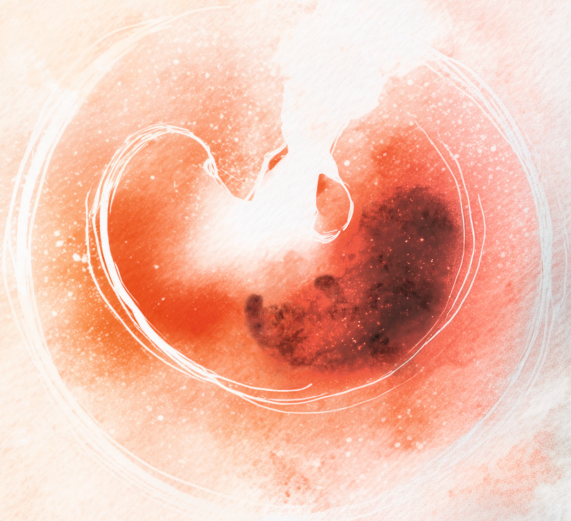
National implementation of the first-trimester anomaly scan: benefits, opportunities and challenges

Bronsgeest, K.



CHAPTER 9

General discussion

The promised land of early screening?

The prevalence of congenital anomalies is estimated around 2.5%[1]. Prenatal detection plays a crucial role in supporting reproductive decision-making, as well as reducing neonatal morbidity and mortality[2-5]. As a result, the second-trimester anomaly scan (SAS) is a standard component of routine antenatal care in most developed countries[6]. Yet, the landscape is shifting: increasing evidence suggests that (major) anomalies can be identified earlier in pregnancy using first-trimester scans[7, 8]. This facilitates earlier diagnostic evaluation and strengthens reproductive autonomy by providing prospective parents more time for genetic testing and informed decision-making. The diagnostic performance and overall impact of the first-trimester anomaly scan (FTAS) within a low-risk, nationwide prenatal screening context have yet to be fully established, despite its promising results in the early detection of fetal anomalies. Assessing the value of the FTAS is inherently complex, yet of indisputable relevance as the outcome directly affects 170,000-180,000 pregnant women in the Netherlands each year[9] and may resonate far beyond our borders, as the Dutch prenatal screening program serves as an international example. This chapter reflects on the first-year results of national FTAS implementation in the Netherlands, carefully weighing its benefits against possible undesired effects. As such, this thesis provides valuable input for broader discussion on the future of the FTAS: whether it should be maintained and if so, how it should be structured.

Does early pregnancy termination reduce psychological burden?

Several countries impose legal limits on the gestational age at which termination of pregnancy (TOP) is permitted, often ranging between 22 and 24 weeks, as displayed in ***chapter 2***. In these contexts, early screening offers a critical benefit: it facilitates timely detection of anomalies within the legal window for TOP, thus enhancing reproductive autonomy. Opponents of the FTAS may argue that early screening might lead to the termination of pregnancies with less severe anomalies, e.g. cases that might otherwise not be terminated at the SAS. It is further suggested that the threshold for making such decisions may be lower in early pregnancy, when the fetus can still be abstract and parental attachment less developed. However, our interview and quantitative data indicate that parents approach such decisions with great deliberation, and that terminations for relatively mild anomalies are rare. This was further illustrated in a personal interview with a woman who chose to terminate her pregnancy due to a missing hand, demonstrating that such decisions are not made lightly. Our conversation was marked by profound love for her child and deep sorrow, reflecting the careful and compassionate consideration behind her choice.

One of the key proposed advantages of first-trimester anomaly screening is that earlier TOP may be associated with less emotional burden, potentially due to lower levels of

fetal attachment and more time for reflection and decision making. Studies conducted more than a decade ago may have limited applicability to current settings, as societal developments have shifted the timing and intensity of fetal attachment. Contributing factors include the increasing availability and uptake of early scans, the rise of commercial ultrasound services and popularisation of gender-reveal parties, facilitating earlier emotional bonding than was common in previous decades. Our findings reinforce the rationale that early termination carries less psychological impact than later in pregnancy. It is important to note that the method of termination (medical vs. surgical) may also influence the emotional experience, a factor unaddressed in our study. This aspect may be relevant given international differences in the timing of first-trimester screening and availability of termination procedures. Moreover, our findings should be framed with caution, as they must not be misconstrued to imply that earlier termination is inherently less distressing. The impact of termination is highly individual and shaped by a range of psychological, relational and contextual factors, including personal coping styles. In our study, women who discontinued their pregnancy between GA 20-24 weeks almost uniformly described a strong sense of fetal attachment, including naming the baby, experiencing a parental identity after birth, and engaging in memory-making rituals. In contrast, experiences following early termination were more diverse. Some participants reported similar emotional bonds and significant impact. For instance, one interview with a partner following termination at 14 weeks' gestation was conducted without the woman, as the topic remained too painful for her to discuss five months postpartum, reflecting the deep emotional burden. The lasting connection was symbolised by a tattoo inspired by the baby's ultrasound image. Other participants in the early group expressed a more emotionally distant experience and reported less psychological burden. One partner returned to work after one day and the woman after one week postpartum. They felt no need for remembrance rituals and experienced no emotional difficulty with potential emotional days such as the original due date. Overall, these narratives show that while early termination may have limited impact at the group level, individual experiences vary widely, from profound emotional burden to apparently minimal effect. They underscore the need for nuanced, patient-centred counselling that acknowledges the diverse emotional responses and supports individually tailored care.

The additional diagnostic value of the FTAS in a population-based setting

In ***chapter 4*** we have demonstrated that the FTAS substantially enhances the detection of fetal anomalies, highlighting the added value of national anatomy screening in addition to routine scans. Although the number of detected first-trimester major anomalies (FTMA) in the first trimester increased only marginally, mainly due to their low prevalence, it is important to note that these cases are all severe anomalies, such

as anencephaly, which were not detected by previous routine scans. Without the FTAS, these women would have been confronted with such a lethal condition deeper into the second trimester, even though numbers are small. Yet, we showed that the main benefit lies in the earlier detection of *often detectable* and *other* anomalies. This is of particular clinical relevance, as these categories may include severe conditions that fall outside our formal FTMA definition but are nonetheless anomalies for which early detection is highly desirable. For *other anomalies* specifically, ***chapter 4*** showed that the introduction of the FTAS resulted in an additional 100 women opting for TOP compared to a situation without the FTAS, underlining the importance of these detected anomalies. Moreover, earlier detection also supports the preferences of those who value early knowledge of potential fetal anomalies, thereby strengthening their reproductive autonomy. Noteworthy, a substantial proportion of trisomy 13, 18, and 21 cases detected by the FTAS could have been identified by non-invasive prenatal testing (NIPT). At the time of the study, NIPT was available for €175 while the FTAS was free of charge. Since 2023, NIPT has been offered free of charge from 10 weeks' gestation, resulting in a 10% increase in uptake[9]. This earlier and costless offer of NIPT will likely reduce the yield of the FTAS, since fewer anomalies will remain to be identified exclusively by the FTAS. In addition to improving detection, the FTAS appears to have a reassuring effect among those with normal results on both the FTAS and second-trimester scan: satisfaction was high, with 97% indicating they would opt for the FTAS again. As one participant stated: "*The 13- and 20-week scans have really helped me experience a worry-free pregnancy*". Furthermore, half of the women who opted for TOP between a gestational age (GA) of 20 and 24 weeks reported feelings of time pressure due to the legal time limit for TOP. For those women, the FTAS is extremely valuable as earlier screening provides more time for evaluation and decision-making. With current exome sequencing times of about three weeks, a woman tested at GA 20 weeks receives results at GA 23 weeks, which leaves only a few days to process the outcome, consult with professionals, and, if desired, prepare for labour. This intense time pressure is avoided when anomalies are detected earlier, allowing decisions to be made with greater deliberation. Importantly, incorporating the FTAS into the prenatal screening program resulted in only a modest delay of time to diagnosis of a few days, indicating that diagnostic trajectories were not substantially extended in general and that uncertainty remained within limits. However, a more detailed examination reveals that, for certain anomalies, prolonged diagnostic trajectories did occur. In cases such as club foot and hydronephrosis, the final diagnosis occurred beyond 19 weeks' gestation, meaning that these women did not benefit from early screening. In the AFTER-cohort, which includes the FTAS, 25.0% of the women received a diagnosis only after 18 weeks' gestation, compared to 16.4% in the BEFORE-cohort without the FTAS. Although such cases were not explored in depth in this thesis, they should not be overlooked. The emotional toll of diagnostic ambiguity

and prolonged uncertainty is reflected in responses from women in our questionnaire study: *"After the 13-week scan, where the results were described as concerning and the worst-case scenarios were explained, we had to wait five weeks for the next scan. That really felt unbearably long."* – 'Fluid in both kidneys, UPJ stenosis', and *"I want to add that the 13-week scan caused a lot of stress for us because the baby is still so small and they actually know very little about the further development of what they see now"* – 'Bilateral fluid in the neck'. These experiences raise the question whether it is desirable to perform such a detailed fetal examination during early pregnancy. An alternative could be to reduce the FTAS protocol. However, a crucial challenge in ultrasound screening remains that anomalies cannot simply be 'unseen' once observed by sonographers. This is reflected in referrals for findings such as clubfoot or cleft lip, even though assessment of the fetal lips and foot position is not included in the FTAS protocol. ***Chapter 6*** further illustrates this, showing that although the primary purpose of the dating scan is obstetric and not intended as a screening tool, it nonetheless may result in the detection of structural anomalies. In the broader context of first-trimester anomaly assessment, ***chapter 6*** also demonstrated that dating scans hold potential for detecting major structural anomalies, even without a structured anatomy protocol. Yet, the true performance of routine scans described in ***chapter 4*** and ***6*** remains unknown as undetected cases were not included, thus restricting direct comparison.

How should 'false' reassurance be weighed?

A systematic evaluation of undetected cases following the FTAS is essential to better understand the limitations, to manage expectations among (prospective) parents and healthcare professionals, and to identify areas for quality improvement. First, such analysis provides insight into whether 'missed' diagnoses are due to protocol execution issues or inherent limitations of anomaly detection at this early gestational age. Secondly, it contributes to informed counselling by clarifying which anomalies can reasonably be expected to be detected in the early trimesters and which cannot. At the same time, it is important to recognize that such evaluation can be sensitive for involved sonographers. An undetected anomaly does not necessarily indicate incorrect or substandard performance. However, to prevent patients from perceiving false-negative cases as individual error, careful use of terminology and framing is essential. The term *undetected* is therefore preferred over *missed*, particularly in clinical communication towards patients, as it more accurately reflects the complexity of prenatal screening without implying personal fault. The term *missed* should be reserved for cases in which an anomaly was demonstrably present and visible during the scan, yet went unrecognized by the examiner.

A total of 1,164 anomalies (0.9%) were diagnosed in the second trimester after a normal first-trimester scan, as presented in ***chapter 5***. Considering that the majority (87%) of these anomalies are inherently undetectable in the first trimester, this rate reflects a relatively good performance for the initial year of FTAS implementation. It should be noted, however, that the true number might be slightly higher as we did not include cases referred between the performed FTAS and before the SAS, e.g. referrals following commercial scans. The 23 undetected FTMA cases, alongside some often detectable anomalies, warrant serious attention. Although the absolute numbers are small, these anomalies are severe and, in theory, should have been visible at the time of the FTAS. Our FTMA image assessment showed that mandatory planes were more frequently missing in FTMA cases, possibly due to the protocol's allowance for incomplete scans, which may have contributed to undetected cases. Now that the FTAS has been implemented for four years, it may be reasonable to apply a protocol similar to that of the SAS, including repeating incomplete scans or referring cases when adequate views cannot be obtained. One woman with a false-positive finding mentioned *"The sonographer had difficulty obtaining the correct measurement due to the fetal position, which resulted in an inaccurate measurement. If she had told me the measurement wasn't possible now but that I could come back at another time, it would have saved me a lot of stress"*. Reducing the incomplete scan rate closer to the 5.7% observed in SAS[9] (from the current 7.7% in FTAS) should be aimed for, yet balanced against the potential increase in referrals and the associated burden on tertiary centres. However, this reduction in incomplete scans might also occur naturally over time as sonographer expertise and confidence increase. In addition, for some women the current policy is appreciated, as one woman with a false-positive finding explained *"... the sonographer couldn't complete the checklist because visibility was limited. If the option had existed to simply check again at the 20-week scan, we would have been fine with that"*. Another factor to improve detection would be to expand the scan protocol. Our spina bifida detection of 46.6% was lower than the 59.5% reported in previous studies[7]. Notably, their protocol included intracranial translucency measurement in the midsagittal plane, which is known to significantly enhance detection rates[10, 11]. If higher detection is a priority, incorporating this assessment could be considered. Similarly, including evaluation of the outflow tracts may improve the detection of cardiac anomalies. It is essential to consider perspectives of pregnant women in this deliberation: how harmful is false reassurance? Our unpublished data on the satisfaction of 438 women carrying a child with a (suspected) structural anomaly (GA 24 weeks) after a normal FTAS result provide some insight. Despite the unexpected diagnosis, the majority reported positive attitude towards the FTAS: 93.8% (totally) agreed with the statement, "*I was glad I had done the FTAS*" and 90.6% with the statement "*If I were to become pregnant again, I would choose to have the FTAS again*". Noteworthy, diagnoses were self-reported, heterogeneous in

severity and cases involving termination of pregnancy were excluded. However, women who decided to terminate their pregnancy due to a fetal anomaly not detected by the FTAS reported similarly high levels of satisfaction with the FTAS. In conclusion, incorporating additional planes to enhance detection is not recommended for our FTAS protocol, given the technical difficulty of such measurements at this early gestational age and the fact that first-trimester scans are performed as population-based screening rather than in specialized diagnostic centres.

The impact of false-positive referrals

Based on our studies, protocol expansion is not recommended in a population-based screening context, especially considering the trade-off between higher detection rates and inherent increase of false-positive results. ***Chapter 3*** described substantial false-positive results of 59.1% after the FTAS, which can be subdivided into false-positive referrals and transient findings (suspected fetal anomaly identified at the referral centre but ultimately not confirmed at 24 weeks' gestation). Fortunately, the impact of false-positive referrals, defined as a normal diagnostic scan immediately after referral in the centre for prenatal diagnosis, in terms of distress, is limited and clinically comparable to those with normal results, as reported in ***chapter 7***. Conversely, women with true- and false-positive scans experienced more decisional regret and reported lower satisfaction. Approximately 25–30% of these respondents reported they would not opt for the FTAS again. While this is a notable proportion, it is not entirely unexpected. Even with adequate pretest counseling, it remains difficult for individuals to anticipate on the emotional impact of receiving unexpected or uncertain results until confronted with a finding they might have preferred not to know in retrospect. One woman mentioned: *"I hadn't realized that a referral after the FTAS would be so stressful, especially because I had a miscarriage during my first pregnancy. All the emotions from that experience came back"*. When opting for the scan, *"[..] you just don't expect it [abnormal scan result] will happen to you, [..]."*. Decisional regret may be influenced by a complex interplay of personal factors, communication quality and level of support from healthcare providers, and the waiting time until the detailed diagnostic scan. Notably, distress scores were measured after a reassuring detailed diagnostic scan and reflect only the preceding seven days. Therefore, these scores likely underestimate the emotional impact during the actual period of stress and uncertainty between referral and the diagnostic scan and may help explain the apparent contradiction between low distress and high regret. Additionally, even when a fetal anomaly was ultimately not confirmed, the diagnostic process may still have disrupted the sense of a carefree pregnancy, prompting a shift in perception and loss of reassurance. Therefore, adequate counselling remains essential, addressing both the benefits and potential downsides. However, placing too much emphasis on the possibility of detecting anomalies and the associated stress, should be avoided

during counselling, as it could unnecessarily worry the large proportion of women who receive normal results. It should also be acknowledged that routinization of the FTAS may influence decision-making, potentially reducing perceived autonomy and contributing to lower satisfaction. This underscores the importance of maintaining high-quality counselling that supports informed, deliberate choices. In parallel, I think that care in the period between an abnormal FTAS result and the follow-up detailed scan could be further improved. Reducing waiting times remains an important objective. In addition, providing structured support, both emotional and informational, during this interim period would help to alleviate distress. Tailored care may also be beneficial in determining whether referral is appropriate or desired in specific situations.

The FTAS in an international context

Placing the findings of this thesis within an international framework provides important insights into how the FTAS is implemented and perceived globally. Crucially, ultrasound screening in a national primary-care setting involving many sonographers, often working independently, differs fundamentally from scans performed in specialized centres. ***Chapter 2*** showed a substantial variability in the organization and quality of first-trimester anomaly screening across developed countries. While most countries have included early anatomical assessment as part of routine obstetrical care, differences in protocols, training, monitoring, and access persist both between and within countries. These inconsistencies may contribute to unequal opportunities and impact reproductive autonomy, especially in settings with restrictive legislation on termination of pregnancy. Insight in these international differences is important, as the diagnostic performance of the FTAS is inherently affected by factors such as the protocol design, sonographer experience, timing of the scan, clinical setting and population characteristics. This builds on previous findings suggesting that sensitivity improves with more detailed protocols and structured sonographer training[8]. All contextual variables should be taken into account when interpreting or comparing screening outcomes, making international comparisons particularly complex. As screening on a population level is rare, the true performance of the FTAS has never been thoroughly investigated on this level. Therefore, our findings might serve as a benchmark, encompassing equitable access, monitoring and uniform organizational aspects, thereby revealing realistic areas for improvement.

Labels are for bottles

A meaningful comparison of international FTAS performance also depends on how anomalies are defined and classified. Even classification and registration systems for congenital anomalies in general vary between countries, as illustrated by differences between EUROCAT and Canadian registries, accentuating challenges in achieving

standardized categorisation of fetal anomalies. When focusing specifically on the detection of first-trimester anomalies, these challenges become even more complex due to factors such as natural fetal developmental and visibility at that stage. Detection also hinges on the scope of the screening protocol: if an anomaly is not included in the protocol, it is unlikely to be found, regardless of sonographer skill. Protocols differ widely, as previously discussed, and there is no universally accepted classification for first-trimester anomalies. Therefore, the terminology used in ***chapters 3-6*** (FTMA, often detectable anomalies, other anomalies, undetectable anomalies), are not familiar to all experts in the field. This lack of standardization complicates comparison of screening outcomes and highlights the need for harmonized categorization frameworks to improve prenatal screening consistency and research comparability.

Every classification system, including ours, remains subject to debate due to broad heterogeneity of fetal anomalies. For example, how should subtle findings such as "mild fluid accumulation" be categorized? From a medical standpoint, such findings may be deemed clinically insignificant and therefore classified as normal. However, from a patients' perspective, even minor findings can provoke anxiety or stress, illustrating the subjective nature of classification outcomes.

Similarly, anomalies such as spina bifida exemplify the complexity of categorization. Should spina bifida be classified as always or often detectable? Large lumbar defects are usually clearly visible in the first trimester, while small sacral defects are subtle and therefore not always detectable early, complicating universal classification. This intra-anomaly variation is mirrored in other conditions as well, such as univentricular heart defects, holoprosencephaly and skeletal dysplasia. A fully nuanced classification system would be impractical in both clinical and research settings, making pragmatic and broadly applicable categories desirable. In my opinion, reaching international consensus on at least a minimum set of anomalies to be classified as FTMA should be realised, enabling meaningful comparison of detection rates and providing a basic reflection of screening quality. Such a core list could include: anencephaly, encephalocele, alobar holoprosencephaly, limb body wall complex, omphalocele, gastroschisis, bladder exstrophy, limb reduction defects, twin reversed arterial perfusion sequence (TRAP), thoracic or lumbar spina bifida and univentricular cardiac defects. While skeletal dysplasia, hydrops and megacystis are important findings, they should not be included in this minimal set, as their onset or expression may occur later in pregnancy, which would limit comparability across studies and reduce the validity of early detection rates as a quality indicator.

It's a matter of perspective

Building on challenges in classifications, the definition of what constitutes an 'undetected case' is not always straightforward and may vary depending on the perspective and intended audience. This highlights the importance of transparency in inclusion criteria and interpretation of false-negative rates in the literature. The primary focus from a medical perspective might lie on the actual diagnostic performance of the scan: which anomalies could realistically have been detected at this gestational age. Also for policy and program evaluation, FTMA and often detectable anomalies are key, as it informs on the effectiveness and potential improvements. In this context, anomalies categorised as *undetectable* are less relevant, as they either fall outside the scope of the protocol or are not yet visible or developed in the first trimester. If we were to exclude such cases, the undetected anomalies would decrease substantially from 0.9% to 0.13%. Accordingly, that's why ***chapter 3*** of this thesis reported the sensitivity for FTMA (85%) next to all anomalies (31%). However, this figure still does not fully reflect screening performance, as it excludes anomalies like univentricular cardiac defects and spina bifida that, while not classified as FTMA, are generally expected to be detectable. Including such anomalies in the analysis would lower the sensitivity to a range between 31% and 85%. However, from the perspective of pregnant women, a reported sensitivity of 85% in ***chapter 3*** may be misleading, as it does not capture the full scope of limitations in first trimester screening. For counselling and expectation management, all undetected anomalies are relevant, regardless of their theoretical detectability. What matters to (prospective) parents is understanding the likelihood of being confronted with a structural fetal anomaly, after a normal FTAS result, and the severity of these anomalies. The fact that a substantial proportion of all undetected anomalies led to termination of pregnancy or intrauterine fetal death underlines their clinical significance. This limitation of the FTAS should be discussed in the context of patient counselling, as well as emphasizing the importance of undergoing the SAS following a normal FTAS result.

National registry for congenital anomalies

As mentioned before, the centrally steered prenatal screening program in the Netherlands serves as an international example. However, when it comes to registration of congenital anomalies, the Netherlands may in turn benefit from the more robust, national systems established in several Scandinavian countries[12-14]. Although the Netherlands has a national perinatal registry (Perined), it is not linked to our prenatal registration system Peridos and its data on congenital anomalies diagnosed after birth are not sufficiently reliable to evaluate screening outcomes. The Dutch EUROCAT registry offers an important source of data on congenital anomalies but also has several limitations. Case reporting depends on active notification by healthcare

professionals, which is likely to result in underreporting. Furthermore, based on only two Dutch regions (Groningen and Limburg), it covers approximately 15% of Dutch births. Its extrapolation to the national level may not accurately reflect the national population, particularly due to the underrepresentation of urban and more diverse areas, such as the Randstad. Establishing a comprehensive national registry remains a significant challenge due to the need for central coordination, legal frameworks, structural funding and a collaborative infrastructure. Independent local scientific initiatives such as the PReCOR database, a collaboration between the University Medical Centres of Amsterdam and Leiden, aim to establish a comprehensive registry of all foetuses diagnosed with congenital heart disease. This registry is extremely valuable as it provides reliable insights and reflects the quality of the Dutch prenatal screening program for congenital heart disease. Despite strong collaboration, high motivation and rigorous data collection efforts, a key challenge remains in capturing undetected cases within the database, as some congenital heart defects may only become apparent weeks to months after birth. A potential, albeit challenging, solution would be to optimize and interlink existing national systems, such as Peridos, Perined and preventive child health services ("consultatiebureau"), to establish a complete, reliable and integrated registration for congenital anomalies.

Future perspectives – one size does not fit all

First-trimester anomaly screening undeniably adds value across various domains. While there is always room for improvement, it is important to acknowledge the exceptionality of the Dutch prenatal screening program in terms of protocol standardization, structured training, equitable access and centralized information provision. The FTAS has been introduced within this robust system and further improvements are expected as experience continues to grow. However, making a conclusive judgement on whether the benefits of the FTAS outweigh the disadvantages is challenging. In my opinion, it is premature to draw such a conclusion as the impact of transient findings and prolonged diagnostic trajectories are highly important and have not been thoroughly evaluated. Therefore, a considerable grey area remains regarding the extent to which we should aim to screen in the first trimester and whether the current FTAS protocol fits the purpose. Regardless of the eventual decision, there is no 'one size fits all'. It will always involve trade-offs: whether in terms of test characteristics, referral threshold, emotional well-being or practical feasibility. Ultimately, it is not possible to meet the preferences or expectations of all relevant stakeholders. Furthermore, whether the FTAS can be considered cost-effective or of *significant* value depends on the context, which is not only country-specific, but may also change over time within the same setting. For example, in the Netherlands, early screening significantly reduces time pressure that would otherwise exist due to the legal limit of 24 weeks, which is currently

seen as a key benefit of the FTAS. In countries without such a limit, this argument is not applicable. Conversely, if the viability threshold were to be lowered[15, 16], this might have consequences for the legal limit for TOP and thus earlier detection through the FTAS would become even more relevant. Similarly, rapid advances in genetic testing could shorten turnaround times from the current three weeks to just days, reducing the urgency created by the 24-week limit and potentially lowering the added value of the FTAS.

Beyond its performance, balance and perceived added value, we must consider: can we go back to a situation without the FTAS? For the past four years, pregnant women in the Netherlands have had access to anomaly screening and most now perceive it as a standard part of care. Discontinuing first-trimester anomaly screening would leave an unmet demand, thereby creating a lucrative opportunity for commercial providers to seize this gap. Such a shift would entail the loss of central coordination, fragmented protocols and limit access to those who can afford it. Furthermore, the current high standard of pretest counseling would decline or disappear altogether. In the Netherlands, prenatal screening is intrinsically bound to reproductive autonomy, with emphasis on enabling well-informed and deliberate choice. Safeguarding this principle depends on preserving both the quality and the equity of the national program. As professionals and policy makers, we carry the responsibility to protect this cornerstone of prenatal care through a regulated, nationally coordinated offer. A key starting point is clarifying the primary objective of the FTAS: should the focus lie solely on the detection of FTMA or should the aim be to identify all detectable anomalies in early pregnancy? I recommend to focus on the new, previously mentioned set of FTMA, with a valuable secondary benefit of the detection of *other* anomalies as defined in ***chapter 4***. A strong performance was demonstrated during this first year of population-based implementation. Detection could be strengthened by targeted sonographer training on the acquisition of correct imaging planes of the four-chamber view for detecting univentricular heart defects, midsagittal plane of the spine for detecting spina bifida and extremity assessment for detecting limb reduction defects. In addition, the use of transvaginal imaging should be further emphasized, especially in cases of suboptimal views, as it was only used in 14.7% of cases in our cohort. Notably, while implementing adjustments with the goal to enhance detection, it is important to acknowledge that screening is not diagnostic, and some anomalies will inevitably remain undetected. To further improve detection rates, policy regarding incomplete scans should be revised. Sonographers should repeat the scan when protocol-specified planes are incomplete. Referral to a diagnostic centre can be implemented in a stepwise manner by initially focussing on only scans with an abnormal four-chamber view or midsagittal spine planes or

on sonographers' request. The impact of this approach should be monitored before considering broader referral indications. Especially, since reducing false-positive referrals would be another important objective. Biometric measurements currently contribute substantially to false-positive results, as the tight distribution of reference growth curves causes even minor measurement differences to lead to large percentile shifts. Our data showed 374 referrals due to isolated abnormal fetal biometry, of which 36 (9.6%) had a structural or genetic anomaly. Thus, the disadvantage of biometric measurements seems to outweigh the advantage in general. Yet, before any definitive changes, in-depth analyses are needed to balance the value of each of the four parameters (HC, AC, FL, CRL) against their contribution to false-positive results. Suggestions for interim policy might include either continuing to measure all parameters but restricting referrals to extreme cases, or limiting measurements to HC and AC only, thereby maintaining alertness for conditions such as triploidy. The pretest counselling is of high quality and should remain this way if the FTAS were to be continued. While there are naturally areas for improvement, expectations should remain realistic regarding the level of information and understanding achievable at the population level, particularly given that 26% of the population has a low educational level and limited health literacy and numeracy. Lastly, NIPT should precede the FTAS if women desire both, as many anomalies detected in our FTAS cohort could already have been identified through NIPT, making this sequence more efficient and cost-effective within this public health funding framework. Any changes to the FTAS, or any other aspect in the prenatal screening program, should be accompanied by a comprehensive scientific evaluation to assess whether the intended outcomes are achieved and to ensure that benefits outweigh potential harms.

REFERENCES

1. EUROCAT. Prevalence charts and tables [updated 07/2025. Available from: https://eu-rd-platform.jrc.ec.europa.eu/eurocat/eurocat-data/prevalence_en.
2. Bonnet D, Coltri A, Butera G, Fermont L, Le Bidois J, Kachaner J, et al. Detection of transposition of the great arteries in fetuses reduces neonatal morbidity and mortality. Circulation. 1999;99(7):916–8.
3. Mahle WT, Clancy RR, McGaurn SP, Goin JE, Clark BJ. Impact of prenatal diagnosis on survival and early neurologic morbidity in neonates with the hypoplastic left heart syndrome. Pediatrics. 2001;107(6):1277–82.
4. Franklin O, Burch M, Manning N, Sleeman K, Gould S, Archer N. Prenatal diagnosis of coarctation of the aorta improves survival and reduces morbidity. Heart. 2002;87(1):67–9.
5. Bardi F, Bergman JEH, Bouman K, Erwich JJ, Duin LK, Walle HEK, et al. Effect of prenatal screening on trends in perinatal mortality associated with congenital anomalies before and after the introduction of prenatal screening: A population-based study in the Northern Netherlands. Paediatr Perinat Epidemiol. 2021;35(6):654–63.
6. Salomon LJ, Alfirevic Z, Berghella V, Bilardo CM, Chalouhi GE, Da Silva Costa F, et al. ISUOG Practice Guidelines (updated): performance of the routine mid-trimester fetal ultrasound scan. Ultrasound Obstet Gynecol. 2022;59(6):840–56.
7. Syngelaki A, Hammami A, Bower S, Zidere V, Akolekar R, Nicolaides KH. Diagnosis of fetal non-chromosomal abnormalities on routine ultrasound examination at 11-13 weeks' gestation. Ultrasound Obstet Gynecol. 2019;54(4):468–76.
8. Karim JN, Roberts NW, Salomon LJ, Papageorghiou AT. Systematic review of first-trimester ultrasound screening for detection of fetal structural anomalies and factors that affect screening performance. Ultrasound Obstet Gynecol. 2017;50(4):429–41.
9. RIVM. Professionalsmonitor 2023 screeningsprogramma de NIPT en het SEO [updated 15–01–2025. Available from: https://www.pns.nl/documenten/professionalsmonitor-2023-screeningsprogramma-nipt-en-seo.
10. Chaoui R, Benoit B, Mitkowska-Wozniak H, Heling KS, Nicolaides KH. Assessment of intracranial translucency (IT) in the detection of spina bifida at the 11-13-week scan. Ultrasound Obstet Gynecol. 2009;34(3):249–52.
11. Chaoui R, Nicolaides KH. Detecting open spina bifida at the 11-13-week scan by assessing intracranial translucency and the posterior brain region: mid-sagittal or axial plane? Ultrasound Obstet Gynecol. 2011;38(6):609–12.
12. Medical Birth Registry of Norway. Purpose and responsibilities. [updated 17–11–2023. Available from: https://www.fhi.no/en/ch/medical-birth-registry-of-norway/medical-birth-registry-of-norway/.
13. Socialstyrelsen. National Register of Congenital Anomalies. [updated 09–02–2024. Available from: https://www.socialstyrelsen.se/en/statistics-and-data/registers/national-medical-birth-register/national-register-of-congenital-anomalies/.
14. Finnish institute for Health and Welfare. Congenital Malformations. [updated 15–01–2024. Available from: https://thl.fi/en/statistics-and-data/data-and-services/quality-and-statistical-principles/quality-descriptions/congenital-anomalies.
15. Halliday S, Romanis EC, de Proost L, Verweij EJ. The (mis)use of fetal viability as the determinant of non-criminal abortion in the Netherlands and England and Wales. Med Law Rev. 2023;31(4):538–63.
16. De Proost L, Verweij EJT, Ismaili M'hamdi H, Reiss IKM, Steegers EAP, Geurtzen R, et al. The Edge of Perinatal Viability: Understanding the Dutch Position. Front Pediatr. 2021;9:634290.