SMART Test®
Comprehensive Guide for Parents

PATIENT INFORMATION BOOKLET - NOVEMBER 2025

LONDON PREGNANCY CLINIC

Summary

The SMART Test® is a cutting-edge prenatal screening service offered exclusively at the London Pregnancy Clinic. It integrates advanced ultrasound technology, the most sophisticated non-invasive prenatal testing (NIPT), and expert fetal medicine review for a thorough assessment of your baby's health as early as 10 weeks of pregnancy.

Key Features:

1. Comprehensive Screening

- Covers over 100 fetal syndromes, genetic disorders, and anomalies.
- Screens for chromosomal abnormalities (like Down syndrome), microdeletions (like DiGeorge syndrome), single-gene disorders (like Rett syndrome), and structural anomalies (like spina bifida).

2. Two-Steps in One Day

STEP 1:
Advanced ultrasound using GE Healthcare Voluson technology to screen for severe structural anomalies.

STEP 2:
KNOVA NIPT analyses cell-free fetal DNA for detailed genetic insights, including chromosomal and genetic conditions.

3. Why 10 Weeks?

- Earliest reassurance and insights into baby’s genetic and structural health.
- Allows time for retesting or confirmatory diagnostic testing if needed.

Introducing SMART Test®

4. Benefits

- Non-invasive and safe.
- Results provide comprehensive insights into your baby's genetic health.
- Includes free genetic counselling for high-chance results.
- Suitable for pregnancies with advanced maternal or paternal age, IVF conceptions, or increased nuchal translucency.
- Competitive pricing for a unique test combining expert ultrasound and cutting-edge NIPT.

5. Limitations

- It is a screening, not a diagnostic test. Positive results may require confirmatory procedures like CVS or amniocentesis.
- Cannot detect all possible genetic conditions and structural anomalies due to the limits of current technology.
- Not applicable for multiple pregnancies, vanishing twin syndrome or donor eggs.

It is offered only between 10 and 16 weeks, as time is needed to manage any high-chance results, but later testing may be possible after discussion with the clinic by email.

6. Exclusivity

- Only available at the London Pregnancy Clinic, ensuring expert handling of scans, genetic counselling, and support.

Welcome to the SMART Test®

The SMART Test®, exclusive to the London Pregnancy Clinic, combines expert ultrasound with advanced non-invasive prenatal testing (NIPT) to provide the earliest and most comprehensive assessment of your baby's health.

The SMART Test® is a one-stop service that includes an advanced version of **10 Week Scan and extended KNOVA NIPT (SMART Test® KNOVA).** This principal panel can be upgraded to include screening for hereditary diseases: **SMART Test® Plus** option.

SMARTTEST PLUS

Structural, Chromosomal, and **M**onogenic **A**nomalies
Recognition **T**wo-step **Test**

SMART Test® integrates expert imaging with cutting-edge genomics. This innovative two-step approach detects structural anomalies, Down syndrome, chromosomal aneuploidies, microdeletions, and monogenic syndromes as early as at 10 weeks.

A registered trademark of the London Pregnancy Clinic, the **SMART Test®** represents excellence in first-trimester prenatal care, delivering unparalleled accuracy and insight.

The **SMART Test®** embodies our holistic approach to prenatal care - offering reassurance, early detection, and tailored support. We appreciate that this document is detailed, but we strongly encourage you to read it carefully. Even if you're not planning to undertake this test, the information it contains can enhance your understanding of the most advanced prenatal screening option available today.

Who will benefit?

Parents Looking for Reassurance

Provides peace of mind by screening for a wide range of genetic and structural conditions as early as 10 weeks.

Advanced maternal or paternal age

Designed for mums over 35 or dads over 40, where risks of certain genetic conditions may be higher:

- Advanced maternal age increases the likelihood of chromosomal abnormalities like Down syndrome.
- Advanced paternal age can result in genetic mutations, such as monogenic (single-gene) disorders, often due to changes during sperm cell division.

Families with Previous Pregnancy Complications

Ideal if you've experienced a baby with anomalies, syndromes, or pregnancy terminations due to fetal conditions in the past.

Those Seeking Early Answers

If performed at 10 weeks, full results are typically available by, or earlier than, the routine NHS 12-week scan and Combined Screening Test (CST).

The best for Increased Nuchal Translucency (NT)

Covers many structural, chromosomal and monogenic conditions associated with the increased NT, meaning it's the NIPT of choice for fetuses with high NT.

- Down syndrome, other aneuploidies
- 22q deletion (DiGeorge syndrome), other microdeletions
- Noonan syndrome, other genetic syndromes
- Congenital heart defects, other structural anomalies

For whom?

Parents-to-Be with Specific Risk Factors

Helpful for pregnancies conceived through IVF. However, couples using a donor egg will require additional guidance.

Couples Seeking More Reassurance After an NHS 11-13 Week Scan

- Most NHS scans are conducted professionally, with sonographers offering thorough explanations and reassurance about the baby's health. However, some parents may feel their scan was rushed or lacked detail, with limited views of the baby's development. This can leave them with questions about whether everything was thoroughly checked.
- Some parents may feel uneasy with low-chance results from the Combined Screening Test (CST), knowing it only screens for trisomy 21, trisomy 18, and trisomy 13, and has a 10-15% false negative rate for trisomy 21 (Down syndrome). The SMART Test® offers a more detailed and comprehensive assessment, addressing these concerns and providing parents with greater peace of mind.

BEFORE SMART TEST®

Pre-Test Genetic Counselling

OPTIONAL

30-minute session with a registered Genetic Counsellor.
Quick, expert support.

30-minute | online | £80

Unsure which NIPT is right for you, or whether SMART Test® is the best option? In this appointment we explain SMART Test® and other NIPT choices, outline what each test can and cannot show, discuss timing, accuracy, limitations, potential next steps (ultrasound and diagnostic tests), and costs. You'll leave with clear, personalised advice to help you make an informed decision. What you'll get:

- Independent, evidence-based guidance on NIPT options (including SMART Test®)
- Benefits, limitations and likely outcomes explained in plain language
- A personalised recommendation and a short written summary

Further info and booking: londonpregnancy.com/nipt-genetic-counselling/

Eligibility is determined by the limitations of NIPT

Suitable for:

- **Pregnancy type:** Singleton pregnancies, including IVF pregnancies using the patient's own eggs.
- **Gestational age:** Starting from 10 weeks of pregnancy to 16 weeks of pregnancy.
- **Parental health:** No history of chromosomal abnormalities in the mother.
- **Age:** Pregnant individuals aged 18 or above.

Ineligible Scenarios:

- **Pregnancy type:** Multiple pregnancies (e.g., twins, triplets).
- **Gestational age:** Above 16 weeks of pregnancy. (more info on page 10)
- **Health History:**
  - Active malignancy.
  - History of bone marrow or organ transplant.
  - Parental mosaicism or maternal chromosomal abnormality.
  - Pregnancy with fetal demise.
- **Maternal age:** Under 18 years old.
- **Factors need to be checked with NIPT Lab for eligibility:**
  - Recent blood or blood components transfusion.
  - Recent immunotherapy.
  - Past malignancy.

Special Situations:

In certain scenarios where our preferred NIPT brand, KNOVA, cannot provide reliable results, we offer **PrenatalSafe Complete Plus NIPT** as part of the SMART Test®. These situations include:

- Vanishing twin syndrome.
- IVF pregnancies using donor eggs.
- Surrogacy pregnancies.

PLEASE NOTE THAT WHILE PRENATALSAFE COMPLETE PLUS IS THE ONLY OPTION FOR THESE CASES, IT HAS LESS OPTIMAL GENETIC COVERAGE COMPARED TO KNOVA. ADDITIONALLY, THIS TEST IS MORE EXPENSIVE AND HAS A LONGER TURNAROUND TIME.

Optimal Time: 10 Weeks

The SMART Test® is ideally performed at 10–11 weeks of pregnancy. This timing has been carefully chosen to provide expectant parents with the most accurate and comprehensive insights into their baby's health while ensuring the earliest possible detection of potential issues. Here are the main reasons why:

NIPT Works Best From 10 Weeks

At 10 weeks, the amount of fetal DNA circulating in the mother's bloodstream is sufficient for reliable analysis. Non-invasive prenatal testing (NIPT) at this stage provides highly accurate results for detecting:

- Chromosomal abnormalities like Down syndrome (trisomy 21).
- Microdeletions, such as DiGeorge syndrome.
- Genetic syndromes, including Noonan syndrome.

Signature 10 Week Scan

At 10 weeks, the fetus is fully formed, though small, making it an ideal time for early assessment. The 10 Week Scan, performed by fetal medicine experts, uses state-of-the-art ultrasound technology to:

- Confirm the pregnancy's viability and gestational age, and check how many babies are developing in your womb.
- Provide high-resolution images with microscopic-level detail, enabling a thorough assessment of the fetus's development.
- Detect severe structural anomalies, including:
  - Spina bifida.
  - Acrania.
  - Major heart defects.
  - Alobar holoprosencephaly.
  - Body stalk anomaly.

3D Scan

- 3D scan is the integral part of 10 Week Scan.
- The 3D ultrasound offers a detailed view of the baby's normal development, including the head, body, and limbs. For technical reasons, a diagnostic 3D assessment of the entire baby is only feasible at 10-11 weeks of pregnancy.

Optimal Time

Reassurance and Informed Decision-Making

The early screening of chromosomal, genetic, or structural anomalies provides:

- Peace of mind for parents, particularly those with advanced maternal or paternal age, or a history of complications.
- An opportunity to explore options and plan for the pregnancy with confidence.

Time for Follow-Up Testing

If abnormalities are detected, there is enough time to:

- Perform confirmatory diagnostic tests such as chorionic villus sampling (CVS) or amniocentesis.
- Schedule these tests promptly, avoiding unnecessary delays.

Comprehensive Results by 12–13 Weeks

The SMART Test®'s timeline ensures you receive a full report, combining ultrasound findings and NIPT results, by the time of your first NHS scan. This synchronised approach allows for:

- A clearer understanding of the baby's health.
- Better coordination with standard NHS care.

By performing the **SMART Test® at 10 weeks**, expectant parents benefit from cutting-edge technology, expert care, and comprehensive insights into their baby's health, all at the earliest possible stage of pregnancy.

Flexibility Across Pregnancy Stages

The SMART Test® also offers unparalleled flexibility and can be performed at various stages of pregnancy, ensuring comprehensive evaluations tailored to your needs.

10-11 WEEKS	**The best SMART Test® Timing** (see above)
12-16 WEEKS	• **Expanded Scope:** From 12 weeks, we offer the Early Fetal Scan, an enhanced version of the anomaly scan that examines additional fetal structures, such as the face and kidneys. • **Who Benefits?** This stage is particularly useful for parents addressing unexpected findings from NHS 11-13 week scans, such as increased NT thickness, structural findings for the baby or high-risk results from the Combined Screening Test (CST). • **Comprehensive Assessment:** Both structural and genetic evaluations remain thorough and effective during this period. • **3D scan:** Unfortunately, clinical 3D assessment of the whole fetus is typically impractical after 11 weeks in most cases.
BEYOND 16 WEEKS **SPECIALIST CARE**	If you are **above 16 weeks of pregnancy you MUST contact us for more information via email** (info@londonpregnancy.com). • **Tailored Approach:** For pregnancies progressing beyond 16 weeks, our clinic provides customised advice and advanced options to suit individual circumstances. • **NIPT Performance:** Rest assured, the accuracy of NIPT remains consistent at later stages of pregnancy, ensuring reliable results.

Why Timing Matters

Performing the SMART Test® earlier allows for timely reassurance and intervention. The SMART Test® adapts seamlessly to different timelines, so no opportunity for advanced screening is missed. Regardless of timing, the SMART Test® provides comprehensive information to support your pregnancy journey.

STEP ONE: ANOMALY SCAN

Ultrasound Scan

SMART Test® scan represents an advanced version of our 10 Week Scan (or Early Fetal Scan) and is performed by a specialist in fetal medicine.

1 Step: Ultrasound Scan - Structural Health

Aim of the Scan:

The SMART Test® relies on the expert scan working synergistic with NIPT. For correct diagnosis, safety, and proper care, extended NIPT like KNOVA must always be guided by an expert scan. There are several critical reasons why.

- **Identifying Severe Structural Anomalies Early:** The primary objective of the 10-week scan is to detect severe structural anomalies at an early stage of pregnancy. Structural anomalies are significantly more common than chromosomal or genetic issues. A notable proportion of severe anomalies identified during our 10 Week Scan are either lethal or associated with poor outcomes. While NIPT is highly effective at screening for genetic conditions, many structural anomalies, such as acrania, are non-genetic and cannot be detected by NIPT at all. Detecting these anomalies beforehand ensures that patients follow the appropriate care pathway and avoid being falsely reassured by normal NIPT results. They also can save money by not performing inappropriate, expensive genetic tests (NIPT).
- **Confirming Viability:** In early pregnancy, there is always a risk of miscarriage. Performing expensive genetic testing without first confirming viability is impractical.
- **Establishing Gestational Age:** KNOVA NIPT requires a minimum gestational age of 10+0 weeks. Accurately determining this ensures the test can be performed at the correct time.
- **Ruling Out Conditions That May Affect NIPT Feasibility:** Situations such as vanishing twin syndrome or multiple pregnancies (twins) may render KNOVA NIPT unsuitable. In these cases, alternative NIPT options available in the London Pregnancy Clinic may be recommended.

Scan Technical Details: Our Ultrasound Equipment

There are various ultrasound machines, each with different diagnostic capabilities. For the SMART TEST®, we exclusively use high-end equipment from GE Healthcare, an internationally recognised leader in medical ultrasound imaging. GE Voluson scanners are specially designed for pregnancy examinations and considered the gold standard for advanced ultrasound diagnostics.

- **Equipment Used:** We use two variants of premium-class scanners: **Voluson Expert 22** and **Voluson Expert 20**.
- **Special high-frequency transducers (probes):** These are not the standard probes used for scanning babies in the second half of pregnancy. Our selection of unique high-frequency transabdominal and transvaginal probes ensures exceptional image quality, even for tiny structures at an early stage of pregnancy. They function like a magnifying glass or even a microscope. With their use, we can see details such as the fingers of a 10-week-old baby who measures just 3 cm.
- **Safety Measures:** Ultrasound scans are considered safe during pregnancy, especially as they pose no radiation hazard. All our scans adhere to the ALARA (As Low As Reasonably Achievable) principle, ensuring minimal ultrasound exposure. We use the lowest possible thermal settings and strictly control the TI (thermal index). For 10-week-old babies, spectral Doppler is avoided. Transvaginal transducers are meticulously decontaminated to guarantee safety.

How We Perform the Scan

The SMART Test® scan is conducted by a doctor or specially trained fetal medicine sonographer, ensuring the highest level of precision and expertise.

Empty bladder request

We kindly ask patients to ensure their bladders are empty before the scan. An empty bladder is essential for optimal imaging during the first trimester, particularly the 10 Week Scan.

PLEASE DO NOT FILL YOUR BLADDER BEFORE THE SMART TEST®, AS A FULL BLADDER CAN REDUCE THE CLARITY AND RESOLUTION OF THE ULTRASOUND SCAN.

Scanning Technique

The scan always begins with a **Transabdominal Ultrasound** using high-frequency probes, providing an initial overview of the pregnancy. This scan is performed by gently moving a probe across your tummy (abdomen). A special gel is used to help the sound waves travel and create clear images of your baby.

Transvaginal scan (TVS)

At 10–11 weeks, the transvaginal scan is our core technique, offering unmatched microscopic resolution to assess fetal anatomy and behaviour. We use it in most cases, unless the baby's position allows clear transabdominal imaging. Only the transvaginal scan can produce true diagnostic 3D images at this early stage.

This scan is done by gently inserting a thin, smooth probe into the vagina. It gives very detailed images of your uterus and the baby, especially in early pregnancy. It's safe and usually not uncomfortable. **Transvaginal scan** is typically performed using specialised high-frequency transvaginal probes for additional detail, particularly for the brain, spine, and heart structures. Our unique transvaginal probes allow for more precise imaging of early fetal anatomy. All transducers undergo meticulous decontamination procedures before and after each use, ensuring a sterile and safe environment. A chaperone (a clinical assistant) is present for every transvaginal scan by male professional and you can also ask for chaperon in the case of female operator.

If you feel uncomfortable with a transvaginal scan (TVS), you can always opt-out. Please note that in most cases, a TVS is crucial for obtaining diagnostic views of the baby's anatomy, especially the heart and spine.

Watch our video on Transvaginal scan vs Transabdominal Ultrasound here.

1 Step: Ultrasound Scan - Structural Health

What SMART Test® Checks the Baby for at 10 Weeks?

CRL (CROWN-RUMP LENGTH)	Measurement of the baby's length (CRL) to confirm gestational age and establish estimated due date (EDD).
FETAL HEARTBEAT	Confirmation of fetal heartbeat and measurement of heart rate, which can be up to 180 beats per minute.
HEART	Evaluation of the four heart chambers and the presence of the two main arteries (aorta and pulmonary artery).
HEAD AND BRAIN	Assessment of normal head and skull development. We check for brain division into two hemispheres and the presence of the fourth ventricle.
NUCHAL TRANSLUCENCY (NT)	Examination of the skin at the back of the baby’s neck and measuring the nuchal translucency (NT), the small pocket of fluid beneath the skin. If the NT is increased (above the 95th centile for CRL), we will explain its clinical significance (a higher risk of fetal health problems). In this situation, we offer our specialist SMART NT pathway (no change in test price).
SPINE	Examination of the spine to assess for deformities and to screen for spina bifida.
ABDOMEN	Verification of normal physiological bowel herniation into the umbilical cord, absence of abdominal cysts, presence of the stomach, and absence of a distended bladder (megacystis).
EXTREMITIES	Presence of arms, hands, legs, and feet. We also check for fingers, though counting them may not always be possible.
UMBILICAL CORD	Confirmation of the presence of the umbilical cord and the number of umbilical vessels.
YOLK SAC	Observation of the yolk sac’s presence & development.
AMNION	Assessment of the amnion’s integrity and exclusion of amniotic bands.

*continued on next page →

1 Step: Ultrasound Scan

*table continued

AMNIOTIC FLUID	Verification of normal amniotic fluid around the baby.
PLACENTA	Exclusion of implantation into a previous caesarean section (CS) scar and confirmation of no subchorionic haematoma.
CERVIX	The examination aims to rule out significant cervical shortening. While we do not routinely measure cervical length, we will assess it if it appears shortened.

3D Scan

- We consider 3D ultrasound as an essential diagnostic tool at 10-11 weeks.
- The 3D image shows the normal development of the baby's head, body, and limbs.
- In most cases (>90%) we can produce a clinical 3D image of the whole baby at 10-11 weeks.

PLEASE NOTE THAT DUE TO TECHNICAL REASONS, 3D IMAGING OF THE FULL BABY BECOMES LIMITED OR IMPOSSIBLE AFTER 11 WEEKS.

Patient Experience

During the scan, real-time images are displayed on a screen for parents to view. We also provide 2D and 3D images, as well as short video clips, which can be sent directly to mobile devices. Our clinician explains the findings throughout the procedure, offering reassurance and answering any questions.

Limitations of the Scan

The quality of the scan largely depends on the baby's position in the womb. If the fetal position is unfavourable, our clinician may ask you to take a 20-40 minute walk and return for a rescan. We recommend allowing flexibility in your schedule.

What We Do If the Scan Cannot Produce Diagnostic Imaging

In fewer than 5% of cases, even after a rescan, diagnostic imaging may remain inconclusive. This can be due to factors such as fibroids, intra-abdominal scarring (for example, after a caesarean section), or a persistently awkward fetal position. If this happens, we'll let you know and offer a complimentary follow-up scan after your NIPT (KNOVA) results are available; usually between 13-16 weeks.

THIS COMPREHENSIVE ULTRASOUND APPROACH ENSURES A DETAILED ASSESSMENT OF THE BABY'S HEALTH WHILE PRIORITISING PATIENT COMFORT AND SAFETY.

Structural Anomalies by Fetal Prognosis

Lethal Anomalies

Here is the list of fetal structural anomalies we screen for at 10–11 weeks. Please note that while we make every effort to detect these conditions, in some cases it may not be possible due to technical or biological reasons.

ACRANIA	Absence of cranial bones, associated with severe brain damage. Common fetal anomaly (about 1 in 1000 pregnancies). Always fatal.
ALOBAR HOLOPROSENCEPHALY	Severe brain malformation where the brain fails to divide into two hemispheres. Lethal in most cases.
BODY STALK ANOMALY (BSA)	A rare condition where the fetus remains attached to the placenta with exposed abdominal contents. Fatal.
LIMB BODY WALL COMPLEX (LBWC)	A severe congenital anomaly involving multiple body systems, characterised by body wall defects, limb anomalies, and internal organ malformations. Fatal.
SIRENOMELIA (MERMAID SYNDROME)	Fusion of the lower limbs, often associated with absent kidneys and severe organ malformations. Usually fatal.
CONJOINED TWINS (CERTAIN TYPES)	Depending on the extent and location of fusion, many types of conjoined twins are lethal.

Anomalies Associated with Severe Disability or Lethal

These conditions often result in significant long-term physical or intellectual impairments.

SPINA BIFIDA	Incomplete closure of the spinal column, which damages spinal cord nerves. Usually, it results in legs paralysis and bladder/bowel incompetence. Common anomaly.
ENCEPHALOCELE	Protrusion of brain tissue through a defect in the skull. Often leads to severe neurological impairment or even death.
CLOACAL EXSTROPHY	Severe malformation of the bladder, intestines, and reproductive organs. Requires complex surgeries, with a high likelihood of disability.
PENTALOGY OF CANTRELL	Complex condition involving defects in the heart, diaphragm, abdominal wall, pericardium, and sternum. Significant long-term issues, even with surgical treatment.
AMNIOTIC BAND SYNDROME (SEVERE CASES)	Constriction of fetal body parts by amniotic bands can result in severe limb deformities or amputations.
SEVERE HEART DEFECTS	We make every effort to detect severe CHD at 10 weeks, but formal performance metrics at this stage are unknown. The NHS benchmark is ~50% detection at 20 weeks. In our experience, some severe defects may be visible at 10 weeks. Examples include: • **Hypoplastic Left Heart Syndrome (HLHS):** Underdevelopment of the left side of the heart, leading to poor blood circulation. • **Tricuspid Atresia:** Absence of the tricuspid valve, disrupting normal heart function. • **Univentricular Heart:** A condition where only one ventricle is functional. • **Ectopia Cordis:** A rare and severe anomaly where the heart protrudes through the chest wall.

Conditions Associated with Chromosomal and Genetic Syndromes

These conditions may indicate an increased risk of underlying chromosomal or genetic abnormalities and syndromes; however, in some cases, they can resolve spontaneously with a favourable outcome.

INCREASED NUCHAL TRANSLUCENCY (NT)	Increased fluid at the back of the fetal neck, detected during early pregnancy. An NT measurement above the 95th centile at 10-11 weeks is considered increased. It may indicate chromosomal anomalies (e.g., Down syndrome), genetic syndromes (e.g., Noonan syndrome), structural heart defects and other problems.
EARLY FETAL HYDROPS	Abnormal accumulation of fluid in two or more parts of the fetal body (for instance under the skin and inside the chest), often associated with chromosomal abnormalities, genetic syndromes, or structural anomalies.
CYSTIC HYGROMA	Fluid-filled sacs around the fetal neck, resulting from a blockage in the lymphatic system, are commonly linked to chromosomal abnormalities such as Turner syndrome and Edwards syndrome or genetic syndromes.

Early fetal hydrops and cystic hygroma are usually associated with significantly increased NT measurements and may indicate higher chances for chromosomal or genetic conditions.

The KNOVA NIPT panel (see below) screens for many chromosomal and genetic conditions linked to increased nuchal translucency, early fetal hydrops, and cystic hygroma, making it the preferred NIPT in these situations.

Potentially Treatable Anomalies

With timely interventions, these conditions may be manageable, offering a good chance of survival and improved quality of life.

ABSENCE OF ARMS, HANDS AND/OR LOWER EXTREMITIES	Missing limbs can be managed with prosthetics and rehabilitation, allowing a good quality of life.
EXOMPHALOS (OMPHALOCELE) WITH LIVER	Protrusion of the liver and other abdominal organs into the umbilical cord. It is treated with surgery, however some babies will have long term problems with lungs or even die.
AMNIOTIC BAND SYNDROME (MILD CASES)	If detected early and mild, surgical intervention after birth can manage deformities.
MONOAMNIOTIC TWINS (MA TWINS)	High-risk twin pregnancy due to shared amniotic sac, leading to cord entanglement. Survival is possible but with high risks of complications.
CONJOINED TWINS (CERTAIN TYPES)	Surgical separation is sometimes possible, leading to survival and an acceptable quality of life.
TRAP SEQUENCE (TWIN REVERSED ARTERIAL PERFUSION)	A rare complication in twin pregnancies where the acardiac twin lacks a functioning heart. Fatal for the acardiac twin and high risk for the normal twin.

SMART Test® 10 Week Scan Compared to NHS 12 Week (Nuchal) Scan

Timing

The 10 Week Scan is conducted much earlier, approximately 2 weeks before the NHS 12-week scan.

Aim

- The 10 Week Scan primarily focuses on screening for lethal or severe structural fetal anomalies. It does not focus on markers for Down syndrome because the NIPT included in the SMART Test® has a 99.9% detection rate for Down syndrome, which is significantly more accurate than ultrasound screening.
- The 12-week scan aims to measure nuchal translucency (NT), which, when combined with a blood test (Combined Screening Test), has only 85-90% detection rate for Down syndrome.
- The 10-week scan also measures NT, and early data suggest that NT at this stage is a more sensitive indicator of fetal health than later, 11-14 weeks, measurements.

Severe Structural Anomaly Detection

Detecting severe structural anomalies is the primary focus of the 10 Week Scan. The NHS formally screens for anomalies at the 20-week anomaly scan, which is 2-2.5 months later, delaying the identification of critical issues during a crucial developmental period. However, some NHS trusts may conduct early screening for selected anomalies at 12 weeks (check with your hospital).

Protocol for Checking Fetal Structures

The 10 Week Scan follows a clear protocol for a systematic check of fetal anatomy (morphological scan). According to a 2019 survey, 25% of NHS trusts in England did not have protocols to check any fetal structures during the first trimester scan.

Screening for Spina Bifida and Severe CHD

Spina bifida and major congenital heart defects (CHD) are associated with severe disabilities and can be lethal. They are key targets of the SMART Test® 10 Week Scan. Less than 20% of NHS trusts in England include checks for the spine and heart in their first trimester protocols.

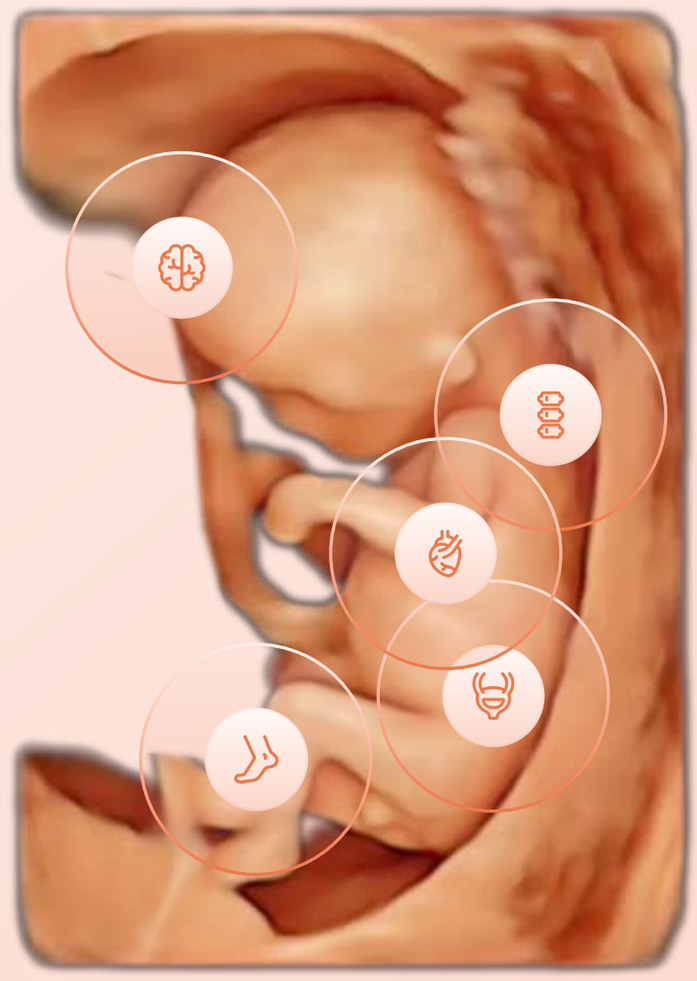
1 Step: Ultrasound Scan - Structural Health

What NHS 12 Week (Nuchal) Scan Checks

VIABILITY | DATING | FETUS NUMBER | NT MEASUREMENT

What 10 Week Scan Checks

VIABILITY | DATING | FETUS NUMBER | NT MEASUREMENT | HEAD | BRAIN | HEART | SPINE | ABDOMINAL WALL | ALL LIMBS



Approach

- The 10 Week Scan mainly uses a transvaginal approach with state-of-the-art scanners and high-resolution transducers. This approach provides highly detailed images, allowing the fetal structures to be viewed with near-microscopic clarity.
- The NHS typically uses a regular transabdominal scan with standard transducers, which offer lower resolution and less detailed imaging.

3D Imaging

The SMART Test® allows for clinically important 3D images of the baby in about 90% of cases using transvaginal scanning. These images demonstrate the integrity of the baby's head, body, limbs, and umbilical cord. The NHS does not use diagnostic 3D imaging in the 1st trimester and also later stages of gestation.

Expertise

The 10 Week Scan is performed by fetal medicine specialists who are specifically trained for this type of early examination.

Sharing of Images with Parents

We share video clips and digital images of the baby securely via our cloud-based system. Additionally, we provide black-and-white and colour printouts.

Diagnostic quality of the scan:

The quality of the scan primarily depends on the baby's position within the womb. If the baby is in an unfavourable position that limits visibility, we may ask the patient to take a brief walk and return for a repeat scan approximately 20-40 minutes later.

Rescan policy:

In rare cases, accounting for less than 10% of scans, we may encounter difficulty obtaining diagnostic images or conclusive findings even after rescanning. Common factors contributing to this include:

- Persistent oblique positioning of the baby in the uterus
- Presence of fibroids
- Intra-abdominal scars (e.g., from a previous caesarean section)
- High position of the womb in the pelvis

If diagnostic imaging is inconclusive after a same day rescan, we may schedule a follow-up free scan in a few weeks after the NIPT results are available, typically between 13-16 weeks.

STEP TWO: NON-INVASIVE PRENATAL TEST

KNOVA NIPT

KNOVA NIPT offers broad coverage, screening for:

- **Common aneuploidies** (6 chromosomal syndromes)
- **Sex chromosome aneuploidies** (4 syndromes)
- **Microdeletions** (12 severe and common ones)
- **56 single genes**, where mutations lead to a wide variety of monogenic syndromes (single-gene disorders), including Rett and Noonan syndromes. *This is the unique feature of KNOVA NIPT.*

2 Step: KNOVA NIPT - Genetic Health

SMART Test® – Advanced NIPT by our LPC team

The second step of the SMART Test® involves the most advanced Non-Invasive Prenatal Test (NIPT) available **KNOVA NIPT.** Contrasting to Harmony Test, Panorama Test or other basic NIPT options, which only check for Down syndrome, and a few common chromosomal anomalies, the KNOVA NIPT goes far beyond and screens for a significantly broader range of genetic conditions. This sophisticated NIPT detects additional genetic disorders, including microdeletions and single-gene (monogenic) diseases.

Why We Chose KNOVA NIPT

At London Pregnancy Clinic, our focus is to offer the most accurate and comprehensive prenatal screening. Over the past three years, we have rigorously evaluated various extended NIPT options from the most advanced laboratories. Only a few leading genomic institutions globally, such as Natera, Eurofins, and Fulgent Genetics, have the capability to perform these complex tests. After a thorough analysis of accuracy, reliability, validation, turnaround time, no-call results, price, and the scope of conditions screened, we selected **KNOVA Prenatal Screening (NIPT/NIPS) Full Panel, provided by Fulgent Genetics Lab,** as our NIPT for SMART Test®. KNOVA excelled across all key evaluation criteria, outperforming other sophisticated NIPT options in every category.

Extended NIPT panels are commonly criticised for producing a high level of false positive results and for testing not clinically important conditions. The genetic panel of KNOVA NIPT was perfectly curated and represents a very balanced genomic product, providing excellent coverage for severe genetic syndromes and trying to reduce the possibility of false positive results. KNOVA does not screen for conditions known to have high false-positive rates, such as testing all chromosomes, rare microdeletions, or variants of unknown significance (VUS).

Why We Choose Fulgent Genetics Lab (California, US) for SMART Test®

Fulgent Genetics stands as a pioneer in next-generation sequencing (NGS) and advanced genetic screening. Their comprehensive offerings include more than 18,000 genetic tests, whole-genome sequencing, and specialised prenatal panels. Fulgent's commitment to evidence-based testing, and robust clinical validation aligns perfectly with our mission at the London Pregnancy Clinic.

Accreditation and Quality.
Fulgent operates under stringent quality standards, holding CAP and CLIA certifications, as well as ISO 15189:2012 accreditation.

2 Step: KNOVA NIPT - Genetic Health

KNOVA NIPT Panel

Fulgent Genetic Lab is a world leader in next-generation sequencing (NGS). Leveraging their expertise, they developed a proprietary technique for comprehensive prenatal analysis of cell-free DNA (cfDNA), which is now implemented in KNOVA NIPT. It uses a unique sequencing approach, combining coordinated allele-aware target enrichment and multidimensional analysis. This ensures high sensitivity in detecting fetal genetic variants while minimising maternal DNA interference. Their method is ideal for screening de novo monogenic disorders. As a result, KNOVA's panel covers a broad range of serious genetic conditions.

KNOVA checks for *de novo* chromosomal and genetic conditions, which occur spontaneously due to errors in chromosomes or genes during conception and are not hereditary. The most widely recognised *de novo* condition is Down's syndrome, but hundreds of others exist. Unlike standard NIPT tests that only detect chromosomal number changes, KNOVA offers a sophisticated analysis across three genetic layers: abnormal chromosome numbers (aneuploidies), structural changes in chromosomes (microdeletions), and faulty genes (monogenic disorders). The test focuses on detecting the most common and severe genetic conditions that current technology can identify.

KNOVA does not detect all genetic disorders. During development of KNOVA Fulgent Genetic uses the SEPH criteria, ensuring that only the most relevant monogenic disorders are screened, reducing risk of false positive and inconclusive results. SEPH criteria include:

- **Severe outcome:** Conditions with serious health impacts and limited variability in symptoms.
- **Early onset:** Disorders typically presenting in infancy or early childhood.
- **Known prevalence:** Conditions with established rates of occurrence.
- **High test performance:** Reliable detection methods for accurate results.

Key Genetic Conditions Screened by KNOVA

1. Aneuploidies (extra copies of chromosomes)

Aneuploidies are genetic conditions caused by an abnormal number of chromosomes. These disorders are significant in prenatal screening because they can lead to severe developmental issues, intellectual disabilities, and physical anomalies.

- **Trisomy 21 (Down Syndrome)**
  The most common syndrome in humans, with a current incidence of 1 in 330 pregnancies in England. It is a chromosomal disorder associated with developmental delays, intellectual disabilities, and characteristic physical features.
- **Trisomy 18 (Edwards Syndrome)**
  A severe chromosomal anomaly resulting in multiple life-threatening organ defects, severe disabilities and a high mortality rate in infancy.
- **Trisomy 13 (Patau Syndrome)**
  This condition leads to severe intellectual disability and multiple congenital anomalies, including heart defects, facial anomalies and brain abnormalities.
- **Trisomy 15**
  An infrequent chromosomal condition associated with developmental delays, growth issues, and potential congenital anomalies.
- **Trisomy 16**
  The most common chromosomal trisomy in early miscarriages is associated with early pregnancy loss and severe developmental defects.
- **Trisomy 22**
  A rare chromosomal abnormality associated with developmental issues and often early pregnancy loss.

2. Sex Chromosome Anomalies

Sex chromosome anomalies occur when there is an abnormal number of sex chromosomes, leading to various developmental, reproductive, and physical differences. These conditions are significant because they can affect growth, fertility, and intellectual development.

- **Turner Syndrome (45,X)**
  A condition affecting females caused by the absence of one X chromosome, leading to short stature, infertility, and possible heart and kidney problems.
- **Klinefelter Syndrome (47,XXY)**
  A condition in males caused by an extra X chromosome, often resulting in infertility, learning difficulties, and low testosterone levels.
- Other sex chromosome disorders

3.Microdeletions

Microdeletions are chromosomal abnormalities where small segments of a chromosome containing multiple important genes are missing. These deletions can result in a range of developmental, intellectual, and physical issues depending on the genes involved.

- **22q11.2 Deletion Syndrome (DiGeorge Syndrome)**
  A disorder caused by a small missing piece of chromosome 22, leading to heart defects, immune system issues, developmental delays and associated with schizophrenia.
- **1p36 Deletion Syndrome**
  A condition caused by a deletion at the tip of chromosome 1, associated with intellectual disability, seizures, and distinctive facial features.
- **Cri-du-Chat Syndrome (5p Deletion Syndrome)**
  A rare genetic disorder caused by a deletion on chromosome 5, leading to intellectual disability, delayed development, and a high-pitched cry in infants.
- **Wolf-Hirschhorn Syndrome (4p Deletion Syndrome)**
  A condition caused by a deletion on chromosome 4, resulting in severe developmental delays, seizures, and distinct facial features.
- **Prader-Willi Syndrome (15q11-q13 Deletion)**
  A genetic disorder caused by the loss of function of genes on chromosome 15. It can lead to obesity, intellectual disability, and short stature.
- **Angelman Syndrome (15q11-q13 Deletion)**
  A neurogenetic disorder caused by a deletion on chromosome 15, characterised by severe developmental delay, lack of speech, and frequent laughter.
- **Smith-Magenis Syndrome (17p11.2 Deletion)**
  A disorder caused by a deletion on chromosome 17, associated with intellectual disability, behavioural issues, and sleep disturbances.
- Other microdeletions.

4. Monogenic Syndromes (single-gene disorders)

Monogenic disorders are caused by mutations in a single gene. The monogenic conditions screened by KNOVA occur as new *(de novo)* mutations and often have significant impacts on physical development, organ function, and overall health. Some of those conditions are associated with intellectual disabilities.
KNOVA does not intend to screen for hereditary syndromes, however **SMART Test® *plus*** provide those options too (see below).

- **Rett Syndrome (MECP2 Gene)**
  A neurological disorder primarily affecting girls, leading to severe cognitive and physical impairments after a period of normal development.
- **Noonan Syndrome (RASopathy – multiple genes involved)**
  A common genetic condition affecting multiple parts of the body, often resulting in heart defects, short stature, varying degrees of intellectual disability, and unique facial characteristics. RASopathies are a group of genetic disorders caused by mutations in the RAS-MAPK pathway, affecting cell growth and development.
- **Cardiofaciocutaneous Syndrome (BRAF, MAP2K1, MAP2K2 Genes)**
  A RASopathy causing distinctive facial features, heart defects, skin abnormalities, and developmental delays.

2 Step: KNOVA NIPT - Genetic Health

- **Costello Syndrome (HRAS Gene)**
  A rare genetic disorder characterised by distinctive facial features, developmental delays, heart abnormalities, and increased cancer risk.
- **LEOPARD Syndrome (PTPN11, RAF1 Genes)**
  A RASopathy leading to multiple lentigines, heart defects, and distinctive facial features, with an increased risk of hearing loss.
- **CHARGE Syndrome (CHD7 Gene)**
  A complex genetic disorder involving multiple congenital anomalies, including eyes, heart defects, nasal airway blockage, and developmental delay.
- **Kabuki Syndrome (KMT2D Gene)**
  A rare genetic disorder characterised by distinct facial features, developmental delay, and skeletal abnormalities.
- **Tuberous Sclerosis Complex (TSC1/TSC2 Genes)**
  A genetic condition that causes benign tumours to form in multiple organs, including the brain, skin, kidneys, and heart. The condition is commonly associated with severe epilepsy.
- **Cornelia de Lange Syndrome (NIPBL Gene)**
  A genetic disorder causing distinctive facial features, limb abnormalities, and intellectual disability.
- **Sotos Syndrome (NSD1 Gene)**
  A condition characterised by overgrowth in childhood, distinctive facial appearance, and developmental delay.
- **Thanatophoric Dysplasia (FGFR3 Gene)**
  The most common severe skeletal dysplasia characterised by extremely short limbs and a narrow chest. The majority of newborns with this condition will die soon after birth.
- **Achondroplasia (FGFR3 Gene)**
  The most common form of dwarfism. The average height of the adult with this condition is about 125 cm (4 ft 1 in).
- **Osteogenesis Imperfecta (De Novo Mutations in COL1A1/COL1A2 Genes)**
  A group of genetic disorders causing fragile bones, frequent fractures, and varying degrees of severity.
- **Achondrogenesis (COL2A1 Gene)**
  A severe skeletal disorder characterised by underdeveloped bones, extremely short limbs, and often perinatal lethality.
- **Apert Syndrome (FGFR2 Gene)**
  A rare genetic disorder characterised by premature fusion of skull bones (craniosynostosis), leading to abnormal head shape and facial features.
- **Pfeiffer Syndrome (FGFR1/FGFR2 Genes)**
  A genetic condition involving premature fusion of certain skull bones (craniosynostosis), resulting in distinctive facial features and possible limb abnormalities.
- Other genetic syndromes.

Technical Overview & Courier

Blood Sample Collection

Two blood tubes are required, collected from your arm during the appointment.

Courier Service

- The blood samples are shipped via **DHL**, a globally trusted courier service known for secure and timely international delivery.
- Samples are transported at **ambient temperature** using specialised Streck tubes, which maintain the stability of cfDNA for **up to 7 days.**
- Each shipment is tracked in real time and is expected to **arrive at the lab within 48 hours,** ensuring prompt and secure delivery.
- Please note that DHL does not operate on weekends, so delivery times may be slightly longer than usual.

Lab Processing and Methodology

- Upon arrival at **Fulgent's El Monte US California Lab** the sample undergoes:
  - Coordinative allele-aware target enrichment sequencing.
  - **Multidimensional genomic analyses** involving read depth, allelic fraction, and cfDNA fragment length.
- This advanced technology enables the detection of **de novo mutations,** inherited conditions, and chromosomal anomalies with high accuracy.
- The status of each KNOVA test is carefully monitored by the London Pregnancy Clinic using Fulgent's dedicated provider portal.

The turnaround time (TAT) for this advanced genetic test is impressively short.

- The expected TAT for KNOVA results is **7 to 10 working days** from the time of sample arrival to the labratory. (slightly longer than as Panorama).
- Since the test involves detailed genetic analyses, delays may occur in rare situations, such as:
  - **Extended analysis requirements** to ensure result accuracy.
  - **Data validation:** KNOVA employs multiple layers of genomic analysis to ensure high sensitivity and specificity, which sometimes adds time to the reporting process.
  - **Sample shipping delays** caused by external factors (uncommon).

Note: In some cases, the date on the report may be listed one or two days earlier than the final result approval by, reflecting when the sample was first processed by the lab.

LONDON PREGNANCY CLINIC WILL CONTACT YOU BY PHONE AS SOON AS WE RECEIVE CONFIRMATION FROM THE LAB THAT YOUR NIPT REPORT IS READY. WE WILL THEN SECURELY SEND YOU THE PDF FILE WITH YOUR KNOVA RESULTS.

No-Call Results for KNOVA

A **'no-call' result** occurs when a non-invasive prenatal test (NIPT) does not produce a reliable result, usually due to **insufficient fetal DNA** in the maternal blood sample (known as low fetal fraction). This can be extremely stressful and frustrating for expectant parents, especially after anticipating reassurance from the test. This situation was very common with once widely used **Harmony test (more than 5%)**.

Based on our ongoing audit and internal records, KNOVA currently has the lowest incidence of no-call results, among all other NIPT brands, (less than 1%), reflecting its exceptional reliability.

If this rare event occurs with KNOVA, we will contact you promptly to explain the situation and offer a complimentary repeat blood test (redraw). The optimal time for a redraw is 2-3 weeks after the initial sample, as this allows time for the fetal fraction to increase naturally. Most of the time, the second blood sample provides a clear result without any further issues.

However, in rare instances, even the redraw may yield insufficient fetal DNA. In such cases, we will issue a refund for the NIPT portion of the SMART Test® (excluding the scan). We understand that this situation can be frustrating, but it is an inherent technical limitation of cfDNA-based testing.

Certain factors can increase the likelihood of a low fetal fraction (FF) resulting in no-call results:

- **Early Gestational Age -** FF is typically lower in pregnancies under 10 weeks. We do not offer the SMART Test® before 10 weeks.
- **Higher Maternal BMI -** Increased maternal cfDNA may dilute fetal DNA, reducing FF.
- **Multiple Pregnancies -** FF levels can vary, impacting test accuracy in twin or multiple pregnancies. We do not offer the SMART Test® for multiple pregnancies.
- **IVF Pregnancies**
  IVF is associated with lower FF, though the exact reasons remain unclear.
- **The Blood Thinner Injections -** The commonly used medication is low molecular weight heparin (e.g. Clexane or Hexaparin), which is injected usually in the tummy area. Blood thinner injections use during pregnancy may increase the likelihood of non-reportable NIPT results due to low FF, though the mechanism is not fully understood.
- **Chromosomal Abnormalities-** Low fetal fraction is not associated with Down syndrome, but it has been linked to trisomies 13 and 18. In such cases, we recommend a targeted Early Fetal Scan (we offer this for a discounted price) to assess for anomalies associated with these conditions. In most cases, this scan can detect structural markers indicative of trisomy 13/18.

Limitations of KNOVA NIPT

KNOVA NIPT is a highly advanced screening tool designed to provide valuable insights into your baby's genetic health early in pregnancy. However, like all medical tests, it has certain limitations that are important to understand. We are committed to transparency and fairness, ensuring you are fully supported throughout the process. Below is a detailed overview of the potential limitations, with explanations of relevant medical terms where necessary:

Screening vs. Diagnostic Testing

While KNOVA NIPT provides a highly accurate risk assessment, it is not a diagnostic test. It check the chance of a condition but doesn't give a definite answer. If a high probability is indicated, confirmatory diagnostic procedures such as **CHORIONIC VILLUS SAMPLING (CVS) OR AMNIOCENTESIS** are recommended to obtain a definitive diagnosis.

False Alarms and Missed Conditions

Sometimes the test may show a problem when there isn't one (false positive).
It might also miss a real problem (false negative).

Atypical and Inconclusive Results

In very rare cases, the test may not yield a conclusive result due to an unusual DNA pattern that does not match any known chromosomal or genetic condition.
In such situations, we will offer comprehensive genetic counselling to help you understand the findings. In some cases, diagnostic testing (such as amniocentesis or CVS) may be recommended to gain a clearer picture of your baby's genetic health.
Fortunately, these complex scenarios are exceptionally rare.

Rare Conditions Might Not Be Fully Covered

The test checks for many rare conditions, but because these conditions are uncommon, the results may not always be accurate.

Extended Waiting Time for Results

You will usually get your results in after two weeks, but it may take longer due to different reasons independent from London Pregnancy Clinic.

Not Suitable for All Pregnancies

This test isn't available if:

- You are pregnant with twins or more (including vanishing twin).
- You are using an egg donor.
- You have a serious illness or recent transplant.

2 Step: KNOVA NIPT - Genetic Health

KNOVA does not report Variants of Unknown Significance (VUS)

This means that KNOVA only reports findings that are well understood to be clinically significant. A Variant of Unknown Significance (VUS) is a genetic change where it is unclear whether it is harmless or related to a health condition.
By not reporting VUS, the test avoids creating unnecessary anxiety or confusion over uncertain results and instead focuses only on genetic conditions known to be serious and well-defined.

Unexpected parental mutations detection

In rare cases, a parent carries a pathogenic or likely pathogenic variant, a genetic change in the DNA sequence (often called a mutation) that is known or likely to cause disease, but has no symptoms or only very mild ones. KNOVA is not intended to screen parents; it's designed to assess the baby. However, because the test analyses cell-free DNA in the mother's blood, it can occasionally detect a maternal variant.

When that happens, KNOVA cannot tell whether the baby has inherited it (maternal DNA dominates the sample). For autosomal dominant conditions, the chance of passing it on is typically 1 in 2; other inheritance patterns (recessive, X-linked) differ and will be explained in counselling. In these situations, we would recommend diagnostic testing (CVS or amniocentesis with targeted single-gene testing) to confirm whether the baby has the variant.

Human genetics can be complicated: some variants can be "inactive" or only partly active in a parent (so-called reduced penetrance/variable expressivity), so if the variant is passed on, it may be hard to predict how, if at all, it will affect the child. Please note that this situation is uncommon but may involve significant additional costs for extended genetic counselling, invasive testing and targeted genetic analysis. It can also create a high level of anxiety for the parents.

Extended NIPT validation:

Extended NIPT screenings for rare genetic diseases, such as those offered by KNOVA, face inherent challenges, particularly regarding the performance for those conditions. The primary difficulty lies in the rarity of these genetic disorders, which makes it challenging to gather a sufficiently large sample size for rigorous validation.

While KNOVA employs cutting-edge technology and represents a significant advancement in genetic screening, it is important to note that comprehensive validation data may not exist for every rare disorder it screens for. Validation typically requires a substantial number of confirmed cases to reliably assess the test's accuracy in detecting specific conditions. For rare disorders, the limited number of confirmed cases makes this level of validation difficult to achieve.

In practical terms, this means that while the KNOVA test offers valuable insights and the ability to screen for a wide range of rare genetic conditions, its level of certainty and accuracy may not match that of more common conditions, such as Down syndrome. Despite this limitation, the test remains a powerful tool for early detection and risk assessment, providing critical information for parents during pregnancy.

Follow-Up Testing Costs

If the test finds a high chance of a condition, further testing is needed, which may cost extra. The NHS may not always cover tests for very rare conditions, so private testing might be necessary.

Emotional and Financial Considerations

- Getting unexpected or unclear results can cause stress.
- Additional counselling and tests may also bring extra costs.

Detection Capabilities and Coverage of Rare Conditions

- KNOVA NIPT screens for a range of rare genetic conditions, including certain chromosomal abnormalities, microdeletions, and monogenic disorders.
- However, the accuracy of detecting these rare conditions can vary, and the test may not detect all potential genetic anomalies.
- There are about 6,000-8,000 rare diseases and understandably KNOVA does not screen for all of them.

Chromosomal Screening

- KNOVA NIPT primarily screens for whole chromosome abnormalities in chromosomes 13, 15, 16, 18, 21, 22, X, and Y.
- Partial deletions or duplications within these chromosomes may not always be detected, and the test does not assess for complex structural changes such as **uniparental disomy, triploidy, tetraploidy, translocations, inversions,** or **ring chromosomes.**

Microdeletion Screening

- The test targets specific regions associated with known microdeletion syndromes.
- However, partial deletions, duplications, or rearrangements within these regions may not be detected or reported.

Monogenic Disorder Screening

- KNOVA NIPT screens for certain single-gene disorders by detecting single nucleotide variants (SNVs) in targeted genes.
- It covers changes in the coding exons and adjacent intronic regions but may not detect:
  - Large deletions or insertions.
  - Complex genetic changes such as indels (insertion-deletion mutations), dynamic variants, structural variants, and single-gene copy number variations.
  - Variants in regions with high GC content, repetitive sequences, homologous sequences, or pseudogenes.
- The test only reports actionable variants classified as pathogenic or likely pathogenic according to guidelines from the American College of Medical Genetics and Genomics (ACMG).
- Variants of uncertain significance (VUS), likely benign variants, and benign variants are not reported.
- **Hereditary monogenic diseases,** such as **Cystic Fibrosis,** are not included in KNOVA's panel. For such conditions, patients can opt for the add-on NIPT "UNITY Fetal Risk™ Screen".

Interpretation and Ongoing Scientific Updates

- The interpretation of results is based on the information available at the time of reporting.
- As scientific understanding and genetic databases evolve, the interpretation of certain variants may change. Patients are advised to seek clarification if they have concerns about their results.

Conclusion

KNOVA NIPT offers a detailed way to check your baby's health early on, but it's important to understand its limits. Talking to our clinician before the test can help you make sense of the results and decide what to do next. This way, you can use the test in the best way possible for your pregnancy.

Managing High-Risk Results

The SMART Test® provides advanced screening for a wide range of genetic conditions, and if your results show a high chance of a genetic or chromosomal condition, we'll guide you through the next steps with care and expertise. Here's what happens if your results indicate a high probability for chromosomal/genetic condition:

Free Targeted Rescan by Dr Fred Ushakov

We offer a complimentary rescan performed by Dr Fred Ushakov, an internationally recognised expert in fetal medicine. This rescan will focus on detecting specific ultrasound findings or structural anomalies associated with the suspected condition. The high-resolution scan aims to provide additional information to support further diagnostic steps and is very helpful for further genetic counselling.

In-House Genetic Counselling

Our in-house genetic counsellor is available to offer a complimentary session to explain your results in detail. During this session, you'll have the opportunity to ask questions and understand the implications of the findings. The genetic counsellor will also discuss the next steps, including the possibility of confirmatory diagnostic tests.

Private Genetic Consultant

In complex genetic cases, we may recommend seeking expert advice from a private clinical genetic consultant. Please note that this counselling may incur additional costs.

Referral to a Fetal Medicine Unit (FMU)

We will facilitate a referral to a specialist NHS Fetal Medicine Unit. Fetal Medicine Units (FMUs) are centres of excellence within the NHS for antenatal care. FMUs are equipped with the expertise and resources to provide advanced diagnostic care and support. Depending on your preference and situation, we will help you explore the best available options for further evaluation.

2 Step: KNOVA NIPT - Genetic Health

Private Invasive Diagnostic Tests

If an FMU or NHS genetics service declines referral for further counselling or testing, we can arrange private CVS or amniocentesis. These procedures are often provided through private services within NHS trusts, using NHS facilities but billed separately. Some FMUs have dedicated private pathways; samples can be sent for targeted single-gene testing or chromosomal microarray, depending on KNOVA findings and the clinical picture. Please note that costs can be substantial; we will outline options and provide clear estimates before arranging those tests. Availability and turnaround times vary by provider.

Financial Considerations

While the initial genetic counselling session by our genetic counsellor and rescan are included in the SMART Test® package, please be aware that further consultations, private diagnostic tests, and additional genetic investigations may incur costs if done privately. We aim to provide transparency and support in helping you make the right choice for your care.

Non Standard SMART Test Options

SMART Test® plus

SMART Test® Genoma

SMART TEST PACKAGES: NON-INVASIVE PRENATAL TEST

SMART Test® plus

SMART Test® plus is an exclusive prenatal screening package offered by the **London Pregnancy Clinic**, combining two advanced NIPT solutions: **KNOVA** and **UNITY**. Together, these tests provide unmatched coverage for inherited and de novo genetic disorders, ensuring the most comprehensive prenatal care available globally.

Comprehensive Overview of UNITY Fetal Risk™ Screen NIPT and SMART Test® plus

SMART Test® Plus is a combination of an early anatomical scan and two advanced, unique NIPTs: UNITY Fetal Risk™ Screen and KNOVA. These tests have complementary strengths, UNITY focuses on inherited autosomal recessive disorders, while KNOVA excels at detecting autosomal dominant de novo mutations. Together, they provide comprehensive screening power. This innovative approach ensures comprehensive prenatal screening by integrating early fetal imaging with cutting-edge genetic testing.

UNITY Fetal Risk™ Screen NIPT by BillionToOne

BillionToOne is an American biotechnology company specialising in advanced molecular diagnostics, including innovative prenatal screening solutions like UNITY. **UNITY Fetal Risk™ Screen** is an advanced **NIPT** designed to screen for **14 autosomal recessive genetic disorders.** These disorders occur when both parents carry mutations in the same gene, potentially passing the condition to their baby. Unlike traditional carrier screening, UNITY can directly assess the baby's risk using only a single maternal blood sample, thanks to its state-of-the-art molecular counting technology and next-generation sequencing.
Conditions Screened by UNITY:

1. Cystic Fibrosis (CFTR Gene)

A life-limiting inherited condition that affects the lungs and digestive system, causing thick mucus build-up and frequent infections. It is the most common severe inherited disorder among people of European descent.

2. Spinal Muscular Atrophy (SMA)

A serious inherited condition that affects the nerves controlling muscle movement. Babies with SMA may have weak muscles, floppy limbs, or difficulty breathing or swallowing. Without early diagnosis and treatment, it can lead to progressive weakness and even death in early childhood.

3. Sickle Cell Disease (HBB Gene)

A blood disorder causing red blood cells to form a sickle shape, leading to pain, anaemia, and risk of stroke or organ damage. It is the most common inherited blood condition in individuals of African ancestry.

4. Alpha-Thalassaemia (HBA1/HBA2 Genes)

A condition affecting the production of haemoglobin, which may cause severe anaemia, especially in its most severe forms.

5. Beta-Thalassaemia (HBB Gene)

An inherited blood disorder that reduces haemoglobin levels, leading to chronic anaemia requiring lifelong treatment.

6. Canavan Disease (ASPA Gene)

A rare inherited brain disorder causing severe developmental delay, weak muscle tone, and early death in childhood.

7. Medium-Chain Acyl-CoA Dehydrogenase Deficiency

A metabolic condition that affects the body's ability to break down certain fats, especially during illness or fasting.

8. Tay-Sachs Disease (HEXA Gene)

A severe neurodegenerative disease of infancy that causes gradual loss of motor skills, vision, and hearing, with no current cure.

9. Familial Dysautonomia (IKBKAP Gene)

A rare condition affecting the autonomic nervous system, leading to poor regulation of blood pressure, temperature, and digestion.

10. Smith-Lemli-Opitz Syndrome (DHCR7 Gene)

A condition causing intellectual disability, growth delay, and facial and limb abnormalities due to disrupted cholesterol production.

11. PMM2-Congenital Disorder of Glycosylation

A metabolic disorder affecting multiple organs and systems, causing developmental delay, low muscle tone, and poor growth.

12. DMD-Associated Dystrophinopathies (DMD Gene)

A group of X-linked muscle disorders including Duchenne and Becker muscular dystrophy, leading to progressive muscle weakness. Mainly affects boys. Females are usually carriers

13. Phenylalanine Hydroxylase Deficiency / Phenylketonuria - PKU (PAH Gene)

A condition where the body cannot break down phenylalanine, leading to intellectual disability if untreated. Managed with a strict diet.

14. Fragile X Syndrome (FMR1 Gene) (optional)

The most common inherited cause of intellectual disability, especially in boys. May also cause autism-like features and behavioural issues.

What Makes UNITY Unique?

Single maternal blood sample

Unlike traditional carrier screening that may require the father's sample, UNITY can directly assess fetal risk using only the mother's blood.

High accuracy

Advanced molecular counting and sequencing methods provide precise risk assessment.

Limitations

UNITY's limitations are comparable to those of KNOVA, as it is also a type of extended NIPT:

- **Not Diagnostic:** UNITY Fetal Risk™ Screen is a screening test, not a diagnostic one. It evaluates the risk but cannot confirm whether the baby will or will not have the condition.
- UNITY may produce false positives, causing unnecessary concern, or false negatives, providing false reassurance, like any screening test.
- **No-Call Results:** Although rare, there is a possibility of receiving no-call results, requiring a repeat test.
- **Delays in Reporting:** Some delays in receiving results may occur due to the complexity of the testing process
- **Validation:** UNITY, like KNOVA, faces challenges with validation due to the nature of the conditions it screens for. Many of these conditions are rare, making it difficult to collect a large enough sample size of confirmed cases to rigorously validate the test's accuracy. Despite these challenges, UNITY remains a valuable screening tool, offering insights into potential risks that can guide further diagnostic evaluations when needed.

The turnaround time for UNITY Fetal Risk™ Screen results varies and usually results for recessive conditions are available in up to three weeks.

Report: BillionToOne Lab issues a separate report for the UNITY Fetal Risk™ Screen, which typically arrives after the results from KNOVA.

Conclusion

SMART Test® plus, combining **KNOVA** and **UNITY**, offers expectant parents the most advanced, comprehensive non-invasive prenatal screening available. This innovative package ensures early detection of genetic and structural anomalies, empowering families with crucial information and expert support for informed decision-making throughout pregnancy.

SMART TEST PACKAGES: NON-INVASIVE PRENATAL TEST

PrenatalSafe Complete Plus

NIPT for SMART Test® in Cases of Vanishing Twins or IVF Pregnancies with Donor Eggs

The PrenatalSafe Complete Plus, provided by Eurofins Genoma Lab (Rome, Italy), is a cutting-edge non-invasive prenatal test (NIPT) specifically designed to address complex pregnancy scenarios, such as vanishing twins or IVF pregnancies with donor eggs. Unlike KNOVA NIPT, which is not suitable for these cases, PrenatalSafe Complete Plus offers a robust alternative with comprehensive screening capabilities.

Key Features

PrenatlSafe, provided by Eurofins Genoma Lab (Rome, Italy), is a cutting-edge non-invasive prenatal test (NIPT) specifically designed to address complex pregnancy scenarios, such as vanishing twins or IVF pregnancies with donor eggs. Unlike KNOVA NIPT, which is not suitable for these cases, PrenatalSafe Complete Plus offers a robust alternative with comprehensive screening capabilities.

Comprehensive Screening:

- Detects a wide range of genetic and chromosomal conditions, including:
  - **All aneuploidies** (e.g., Down syndrome, Edwards syndrome, Patau syndrome).
  - **Microdeletions** (e.g., DiGeorge syndrome).
  - **Monogenic disorders** (e.g., Noonan syndrome).
  - **Single-gene inherited conditions** (e.g., cystic fibrosis).
- Covers sex chromosome abnormalities and provides optional fetal sex determination.

Designed for Complex Pregnancies:

- Tailored for **vanishing twin cases** or **IVF pregnancies using donor eggs.**
- Utilises advanced bioinformatics to resolve challenges such as mixed fetal and maternal DNA profiles.

✳ If you've had a vanishing twin, **we must wait at least 5 weeks from the time of the event** before testing to ensure optimal accuracy.

Methodology:

- Employs **whole genome sequencing (WGS)** and advanced techniques to isolate and analyse cell-free fetal DNA (cfDNA).
- Uses cutting-edge deconvolution methods to distinguish fetal DNA from maternal DNA, ensuring high accuracy even in complex cases.

Testing Details:

- Requires a maternal blood sample (two tubes).
- Optional paternal DNA mouth swab can enhance detection accuracy for specific conditions.
- Results are delivered in two stages: **10-14 days** for chromosomal anomalies and microdeletions, and **22-28 days** for monogenic conditions.

Limitations:

- As with all NIPTs, it is **a screening test, not diagnostic**. Positive results should be confirmed with invasive diagnostic procedures (e.g., CVS or amniocentesis).
- Other advanced NIPT limitations are the same as those of KNOVA.

Why Choose PrenatalSafe Complete Plus?

PrenatalSafe Complete Plus provides unparalleled insight into the baby's genetic profile for complex cases like IVF with donor pregnancies. It ensures early, non-invasive evaluation with high accuracy and reassurance.

While KNOVA's panel offers broader coverage, faster turnaround times, and a lower price (£990 vs. £1490), PrenatalSafe Complete Plus remains a trusted and comprehensive alternative, tailored to address scenarios that KNOVA cannot accommodate, such as vanishing twins and donor egg pregnancies.

By leveraging advanced genomic and bioinformatic techniques, PrenatalSafe Complete Plus ensures clarity and confidence for parents during their prenatal journey.

Comparison Table of SMART Test® Options

FEATURE	SMART TEST® KNOVA	SMART TEST® PLUS	SMART TEST® GENOMA
TEST NAME	KNOVA NIPT	KNOVA NIPT + UNITY Fetal Risk™ Screen	PrenatalSafe Complete Plus
ELIGIBILITY	Singleton pregnancies (no donor eggs)		Vanishing twin Donor eggs
STRUCTURAL SCREENING	10 Week Scan (the earliest anomaly scan)		
FETAL STRUCTURAL ANOMALIES	Severe anomalies detectable via ultrasound in the 1st trimester (e.g., acrania, spina bifida, major heart defects)		
CHROMOSOMAL	Trisomies 21, 18, 13, 22, 16, 15		All trisomies
SEX CHROMOSOMAL	Turner syndrome, Klinefelter syndrome, etc		
MICRODELETIONS	12 microdeletions		9 microdeletions
DE NOVO SYNDROMES	56 monogenic conditions		25 monogenic conditions
INHERITED RECESSIVE CONDITIONS	Not included	14 conditions	5 conditions
TURNAROUND TIME (WORKING DAYS)	7–10 days	7–21 days	10–28 days

*continued on next page →

SMART Test® Comparison Table

*table continued

FEATURE	SMART TEST® KNOVA	SMART TEST® PLUS	SMART TEST® GENOMA
OPTIONAL FETAL SEX REVEAL	Yes	Yes	Yes
NUMBER OF NIPT REPORTS	One	Two	Two
PARTNER SAMPLE REQUIRED	No	No	Yes (mouth swab)
NUMBER OF BLOOD TUBES FROM MOTHER	2	4	2
PRETEST GENETIC COUNSELLING	Optional	Optional	Optional
PRICE	**£990**	**£1490**	**£1490**

THIS TABLE PROVIDES A CLEAR COMPARISON OF THREE SMART TEST® OPTIONS, HIGHLIGHTING THE DIFFERENCES IN GENETIC CATEGORIES, PARTNER SAMPLE REQUIREMENTS, NUMBER OF BLOOD TUBES REQUIRED, PRETEST GENETIC COUNSELLING, AND ELIGIBILITY TO HELP PARENTS MAKE AN INFORMED DECISION.

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Medical disclaimer

This booklet is for general information and education only. It does not replace advice from your midwife, GP, obstetrician, or fetal medicine specialist. SMART Test® is a screening service. Screening cannot find every problem, and no test can guarantee a completely healthy baby.

A low-chance result does not rule out all conditions.
A high-chance result does not mean your baby is definitely affected.

In many cases, diagnostic tests such as CVS or amniocentesis are needed to confirm or exclude a condition.

Your own care should always be planned with a qualified health professional who knows your medical history and pregnancy details.

PLEASE DO NOT DELAY, IGNORE, OR STOP MEDICAL ADVICE BECAUSE OF SOMETHING YOU HAVE READ HERE.
SERVICE DETAILS, AVAILABILITY, AND PRICES MAY CHANGE OVER TIME.

FOR THE MOST UP-TO-DATE INFORMATION, PLEASE CHECK OUR WEBSITE OR CONTACT LONDON PREGNANCY CLINIC DIRECTLY.

If you are worried about your pregnancy, **contact** your maternity unit, **GP, NHS 111, or emergency services (999 in an emergency)** without delay.

SMART Test® Pricing Policy

Advanced tests like KNOVA are understandably costly, reflecting the immense complexity of cutting-edge genetic evaluation. Expert ultrasounds conducted on state-of-the-art scanners also carry a significant expense. However, at the London Pregnancy Clinic, we believe that early and comprehensive screening should not be a privilege but an opportunity available to all. Driven by this vision, we and our partners Fulgent Genetics have worked tirelessly, sparing no effort, to shatter the barriers of cost. Against all odds, we have achieved what seemed impossible: offering the SMART Test® KNOVA for less than £1,000. This outstanding achievement ensures more parents can access the most advanced screening available, providing peace of mind and the earliest possible insight into their baby's health.
Five reasons why the SMART Test® maintains a highly competitive price, for such an advanced prenatal screening service:

1. Efficient Workflow

The test integrates state-of-the-art ultrasound and NIPT technologies into a single streamlined package. This "one-stop clinic" approach reduces redundancy, enhances efficiency, and minimises additional costs.

2. Advanced Technology

Using cutting-edge equipment like the Voluson Expert range scanners and Next-generation sequencing (NGS), the test maximises diagnostic accuracy while ensuring cost-effectiveness due to reduced repeat procedures and need to rescan due to not diagnostic views.

3. Expertise Consolidation

The service is exclusively provided by fetal medicine specialists and genetic counsellors at the London Pregnancy Clinic. This eliminates the need for referrals and external consultations, further lowering costs.

4. Specialised Lab Partnerships

Collaborating with trusted international lab ensures high-quality genetic testing at negotiated rates.

5. Volume and Audit Practices

The London Pregnancy Clinic is the leading provider of NIPT in London. By conducting high volumes of tests with rigorous internal auditing and streamlined logistics, we achieve economies of scale while ensuring exceptional quality and reliability.

THROUGH THESE MEASURES, THE SMART TEST® DELIVERS EXCEPTIONAL VALUE WITHOUT COMPROMISING QUALITY, OFFERING PARENTS AN EARLY, COMPREHENSIVE, RAPID, AND RELIABLE PRENATAL SCREENING SOLUTION.