be located for a particular child (growth channel).

TH is determined by the formula of Tanner :

TH boy = (Hm + Hf + 13) / 2

TH girl = (Hm + Hf - 13) / 2

The target range (TR) of the deviation of normal height for each child was defined as the range ± 9 cm for boys and ±7.5 cm for girls (on Tanner).

The body mass index (BMI) was calculated using the Quetelet formula and compared with the CDC reference data:

BMI = weight (kg)/ height^2 (m^2)

or directly through the calculator on the site of the Center for Disease Control and Prevention (https://www.cdc.gov/healthyweight/bmi/calculator.html). BMI and weight are evaluated by the standards of the respective sex and age of the CDC.

5. Methods of scientific-applied nature.

In order to fully assess the degree of application (implementation rate) of the pilot Programme, a survey described above in the questionnaire method section of Materials and Methods is planned.

The hired the PR-specialist under programme received instructions to search for interested media, as well as to distribute all activities under the Programme in a timely manner. A plan for dissemination of objectives, methods and current results was made. In addition to the usual ways through participation in scientific events and media channels (television, videos, YouTube, FaceBook, magazines, newspapers and sites), more recent methodologies and techniques such as publishing banners on the most visited health sites and interviews of young professionals working on the Programme were used in the dissemination of the activities and results. The participating coordinators, representatives of BNA and VAPES did not miss an opportunity to promote the Programme, the difficulties it faces and its achievements.

A comprehensive assessment of media monitoring was planned and carried out (assessment of the recognisability and societal impact of the project). This was done by evaluating the visits to the site, the email requests and the FaceBook page of the Programme. The data was collected with the help of the IT specialist working on the project.

At the beginning and at the end of the pilot programme, the expected and detected facilitators and barriers that had an impact on the degree of project application were analysed. All data from the surveys, as well as from the opinions of the participating neonatologists during the monthly telephone reports and congresses at which the project is presented, are taken into account.

6. Statistical methods.

When collecting the monthly results of determining the frequency of SGA births, it is also planned to collect the auxological data of the enrolled SGA children.

The analysis of data on the auxological indicators of newborn SGA children was finalized through SPSS version 25 software. The data are further processed by the automatic software Fenton Growth Calculator for Preterm Infants (https://peditools.org/fenton2013/index.php). Thus, in addition to further cleaning and excluding the data of children who are not born SGA or do not meet the inclusion/exclusion criteria otherwise, the data on length at birth and weight in z-score (SDS) are converted.

With the help of SPSS, several analyses of the obtained data were carried out:

- variance analysis of quantitative data: mean, standard deviation.
- descriptive analysis of qualitative data: absolute number, relative share

– comparative analysis using Fisher's t-criteria, differences with $p<0.05$ were accepted as statistically significant.

II.2.Participants.

The selection of participants took place on several levels. After the presentation of the idea for the project and the more significant moments of the roadmap for its holding of the conference in Hisarya, the selection of the wards was made on the basis of a expressed desire by the neonatologists and in response to a survey sent a little more than a year later (January 2021). The survey was specially created by the Programme team (author) and described above.

The criteria for inclusion or exclusion of participants are as follows:

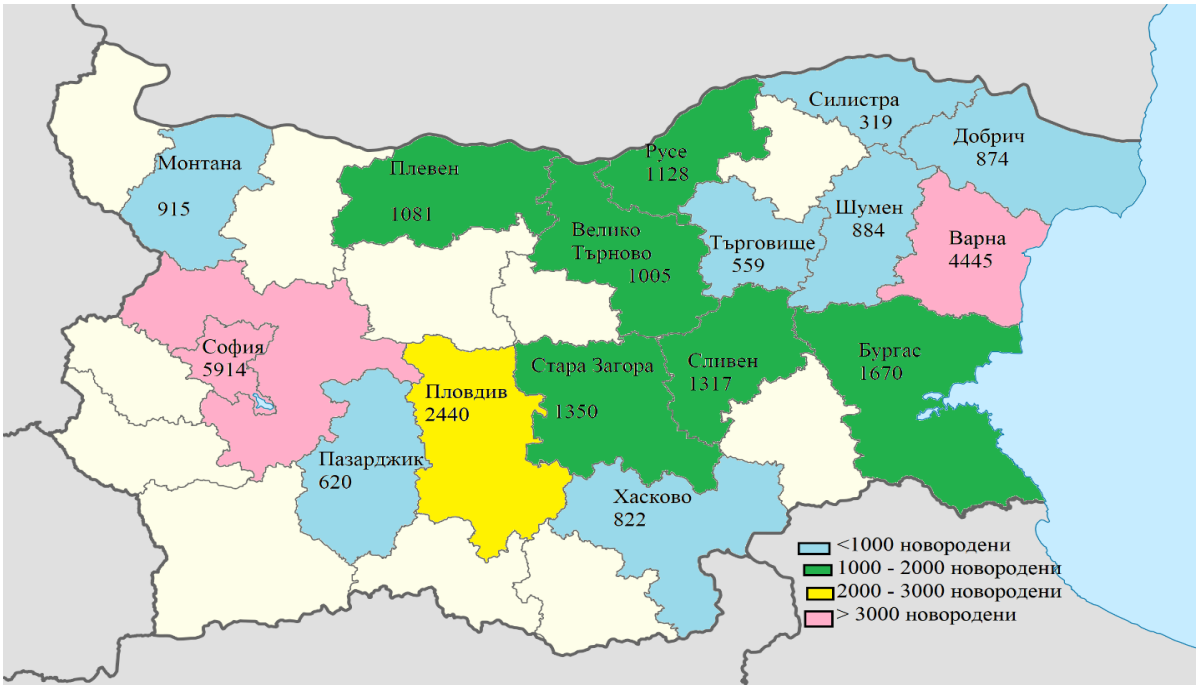
Criteria for the inclusion ofSGAparticipants:

1-st

An additional reference was made in the library and 11 full-text publications of Iotova were found, addressing the problems of the full-term SGA children. It introduces the terms and definition related to the SGA sizes at birth and the growth of children (postnatal catch-up/catch-up) in a cohort longitudinal study of adults from Varna and the region. Later problems related to SGA birth – lack of growth catch-up, obesity, metabolic syndrome, metabolic and cardiovascular risk have been thoroughly studied. Later in a dissertation paper for a scientific degree „Doctor of Sciences" were added studies on pubertal development, abdominal obesity and related cardio-metabolic and cardio-renal risk factors. Unfortunately, in the international literature, no traces of these large-scale studies are found.

In order to assess the available knowledge of the neonatologists who have applied for participation in the Programme and the preliminary data reg. SGA newborns, an online survey among 23 neonatological structures was conducted. Response was obtained from 90.9% (n=20) of participants. One of the clinics that did not respond to the survey did not start participating in the first stage of the Programme.

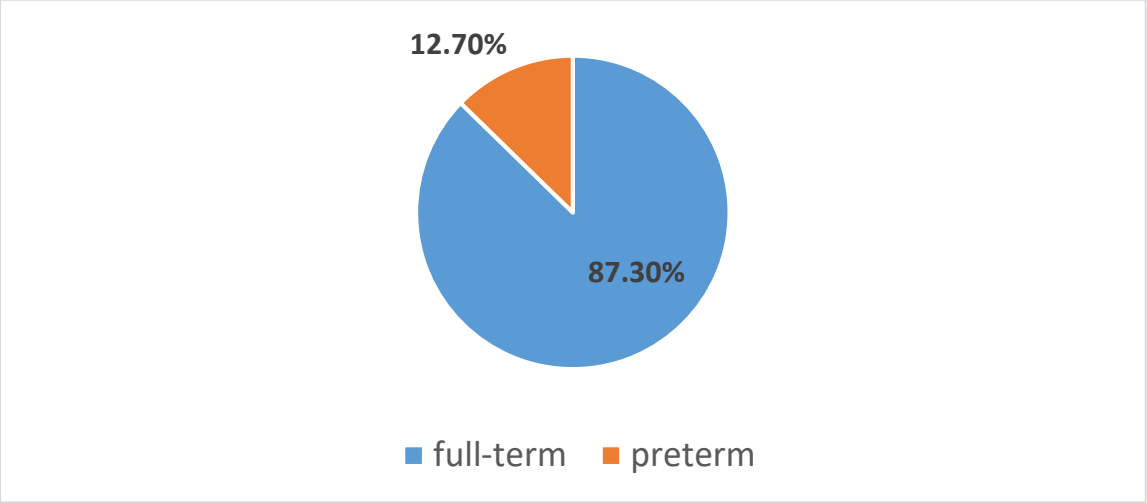
Fig. 1 Distribution of the number of newborns in the participating clics for 2020 by region



In 2020, according to the statistics led by the participating neonatological structures, a total of 25,343 children were born, including 87.3 % (n=22 113) were full-term and 12.7% (n=3 230) were premature. No clinic have systematically determined SGA/AGA/LGA status at birth. Fig. 1 shows the distribution of the number of newborns by region for 2020. Fig. 2

shows the ratio of preterm and full term children born in the willing neonatological structures for 2020.

Fig.2 Ratio full-term-preterm SGA children born in 2020 in the participating neonatology units



When asked what device they measure children's height, 80% (n=16) say they use a tailoring meter for this purpose. In one of the polls, there is a response „rolet", which was used as a meter. Only 20% say they have different tools (5% - Gima standard height meter, 5% - graduated adhesive tape per centimetres, 5% - a height meter to a drawbar and 5% - a meter placed on a hard plane) (Fig. 3).

Fig. 3 Material security of neonatal units with devices for measuring the height

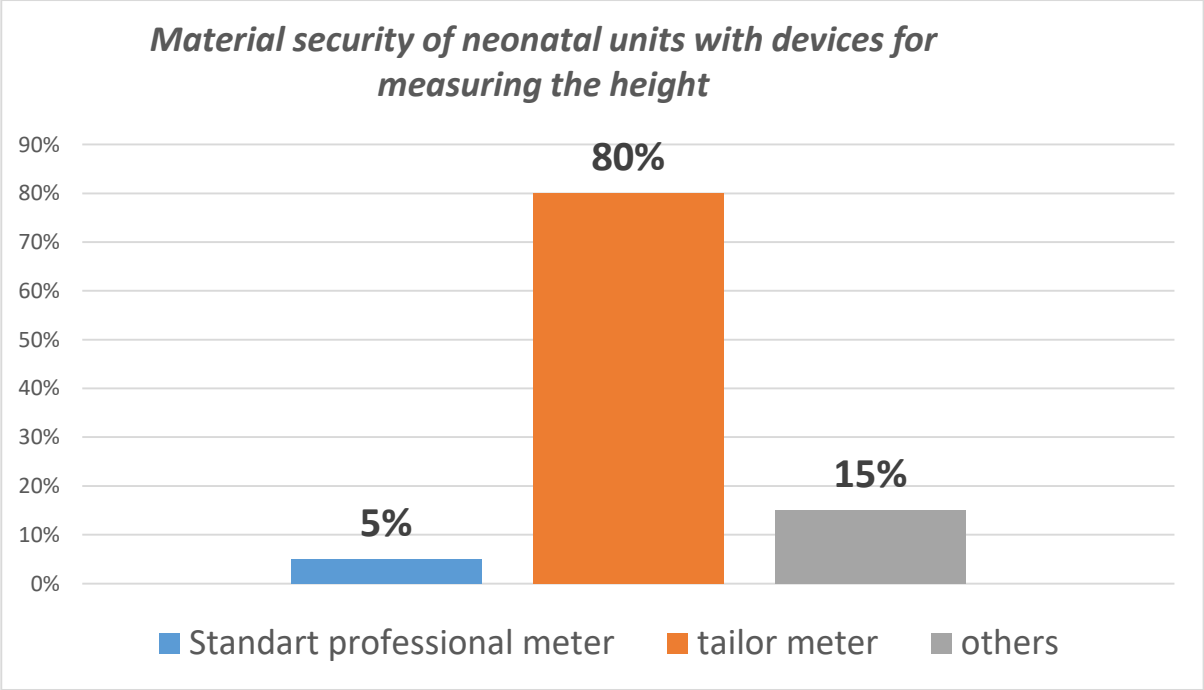
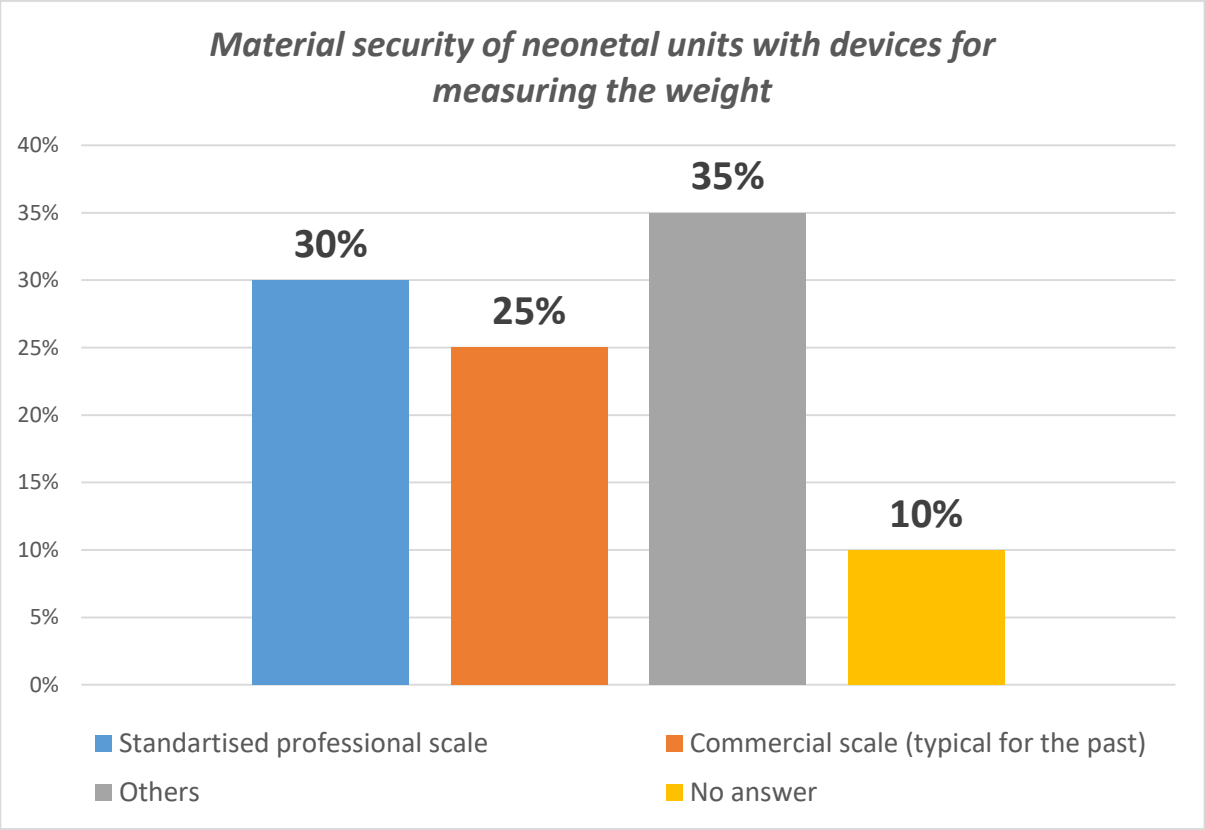


Fig. 4 Material security of neonatal units with devices for measuring the weight



Almost all respondents (95%, n=19) stated that they use a tailoring metre to measure head circumference (HC), with only one reported for the presence of specialized HC measuring tapes, „given by pharmaceutical company". Fig. 4 presents the material security of neonatal units with devices for measuring weight. It is evident from both figures that in most neonatological structures there is no good material basis for performing their daily work related to measuring newborns.

When asked how they rated the gestational age, the respondents gave more than 1 answer, relying most on clinical signs and PDD, determined by the Negele formula. It is important to note that in the category „other response", 20% (n=4) replied that antenatal ultrasound is relevant.

To estimate gestational age, five respondents (25%) said they used Rautenbach-Hoepffner's clinical criteria, two (10%) used the 1991 New Ballard Score. The majority of respondents (75%, n=15) said they used the auxological criteria of Fenton to determine a full-term and premature SGA child. The Rautenbach criteria were used by 10% (n=2), and one neonatologist (5%) said he most often used the Lubchenco criteria.

By checking the knowledge of the reasons for tracking SGA children and targeting PEs, all respondents said that tracking physical development is of particular importance. The reasons

that neonatologists indicate as grounds for referral to PE are different – „osteogenesis imperfecta", „delayed growth", „achondroplasia", „hypoglycemia", etc. For reasons of follow-up of SGA children, the most commonly indicated response was growth retardation and high metabolic risk. Only one person surveyed said they were conducting routine blood glucose (BG) tests on all newborns.

After analyzing the data from the survey and on their basis, the preparation of the materials for the Programme was started. Meetings were held with artists, PR and IT specialists. They helped the organization, the production of a logo, flyers, posters and the site, as well as the filming of the videos. Given that there was already an inertia on the part of neonatal structures, the preparation of materials was carried out in parallel, as well as the re-calling of the structures willing to participate.

A learning video explaining the definition of a SGA child and the need to track the condition due to frequent late complications is captured. Two training videos were shot to measure a small infant (as a demonstration to measure a newborn), an older child (over 2 years of age). The videos are available on the Programme's website (https://mgv.growinform.org/%D0%BD%D0%BE%D0%B2%D0%B8%D0%BD%D0%B8/%D0%B2%D0%B8%D0%B4%D0%B5%D0%BE-%D0%BF%D1%80%D0%B5%D0%B4%D1%81%D1%82%D0%B0%D0%B2%D1%8F%D0%BD%D0%B8%D1%8F).

The project is under the joint auspices of the Bulgarian Neonatology Association (BNA) and the Varna Society for Pediatric Endocrinology (VAPES). The introductory video announcing the beginning of the pilot Programme was broadcast on 01.03.2021. This is not accidental, but is also tied to the logo of the project, made together with an artist-graphics (fig. 5). Using the martenitsas – large and small, a greater and easier recognition of the Programme was sought. The meaning of the small and large martenitsa was to show that this specific group of „small" children have great opportunities to catch up on their growth and be indistinguishable from their peers. Prof. Iotova gave the idea to title the site and FaceBook page „Small with Great Potential (SGA)".

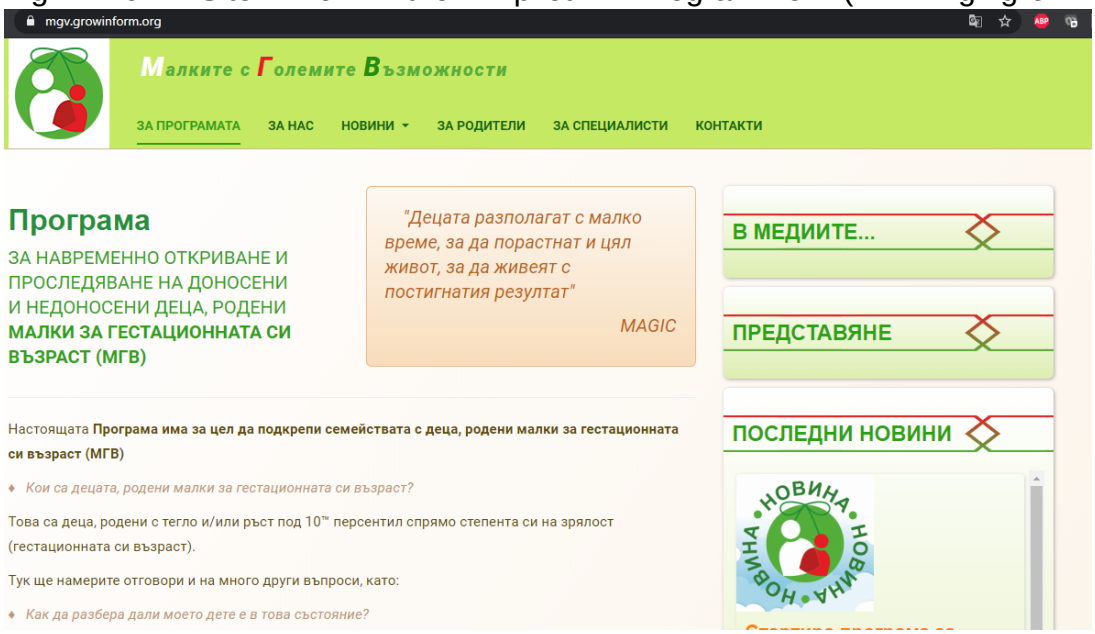
Fig. 5 Logo of the Programme

In order to promote the Programme, three types of leaflets were prepared:

- for future parents,
- for parents of SGA children
- for doctors and especially general practitioners (GPs) pf the future newborns

A poster is prepared for each participating neonatology unit. The purpose of the leaflets provided was to make parents, future or current, aware of the condition and if interested, to seek more information on the indicated FaceBook page (Small with Great Potential), email (21mgv21@gmail.com) and/or site (www.mgv.growinform.com, figure 6). The website of the Programme provides free download of the curves of Fenton, a graphically presented differential diagnosis of the most common syndromes associated with SGA birth, translated by the publication of Finken and others.

Fig. 6 Site of the pilot Programme (www.mgv.growinform.org)



In order to further facilitate the promotion of the Programme, the FaceBook page and site information about the condition are continuously supplemented. Data on the progress of the Programme shall be reported. With the help of the IT specialist, online platforms for communication with parents are supported. With the help of the PR specialist, the Programme is actively reflected in various newspapers, online editions, televisions. It is planned to maintain the site, e-mail and FaceBook page after the end of the pilot Programme.

The initial survey proved the lack of sufficient measuring instruments for both height and weight in many of the participating units. The different criteria for accepting a diagnosis of SGA are also alarming. Thanks to VAPES, all neonatal units were equipped with new standardized Seca baby height meters, and those with the greatest need and with new Gima electronic weights.

The programme provides for a mandatory review and assessment of catching up in the growth of enrolled children at the age of 2 years, but if desired by parents, such can be done earlier. The materials were prepared in folders and together with the measuring equipment were sent by courier company in March 2021.

A few days after the distribution of the materials, the first trainings were held. Given the start of the project during the COVID-19 pandemic, it was not possible to conduct the sessions in person, so the Google Meetings platform was used. The trainings, which took place in two consecutive days (30.03 and 31.03.2021), were attended by almost all neonatological units (86.95%, n=20). The trainings were attended not only by the heads of the structures, but

also by young specialists and post-graduate students. Each head of department made a separate decision on how to work on the – Programme alone, with the help of colleagues or to include support staff – midwives and nurses. The two units, which failed to participate in the online trainings, participated in sessions on the phone at a convenient time for them. Only one unit at a personal meeting for the transmission of materials refused to participate in the trainings, because „The Programme does not seem difficult“.

After conducting the survey and the first online trainings, expected barriers and predisposing factors (facilitators) in the implementation of the Programme were outlined. They are presented in Table 2.

Table 2 Expected barriers and facilitators.

Expected barriers	Expected facilitators
Lots of clinical work	Training of neonatologists and providing easily accessible and simple tools for assessing and registering newborns
Cultural and social factors	Media covering of the Programme
“Fear” in parents; unusual approach	Maintenance of online platforms and constant telephone connection for communication with the team of the Programme
Differences in the measurement of the height of children and poor provision of measuring instruments	Provision of new modern Secca height meters to all participating neonatological units.
Differences in the methods used for the determination of SGA	Trainings and accessible videos on the Programme's website

In conversations with the participating units on the organization of the Programme, it was very often touted as a problem that „the person responsible for the Programme” works on schedule and so sometimes children are missed. A big concern among neonatologists was how to choose when and how to explain the condition to parents. The many clinical work combined with the fact that in many places one on duty is responsible for births, physiologically healthy

newborns, at-risk and those in an intensive sector, proved to be the first, most sustainable and largest barrier identified in the study. The trainings were able to calm the worries, as well as to explain possible future problems and ways to solve them.

Cultural and social factors are considered as a likely barrier in the Programme. In our country, there are not enough preventive programmes in general. This, along with the fear that arises in any parent at the first meeting with a new and unknown diagnosis, are reported as adverse factors. To reduce the effect of these factors, each participating neonatal unit was provided with posters and flyers. Part of the neonatal structures in the country have „Open days“. With this in mind, the team sent two posters and enough leaflets to each neonatology, and it was explained to everyone that if desired and/or needed more can be sent. The purpose was to visit the unit of future parents, to get them acquainted early with the pilot Programme, its goals and what the condition is.

Other expected barriers were the poor material base in the units and the height and weight differences associated with it. Thanks to VAPES, this barrier was easily overcome. As an unfavorable factor at the beginning, the difference in the definition of SGA child at birth was also reported. The team of the Programme conducted online trainings, which were repeatedly reminded of the definition used in the project, as well as provided enough printed and easily accessible Fenton curves through the website of the Programme.

After the start of the project, data from the participating neonatological units for the number of newborns, the number of SGA children detected and recorded, were actively collected by phone every month. The data was collected by the two coordinators. At the very beginning, each participating clinic handed „ the responsible“ for the Programme to facilitate the communication process. The calls were made at a convenient time for both sides, without unnecessary rigor and formality in their conduct, and in the most collegial and empathic way possible.

When taking into consdideration the results of the first 3 months, in six of the neonatal units a complicating factor turned out to be the introduction of the Fenton criteria for defining a SGA child. Despite the trainings, „the habit of“ to use the 3rd percentile was reported in these places. Several clinics did not provide data for the period or presented reasons why starting the project with them was impossible. Some of the reasons presented are as follows:

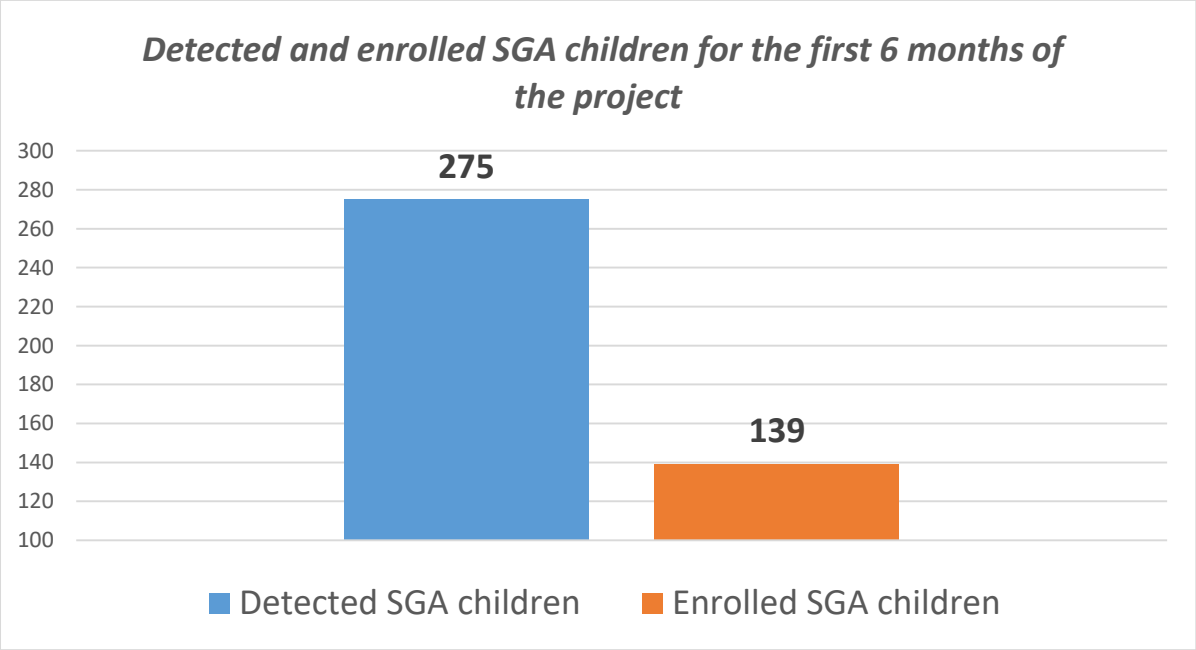
- lots of clinical work, insufficient staff
- unwillingness of the staff to work on the project,

x “forgetting” about the Programme

For these and possibly other unnamed reasons, two units did not start work on the Programme. These are two (8.7%) of the participants - in Pazardzhik and one neonatology in a large OB hospital in Sofia. There were gaps in the data of more compartments or they were not received on time or were not received at all, despite the current assurances that they would be provided.

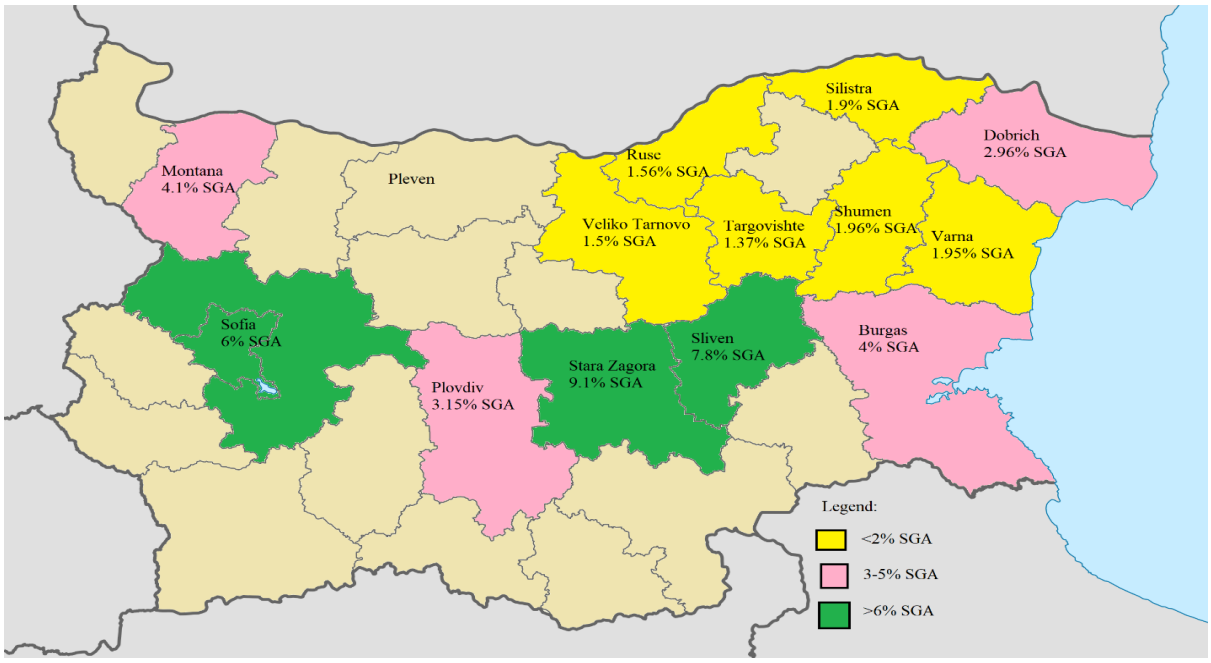
After the first 6 months of the Programme, an analysis of the results was made. For the above period, 275 SGA newborns were found. They represent 3.7% of all newborns in the participating clinics for the period (n=7424). The families that have agreed to participate in the Programme are 139 (50.54%) (Fig. 7).

Fig. 7 Detected and enrolled SGA children for the first 6 months of the project



During the preparation of the pilot Programme, it was expected to detect at least about 5% SGA newborns. Given the birth data for 2020, 1,267 children per year or 633 children for the first 6 months were expected. The 275 children found for the period were 43.4% of the expected. The frequency distribution of detected SGA newborns by area is shown in Fig. 8

Fig. 8 Frequency distribution offound SGAchildren by districts.



Differences in areas are evident. It is important to note that for the city of Sofia from 5 participating departments, only one presented data for the period. Of the remaining 4 (20% of all) did not start their participation in the Programme at all, and 60% did not report their data for the first 6 months. One of the three participating structures from Varna did not send data for the whole period. This is the same structure that at first claimed that „work on the Programme seems easy“.

In Pleven, for the first six months, a change of the neonatologist working under the Programme was required. That is why a new individual training was held and a new beginning of data collection from the clinic.

Of the other 13 participating structures, it is important to distinguish the work of two regional neonatal units – Sliven and Stara Zagora. There were 9.1% and 7.8% SGA newborns, respectively. The next neonatological structures with a close-by frequency are Montana – 4.1%, Burgas 4.0%, Plovdiv 3.15% and Dobrich 2.96%. The remaining 6 districts of Northeastern Bulgaria managed to register only < 2% of their newborn babies.

In order to establish the degree of application of the project (implementation rate), a new online survey was conducted through the MonkeySurvey platform a month after the analysis. The two coordinators contacted the departments that started their participation and all declared an oral desire to continue working on the pilot Programme. According to the declared

desire to continue (n=21) clinics, the poll was sent to 27 neonatologists from these clinics/departments in the country. Response was obtained from 44.4% of targeted neonatologists (n=12).

When asked how the work on the Programme goes, 84% of respondents answered well or very well. While 2 respondents (17%) said that they often have rejections, more than half (58%) share about drop-outs „only sometimes" (fig. 9).

According to half of the respondents, most often lead to refusal cultural-social reasons, and according to 25% of respondents, „parents do not understand the essence of the Programme" (Fig. 10). In another response, a neonatologist says that parents are often afraid of blood tests and have to reassure them that they will not be needed. Only a neonatologist claims that there are no refusals on the part of parents in its structure.

Fig. 9 Refusals from parents

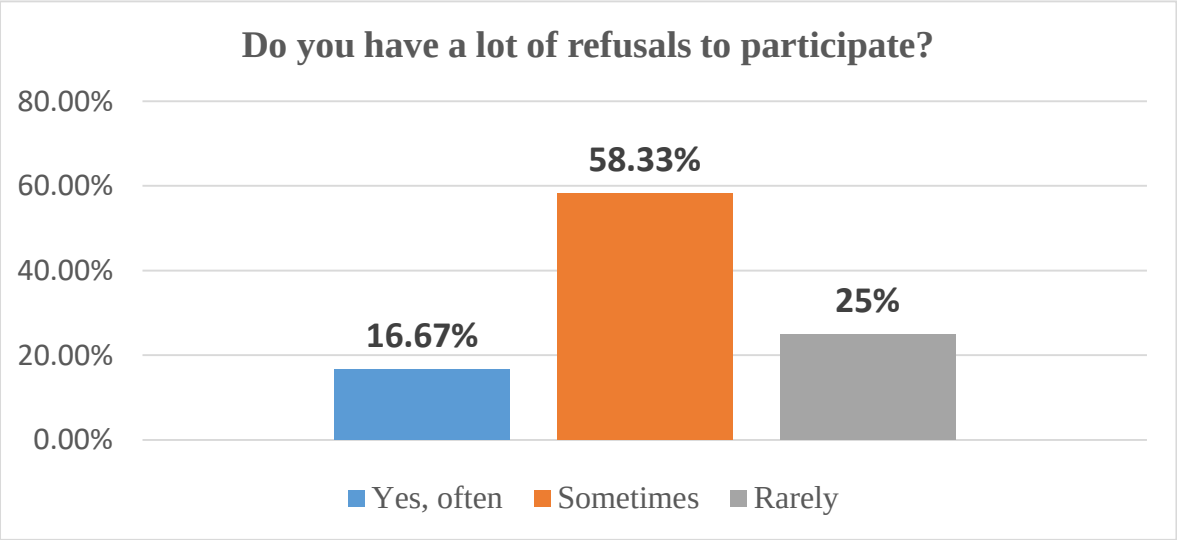
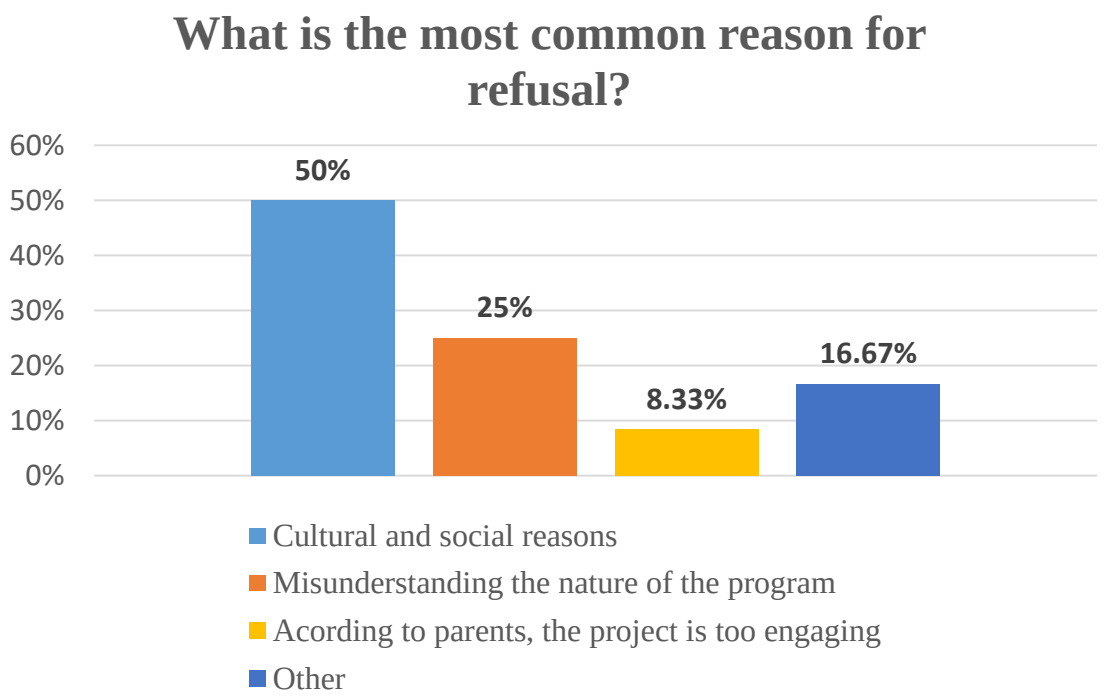


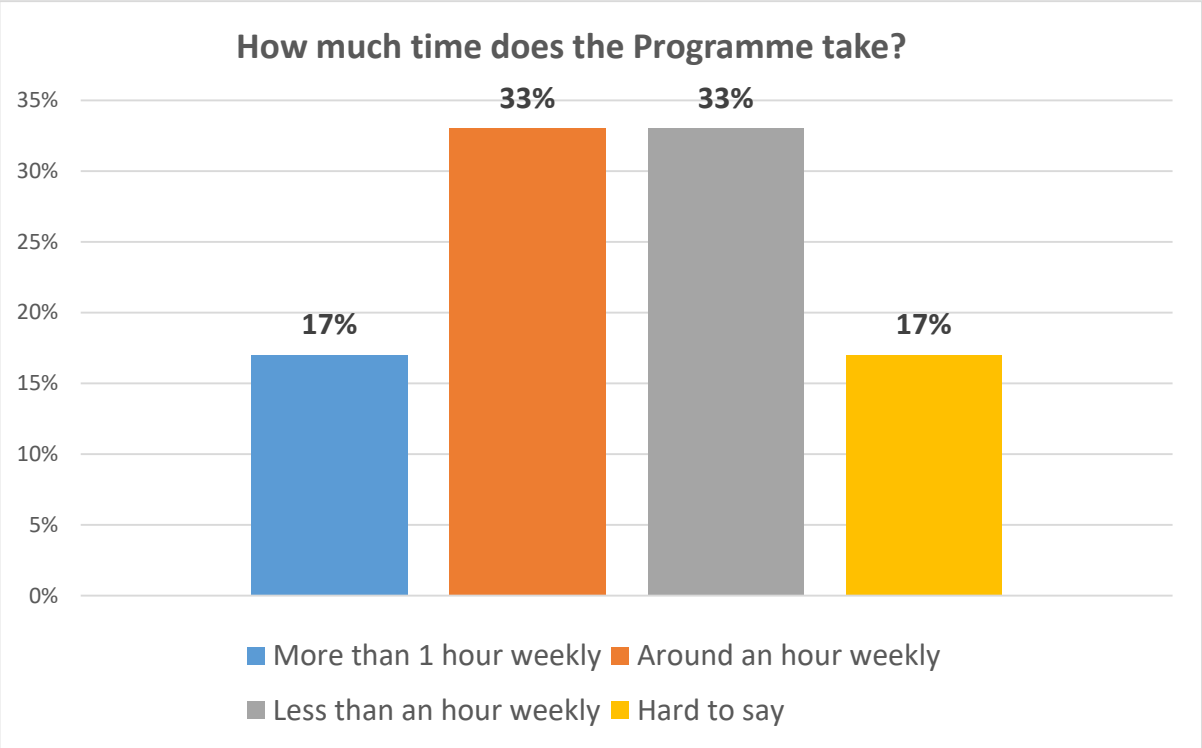
Fig. 10 The most common reasons for refusing to participate by parents.



When asked what other obstacles he encountered during his work, the majority of neonatologists surveyed did not share such. Only one respondent (9%) said they often had difficulty because of their parents' fear of blood tests. More than half (58%) of respondents said that future parents rarely pay any attention to the Programme at all. An even higher percentage (67%) of neonatologists say that their colleagues have very little interest in the Programme.

Half of the respondents said they devote 1 hour per week to work on the Programme, 33% less than an hour and 17% could not determine (Fig. 11). In an informal telephone conversation with the two most actively involved neonatal units, the colleagues said that it takes about 1 minute to define a child as SGA and between 5 and 10 minutes to talk with the family and explain the condition and complications associated with it. In their opinion, the activities under the Programme could be included in their daily practice after the end of the project without significant difficulties. In most clinics (67%), however, only doctors are familiar with the Programme, and in one case only the programme worker is aware of it.

Fig. 11 Time, spent working on the Programme



When asked if there is support from the hospital, 42% say that the management fully supports them, and according to 42% the hospital is not excited about this type of work.

Neonatologists rarely receive questions from parents related to the growth of children. Only 25% of the respondents said that parents outside the project were interested in conditions related to delayed growth.

Table 3 presents the identified barriers and facilitators in the first stage of the – project both in the course of work and through the survey conducted. The lack of sufficient medical specialists in some medical specialties is a known problem affecting the specialty of neonatology. This factor, together with the many clinical work, staff absent and the COVID-19 pandemic during which the project was being carried out, proved to be a bigger obstacle than foreseen. This adverse factor was at least partially overcome with more frequent calls and reminders for the Programme.

Table 3 Found barriers and facilitators during the first stage of the Programme

Found barriers	Found facilitators
Lack of medical staff (neonatologists and midwives), including in relation to the Covid pandemic	Frequent calls and reminders for the Programme Introducing the application of Fenton curves into the disease history of every newborn
COVID-19 pandemic	Extension of the Programme by 3 months
Lots of clinical work	Promote close collegial relationships with interchangeability
Application of new auxological curves and criteria for SGA child	Educational videos available on the Programme's website
SGA children who go to a foster family or homes for medical and social care	Leaflets and documents of the Programme, which remain with the documents of the child
Case of withdrawn IC after a conversation with the GP	Continuing media coverage of the Programme and maintaining online platforms for communication with the team of the Programme Frequent presentations of medical forums on neonatology and pediatric endocrinology, as well as those of general practitioners

After the first 6 months, two children (1.4%) dropped out of the Programme. Both cases are from Stara Zagora. Unfortunately, one with a newly discovered congenital oncological disease (nephroblastoma that is not associated with the SGA condition) and parents do not want to continue their participation. The second case of withdrawn IC is after discharge of the child from the clinic and return of the family to the home and visit by the GP. After the negative statement of the GP, the family called to withdraw the IC and its participation in the project. As a reason it is pointed out, „the fear that the child will be placed on hormonal treatment without the need for such“.

After presenting the Programme of the National Congress of Neonatology in 2021 in Starosel, two neonatological units declared their willingness to participate in the second 6 months of the Programme. So another neonatal ward in Ruse started its work from January 2022. Unfortunately, despite the expressed desire and repeated calls from the two coordinators, the second structure did not join the project.

After the extension of the Programme to 30.06.2022 and taking into consideration the new methods of calling and improving communication with colleagues, despite the improvement, the effect was less than expected. In some places, there was an increase in data reporting, but in other clinics, this increase was only temporary.

Fig. 12 Discovered and enrolled children in the three most active clinics for the first 6 months of the Programme

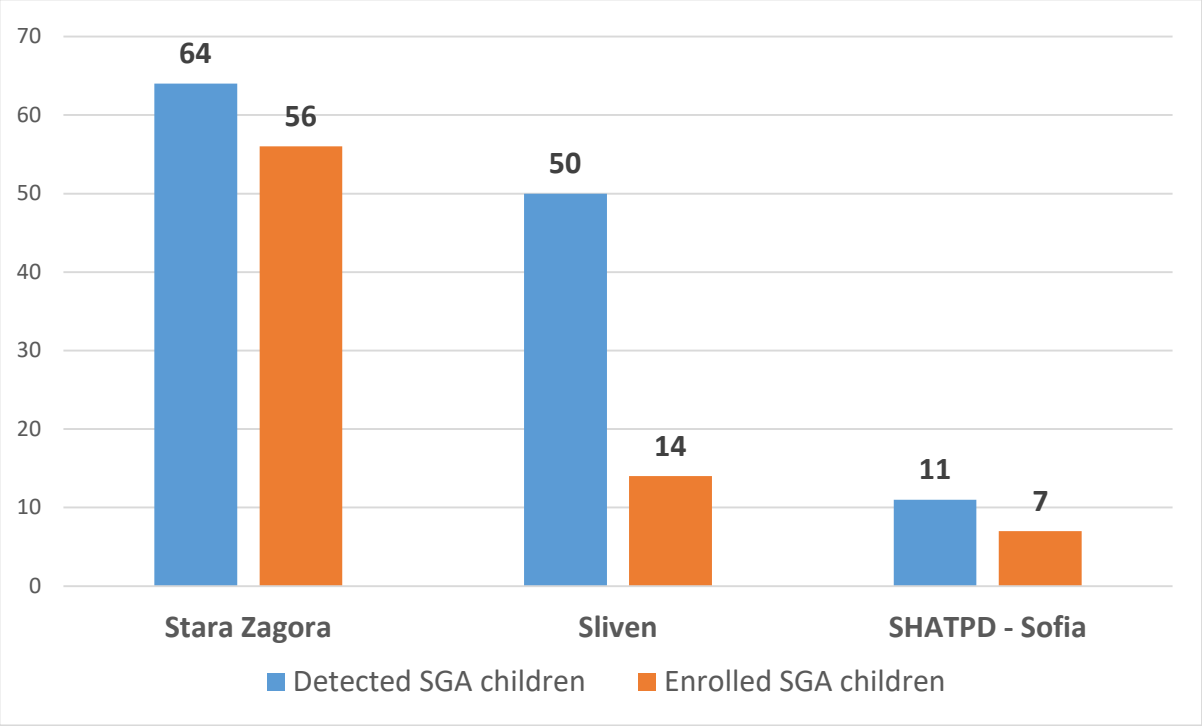
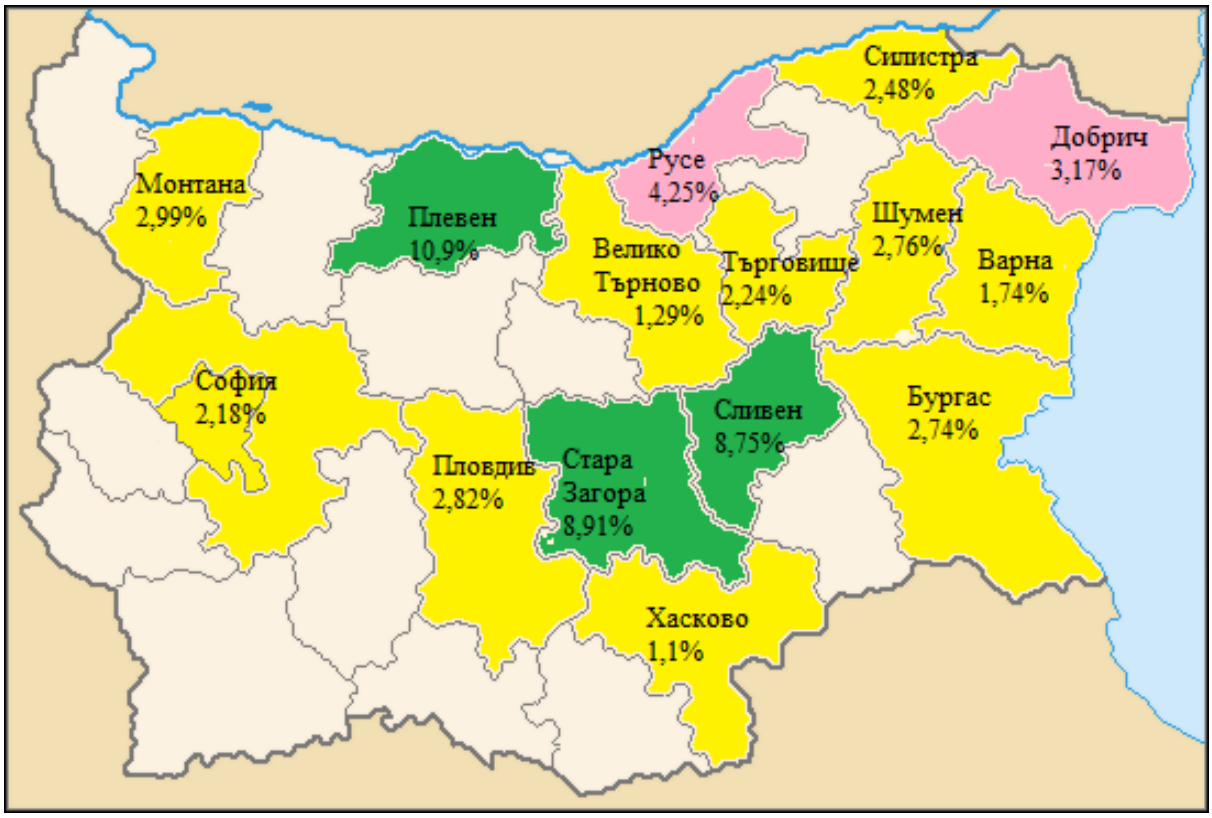


Fig. 12 shows the number of detected and enrolled SGA children in the three most actively working neonatological units for the first 6 months of the Programme. The graph shows that Stara Zagora works most actively for the period. SHATPD - Sofia, finds and records a small number of patients, which is mainly due to the fact that this is the only participating neonatological structure that is not located on the territory of OB complex in the country. Sliven has a slower start, but after the active introduction of all staff in the work on the pilot Programme, they found a close percentage of SGA to that of Stara Zagora. It is also the unit that often encounters cultural-ethnic problems with families. Regardless of them, the team of neonatology is highly ambitious for work and even in case of refusal to sign the IC, sends the documents together with the rest to the child's home.

At the end of the Programme, it was reported that it led to the opening of 794 SGA newborns, which account for 3.2% of all newborns for the period in the participating clinics

in the country. The IC are collected from 443 families with SGA newborns (55.8%). Fig. 13 presents the frequency of SGA births in the participating structures for the whole period.

Fig. 13 Prevalance of SGA births by regions



In Haskovo, the registered prevalaence is 1.1%. The project was difficult there. The lack of neonatologists, as well as a lot of clinical work, had a great impact, which could not be overcome, despite the measures taken. The only neonatologist working on the project was often absent from the ward, but no one else from the unit expressed a desire to participate in the project. For the entire period under the Programme, only one family has signed the IC in this structure.

After receiving the data from the clinics for the entire period, the incidence of SGA births in Sofia dropped to 2.18%. In the different departments here the barriers were not overcome and again the highest percentage of SGA children were found in the only clinic, which is not even on the territory of the obstetric-gynecological complex.

After the change of the person responsible for the Programme in Pleven, 10.9% SGA births were reported for the second part of the stage. The prevalance increased in Ruse after the start of the second neonatological structure. The frequency of registered SGA children in Plovdiv has further decreased. According to the analysis, this is most likely due to the large

continuous migration of neonatologists from the public to the private sector. For the period of the project in several clinics in the country, some of the colleagues changed their workplace from a participating unit to a private one that does not work on the project. The private OB hospital in Plovdiv, according to colleagues, is attracting more and more neonatologists from the public sector. The same, despite the declared oral desire to participate in the project during the National congress of neonatology in October 2021, did not confirm and did not start its participation.

Dobrich reported an increase in the percentage of detected SGA children, but not in the percentage of children enrolled. In the other structures, the frequency is similar to that of the first 6 months of the pilot Programme.

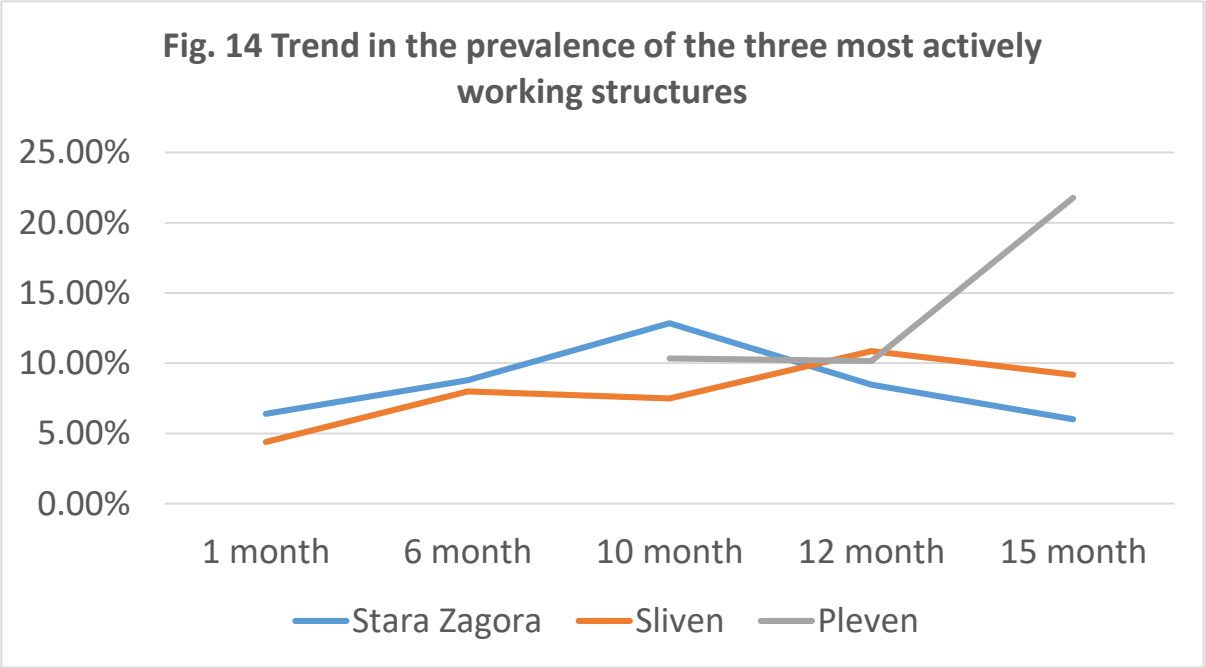


Fig. 14 shows the trend for prevalence in the three most actively working units – Pleven, Stara Zagora and Sliven. For Pleven the results start from January 2022, after the active work of the new project manager, while in the other two structures the active work was visible from the beginning of the pilot Programme.

After completing the first stage of the Programme, all clinics were asked to submit their data on paper. The aim of this action was to facilitate the process of data analysis and to collect missing data. A single entity did not send its data. After repeated calls and reminders, despite monthly data on the number of detected and recorded SGA children, as well as the number of newborns, the project team did not receive the recorded data from this maternity home. The

explanation of the neonatologist was that the data „are not filled in a table, but are on separate sheets” and can not be sent.

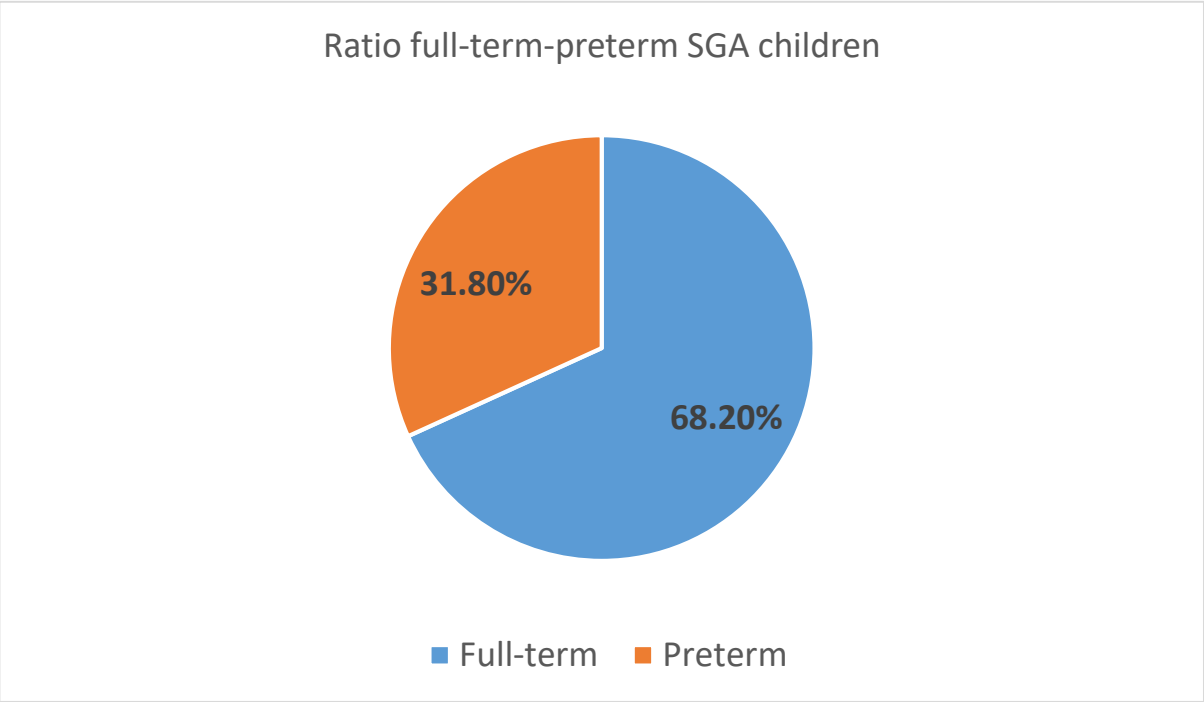
The analysis of the data on the auxological indicators of newborn SGA children was finalized by SPSS version 25 software, as indicated in chapter „Material and methods”. The data were further processed by the automatic software Fenton Growth Calculator for Preterm Infants - https://peditools.org/fenton2013/index.php. So besides additional cleaning and exclusion of children who were not born SGA, the data on length at birth and weight in z-score were converted.

After cleaning the data, of the 443 recorded SGA children, 409 SGA children remained in the analysis. The remaining 34 children were excluded for two reasons – or did not meet the criteria for height and/or birth weight below the 10th percentile (<-1,28 SD) or were born before and/or after the start of the Programme, and for 4 of the children no data were submitted at all.

All children who are not SGA have been contacted by a coordinator and explained how to interpret their growth data at birth. The children who were not born for the period of the pilot Programme were contacted again by one of the coordinators and they were planned to be followed up without being included in the analysis of the data. No child with syndrome was found at the neonatal stage of the project.

In the resulting group, the distribution by sex was almost 1:1 (196 boys: 213 girls). Below, the data are presented as an average of +/- 1 SD (X±SD). The average weight in the cohort studied was 2062.16±522.4g and the average height was 44.35±5.0cm. The average weight for girls in the entire cohort is 2050±515.8g, while for boys it is 2074.31±530.5g. In the group of participating SGAs, around two thirds of children were full-term (68.2%, n=279), figure 15.

Fig. 15 Ratio of full-term and premature SGA children found in the Programme



The average weight in the group of full-term SGA children was 2338.49±283.6g, which is significantly greater than that of premature 1469.12±412.4g. With height, the same regularity is observed. Table 4 shows the differences in weight and height for the respective sex in the full-term and premature group.

Table 4 Height and weight in full-term and preterm boys and girls

Full-term (≥37 г.с.)	Weight (g)	Height (cm)	Preterm (≤37 г.с.)	Weight (g)	Height (cm)
Boys	2368,4±301,8	47,0±2,1	Boys	1520,8±412,8	40,1±4,4
Girls	2313,2±265,7	46,2±4,1	Girls	1412,4±407,8	38,9±4,9

In the group of SGA children HC in boys and girls there is no significant difference (32,11±1,40 a/st 32,0±1,24 cm). The average head circumference of full-term SGA children is 32.05±1.32 cm, while in premature infants it is 29.27±2.64. The average HC value in boys is 29.56±2.61, while in girls it is 28.93±2.66 cm.

In the total cohort, 4.2% SGA children defined by birth length (n=17), 48.4% SGA children versus birth weight (n=198) and 47.4% SGA children were detected concurrently relative to length and weight.

Table 5 Distribution of full-term and premature SGA children by height, weight and height and weight

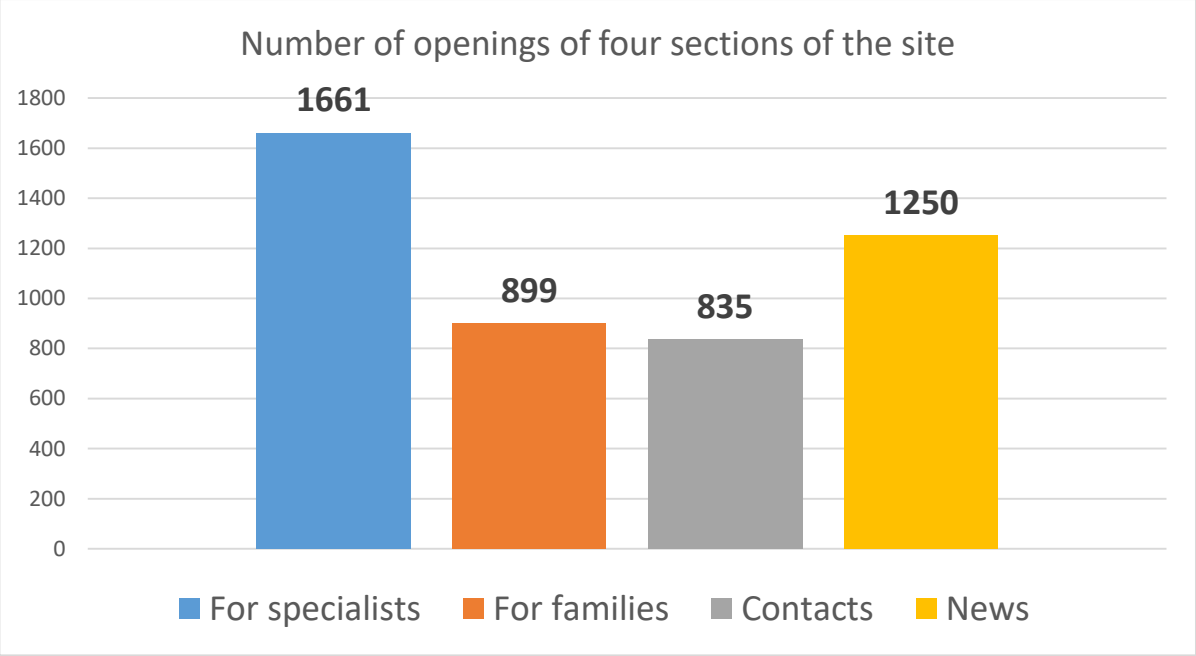
	SGA by height	SGA by weight	SGA by height and weight
Full-term	1.8%	55.9%	42.3%
Preterm	9.2%	32.3%	58.5%

In order to assess more fully the impact of the pilot Programme, an evaluation of media monitoring has been carried out. With the active support of a professional PR specialist, articles on the nature and results of the project were actively distributed in the media, with a total of 15 publications, interviews and video reflections during the Programme. The playlist was created on the YouTube channel of MU-Vi.tv. It added what videos from the creation of the project and subsequent videos on the progress of work. Banners have been published in several well-known healthy sites (www.zdrave.net, www.medconsult.bg), which are active as of 25.02.2024.

The website of the Programme was actively visited. According to the IT-specialist, supporting the platform, the project site is open 12 444 times for the period from its creation to 25.02.2024. Fig. 16 shows the number of openings in the individual sections (for specialists, families and team contact page).

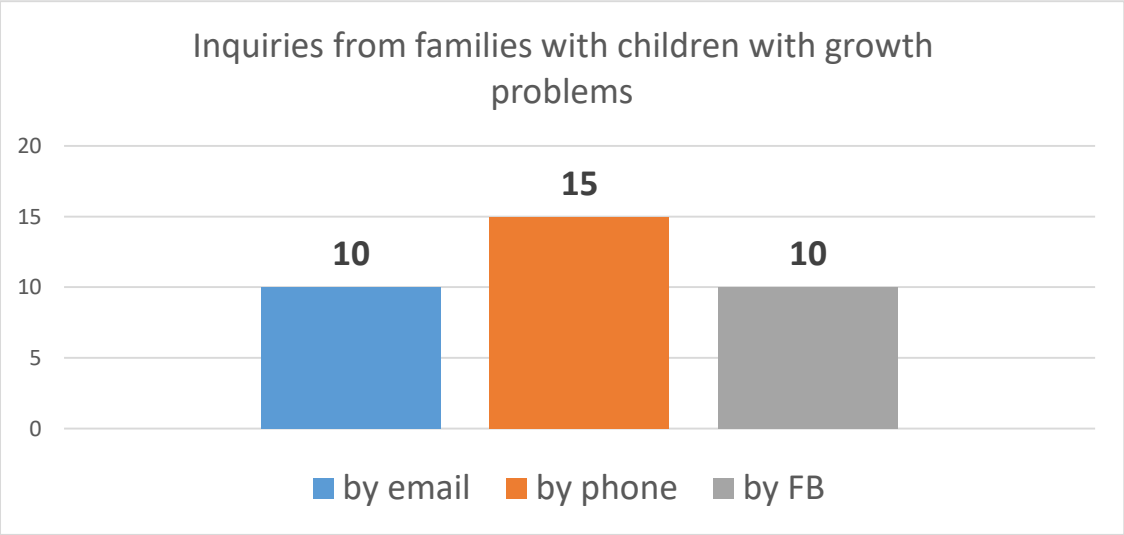
The chart points to the conclusion that the page was visited by both families of SGA children and by numerous doctors. Given the prepared leaflets for GP, we sincerely hope these visits to the page for specialists are not only by neonatologists and PE, but also by GPs who were willing to find out more about the Programme.

Fig. 16 number of openings of four sections of the site (www.mgv.growinform.org)



For the period until 31.12.2023, active inquiries were made both on the project email and on FaceBook. Fig. 17 shows the number of inquiries about the Programme from families with children born of small size outside the period of the project. It is important to note that inquiries were received through the page and the previous programme of VAPES - awareness raising programme regarding postnatal growth deviations – Growinform (www.growinform.org), which continues to be active in FB. All families who have sought our support have received a response and, if necessary, have been referred for review to the PE.

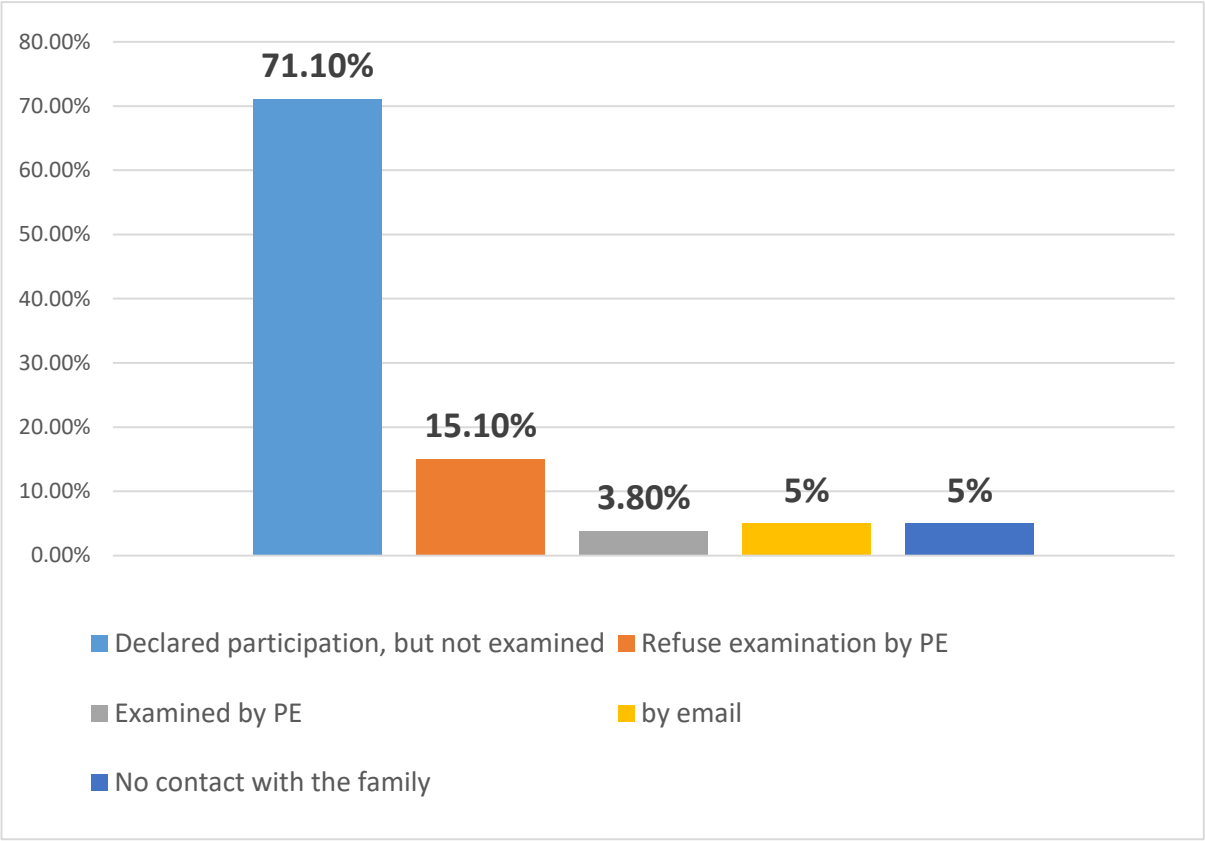
Fig. 17 Inquiries from families with children born outside the Programme.



At the time of the completion of this dissertation, the second stage is not yet complete. The second stage will be completed in June 2024, and for children who need additional follow-up until the age of 3 in June 2025. The data below are as of 31.12.2023. As of that date, one of the coordinators has sought contact with the families who signed the IC.

For the period 01.04.2021 – 31.12.2023, 239 (58.4%) children are due for an examination of PE. When calling and reminding about the pilot Programme, 170 (71.7%) families confirmed their participation, but have not yet visited a children's endocrinologist. Contact was not made with 12 families (5.0%) due to lack of phone number or changed one.

Fig. 18 Results from the second stage of the Programme.



The same number – 12 (5.0%) time converted by email, all of why recorded their growth. This was necessary due to the great distance between home of the families and the nearest pediatric endocrinologist. A visit to the PE was reported in 9 (3.8%) families. Unfortunatelly, a large percentage - 15.1% (36 families) do not wish to follow-up at de due to the belief thatat GP service is serviceient. The data are presented in Fig. 18.

Due to the non-completion of the second stage, the expected and detected barriers and facilitators are assessed together and presented in Table 6.

Table 6 Expected and detected barriers and facilitators in the second stage of the Programme.

Expected and detected barriers	Expected and detected facilitators
Lack of interest from parents	Increase media activity
"Forgetting" about the Programme	Reminder by phone call at 2-years-of-age
Lack of sufficient knowledge about its condition and complications from the GPs	Participation in congresses and presentation of the pilot Programme Maintaining online and FB platforms for communication with the team of the Programme
Remoteness of the nearest pediatric endocrinologist	Pre-development of growth curves and evaluation of SGA children by e-mail

Algorithm for tracking SGA children

On the basis of the results obtained from the analysis of literature, as well as their own, an algorithm for behavior with SGA children was prepared. It is extremely easy, in a few steps:

Step1: Defining SGA children, using Fenton criteria

Step2: Conversation with the family about the condition and possible complications

Step3: Monthly monitoring of the length and weight of the child in outpatient settings by the GP or pediatrician (possibly and according to data from measurements in the home by a parent)

Step4: Examination by PE at the age of 2.

When defining SGA child, Fenton's criteria are appropriate for use. They are freely available on the Internet as well as on the pilot Programme`s website. It is appropriate to consider whether there is any evidence of newborn syndrome. Quick and easy reference for this is possible when using the translated schemes of Finken, available also on the project website.

Given the trainings and information from a site, flyers and posters, we believe that talking with parents would not make neonatologists difficult. A large proportion of them are

already familiar with the early and late complications, due to participation in the project or by giving presentations at various scientific forums.

Step 3 normally implemented in the routine practice of GPs and paediatricians in outpatient settings. There are no changes in their previous work. The only thing that will be needed is for the child to be referred to the PE for growth assessment.

The final step offers an early assessment of late complications in these children. Even if they are not available, families would benefit from talking to PE and getting additional advice on feeding and developing their children. At PE's discretion, some of these children will be left for follow-up until the age of 3.

We believe that the algorithm is easy to use and implement in daily practice. With good preparation, even if the assessment of the MGV status in the neonatal structure is missed, it would be easily performed by the GP/pediatrician/neonatologist by the age of 2.

IV. DISCUSSION.

Despite the deep demand for literature, access to articles in Bulgarian literature is very limited. Searching the national library did not produce the desired result, necessitating a second search in a local library. The open publications in the Bulgarian literature are insufficient to assess the frequency of SGA births in our country. As already mentioned in the Results section, most publications focus on the early problems of SGA children and especially premature children. At the moment of our work we know only one population study of Iotova on SGA children from single pregnancies in Varna. In her studies, Iotova conducted extensive research on metabolic, pubertal, cardiovascular and cardiorenal problems of SGA children. The publications also present a longitudinal growth assessment of the studied SGA cohort. The Iotova incidence of 5.19% of full-term SGA children is in our opinion relevant and comparable to literature worldwide. After her extensive research, no new comprehensive studies have been found to describe the diversity of issues associated with SGA birth.

Some of the published studies we have found are missing in the national library, which is a worrying fact about the preservation of the works of Bulgarian researchers. It is possible that despite the efforts and thorough search for the dissertant, articles on the frequency of the condition and the complications associated with it in our country have been omitted.

It is also worrying that while in Bulgaria for the 30-year period there are about 100 articles related to SGA children in general, for the same period in Pubmed 16 627 results were found (search with the term small for the gestational age). Despite the importance of the problem in our country, it is not fully appreciated by many scientists. Perhaps this is the reason for the lack of a thorough approach in these children and the lack of sufficient knowledge on the part of neonatologists, as the survey in the present study showed.

The initial survey among neonatologists received high response and achieved great participation. Our percentage of participants is higher than other similar studies. Halvadzhiyan and others conducted a survey among the GPs in Varna and Pleven on the practices for referral to specialists in PE. They received a response of 67% in Pleven and 80% in Varna, while in the current poll 90.9% of respondents answered.

It is noteworthy f the uneven distribution of the number of newborns by area. It is important to note that more than one neonatal unit is involved in several cities. These are Plovdiv, Sofia and Varna. It has the highest average number of births per year. The participation of so many neonatal units speaks of sensitizing colleagues to the problems of SGA children.

Unfortunately, the Programme did not include absolutely all neonatological compartments from each of the mentioned areas. However, given the large number of newborns in the participating structures and the fact that more than half of the districts in the country joined (n=16; 57.1%), it can be assumed that the study was population-based. For 2020, according to data from the National Statistical Institute in the Republic of Bulgaria, there are 59,440 births, of which 59,086 are live births. 42.9%of these children passed in the departments that applied for participation in the Programme, which also confirms the population character of the study.

According to self-reported data for 2020, neonatological structures in our country were born 3,230 premature babies or 12.7% of all newborns. According to Ohuma and co-authors for 2020, premature babies make up 9.9% of all newborns worldwide. According to Purisch, the incidence of premature babies rose from 9.5% in 1981 to 12.8% in 2006. Data from a WHO multicentre study suggest that the incidence of prematurity ranges from 3.6% in Germany to 14.7% in Egypt.

As we have already pointed out, after the statistics on the number of births for 2020, the assessment of the participating neonatology clinics continued with an assessment of their material security. In his 2014 article Foote reminds not only of the need for proper measurement technique, but also of the importance of using only standardized measuring instruments, especially height meters, when tracking the growth of children. The high proportion of clinics with a lack of measuring devices detected by the first survey is extremely alarming. This is one of the reasons why VAPES has given new standardized Seca height meters to all participating neonatological units, as well as electronic Gima weights with a division up to 5g to those in need.

The data from the poll for determining the term of pregnancy and prematurity are one-way – according to neonatologists a complex method for such assessment is needed. This is in line with the World Health Organization (WHO) criteria. On the question of determining the gestational age, some differences in responses are found. Although most respondents answered that most often it is defined by the Negele formula for determining PDD – Date of LMP - 3 months + 7 days, as well as by clinical signs and data from ultrasound examination during pregnancy, not a small relative share of respondents use the criteria of Rautenbach-Hoepffner and New Ballard Score. Despite its use in all newborns, not one study found that New Ballard Score overestimated the gestational age in SGA children.

The result, indicating that most of the colleagues surveyed used Fenton's criteria, was extremely encouraging at first. Despite the declaration of knowledge of the definition, in all primary and secondary structures that applied for participation, there is a lack of data for systematic assessment and definition of SGA children, both according to Fenton criteria and according to any other criteria .

More and more authors talk about the need for active tracking of children at risk for stunted growth, as well as the need for joint work between all specialists working with children. This supports the initiative to create the Programme for timely detection and tracking of premature and premature infants born SGA. The idea set in the project is not only to actively follow-up all SGA newborns until the age of 2, as well as to create a protocol for directing such children, but also to improve communication between neonatologists, GPs and PE.

Organization, as we have already shown in the Results section, is a multistage process. Following the steps described by O`Cathain, a status definition was first selected. Fenton criteria use a wider definition limit (<10th percentile), and many authors deny them. Most of the SGA children who did not catch up on their growth were born < -2SD against the national reference curves, but using the limit set by Fenton, they were more able to timely reach children prone not only to growth disorders, but also to early development of obesity and metabolic changes. Abali and co-authors investigated early complications such as hypoglycemia and polycythaemia, as well as some late – non-invasive growth and disability in three groups of children – SGA <-2SD, SGA <10th percentile and AGA children. Most early complications were found in the < -2SD group, but the obesity was found at a higher rate in the SGA children group <10th percentile. Given that the pilot Programme examines late-term disorders in SGA childbirth, it is the 10th percentile limit that seems more appropriate to detect not only non-invasive growth, but also obesity and metabolic complications at an early age.

As Derman and co-authors remind in their 2018 article on successful intervention delivery, especially in low- and middle-income countries, training is needed. Bana and her team used brochures with information about the symptoms that cancer treatment can lead to. Marín-González and co-authors allot part of their budget under the SOPHIE project (Evaluating the Impact of Structural Policies on Health Inequalities and Their Social Determinants and Foster Change) for both flyers and logos that are easily recognizable. The team also describes the need for active work with the media to improve the dissemination of information. All this proves the need and supports the use of IT- and PR-specialists in such population-oriented work.

The pilot Programme started during the COVID-19 pandemic. Cook and co-authors describe the importance of continuing non-pandemic clinical trials during COVID-19. In their 2020 paper, the researchers said that the findings of studies conducted in patients without COVID-19 were also appropriate for patients with coronavirus infection. This further confirmed the need for timely start of the project without further delay in time.

When the epidemic broke out, many studies found themselves in a difficult position on how to continue working. Columbia University in New York offers its approach to launching new research and criteria for continuing or temporarily suspending studies that have already begun. According to the 2022 article, the university management allowed to continue their activities only studies leading to direct benefit to participants, and the inclusion of new subjects was temporarily suspended. In our case, there was no risk to the fate, and only benefits were expected – inclusion in the project did not require an additional visit to a doctor, but took place during the hospital stay after childbirth. Growth assessment at 2 years of age is carried out at a convenient time for the family, and already in preparation for the project, a distancing method was prepared to assess the catch-up in growth – preparation of individual growth curves by email.

According to data from Juckett and co-authors, building „deployment capacity“ of scientifically applied projects is key to implementing a programme. In our project, this happened through trainings, telephone conversations and meetings at various conferences, where the topic of SGA children was discussed. According to Cooper, the factors influencing differences in the health care system are multifaceted, complex and interrelated.

Given the data from Kalpazidou Schmidt on the need for constant change and improvement of the scientifically applied investigations, the Programme has been adapted several times to the situation, especially in view of the pandemic, during which its first phase took place. Cronin and team used the pandemic to improve distancing work on clinical trials. Through training of remote scientific collaborators and use of electronic health records, the team proves the possibility of continuing work on important studies in emergency hospital units. A similar approach was applied in the pilot programme. Online trainings of interested neonatologists (remote training) were conducted, which facilitated their work and helped to carry out the project work. In addition, the pilot Programme was supported by the active work of IT and PR specialists.

In order to support and facilitate the work on the scientifically applied programmes, it is necessary to provide for possible barriers and facilitators, or as they are called by Waltz et al., „contextual determinants“. According to a large meta-analysis of 252 publications related to SARs, for a study to be applicable and sustainable, it must be constantly re-evaluated and appropriate measures taken for the application in different situations (and populations).

Our survey showed that in most cases the Programme is only familiar to medical staff, with the majority of participants having no support from their colleagues. Only in one clinic and midwives were involved in the work on the Programme entirely. As already mentioned, according to data from Bana et al., the active participation of nurses and the distribution of leaflets has contributed to the success of the work on the programme for tracking cancer patients. Both this publication and our Programme prove that the active work of nursing staff is important for both clinical and applied research.

The gaps identified by us in the definition of SGA birth and subsequent re-training are important in the context of the fast-growing Programme. The idea of online training is increasingly popular worldwide, especially after the impact of the COVID-19 pandemic. In their article McGuire and co-authors share their experience on the online training of GPs from Sub-Saharan Africa. In addition to the high percentage of participants who successfully completed the training (80%, only 2 people did not meet the goals set at the beginning of the programme), most of the participants have built personal positive relationships with their mentors and continue to work actively with them outside the programme. In our case, the established positive links help for easier reporting and improvement of places of results.

Work on such projects often encounter problems in continuing the path of the patient. Many authors appeal for joint work between several types of specialists. Our case of a single withdrawn IC speaks of poor collaboration with some GPs and the need not only for additional training of all healthcare professionals working with children, but also for the introduction of measures at central level.

A known fact is the lack of medical specialists in many regions of our country, and the problem is particularly pronounced in the neonatal sphere. According to the Bulgarian Association of Neonatology (BNA), about 150 people work in neonatological structures throughout the country. Half of them are located in Sofia and Plovdiv. These are the two cities with the most private hospitals in the country. The migration of specialists is exclusively represented from the public into the private sector.

Given the data on the insufficient number of neonatologists in the country, the difficulties in work due to staff shortages are expected. The programme was implemented in most major cities - 16 districts in the country declared participation (57.1%). Given the large distance between the centers and the multiple units, it is expected that there will be errors in measurements. As of 1994. Voss and others made a study on the technique of measuring and using different height meters. The article shows that in practice, mistakes can often be made when measuring height and its subsequent evaluation, if some basic rules are not followed.

For the period 2017 - 2019, 13 cities are covered by the GrowInform – project of VAPES, aimed at timely diagnosis of children with growth disorders. To raise public awareness of this project, the team created flyers, posters and worked with over 100 media channels to spread information. The Programme evaluated the growth of 237 children, actively using Facebook or other Internet-based media. During the project, families whose children did not participate in these examinations learned about the Programme and actively sought out a pediatric endocrinologist. Considering this data from previous experience, the team is working hard with PR specialist to maintain online platforms (Facebook, email) that inform the general audience about the implementation of the Programme, its goals and organization, and to facilitate the contact of families with born SGA children with non-catch in growth.

Various definitions of SGA children are used in literature. Most neonatal editions use a limit of 10th percentile, while in pediatric endocrinology publications a limit of <-2SD is preferred. In the context of the latest consensus on SGA children, the curves to be used must be reference for the population concerned. The Lubchenco curves known to all neonatologists have been replaced by the more detailed and contemporary Fenton curves.

Publications of recent years mention even the unification of the concepts „premature", SGA and „child born with low weight" with the general term "small vulnerable child". An article by Gardosi in Hormone Reasearch talks about the need to apply an individual approach in defining each newborn's SGA status and offers routine implementation of software for assessing birth sizes. During the organization of the project, it was taken into account the fact that this would probably be difficult for many neonatologists to quickly assess the condition. Therefore, the team uses software to further verify and evaluate recorded SGA children (https://peditools.org/fenton2013/index.php), as already explained in the Material and Methods section. The time it took to evaluate each child using the software was about 1 minute. The site offers an estimate based on gestational age, height, weight, and head circumference, and presents the data against the Z-score. According to the dissertant's personal opinion, the

software is convenient to analyze the data, especially in the more difficult cases for assessing newborns and would be a good choice for use in routine practice.

For the first 6 months in the pilot Programme, an incidence of 3.7% SGA births was detected, which is comparable to a small amount of literature. According to data from a Swedish retrospective study for the period 1990-2004, 3.6% of all single pregnancies are SGA. According to a review article by Janchevska, about 5% of children are born SGA using consensus criteria. According to data from a major meta-analysis by Christian and co-authors, the incidence of SGA birth ranges from 6.1% in China to 64.5% in India. According to Lee and co-authors and Black, about 27% of all births in low- and middle-income countries are SGAs. The apparent discrepancy with our cohort is probably due to several factors:

- Short period of the Programme
- Not all neonatological structures in the country participate in it
- - At the beginning of the work, difficulties were encountered and „forgetting“ for the pilot Programme, which is probably due to the smaller relative share of detected SGA children.

Assessing the degree of application (implementation rate) has proved to be a difficult task. The reply to the author's questionnaire was received from only 44.4% of the participating entities. Compared to the initial survey, the relative share of neonatologists who responded fell by almost half. This is a much lower level also compared to the return of the survey of Halvadjian and collaborators held among the GPs in the Varna and Pleven region. In a scientific application study on antibiotic use, Kühn and co-authors responded between 63% and 76% in the first physician survey and 68 and 95% in medical assistants. In contrast to the above answers is the return (response rate) of the web-based questionnaire of the European Association of endoscopic surgery. When emails were sent to 3,728 members of the association, the survey was answered by 4.8% (179 people).

In our country, there are not enough preventive programmes, and in some cases even mandatory preventive measures are not implemented. According to data from a 2023 own study, a large relative share of GPs do not complete mandatory vitamin K prophylaxis. This has been shown to impair the prevention of bleeding due to vitamin K deficiency in newborn and exclusively breastfed children. Therefore, the team of the pilot Programme was not surprised with the high percentage of refusals to participate.

According to a study on the prevention of relapses of depression and anxiety, the most common reasons for refusing to participate in the study are the lack of sufficient knowledge about the risk of recurrence of the condition, misunderstanding the condition, as well as refusal for logistical reasons. In our cohort, on the second place, after cultural-ethnic reasons, is a misunderstanding of the essence of the Programme. Cultural-social factors are difficult to compare with other studies, as they are nowhere in the literature cited as the leading reason for refusal. On the contrary, a variety of patients are sought in many places to make the study more credible. According to Aguwa, selecting a multicultural team to work is crucial for better patient care.

Data obtained on the interest of the team and future parents are not surprising given the data of the analysis of the first results. As already mentioned, some of the families who refused to participate did not understand the essence of the Programme. According to data from the two actively participating units, the telephone conversation with the time it takes to work with one family is between 5 and 10 minutes in total. Given the data from our author's questionnaire, we can evaluate that the pilot Programme is not time consuming and does not require additional stay after the working day of the participating neonatologists. The readiness of two of the units to continue work on the project further speaks in support of the latter claim.

The difficulties in the work on the Programme for timely detection and follow-up of premature and full-term children born SGA are also due to the lack of support from the management of the medical institution. This fact further reinforces the thesis that the registration of the born SGA children at birth and the definition of the path for their tracking should be introduced at a central level.

Comparing the prevalence we find, both in the country and by districts, is difficult. This, as we have already said, is due to several factors, the most important of which is the use of different definitions and curves. The incidence we detected (3.2%) is extremely low. Compared with the preevalence detected by Iotova of full-term SGA children from single pregnancies and with the data from the implementation of the project, we assume that this is not the true frequency of the condition in our country.

According to data from Lwin and co-authors for the period 2010 – 2014 in a Swedish survey and using the Swedish standard for definition of SGA birth, 1.6% SGA newborns from single pregnancies were found. In a study of birth weight trends, Morisaki and co-authors found

7.5%, 7.6%, and 8.2% for 2000, 2004, and 2008 using the 10th percentile limit and the U. S. national curves.

The prevalence detected for the whole period in Pleven, Stara Zagora and Sliven is closest to the prevalence of the condition in most publications. In the literature, the incidence rates ranged from 2% to 20%. According to data from a Canadian study on educational differences in mothers of premature and SGA children, 11.3% of full-term SGA children were detected for the period 1981 – 2004. According to data from He and associates, the incidence of SGA births over a 15-year period (2001 – 2015) was 6.2% using a 10th percentile limit compared to their national reference curves. In most definition recommendations used, head circumference is not the primary method for defining an SGA child. It is important for the determination of „asymmetric“ and „symmetrically“ SGA child. Galvão and collaborators conducted a prospective study on pregnant and newborn infants to determine the incidence of SGA births and related maternal factors and fetal complications. When using the limit < 10th percentile, the frequency is compared against 4 different curves – INTERGROWTH-21, Brazil national reference curves, WHO curves and GROW-reference curves. The relative share of SGA births is as follows – 7.0%, 9.6%, 10.9% and 11.6%.

The detected frequency between 3 and 4.5% is comparable to some European countries. According to data from Karlberger and a team from a study conducted in 1992, 5.4% SGA children were found using the Swedish SGA definition criteria. According to data from a similar study of the same team, 3.8% SGA births were detected using a limit of < -2SD for the national reference curves of Sweden. Incidence below 2% is found in a small literature and more frequently in the study of specific subpopulations of SGA births. According to Revollo and collaborators, the incidence of SGA births in Ethiopia varies between 2.3% using a 3rd percentile limit versus the INTERGROWTH-21 and 7% curves at the 10th percentile limit of the same curves.

In our SGA population, the ratio of boys:girls is approximately 1:1 (196:213), which is similar to the data of Tamaro and co-authors – in them found a ratio of boys:girls 65:53. According to the Ha team's article, when they looked at factors in the environment that affected SGA births, they found 51.1% boys and 48.9% girls in the SGA group.

According to data from the initial survey, the number of prematurely born children in 2020 is 12.7%, while for the period of the Programme the number of prematurely born SGA children is nearly 1/3 of all enrolled SGA children or 16.4% of all detected SGA children.

According to Rai and a team from a large cohort study in India, 16% were premature, 38.2% were born SGA, and 1.2% were premature SGA children.

The distribution of SGA children in three categories – by height, by weight and by height and weight at the same time is also not always described in the literature. According to Fujita data for the period 2006 – 2008 in Japan, 3.5% SGA children were found using the criterion of < -2SD compared to their national gender-specific curves. The study found 1.2% SGA children versus weight, 1.5% SGA versus height, and 0.8% versus weight and height. With us, the relative share of SGA children in terms of weight, in relation to height, compared to both is much lower, most likely because we have the data only of the children enrolled in the SGA Programme. This is a shortcoming of the Programme, which was reported at the end of the first (neonatological) stage. Given the difficult collection of even just this data by some structures, in the personal opinion of the dissertant, it would not have been possible to collect the data on all births under the units. This leads to the idea of a mandatory centralized system that not only facilitates the work of neonatologists, but also to automatically determine the SGA status of each newborn. This would increase the proportion of timely diagnosis of these children, as well as help make it easier to follow up further in outpatient practice.

Rankin and his team remind us of the need to use social media not only personally, but also professionally. According to data from Huber and collaborators from an analysis of how healthcare professionals and patients respond to comments on different platforms. The most commonly used platform turned out to be FaceBook, followed by comments on the New York Times online platform. In 2021. Cooper and collaborators said they used closed („secret“) virtual groups on social networks to support people with HIV. According to the article, most of the respondents said that they have improved their overall well-being and at the same time received support. This data only confirms the need for active work with PR specialists and at the same time reinforces the need for active use of social networks. In this case, FaceBook was selected. In addition to it, the project site is actively maintained, as well as the email. The numerous visits to the site show the interest of the society about the problems of the SGA children.

In 2021, a team in the Journal of Medical Internet Research published a meta-analysis on disinformation on social media. According to the article, the most common topics related to misleading or erroneous information are vaccines, medicines and smoking, non-communicable diseases, the pandemic and the treatment of certain diseases. The SGA diagnosis and its treatment, in our opinion, fall into the category of misinformation not only because it refers to

a non-contagious disease in need of follow-up and treatment, which is not yet well known to society, but also because of the norms and understandings in our country.

Fear in patients occurs not only with a new diagnosis. Mohanty et al. described in their 2020 publication their data on barriers encountered in the hepatitis B vaccination. The analysis included 36 studies, with the most common reason for refusing vaccination being the lack of sufficient information on vaccination. Secondly, there are wrong beliefs about the possible complications of hepatitis B vaccination.

At the time of writing this development review by PE subject almost 60% of enrolled SGA children. Although a large percentage of families declare continuation of their participation, but no review has yet been carried out at the PE. Our relative share of families willing to participate in the second part is comparable to other large surveys. Bowden et al. described a large SAR in Australia working with cancer patients. Among them, of the 104 studies included in the „The Beat Cancer Project“ project, 92 (88%) were successfully completed. According to McKevitt's team, from a survey of stroke survivors, 74% took part in the study's records. The article notes that 20% of participants were unaware that they were participating in such a register. Knowledge about the objectives and results of the study is even more alarming - 73% say they have not received results from their participation, and 57% are not close to the purpose of the register in which they are included.

Families who are at a long distance from the PE are assessed by email after sending the growth data. According to the WHO, telemedicine is the provision of medical services to people in need, where distance is critical for access to medical professionals for the diagnosis and treatment of diseases. According to data from Mahar and co-authors, telemedicine was used by various specialists – neurologists, radiologists, pathologists, etc. Algahtani and collaborators remind that telemedicine is increasingly involved in frontline practices due to the search for prevention strategies. Given these data, as well as the presence of a COVID-19 pandemic at the start of the project and the remoteness of some families to the nearest endocrinologist, it was necessary to draw growth curves by email. This facilitates the process of evaluation and access to family medical services.

There is more and more talk not only about telemedicine, but also specifically about routine implementation of applications to facilitate access to medical services. A 2020 article in a specialized journal of mobile apps and health-promoting computer techniques described a 4-step model for developing applications to facilitate access to medical care. Such applications

would be a great facilitator in the daily work of the medical profession. This is what the Ardito team thinks.

According to Nelson's data and co-authors of a study on patient assistance in treating DM, a large number of respondents said they forgot to take their dose. In our case „forgetting“ for the Programme is clearly evident from the still small number of SGA children who visited PE for a control examination at the age of 2 years.

According to Burns data and collaborators, in order for a SAR to be successful, an approach covering the entire – “top-down” approach chain should be applied. Thus, from starting at the central level and going down to the next levels, the implementation of programmes in everyday life is possible. According to the results obtained in this Programme, this is the necessary approach in our country. The Programme once again proved that in many cases, despite the great desire for change, everyday problems such as lack of staff, a lot of clinical work, disinterest in the majority of the team, can prove detrimental to the introduction of new practices.

V. CONCLUSION.

The presented results in this dissertation work proved that the pilot Programme has great potential. There were some very difficult factors which were not in all cases easy to overcome. Despite the measures taken to raise awareness of both the public and the medical community, more efforts are needed in this direction.

When conducting a new similar Programme or continuing the current one, we consider the need to collect auxological and passport data of all newborns to be proven. The need for introducing measures at central level to define SGA children immediately after birth and introducing the diagnosis to a routine practice of both neonatologists and the practice of GP has been clearly demonstrated. The introduction of automatic status assessment software would help to assess the condition more quickly and for fewer missed cases, especially at the beginning.

The lack of sufficient neonatological staff and the constant migration to the private sector is a fact that should be paid particular attention. Strict and rapid measures are needed to preserve the narrow specialists in the main hospitals with universal accessibility. The Programme proved that there is no way in units with a lack of staff to cover all children, despite their desire and efforts. Part of the structures in neonatology showed that they are ready to continue actively working to define and guide SGA children on their further path. Once again, the key role of nursing and obstetric staff for the successful outcome of the work on the Programme, as well as for any such initiative in the future, became clear.

As one of the most important results of this work we draw the importance of working with society to better understand and accept preventive intervention programmes of public health importancethe better health of Bulgarian children.

VI. DEDUCTIONS.

1. The analysis of publications concerning SGA children in Bulgaria shows insufficient interest in the SGA condition and almost complete lack of epidemiological data.
2. Currently, neonatologists are not sufficiently familiar with modern criteria for defining SGA birth, as well as the incidence and complications associated with the condition. No formal algorithms were found to define SGA newborns.
3. The assessment of the problem of recognition and definition of SGA children has created a basis for the development of the pilot Programme for timely detection and follow-up of full-term and premature infants born SGA.
4. On the basis of the pilot Programme, the prevalence could not be estimated in all the neonatological structures involved. The estimated frequency, from the data of the 3 most actively involved clinics, is 9.14%. Not a single child with syndrome was found in the First Stage of the Programme.
5. Despite the work and efforts for coordination, the expected results were achieved only in 3 of the participating 22 clinics. The analysis showed that to achieve results, it is imperative to involve all staff of the participating structure and to adapt its daily clinical practice.
6. The active media coverage of the Programme increased the interest in the condition, as evidenced by the consulted and targeted for treatment children born in medical institutions and terms other than those of the Programme.
7. Despite the many confounding factors, the ongoing analysis and the timely steps taken to address them have yielded results. The constant re-evaluation of the limiting and predisposing factors (barriers and facilitators), as well as the adaptation to them, showed that in our country there are all prerequisites for this activity to be integrated into the routine neonatological practice.
8. The results of the pilot Programme showed at the moment that routine introduction for assessing the dimensions of childbirth and conversation with parents about the patching of the path for further application require relatively little time and effort. In the form of a protocol, they will be offered to health authorities for integration into the requirements for the service of newborns under the CP.

VII. CONTRIBUTIONS.

- The present Programme is the first known pilot scientific-applied research for covering the born SGA children at birth and thus avoiding early and late complications of the condition.
- In result in the implementation of the Programme 3 Neonatological units from different parts of the country (Stara Zagora, Sliven and Pleven) can be judged for the current incidence of SGA in full-term and premature newborns.
- Increasing public awareness - families of SGA children are estranged and begin to actively seek help and support.
- The need for additional work to raise the awareness of the medical community, especially in outpatient practice, for detection and timely referral of SGA children without postnatal catch-up growth to a pediatric endocrinologist has been demonstrated.
- 4-step structured and easy-to-execute protocol for defining and tracking SGA children.
- A network of specialists – neonatologists and pediatric endocrinologists who are well aware of the SGA condition, features and complications was created.

VIII. LIST OF PUBLICATIONS AND PARTICIPATIONS, RELATED TO THE DISSERTATION

Articles, related to the dissertation:

1. T. Zlateva, Small for gestational age children, Varna medical Forum, 2024 (1), online first DOI: http://dx.doi.org/10.14748/vmf.v13i1.9547
2. Zlateva T, Krumova D, Tsochev K, Pramatarova T, Georgieva R, Krasteva-Vilmosh M, Petleshkova-Angelova P, Mumdzhiev H, Stoyanova H, Iotova V. Design and specific features of the Programme for Early Detection and Follow-Up of Full-Term and Preterm Children, Born Small for Their Gestational Age. Journal of the Union of Scientists-Varna. Medicine and Ecology Series. 2022 Jun 15;27(1):8-14.
3. Zlateva T, Krumova D, Kamburova T, Georgieva R, Krasteva-Vilmosh M, Mumdzhiev H, Stoyanova H, Iotova V. Barriers and facilitators in the Programme for Early Detection and Follow-Up of Full-Term and Preterm Children Born Small for Gestational Age. Izvestia Journal of the Union of Scientists-Varna. Medicine and Ecology Series. 2023 Dec 19;28(2).

Participations in medical forums:

1. Stefanova T., T. Pramatarova, D. Krumova, D. Yordanova, M. Krasteva, V. Iotova. Pilot programme for timely detection and follow-up of small-for-gestational-age short children. Fifth International Meeting of the Bulgarian National Society for Pediatric Endocrinology “PEDIATRIC ENDOCRINOLOGY AND THE EPIDEMIC”, 11th – 12th November 2021, Sofia, Bulgaria

2. Zlateva T., D. Krumova, T. Pramatarova, M. Krasteva-Vilmos, R. Georgieva, V. Iotova, Preliminary Results Of The Programme For Early Detection And Follow-up Of Short SGA Children In Bulgaria, 4th Summer Discussion of Neonatology, 15-18.06.2022, Avignon. France - e-poster

3. Златева Т., Крумова Д., Праматарова Т., Георгиева Р., Кръстева М., Стоянова Х., Мумджиев Х., Йотова В., Програма за навременно откриване и проследяване на МГВ деца - опит от първия етап на програмата, Национална конференция по неонатология, гр. Хисаря, 21-23.04.2023 г.

4. Златева Т., Крумова Д., Йотова В., Физическо развитие на недоносените и родените с ниско тегло, Шеста мултифасетна конференция за детското развитие, гр. Пловдив, 07-08.04.2023 г.

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