HTA Austria
Austrian Institute for
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GmbH

Regulation and financing of prenatal screening and diagnostic examinations for fetal anomalies in selected European countries

Policy Brief

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List of abbreviations

AC .....amniocentesis
AIHTA .....Austrian Institute for Health Technology Assessment
CH .....Switzerland
CT.....Combined Test
CVS .....chorionic villus sampling
DE .....Germany
EUROCAT .....European network of population-based registries for the epidemiological surveillance of congenital anomalies
FTS.....First Trimester Screening
GP.....general practitioner
IT.....Italy
n/a .....not applicable
NIPT .....non-invasive prenatal test
NL .....Netherlands
NO.....Norway
RQ .....research question
T13 .....trisomy 13
T18 .....trisomy 18
T21 .....trisomy 21
UK.....United Kingdom
US.....ultrasound

Zusammenfassung

Hintergrund und Forschungsfragen

Pränataldiagnostik (PND): vorgeburtliche Untersuchungen zu Feststellung kindlicher Erkrankungen oder Fehlbildungen

Unter Pränataldiagnostik (PND) versteht man vorgeburtliche Untersuchungen der Schwangeren und/oder des ungeborenen Kindes zur Feststellung kindlicher Erkrankungen oder Fehlbildungen. Man unterscheidet nicht-invasive (z. B. Ultraschalluntersuchungen, Ersttrimester-Screening, Nicht-invasiver Pränataltest) und invasive Verfahren (Amniozentese, Chorionzottenbiopsie). Der Bericht fokussiert auf folgende Untersuchungen:

Tests: First-Trimester-Screening (FTS)/Combined Test (CT), Nicht-invasiver Pränataltest (NIPT), invasive Tests, Ultraschallscreening im 2. Trimester

- First Trimester Screening (FTS)/Combined Test (CT): Screening auf Trisomie 21 (T21), Trisomie 18 (T18) und Trisomie 13 (T13)
- Nicht-invasiver Pränataltest (NIPT): Screening auf v. a. T21, T18 und T13[1]
- invasive Tests (Amniozentese/Chorionzottenbiopsie): zur diagnostischen Abklärung
- Ultraschallscreening im zweiten Trimester („Organscreening"): Screening auf fetale Anomalien

unterschiedliche Regelung und Finanzierung der PND in anderen Ländern

Die Regelung und Finanzierung der PND ist in den einzelnen Ländern sehr unterschiedlich. In diesem Bericht sollen das Angebot und die finanziellen Rahmenbedingungen der oben genannten Untersuchungen in ausgewählten europäischen Ländern untersucht und zusammengefasst werden.

3 Forschungsfragen fokussieren auf Angebot, Finanzierung und Setting

Die folgenden Forschungsfragen stehen im Fokus des Berichts:

- FF1: Welche der oben genannten Untersuchungen werden in den ausgewählten Ländern für alle Schwangeren bzw. bei bestimmten Indikationen, Risikofaktoren oder anderen Kriterien angeboten?
- FF2: Wie werden diese Untersuchungen in den ausgewählten Ländern finanziert (aus öffentlicher Hand, Ko-Finanzierung, privat)?
- FF3: Wo werden die Untersuchungen in den ausgewählten Ländern durchgeführt (in Krankenanstalten, im niedergelassenen Bereich)?

auch Recherche zu Inanspruchnahme und Beratung

Zusätzlich wurden auch Informationen zur Inanspruchnahme der Untersuchungen und zur Beratung im Zusammenhang mit PND in den ausgewählten Ländern recherchiert und zusammengefasst.

Methoden

Auswahl von 6 europäischen Ländern: DE, CH, NL, UK, NO, IT

Es wurden 6 europäische Länder ausgewählt, die sich in verschiedenen relevanten Kriterien unterscheiden (z. B. Gesundheits-/Versicherungssystem, geografische Lage, Berufsgruppen, die überwiegend an der Schwangerenvorsorge beteiligt sind, usw.), um die Bandbreite möglicher Regelungen und Finanzierungsformen zu veranschaulichen. Die Auswahl umfasst die folgenden Länder: Deutschland (DE), Schweiz (CH), Niederlande (NL), Vereinigtes Königreich (UK), Norwegen (NO), Italien (IT).

[1] Screening auf weitere Aneuploidien, Mikrodeletionen bis hin zur Sequenzierung des gesamten fetalen Genoms prinzipiell möglich

Datenerhebung mittels Handsuche und schriftliche Expert*innen-Konsultation mittels Fragebogen

Datenextraktionstabellen für jedes Land

Für die Datenerhebung wurde eine Handsuche in Google/Google Scholar sowie auf relevanten Webseiten (z. B. der Gesundheitsministerien, Public Health Institutionen, bzw. der entsprechenden Screening-Programme, wenn vorhanden) durchgeführt. Zusätzlich erfolgte im Februar und März 2022 eine schriftliche Expert*innen-Konsultation mittels Fragebogen. Es wurden die Vertreter*innen des EUROCAT-Netzwerks[2] der ausgewählten Länder sowie die Vorsitzenden der relevanten medizinischen Fachgesellschaften (z. B. Gesellschaft für Gynäkologie und Geburtshilfe, Gesellschaft für perinatale Medizin) kontaktiert. Für jedes Land wurde eine Datenextraktionstabelle erstellt, welche die Informationen aus der Literaturrecherche und der Expert*innenbefragung kombiniert (siehe Appendix).

Ergebnisse

11 ausgefüllte Fragebögen, 22 Quellen aus Handsuche

Es wurden insgesamt 11 ausgefüllte Fragebögen retourniert: 3 aus Deutschland, je 2 aus der Schweiz, den Niederlanden und Italien sowie je 1 aus UK und Norwegen. Zusätzlich wurden 22 relevante Quellen (Artikel, Webseiten, Policy Dokumente) aus der Handsuche zur Ergänzung der Informationen aus der Expert*innenbefragung herangezogen.

für alle 6 Länder Leitlinien o. ä. Dokumente zur Schwangerschaftsvorsorge verfügbar; tw. auch mit Infos zu PND; tw. spezifische, staatlich geregelte Screening-programme

Für alle 6 Länder wurden Leitlinien oder andere Dokumente identifiziert, die Informationen zur Schwangerenbetreuung auf nationaler Ebene enthalten bzw. diese regulieren (teilweise gibt es jedoch zusätzlich regionale Zuständigkeiten und somit Unterschiede). Für komplikationslose Schwangerschaften sind in den 6 ausgewählten Ländern zwischen 6 und 10 bzw. monatliche (gegen Ende der Schwangerschaft auch öfter) Routineuntersuchungen vorgesehen, die in 3 Ländern überwiegend von Gynäkolog*innen (DE, CH, IT) und in 3 Ländern von Hebammen (NL) bzw. Hebammen und Hausärzt*innen (UK, NO) durchgeführt werden. Informationen zu pränatalen Screening- und diagnostischen Untersuchungen auf Trisomien oder fetale Anomalien finden sich teilweise in den gleichen Dokumenten, teilweise gibt es spezifische, staatlich geregelte Screeningprogramme (NL, UK).

FTS/CT: Angebot und Finanzierung für alle Schwangeren in CH, UK, IT; in DE IGeL-Leistung; in NO und NL seit 2021 nicht mehr verfügbar;

unterschiedliche Settings

Das **FTS/CT** wird in 3 Ländern (CH, UK, IT) allen Schwangeren angeboten und öffentlich finanziert. In DE gaben die befragten Expert*innen widersprüchliche Antworten, ob das Screening allen oder jenen Schwangeren mit Risikofaktoren angeboten wird; es ist jedenfalls komplett privat zu bezahlen (IGeL-Leistung). In 2 Ländern (NL, NO) wird das FTS/CT seit 2021 nicht mehr angeboten, sondern wurde durch den NIPT ersetzt. In beiden Ländern ist jedoch ein Ultraschallscreening im ersten Trimester bereits verfügbar (NL, im Rahmen einer wissenschaftlichen Studie) oder soll im Laufe des Jahres 2022 etabliert werden (NO). Das FTS/CT wird in UK nur in Krankenhäusern und in 3 Ländern (IT, CH, DE) in Krankenhäusern, Arztpraxen, Privatkliniken, Pränatal- und Ultraschallzentren durchgeführt. In IT ist das Screening im Rahmen des Gesundheitssystems in Krankenhäusern kostenlos, kann aber auf privater Basis (Selbstzahler) in Arztpraxen und Privatkliniken angeboten werden.

NIPT: als primäres Screening in NL mit 175€ Selbstbehalt;

Der **NIPT** wird derzeit in einem Land (NL) allen schwangeren Frauen als primäres Screening angeboten; Frauen können den Test mit einer Selbstbeteiligung von 175 € im Rahmen einer wissenschaftlichen Studie (TRIDENT) in Anspruch nehmen. Für Schwangere mit erhöhtem Risiko wird der NIPT zur Gänze öffentlich finanziert. In 3 Ländern (CH, UK, NO) wird der NIPT als

[2] EUROCAT = European network of population-based registries for the epidemiological surveillance of congenital anomalies

sekundäres Screening angeboten und bei den entsprechenden Risikofaktoren zur Gänze finanziert: in NO für Frauen mit Risikofaktoren (z. B. mütterliches Alter >35 Jahre, erbliches Risiko, auffälliger Ultraschallbefund), in CH für Frauen mit einem FTS/CT Ergebnis von >1:1000 und in UK für Frauen mit einem FTS/CT Ergebnis von >1:150. In IT ist das Angebot und auch die Kostenübernahme des NIPT regional unterschiedlich geregelt. In DE wird der NIPT im Jahr 2022 in die Mutterschaftsrichtlinien aufgenommen und in bestimmten Fällen von der Gesetzlichen Krankenversicherung übernommen: z. B. wenn sich aus anderen Untersuchungen ein Hinweis auf eine Trisomie ergeben hat oder „wenn die Möglichkeit einer Trisomie die Frau so stark belastet, dass sie dies abklären lassen möchte".

als sekundäres Screening bei Risikofaktoren (NO) bzw. FTS/CT Ergebnis von >1:1000 (CH) und >1:150 (UK); in IT regional unterschiedlich; in DE Aufnahme als Kassenleistung in best. Fällen in 2022

Der Umfang des NIPT, wenn er im Rahmen dieser Screeningprogramme durchgeführt wird, ist auf das Screening auf Trisomie 21, 18 und 13 beschränkt; mit der Ausnahme von NL, wo das gesamte Genom des Fetus analysiert wird (andere Auffälligkeiten als T21, T18 und T13 werden nur auf Wunsch mitgeteilt, 78 % der Frauen entscheiden sich jedoch dafür, dass sie alle Ergebnisse erfahren möchten). Der Test wird in den meisten Ländern ab der 11. Schwangerschaftswoche durchgeführt. In 2 Ländern (UK, NO) wird der NIPT nur in Krankenhäusern durchgeführt. In NL wird der NIPT in Krankenhäusern für Frauen mit erhöhtem Risiko und in Hebammenpraxen für Frauen als Screeningtest durchgeführt. In den übrigen 3 Ländern wird der NIPT in Krankenhäusern und Arztpraxen (DE, CH, IT), Privatkliniken (IT) sowie in Pränatal- und Ultraschallzentren (DE, CH) durchgeführt.

Umfang des NIPT auf Trisomie 21, 18 und 13 beschränkt; Ausnahme NL (Analyse des gesamten Genoms);

Durchführung meist ab 11. Schwangerschaftswoche

unterschiedl. Settings

Invasive Tests werden in allen ausgewählten Ländern ausschließlich schwangeren Frauen mit entsprechenden Risikofaktoren angeboten und in diesen Fällen öffentlich finanziert, z. B. bei auffälligen Ultraschallbefunden oder Ergebnissen von FTS/CT oder NIPT, die auf ein hohes Risiko hinweisen. In 3 Ländern (UK, NL, NO) werden invasive Tests nur in Krankenhäusern durchgeführt. In den übrigen 3 Ländern werden diese Untersuchungen in Krankenhäusern, aber auch in Arztpraxen mit Spezialisierung auf feto-maternale Medizin und Ultraschallzentren (CH), in Pränatalzentren und Instituten mit spezieller Qualifikation (DE) sowie in Arztpraxen und Privatkliniken (IT) durchgeführt.

invasive Tests: in allen Länder Angebot und Finanzierung nur bei Risikofaktoren

Durchführung in Krankenhäusern bzw. spezialisierten Zentren

Das **Ultraschallscreening auf fetale Anomalien im zweiten Trimester** wird in den ausgewählten Ländern allen schwangeren Frauen angeboten (in DE gab es unterschiedliche Informationen aus der Expert*innenbefragung, ob das Screening-Angebot allen Frauen oder jenen mit Risikofaktoren gilt). Es wird in allen Ländern öffentlich finanziert, in DE brauchen Schwangere jedoch eine Überweisung aufgrund erhöhten Risikos für eine Kostenübernahme durch die Krankenversicherung. Das Screening wird in Krankenhäusern (alle Länder), Arztpraxen (DE, CH, UK, IT) und Pränatal-/Ultraschallzentren (DE, CH, NL) durchgeführt.

Ultraschallscreening auf fetale Anomalien: Angebot und Finanzierung für alle Schwangeren (in DE Überweisung nötig), unterschiedliche Settings

Im Fragebogen wurden die Expert*innen auch um Angaben oder Schätzungen zur **Inanspruchnahme** der Tests gebeten. In Ländern mit kostenfreien Angeboten des FTS/CT für alle schwangeren Frauen liegen die Schätzungen/Daten für die Inanspruchnahme zwischen 72 % und (fast) 100 % (CH, UK, IT). In NL ist die Inanspruchnahme des FTS/CT von 34 % im Jahr 2016 auf nur 1 % im Jahr 2020 gesunken (und wird seit 2021 nicht mehr angeboten). Für Deutschland wurde etwa 60 % geschätzt, je nach Region, Versicherung und sozioökonomischem Status. Für den NIPT sind die meisten Daten Schätzungen: Sie reichen von 15 % in IT, 10-35 % in CH, 20 % in NO und 30 % in DE. In NL haben sich 51 % der schwangeren Frauen im Jahr 2020 für den

Inanspruchnahme der Tests: FTS/CT: 72 % bis fast 100 % bei Ländern mit kostenfreiem Angebot; NIPT: zw. 10 % und rd. 50 %; invasive Tests: 1-3 %; Ultraschallscreening: 70 % bis fast 100 %

NIPT entschieden. Für UK liegen noch keine Daten vor. Die Inanspruchnahme invasiver Tests war teilweise unbekannt und eher gering; Schätzungen wurden meist mit 1 bis 3 % angegeben. Die Daten und Schätzungen zur Ultraschalluntersuchung im zweiten Trimester sind in allen ausgewählten Ländern hoch und reichen von 70 % bis (fast) 100 %.

Beratung im Kontext von PND besonders wichtig

z. B. UK, NL: Beratung durch Hebammen als Teil des Screening-Programms, kontinuierliche Fortbildung und Qualitätssicherung; ausgewogene und evidenzbasierte Informationen thematisieren z. B. Risiken & Nutzen des Screenings, Limitationen, mögliche Ergebnisse

Die **Beratung** ist im Kontext von PND von besonderer Wichtigkeit. Insgesamt gibt es laut der Expert*innenbefragung in allen 6 ausgewählten Ländern eine Beratung im Zusammenhang mit pränatalen Screening- und diagnostischen Untersuchungen. Die konkrete Ausgestaltung, die Anforderungen und die beteiligten Berufsgruppen scheinen jedoch von Land zu Land unterschiedlich zu sein. In UK und NL wird die Beratung explizit als Teil des Screeningprogramms gesehen und wird meist durch zertifizierte Hebammen zu Beginn der Schwangerschaft durchgeführt. In NL gibt es zur Qualitätssicherung z. B. eine Mindestzahl an Beratungen pro Jahr und kontinuierliche Fortbildung der Berater*innen. Jede Frau, der ein Screening angeboten wird, sollte auf der Grundlage zugänglicher, ausgewogener und evidenzbasierter Informationen, die z. B. Risiken und Nutzen des Screenings, Limitationen und Unsicherheiten, mögliche Ergebnisse und Schwangerschaftsoptionen thematisieren, eine persönliche, informierte Entscheidung über die Annahme oder Ablehnung eines Tests treffen. In DE und CH sind in erster Linie Gynäkolog*innen an der Beratung zu PND beteiligt. Der NIPT wird in DE im Jahr 2022 als Kassenleistung für Schwangere mit bestimmten Kriterien eingeführt. Voraussetzung für die Einführung dieses Screening-Tests war die Entwicklung einer Versicherteninformation durch das Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (IQWiG).

Diskussion

unterschiedliche Ausgestaltung von Angebot, Regulierung und Finanzierung der PND in den 6 Ländern; z. B. in Bezug auf Wahl des primären Screening-Test, Kostenübernahme, NIPT-Implementierung, …

Dieser Policy Brief zeigt, dass die Bereitstellung, Regulierung und Finanzierung der pränatalen Screening- und diagnostischen Untersuchungen auf fetale Anomalien in den 6 ausgewählten Ländern sehr unterschiedlich ausgestaltet sind. Dies betrifft v. a. die Wahl des primären Screening-Tests auf fetale Trisomien (FTS/CT, NIPT oder die Identifizierung von Risikofaktoren), die Implementierung des NIPT, die Kostenübernahme der Tests, die Inanspruchnahme der Untersuchungen, aber auch die allgemeine Schwangerschaftsbetreuung, insbesondere die dafür zuständigen Berufsgruppen. Gemeinsamkeiten zwischen den Ländern gibt es v. a. hinsichtlich der Durchführung und Finanzierung von invasiven Tests und des Ultraschallscreenings auf fetale Anomalien im zweiten Trimester.

mögliche Gründe für Heterogenität: z. B. gesellschaftliche Einstellung zu Behinderung sowie zu Schwangerschaftsabbruch, Qualität der Beratung, …

Die Heterogenität der Regelungen, der Implementierung und der Inanspruchnahme dieser Untersuchungen zeigte sich auch in anderen Studien. Folgende mögliche Gründe werden genannt: die gesellschaftliche Einstellung zu und der Umgang mit Behinderung, die gesellschaftliche Einstellung zu Schwangerschaftsabbruch sowie der entsprechende rechtliche Rahmen, der öffentliche und politische Diskurs zum Thema PND/Screening auf fetale Anomalien, die Möglichkeit einer informierten Entscheidungsfindung der schwangeren Frauen/Paare sowie das Vorhandensein und die Qualität der Beratung (und wer diese durchführt).

Debatte aufgrund NIPT-Einführung als Kassenleistung in DE, da kein medizinischer Nutzen des Tests

In Deutschland hat die kürzlich getroffene Entscheidung, den NIPT in bestimmten Fällen als Kassenleistung einzuführen, eine große Debatte ausgelöst. Wesentlicher Kritikpunkt ist z. B., dass der NIPT keinen medizinischen Nutzen hat (weil er weder die Gesundheit der Schwangeren noch die des Kindes erhalten, wiederherstellen oder verbessern kann) und daher nicht die Kri-

zahlreiche ethische Fragen und Bedenken im Zusammenhang mit NIPT bzw. allgemein mit Screening auf Trisomien

terien für eine Aufnahme in den Leistungskatalog der gesetzlichen Krankenversicherung erfüllt. Das ist auch einer der Gründe, wieso der NIPT bzw. das Screening auf T21, T18 und T13 im Allgemeinen so viele ethische Fragen und Bedenken aufwirft: das Screening dient nicht wie andere Tests in der Schwangerschaft der Förderung der Gesundheit von Mutter und/oder Kind, sondern soll fetale Anomalien finden, für die es keine therapeutischen oder präventiven Interventionen gibt. Stattdessen sollen diese Tests darauf abzielen, die reproduktive Autonomie der werdenden Eltern zu fördern, indem sie ihnen die Möglichkeit geben, Informationen über ihr zukünftiges Kind zu erhalten und zu entscheiden, ob sie die Schwangerschaft im Falle einer genetischen Störung fortsetzen oder abbrechen wollen.

derzeit hauptsächlich Einsatz für Screening auf Trisomien 21, 18 und 13; mögliches Spektrum aber deutlich größer

Sensitivität und positiver Vorhersagewert variiert stark je nach Anomalie und untersuchter Population

Der NIPT wird in erster Linie für das Screening auf T21, T18 und T13 eingesetzt. Die Testhersteller bieten jedoch auch andere Optionen an, wie z. B. das Screening auf Aneuploidien der Geschlechtschromosomen, seltenere Trisomien, Mikrodeletionen (und sogar die Sequenzierung des gesamten Genoms wird bereits durchgeführt), aber die Sensitivität und der positive Vorhersagewert (PPV) für diese Anomalien sind deutlich geringer. Der PPV (die Wahrscheinlichkeit, dass bei Personen mit einem positiven Screening-Testergebnis tatsächlich die betreffende Trisomie vorliegt) variiert je nach untersuchter Anomalie und Prävalenz in der entsprechenden Population. So liegt beispielsweise die Wahrscheinlichkeit, dass eine 40-jährige schwangere Frau, die ein Hochrisiko-NIPT-Ergebnis für T21 erhält, tatsächlich ein Kind mit T21 zur Welt bringt, bei etwa 93%. Im Vergleich dazu beträgt die Wahrscheinlichkeit bei einer 25-jährigen Frau aufgrund des unterschiedlichen Basisrisikos nur 51%. Dies muss berücksichtigt werden, wenn entschieden wird, welchen schwangeren Frauen der Test angeboten wird, und es muss auch den Frauen/Paaren bei der Beratung erklärt werden.

qualitativ hochwertige, neutrale Beratung unerlässlich für autonome, informierte Entscheidungsfindung

Beratung in manchen Ländern gut organisiert, in anderen Ländern Mangel an geschulten Berater*innen & neutralem Infomaterial

Viele Länder und Institutionen betonen, wie wichtig gute, ausgewogene Informationen für schwangere Frauen/Paare sind, die alle Screening-Entscheidungen gleichermaßen unterstützen, und wie wichtig es ist, dass genügend Zeit zur Verfügung steht, um alle Bedenken im Zusammenhang mit dem Screening und den potenziellen Folgen zu erörtern und ein Umfeld zu schaffen, das schwangere Frauen in die Lage versetzt, eine autonome, informierte Entscheidung zu treffen. Ein weiterer entscheidender Aspekt, damit schwangere Frauen eine informierte Entscheidung ohne Druck treffen können, ist die Verfügbarkeit von qualitativ hochwertiger Versorgung und Unterstützung für Menschen mit Behinderungen. Während die Beratung in manchen Ländern (z. B. UK, NL) gut organisiert ist, scheint es in vielen Ländern jedoch an geschulten Berater*innen und an hochwertigem und neutralem Informationsmaterial zu mangeln, insbesondere in den Ländern, in denen NIPT überwiegend oder ausschließlich im privaten Sektor angeboten wird.

breiter gesellschaftlicher Diskurs notwendig

besonderes Augenmerk auf gute, nicht-direktive Beratung mit ausreichend personellen Ressourcen

Abschließend ist festzuhalten, dass aufgrund der vielen ethischen Aspekte des Themas ein breiter gesellschaftlicher Diskurs mit den relevanten Interessengruppen und Beteiligten notwendig scheint. Besonderes Augenmerk sollte auf qualitativ hochwertige und nicht-direktive Information und Beratung gelegt werden. Hierfür sind eine qualitätsgesicherte Ausbildung und kontinuierliche Fortbildung der beteiligten Berufsgruppen unerlässlich. Um ein qualitativ hochwertiges pränatales Screening einschließlich professioneller Beratung anbieten zu können, sind ausreichende personelle Ressourcen erforderlich. Die Einbeziehung von nicht-ärztlichen Berufsgruppen, wie es in mehreren Ländern üblich ist, sollte für die Umsetzung in Betracht gezogen werden.

Executive Summary

Background

Bericht fokussiert auf Regulierung und Finanzierung von pränatalen Screening- und diagnostischen Tests auf fetale Anomalien in ausgewählten europäischen Ländern

There are several prenatal screening and diagnostic tests to detect fetal structural and chromosomal anomalies, classified as non-invasive and invasive methods. The regulation and financing of these examinations are heterogeneous across countries. On behalf of the Austrian Federal Ministry of Social Affairs, Health, Care and Consumer Protection, this project focuses on the offer, financing and setting of the following tests in selected European countries: First Trimester Screening (FTS)/Combined Test (CT), Non-invasive Prenatal Test (NIPT), amniocentesis (AC)/chorionic villus sampling (CVS), and second-trimester ultrasound screening for fetal anomalies.

Methods

Auswahl von 6 Ländern: DE, CH, NL, UK, NO, IT

We chose 6 European countries that differ in various relevant criteria (e.g., health/insurance system, geographical location) to illustrate the range of possible regulations and forms of funding. The selection includes the following countries: Germany (DE), Switzerland (CH), Netherlands (NL), United Kingdom (UK), Norway (NO), Italy (IT).

Handsuche und Expert*innen-Konsultation mittels Fragebogen

We conducted a hand search in Google/Google Scholar and on relevant websites (e.g., ministries of health, public health institutions, national screening programmes). In addition, an expert consultation was conducted through a questionnaire among the EUROCAT (European network of population-based registries for the epidemiological surveillance of congenital anomalies) representatives of the 6 countries and the chairpersons of the relevant medical societies (e.g. Society for Gynaecologists and Obstetricians).

Results

11 Fragebögen und 22 Literaturquellen

11 completed questionnaires were returned: 3 from DE, 2 each from CH, NL and IT, and 1 each from UK and NO. In addition, 22 relevant sources from the hand search were used to supplement the information from the expert consultation.

Angebot, Finanzierung und Setting der Tests unterschiedlich in den 6 Ländern, z. B. bzgl. Wahl des primären Screening-Tests, NIPT-Implementierung, öffentl. Finanzierung

The provision, regulation and financing of prenatal screening and diagnostic tests for fetal anomalies vary widely across the 6 selected countries. This concerns in particular the choice of the primary screening test for fetal trisomies (FTS/CT, NIPT or the identification of risk factors), the implementation of the NIPT, the reimbursement of the tests, the uptake of the examinations, but also the general antenatal care, especially the professional groups responsible for it. There are similarities between countries, particularly concerning the implementation and financing of invasive tests and of the ultrasound screening for fetal anomalies in the second trimester.

Conclusion

aufgrund zahlreicher ethischer Fragen breiter gesellschaftl. Diskurs notwendig

This policy brief highlights the significant heterogeneity between European countries regarding the provision, regulation and funding of prenatal screening and diagnostic testing for fetal anomalies. In conclusion, it should be noted that due to the many ethical aspects of the topic, a broad societal discourse with the relevant interest groups and stakeholders seems to be necessary.

qualitativ gute, nicht-direktive Beratung besonders wichtig

Particular attention should be paid to high-quality and non-directive information and counselling. Quality-assured education and continuous further training of the professional groups involved in counselling are crucial.

1 Introduction

There are several prenatal screening and diagnostic tests to detect fetal structural and chromosomal anomalies, which can be classified as non-invasive (e.g., ultrasound examinations, first-trimester screening, non-invasive prenatal test) and invasive methods (e.g., amniocentesis and chorionic villus sampling) [1]. The regulation and financing of prenatal screening and diagnostic examinations for fetal anomalies are heterogeneous across countries [2, 3]. On behalf of the Austrian Federal Ministry of Social Affairs, Health, Care and Consumer Protection, this project aims to investigate and summarise the provision and the financial framework conditions of the tests mentioned above in selected European countries.

Ziel des Berichts: Recherche und Zusammenfassung der Regulierung und Finanzierung von pränatalen Screening- und diagnostischen Tests in ausgewählten europäischen Ländern

1.1 Definitions

Prenatal testing is defined as any screening and diagnostic tests that provide information on the health of the fetus. Prenatal *screening* tests are usually performed to assess the child's probability of being affected by certain conditions or anomalies. Prenatal *diagnostic* tests can be carried out when the screening tests indicate an increased risk to confirm the presence of a disorder or anomaly [4].

Screening-Test gibt Wahrscheinlichkeit an, diagnostischer Test zur Bestätigung nötig

1.1.1 Test methods

The following prenatal screening and diagnostic tests will be addressed in this policy brief:

- First Trimester Screening (FTS)/Combined Test (CT),
- Non-invasive prenatal test (NIPT),
- Amniocentesis (AC)/chorionic villus sampling (CVS),
- Ultrasound screening for fetal anomalies in the second trimester.

4 unterschiedliche Arten von Tests werden berücksichtigt:

First Trimester Screening (FTS)/Combined Test (CT)

This test is performed in the first trimester, usually between 10+0 and 13+6 weeks of gestation. It combines an ultrasound examination, measuring nuchal translucency, and a blood test, determining the levels of beta-human chorionic gonadotropin (beta-hCG) and pregnancy-associated plasma protein-A (PAPP-A). Together with maternal age, these three markers provide an individualised risk for trisomies 21, 18 and 13. The detection rate for trisomy 21 is stated to be 85% [5].

First Trimester-Screening (FTS)/Combined Test (CT): kombiniert Ultraschall & Bluttest, Screening auf Trisomie 21, 18 und 13

Non-invasive prenatal test (NIPT)

The so-called NIPT is a prenatal screening method that is currently primarily used for trisomy 21, 18 and 13 and selected sex chromosome aneuploidies. It is performed using next-generation sequencing of fetal cell-free DNA in maternal plasma. The detection rates vary by trisomy (trisomy 21: 99.5%; trisomy 18:

nicht-invasiver Pränataltest (NIPT): Analyse von fetaler DNA aus dem mütterlichen Blut, …

… derzeit v. a. als Trisomie-Screening

87.7%; trisomy 13: 96.1%) [6]. Test manufacturers also offer tests for rarer trisomies, copy number variants, and several microdeletions, but the sensitivity and positive predictive value for these conditions are significantly lower [7].

Einsatz des NIPT als „second-line" Screening für Schwangere mit hohem Risiko (aufgrund FTS/CT-Ergebnis oder bei Risikofaktoren) oder als „first-line" Screening für alle Schwangeren

The NIPT can be used as a secondary screening test, i.e., a follow-up, nondiagnostic test offered to a population already identified as high risk in a previous screening test (e.g., by First Trimester Screening or by identifying risk factors such as high maternal age or abnormal ultrasound findings). It can also be used as a primary screening test for all pregnant women, i.e. without previous tests or risk stratification. Fetal cell-free DNA can be detected in maternal blood as early as 5 weeks of gestation; however, the fetal fraction (the percentage of all cfDNA in maternal blood that is derived from the fetal-placental unit) is substantially lower before 10 weeks of gestation, so mostly, the test is not carried out before 10 weeks of gestation. About 1-5% of the tests do not yield a result (e.g., women with obesity are at higher risk of having a test failure) [6]. The NIPT was introduced in 2011 and has since become available in more than 60 countries worldwide. In 2018, 10 million NIPT tests were performed [7].

Invasive tests (AC/CVS)

invasive Tests (Chorionzottenbiopsie oder Amniozentese): zur Diagnostik, geringes Fehlgeburtsrisiko

An invasive procedure has to be carried out to confirm or exclude the presence of a fetal anomaly (e.g., trisomy). CVS can be performed between 10 and 13 weeks of gestation, whereas AC is optimally carried out after 15 weeks of gestation. During CVS, small placenta samples are taken for prenatal genetic diagnosis. In AC, amniotic fluid is withdrawn from the uterus using a needle via a transabdominal approach. Both procedures are performed under ultrasound guidance. After these invasive tests, there is a small procedure-related risk of pregnancy loss [8, 9].

Ultrasound screening for fetal anomalies in the second trimester

Ultraschalluntersuchung auf fetale Anomalien im zweiten Trimester („Organscreening")

Ultrasound screening for fetal structural anomalies is usually performed between 18 and 22 weeks of gestation. It is also called a 20-week screening scan, mid-pregnancy scan, anomaly scan or (in Austria) "Organscreening" and (in Germany) "Feindiagnostik". During this ultrasound examination, the baby's bones, heart, brain, spinal cord, face, kidneys and abdomen are assessed in detail. It can detect several fetal anomalies, such as open spina bifida, congenital heart defects, or cleft lip [10].

1.1.2 Fetal anomalies

Trisomy 21 (Down syndrome)

Trisomie 21/ Down Syndrom: 1 von 700 Neugeborenen, Auswirkungen sehr unterschiedlich

Trisomy 21 (T21) or Down syndrome is the most common chromosomal aneuploidy among liveborn children. The incidence is reported to be 1 in 700 live births [11]. T21 is characterised by various dysmorphic features, congenital malformations such as heart defects, other health problems, and cognitive impairment. However, the impact of Down syndrome on each affected person is individual; some are profoundly impacted while others live healthily and independently as adults [12].

Trisomy 18 (Edwards syndrome)

Trisomy 18 (T18) or Edwards syndrome is the second most common autosomal trisomy, occurring once in 5,500 live births. The clinical spectrum of trisomy 18 may involve any organ system and includes various severe malformations, e.g., congenital heart disease and abnormalities of the gastrointestinal system. The majority of prenatally diagnosed cases of T18 die in utero. Only 5-10% survive the first year of life [13].

Trisomie 18/ Edwards Syndrom: 1 von 5.500 Neugeborenen, breites klinisches Spektrum, meist schwere Fehlbildungen

Trisomy 13 (Patau syndrome)

Trisomy 13 (T13) or Patau syndrome is a severe chromosomal disorder caused by an extra copy of chromosome 13. It is characterised by severe, multiple congenital anomalies, usually involving the central nervous system, heart, face, skin, limbs and genitals. The prevalence in newborns is 1 in 5,000, the majority of prenatally diagnosed children with T13 die in utero, and 90% of liveborn children die within the first year [13].

Trisomie 13/ Patau Syndrom: 1 von 5.000 Neugeborenen, schwere Fehlbildungen mehrerer Organe

Structural anomalies

Structural anomalies present at birth, also called birth defects, can be caused by genetic abnormalities and/or environmental exposures. Major congenital anomalies with medical, surgical or cosmetic implications (such as neural tube defects or cleft lip and palate) occur in approximately 2-4% of live births. Minor anomalies have mostly cosmetic significance but are not medically significant and are seen more frequently than major anomalies. Birth defects can be isolated or present in a characteristic combination or pattern that can indicate the presence of a syndrome [14].

strukturelle fetale Anomalien verschiedener Schweregrade, betreffen ca. 2-4 % der Neugeborenen

1.2 Current regulation in Austria

In Austria, the mother-child pass ("Mutter-Kind-Pass") documents examinations and health data during pregnancy and after birth until the child's fifth birthday. Five gynaecological examinations, two blood tests, and three ultrasound screenings are scheduled during pregnancy. The before-mentioned prenatal screening and diagnostic tests (FTS/CT, NIPT, invasive tests, second-trimester fetal anomaly screening) are not part of the routine prenatal screening programme as provided in the mother-child pass. If there is a medical reason for one (or more) of these examinations, they are paid for publicly [15].

Mutter-Kind-Pass in Österreich: die vorher genannten Screening-Tests sind nicht Teil des Routine-Programms

These indications include the following (indicated examinations are listed in parentheses):

Kostenübernahme nur von bestimmten Tests bei entsprechender medizinischer Indikation

- maternal age >35 years (non-invasive test [nuchal translucency measurement or CT] or invasive test [AC or CVS]),
- consanguinity of the partners (after genetic counselling, possibly second-trimester fetal anomaly ultrasound screening [Organscreening]),
- a previous child with malformations that have an increased risk of recurrence in further pregnancies and that can be diagnosed prenatally (FTS, second-trimester fetal anomaly ultrasound screening),

- increased familial risk for the occurrence of a genetic defect with known inheritance (AC or CVS, possibly second-trimester fetal anomaly ultrasound screening).
- suspicion of mutagenic or teratogenic damage (FTS, second-trimester fetal anomaly ultrasound screening, possibly AC or CVS) [16, 17].

diese werden im Rahmen der „Leistungsorientierten Krankenanstaltenfinanzierung" vergütet

For these indications, the respective examinations are covered by the Austrian performance-oriented hospital financing framework [Leistungsorientierte Krankenanstaltenfinanzierung, LKF] via the State health funds [Landesgesundheitsfonds] and should be carried out in particularly suitable centres for reasons of quality assurance. These centres should ideally be connected with obstetric departments [17].

1.3 Ethical aspects of prenatal testing

neue Technologien, z. B. NIPT, sind mit komplexen medizinischen, politischen und v. a. ethischen Fragen verbunden

Around the world, policymakers, healthcare professionals and the public are confronted with how to deal with the ever-expanding possibilities in biotechnology. Regarding prenatal testing, new technologies (such as the NIPT) come with complex medical, political, practical and, above all, ethical questions. In some countries, novel prenatal tests have been introduced with little controversy and public discussion, whereas in others, broad public debates have taken place [18].

NIPT hat in versch. Ländern unterschiedlich breite & intensive Diskussionen ausgelöst

Although prenatal screening for fetal anomalies has been available before (e.g., by using the FTS/CT), the introduction of the NIPT provoked ethical debates in many countries. The NIPT offers some advantages, e.g., it is more accurate than other screening tests, carries no risk for miscarriages, and can provide earlier results than other tests. However, it is not a diagnostic test but a screening test, i.e. false-positive results occur, and therefore, an invasive test is needed to obtain a definitive diagnosis [19].

relevante Werte sind z. B.:

The Nuffield Council on Bioethics [19] summarised the values playing an essential role in context with the NIPT as follows:

Wahlfreiheit, Autonomie und Einwilligung

- *Choice, autonomy and consent:* NIPT can facilitate reproductive autonomy by enabling women and couples to prepare for a child with a genetic condition or by deciding to have a termination, potentially at an earlier stage of pregnancy. NIPT can also undermine autonomy and choice, e.g., if accurate and balanced information about the tests and the conditions is not available or if pregnant women/couples have the feeling that they are expected to make a particular decision.

Vermeidung von Schäden

- *Avoidance of harm:* on the one hand, NIPT can reduce harms when it can replace or reduce the need for invasive tests; on the other hand, NIPT could lead to anxiety and more invasive tests in the case of inaccurate or unreliable results. If fewer people are born with genetic conditions or impairments because of the use of NIPT, it could also lead to fewer resources for research and health and social care relating to people with genetic conditions and to psychological harms of disabled people who may view prenatal testing as expressing a negative view or judgment about the value of disabled people and their lives.

- *Equality, fairness and inclusion:* NIPT can enhance the ability of pregnant women to choose the circumstances of their pregnancy, which can promote equality for women more generally. However, NIPT may lead to the perception that people are "to blame" for having a baby with a disability, it may change the perception of pregnancy and parenthood, and it may lead to disabled people and their families being more vulnerable to stigma and discrimination.

Gleichheit, Fairness und Inklusion

1.4 Project aim and research questions

The project aims to investigate and summarise the availability and financial conditions of the prenatal screening and diagnostic tests mentioned above in selected European countries.

Ziel des Berichts: Recherche und Zusammenfassung unterschiedlicher Regelungen in europäischen Ländern

According to the primary interests of the Austrian Federal Ministry of Social Affairs, Health, Care and Consumer Protection, we focused on the following research questions (RQ):

- RQ1: Which prenatal screening and diagnostic examinations for fetal anomalies are offered in the selected countries for all pregnant women or specific indications, risk factors, or other criteria?
- RQ2: How are those tests financed in the selected countries (publicly, co-financed, privately)?
- RQ3: Where are the prenatal screening and diagnostic tests carried out in the selected countries (e.g., in hospitals, in doctor's practices)?

Forschungsfragen fokussieren auf Angebot, Finanzierung und Setting der Tests

Additionally, we were interested in the following aspects:

- RQ4: What is the uptake of the examinations in the selected countries?
- RQ5: How is counselling organised in connection with these tests?

zusätzlich Forschungsfragen zu Inanspruchnahme und Beratung

2 Methods

2.1 Selection of countries

We selected 6 European countries that differ in various relevant criteria (e.g. health/insurance system, geographical location, professional groups predominantly involved in antenatal care, etc.) to illustrate the range of possible regulations and forms of financing. The selection includes the following countries:

6 europäische Länder ausgewählt: Deutschland (DE), Schweiz (CH), Niederlande (NL), Vereinigtes Königreich (UK), Norwegen (NO), Italien (IT)

- Germany (DE),
- Switzerland (CH),
- Netherlands (NL),
- United Kingdom (UK),
- Norway (NO),
- Italy (IT).

Relevant criteria that we applied to select the countries were, e.g., the health/insurance system (national health service [Beveridge]: UK, IT, NO; insurance-based system [Bismarck]: DE, CH, NL) and the organisation of antenatal care, i.e., the involved professional groups (mainly primary care involved [general practitioners, midwives]: NL, UK, NO; mainly specialist care involved [gynaecologists/obstetricians]: DE, CH, IT). We also aimed to select countries from different parts of Europe, with a particular focus on neighbouring countries: Western Europe (DE, CH, NL), Northern Europe (UK, NO), Southern Europe (IT). Additionally, we tried to include countries with different religious influences, based on the assumption that religious orientation also co-determines the approach to prenatal diagnostics (e.g., predominantly catholic: IT, CH; largely non-religious: UK, NO, NL; catholic, protestant and non-religious groups similarly large: DE).

Länder unterscheiden sich in Bezug auf z. B. Gesundheitssystem, Organisation der Schwangerenbetreuung (involvierte Berufsgruppen), Religion, Geographie

Table 2-1: Relevant criteria for country selection

	DE	CH	NL	UK	NO	IT
Health/insurance system[3]:						
■ national health service (Beveridge)				X	X	X
■ insurance-based system (Bismarck)	X	X	X			
Organisation of antenatal care/involved professional groups:						
■ mainly primary care (GPs, midwives)			X	X	X	
■ mainly specialist care (gynaecologists/obstetricians)	X	X				X

[3] See: https://www.pnhp.org/single_payer_resources/health_care_systems_four_basic_models.php, https://bmchealthservres.biomedcentral.com/articles/10.1186/s12913-018-3323-3/tables/1, https://www.hca.wa.gov/assets/program/major-final-frameworks-international-models.pdf (cited 14/03/2022)

	DE	CH	NL	UK	NO	IT
Geographical location within Europe[4]:						
■ Western Europe	X	X	X			
■ Northern Europe				X	X	
■ Southern Europe						X
Largest (non-)religious group[5]:						
■ 50–75% catholic						X
■ relative catholic majority		X				
■ 30% catholic, 30% non-religious; 24% protestant	X					
■ relative non-religious majority				X	X	
■ 50–75% non-religious			X			

2.2 Literature search

Handsuche nach Informationen in Datenbanken/Webseiten

Between January and March 2022, a hand search was conducted in the following databases and websites of the selected countries for information on the research questions:

- Google/Google Scholar,
- websites of ministries of health and relevant national institutions (e.g., public health institutes) of the respective countries,
- websites of prenatal screening programmes of the respective countries, if available.

Suchbegriffe

For the literature search, various keywords relating to the test (methods) [e.g., prenatal diagnostics, prenatal testing, First-trimester screening, Combined test, Non-invasive prenatal test/NIPT, second-trimester ultrasound screening, amniocentesis, chorionic villus sampling] were combined with the respective country as well as with relevant keywords such as regulation, offer, financing, funding, reimbursement, setting.

[4] Classification according to the UN Geoscheme: https://www.worldatlas.com/articles/the-four-european-regions-as-defined-by-the-united-nations-geoscheme-for-europe.html (cited 20/01/2022)

[5] Classification according to Eurobarometer survey 2019 and 2010: https://en.wikipedia.org/wiki/Religion_in_Europe#/media/File:Largest_(non-)religious_group_by_EU_member_state_-_Eurobarometer_2019.svg, https://en.wikipedia.org/wiki/Religion_in_Europe#/media/File:Largest_(non-)religious_group_by_EU_member_state_(and_5_other_countries)_-_Eurobarometer_2010.svg (cited 10/02/2022).

2.3 Expert consultation

zusätzlich Expert*innen-Befragung mittels Fragebogen

In addition to the data collection using available literature and relevant websites, we created a questionnaire to consult experts. The questionnaire focused on the 3 main research questions and was prepared as Word form. The questionnaire combines options to select and free text fields and can be found in Appendix (Questionnaire for expert consultation).

konsultierte Expert*innen: EUROCAT-Vertreter*innen, Präsident*innen von relevanten Fachgesellschaften

The expert consultation was conducted in February and March 2022. The questionnaire was sent and answered by e-mail. We contacted the country representatives of the EUROCAT[6] network and the chairpersons of relevant medical societies of the 6 countries, such as societies of gynaecologists and obstetricians or associations for perinatal medicine. In total, 11 experts from the EUROCAT network and 14 experts from medical societies were contacted. Some recipients also forwarded the questionnaire to other experts working in this field. The list of the contacted institutions can be found in Appendix (List of contacted institutions).

2.4 Data analysis and synthesis

kombinierte Datenextraktionstabelle für jedes Land, Übersichtstabelle, Ländervergleich

A data extraction table was prepared to combine the information from the literature search and the information from the expert consultation for each country. The results were summarised in an overview table and analysed in a country comparison. The data extraction tables for each country can be found in Appendix (Data extraction tables for each country).

[6] EUROCAT = European network of population-based registries for the epidemiological surveillance of congenital anomalies, https://eu-rd-platform.jrc.ec.europa.eu/eurocat/eurocat-members/registries_en (cited 28/03/2022)

3 Results

In this chapter, the results for each research question will be summarised. Before that, a brief overview of the routine prenatal screening programmes will be presented for each of the 6 countries (see also Table 3-1).

Präsentation der Ergebnisse anhand der Forschungsfragen

3.1 "Body of evidence"

We received a total of 11 completed questionnaires: 3 from Germany, 2 each from Switzerland, the Netherlands and Italy, as well as 1 each from the UK and Norway. Additionally, 22 relevant sources (articles, websites, policy documents) identified from the hand search were used to complement the information from the expert consultation. The comprehensive data extraction tables for each of the 6 included countries, combining expert consultation and hand search information, can be found in Appendix (Data extraction tables for each country). The information provided by the experts is written in italics; other sources have been referenced.

11 ausgefüllte Fragebögen, 22 Literaturquellen

Datenextraktionstabellen für jedes Land im Anhang

3.2 Overview of prenatal care and screening programmes in the 6 countries

Germany

In Germany, the maternity guidelines [Mutterschaftsrichtlinien] regulate the medical care during pregnancy and after childbirth on a national level, in particular the scope and timing of services, cooperation with midwives and documentation in the so-called "Mutterpass". In a normal pregnancy, regular check-ups (except, e.g., ultrasound screenings) can be conducted by a gynaecologist, a midwife or alternately by both [20, 21]. However, the majority of pregnant women have their check-ups carried out by their gynaecologists [22]. Usually, the examinations take place at intervals of 4 weeks, in the last two months of pregnancy at intervals of 2 weeks. Prenatal screening and diagnostic tests for fetal anomalies are also regulated in the maternity guidelines by the Federal Joint Committee [Gemeinsamer Bundesausschuss, GBA] [20, 21].

DE: Schwangerenbetreuung und PND laut Mutterschaftsrichtlinien des G-BA; regelmäßige (monatliche) Vorsorgeuntersuchungen meist durch Gynäkolog*in

Switzerland

According to the Swiss Federal Office of Public Health [Bundesamt für Gesundheit], seven check-ups are reimbursed in a normal pregnancy which can be carried out by either the gynaecologist or the midwife [23]. Although midwives have been able to take over the care of pregnant women in principle since 1996, midwifery-led care models are still relatively rare in Switzerland [24]. Prenatal non-invasive risk assessment/screening for fetal aneuploidies is provided according to an expert letter from the Swiss Society for Gynaecology and Obstetrics, in consultation with the Federal Office of Public Health [25].

CH: 7 Vorsorgeuntersuchungen, meist durch Gynäkolog*in; PND-Regelung anhand von „Expert Letter" der Fachgesellschaft für Gynäkologie & Geburtshilfe

Netherlands

NL: Betreuung durch Hebamme bei komplikationsfreier Schwangerschaft, Fachärzt*in nur bei Komplikationen; „Centre for Population Screening" regelt Screening-Programm auf fetale Anomalien und Trisomien

In the Netherlands, midwives are the leading medical professionals providing prenatal care to women with 'normal' pregnancies. In case of complications or an increased risk of complications during pregnancy, the midwife refers the woman to a gynaecologist for further care. Midwives work independently in a midwifery practice or as part of a group. The routine check-ups during pregnancy are scheduled once a month in the beginning and more frequently as the pregnancy progresses [26]. Prenatal care is provided according to the "Standards for prenatal care" from the Dutch Midwifery Association (KNOV) [27] and the "Standards for Integrated care during pregnancy and childbirth" from the "College Perinatale Zorg" (a collaboration of the associations for midwifery, gynaecology, paediatrics, patients and health care insurance companies) [28]. The screening for Down's, Edwards' and Patau's syndromes in pregnancy, as well as the 'Structural Ultrasound Scan' (SEO, anomaly scan), are coordinated and monitored by the Centre for Population Screening as part of the National Institute for Public Health and the Environment, which is commissioned by the Ministry of Health, Welfare and Sport [29, 30].

United Kingdom

UK: bei komplikationsfreier Schwangerschaft Betreuung durch Hebamme oder Hausärzt*in; "Fetal Anomaly Screening Programme" des NHS

In the UK, pregnancy care is regulated by the National Health Service (NHS). In uncomplicated pregnancies, it is usually provided by a midwife or a general practitioner; gynaecologists are consulted in case of complications. In the first pregnancy of a woman, 10 prenatal visits are scheduled. If the woman already has children, she usually has 7 prenatal check-ups [31]. Regarding prenatal screening and diagnostic examinations, there is a national screening programme called NHS Fetal Anomaly Screening Programme (FASP) for England, offering information on commissioning, quality assurance, education and training [32].

Norway

NO: Betreuung von Niedrig-Risiko-Schwangerschaften durch Hebamme oder Hausärzt*in; nationale Leitlinie regelt auch PND

Pregnancy care in Norway is provided according to the national professional guideline issued by the Norwegian Directorate of Health [Helsedirectoratet]. This guideline also includes information on prenatal screening and diagnostic examinations. Results of tests and consultations are documented in the Health Card for pregnant women. In a low-risk pregnancy, women are scheduled for up to 9 check-ups and can choose between care by a midwife or a general practitioner [33, 34].

Italy

IT: nationale Leitlinien für Schwangerschaftsbetreuun g, jedoch regionale Unterschiede; Vorsorgeuntersuchungen v. a. durch Gynäkolog*innen

The National Health Service [Servizio Sanitario Nazionale] offers services for low-risk pregnancies accessible to all women, in the context of the "Specialized outpatient assistance for pregnant women and for the protection of maternity" of the "National standard levels of assistance" which were updated in 2017. During a low-risk pregnancy, 6 routine examinations are scheduled and provided by a gynaecologist/obstetrician [35, 36]. In Italy, the public national healthcare system is organised under the Ministry of Health but administered on a regional basis; i.e. there are national guidelines, but some items are decided regionally. Moreover, private structures, which are more prevalent in some regions, are accessible to carry out screening tests, but with partial or complete payment by the pregnant women.[7]

[7] information provided by expert via e-mail

Table 3-1: Overview of prenatal care and screening programmes in the 6 countries

	DE	CH	NL	UK	NO	IT
Regulation of prenatal care (national/regional)	regulated by the maternity guidelines ("Mutterschaftsricht-linien") by the Federal Joint Committee (GB-A) on a national level	provided according to the Federal Office of Public Health (BAG)	provided according to "Standards for prenatal care" from the Dutch Midwifery Association and "Standards for integrated care during pregnancy" from the "College Perinatale Zorg"	regulated by the National Health Service (NHS)	provided according to the national professional guideline issued by the Norwegian Directorate of Health	provided according to the "National Standard Levels of Assistance" regulated by the National Health Service; however, pregnancy care can be regionally different
Prenatal care for low-risk pregnancies	regular check-ups every 4 weeks; in the last 2 months, every 2 weeks	7 check-ups during pregnancy	routine check-ups once a month, more frequently as the pregnancy progresses	10 prenatal visits in the first pregnancy, 7 check-ups for multiparous women	up to 9 check-ups during pregnancy	6 routine check-ups during pregnancy
Involved professional groups in low-risk pregnancies	gynaecologist, midwife or alternately both*	gynaecologist or midwife*	midwife	midwife or general practitioner	midwife or general practitioner	gynaecologist
Regulation of prenatal screening and diagnostics	also regulated in the G-BA maternity guidelines	provided according to an expert letter from the Swiss Society for Gynaecology and Obstetrics, in consultation with the BAG	screening for trisomies and fetal anomalies coordinated and monitored by the Centre of Population Screening as part of the National Institute for Public Health and the Environment	NHS Fetal Anomaly Screening Programme (FASP) for England	also regulated in the guidelines from the Norwegian Directorate of Health	also regulated in the "National Standard Levels of Assistance", but regional differences

Abbreviation: BAG – Bundesamt für Gesundheit (CH), GB-A – Gemeinsamer Bundesausschuss (DE), NHS – National Health Service (UK)

** in both countries, however, routine check-ups are mainly carried out by gynaecologists*

3.3 Offer of prenatal screening and diagnostic examinations for fetal anomalies (RQ1)

***Forschungsfrage 1* fokussiert auf PND-Angebot**

The first research question is: Which prenatal screening and diagnostic examinations for fetal anomalies are offered in the selected countries for all pregnant women or specific indications, risk factors, or other criteria?

First Trimester Screening (FTS)/Combined Test (CT)

FTS/CT: Angebot für alle Schwangeren in 3 Ländern (CH, UK, IT); unterschiedliche Angaben für DE; in 2 Ländern (NL, NO) wird Test nicht mehr angeboten (Ultraschall im 1. Trimester wird derzeit eingeführt)

The FTS/CT is offered for all pregnant women in 3 of the 6 selected countries (CH, UK, IT). In 1 country (DE), the experts gave differing information regarding the offer of this test (for all pregnant women/women with risk factors, "offered on a private basis", "obstetrician's choice"). In 2 countries, the FTS/CT is not offered anymore since 2021 because it has been replaced by other tests (NL, NO). However, in these 2 countries, an ultrasound examination in the first trimester is available or will be made available: In the Netherlands, all pregnant women can opt for a 13 weeks ultrasound scan which is currently introduced as part of a nationwide study.[8] In Norway, it is planned that all pregnant women will be offered an ultrasound examination during the first trimester (between 11+0 and 13+6) through the national health service; this service will be made available in 2022.

Non-invasive prenatal test (NIPT)

NIPT: als "first-line" Screening für alle Schwangeren in NL;

als „second-line" Screening in 3 Ländern (CH, UK, NO): bei Risikofaktoren (NO), bei FTS/CT-Ergebnis von >1:150 (UK) bzw. >1:1.000 (CH); regional unterschiedliches Angebot in IT; Einführung in bestimmten Fällen als Teil der Mutterschaftsrichtlinie in DE in 2022

1 of the selected 6 countries (NL) has recently introduced the NIPT as a first-line screening: all pregnant women are offered to have the NIPT (with co-payment)[9] in the Netherlands. In 3 of the selected 6 countries (CH, UK, NO), the NIPT is being provided as a second-line screening: In Norway, it is offered to pregnant women with risk factors (e.g., maternal age >35 years, hereditary risk, abnormal findings at ultrasound). In CH and UK, the NIPT is also offered as a second-line screening, but to women with increased risk based on the FTS/CT screening. However, the risk threshold is defined differently in the 2 countries: >1:150 in the UK and >1:1,000 in Switzerland. While the test was made available as part of national antenatal care in Switzerland in 2015, it was only introduced in 2021 in the UK (as part of an evaluative roll-out) and Norway. In Italy, the offer of NIPT is regionally different, e.g., in some regions, it is offered for pregnant women with risk factors (second-line screening based on the results of the FTS/CT), and in some regions, it is offered for all pregnant women. In Germany, the NIPT is currently provided on a private basis but will be included in the national maternity programme in 2022 for women with increased risk (i.e., "indications of a trisomy from other examinations", e.g., from FTS/CT or a routine check-up) or if a woman, together with her doctor, concludes that the test is necessary for her personal situation (e.g., if "the uncertainty of not knowing represents an unreasonable burden for the woman"). There is no detailed list of risk factors.

[8] IMITAS study, https://13wekenecho.org/ (cited 10/03/2022)

[9] The NIPT was introduced in 2014 for high-risk pregnant women (based on the Combined Test results) and in 2017 for all pregnant women within 2 scientific studies (TRIDENT-1 and TRIDENT-2, https://www.meerovernipt.nl/de-studies-trident-1-en-trident-2) (cited 10/03/2022)

The scope of the NIPT in the selected countries, when accessed as part of some prenatal screening programmes, is limited to trisomies 21, 18 and 13. The exception is NL, where whole genome sequencing is carried out as part of the TRIDENT study. Findings other than T21, T18 and T13 were reported to women only on request; however, 78% of women chose to have these reported [37].

Umfang des NIPT meist auf T21, T18 und T13 beschränkt, Ausnahme: gesamtes fetales Genom in NL

The recommended time frame for the NIPT includes from 10 weeks of gestation (DE), at or after 11 weeks of gestation (NL, IT[10]), between 11 and 14 weeks of gestation (CH, NO) or up to 21+6 weeks of gestation (UK).

NIPT meist ab 11. Schwangerschaftswoche empfohlen

Invasive tests (amniocentesis [AC]/chorionic villus sampling [CVS])

In all 6 countries, invasive tests are offered to those women who have certain risk factors: e.g., maternal age, high-risk results from screening tests (FTS/CT or NIPT), abnormalities on ultrasound screening, known genetic or familial conditions.

AC/CVS: in allen Ländern für Frauen mit Risikofaktoren

Ultrasound (US) screening for fetal anomalies in the second trimester

In all 6 countries, a second-trimester ultrasound screening for fetal anomalies is offered to all pregnant women. However, there were divergent responses from the German experts, who disagreed on whether screening is offered to all pregnant women or those with risk factors.

Ultraschallscreening im 2. Trimester: in allen Ländern für alle Schwangeren

[10] refers to Emilia-Romagna region only

3.4 Financing of prenatal screening and diagnostic examinations for fetal anomalies (RQ2)

***Forschungsfrage 2* fokussiert auf Finanzierung**

The second research question is: How are prenatal screening and diagnostic examinations for fetal anomalies financed in the selected countries (publicly, co-financed, privately)?

FTS/CT

FTS/CT: öffentliche Finanzierung in 3 Ländern (CH, UK, IT); Selbstzahlerleistung in DE

In 3 of the 6 selected countries, the FTS/CT is fully publicly reimbursed for all pregnant women who choose to have the test (CH, UK, IT). In 1 country (DE), the screening is completely self-paid by the pregnant women [IGeL-Leistung]. The remaining 2 countries (NL, NO) have recently replaced the FTS/CT with the NIPT and are therefore no longer reimbursing this type of screening.

NIPT

NIPT: öffentliche Finanzierung für Frauen mit Risikofaktoren in 3 Ländern (CH, UK, NO); in IT regional unterschiedl. Regelungen; in DE Kostenübernahme in best. Fällen ab 2022; in NL Selbstbehalt für Frauen ohne Risikofaktoren (bei erhöhtem Risiko komplette Finanzierung)

In 3 of the selected 6 countries (CH, UK, NO), the NIPT is fully publicly financed for pregnant women with the respective risk factors: increased risk according to FTS/CT of >1:150 (UK) or >1:1,000 (CH) or risk factors such as maternal age >35, hereditary risks, abnormal ultrasound findings (NO). In 1 country (IT), reimbursement and offer of NIPT are currently regionally different and can be fully reimbursed, partly reimbursed with co-payment or completely self-paid, depending on the region. In 1 country (DE), NIPT will be introduced in 2022 and will be reimbursed by the health insurance in certain cases (e.g., if a woman, together with her doctor, concludes that the test is necessary for her personal situation, i.e., the possibility of trisomy is such a burden on a woman that she wants to have this clarified). In the remaining country (NL), all pregnant women can take the NIPT at the cost of 175€; the rest of the costs are publicly subsidised. However, NIPT for pregnant women with increased risk is entirely covered by health insurance.

Invasive tests (AC/CVS)

AC/CVS: Kostenübernahme bei med. Indikation (alle Länder)

In all 6 countries, invasive tests – if necessary – are completely publicly reimbursed.

US screening for fetal anomalies in the second trimester

Ultraschallscreening im 2. Trimester: öffentlich finanziert in allen Ländern; in DE Überweisung aufgrund erhöhten Risikos nötig

Second-trimester ultrasound screening is publicly financed in all 6 countries. However, in Germany, women need to have a referral to the US screening [Feindiagnostik] from their gynaecologists/obstetricians due to certain risk factors (e.g., suspicious findings) in order for the ultrasound screening for fetal anomalies to be reimbursed by the health insurance.

3.5 Setting of prenatal screening and diagnostic examinations for fetal anomalies (RQ3)

The third research question is: Where are the prenatal screening and diagnostic tests for fetal anomalies carried out in the selected countries (e.g., in hospitals, in doctor's practices)?

Forschungsfrage 3
fokussiert auf Setting

FTS/CT

The FTS/CT is carried out only in hospitals in 1 country (UK) and in hospitals, doctor's practices, private clinics, and prenatal and ultrasound centres in 3 countries (IT, CH, DE). In Italy, the screening is free of charge within the healthcare system in hospitals but can be provided on a private basis (self-paid) in doctor's offices and private clinics. In Germany, the screening is primarily performed in outpatient settings. NL and NO don't offer this screening anymore.

FTS/CT:
im Krankenhaus (UK), unterschiedliche Settings in IT, CH, DE

NIPT

In 2 countries (UK, NO), the NIPT is only performed in hospitals. In the Netherlands, the NIPT is carried out in hospitals for women with increased risk and in midwifery practices for women as a screening test. In the remaining 3 countries, the NIPT is performed in hospitals and doctor's practices (DE, CH, IT), private clinics (IT) as well as prenatal and ultrasound centres (DE, CH). In Germany, the screening is primarily performed in outpatient settings.

NIPT:
ausschließlich Krankenhaus in UK, NO; Krankenhaus und Hebammenpraxis in NL; unterschiedliche Settings in DE, CH, IT

Invasive tests (AC/CVS)

In 3 countries (UK, NL, NO), invasive tests are only performed in hospitals. In the remaining 3 countries, AC and CVS are performed in hospitals, but also in doctor's practices with specialisation in feto-maternal medicine and ultrasound centres (CH), prenatal centres and institutes with special qualification (DE) and doctor's practices and private clinics (IT).

AC/CVS:
Krankenhaus bzw. spezialisierte Zentren

US screening for fetal anomalies in the second trimester

The settings of the second-trimester ultrasound screening include hospitals (all countries), doctor's practices (DE, CH, UK, IT) and prenatal/ultrasound centres (DE, CH, NL).

US-Screening:
Krankenhaus, Arztpraxen, US-Zentren

Table 3-2 gives an overview of the results for the 3 primary research questions.

Table 3-2: Summary of results of the 6 countries for research questions 1-3

	DE	CH	NL	UK	NO	IT
Offer of prenatal screening/diagnostic tests (for all pregnant women, women with risk factors, other criteria)						
First Trimester Screening (FTS)/ Combined Test (CT)	for all pregnant women (but offered on a private basis, "IGeL")	for all pregnant women	n/a (not offered anymore since 10/2021)	for all pregnant women	n/a (not offered anymore since 09/2021)	for all pregnant women
Non-Invasive Prenatal Test (NIPT)	currently offered on a private basis, will be included in the national programme in 2022 for women with specific criteria (test scope: T21, T18, T13)	*second-line* screening for pregnant women with increased risk from FTS/CT >1:1,000 (test scope: T21, T18, T13)	*first-line* screening for all pregnant women (test scope: whole-genome sequencing*)	*second-line* screening for pregnant women with increased risk from CT >1:150 (test scope: T21, T18, T13)	*second-line* screening for pregnant women with risk factors (e.g., age >35, hereditary risks, abnormal US findings) (test scope: T21, T18, T13)	depending on the region
Amniocentesis (AC)/ chorionic villus sampling (CVS)	for pregnant women with increased risk (e.g., maternal age, abnormal US findings)	for pregnant women with increased risk (e.g., risk of >1:380 in FTS/CT, positive NIPT, abnormal US findings, family history)	for pregnant women with increased risk based on NIPT, prior pregnancy or abnormal US findings	for pregnant women with risk factors (previous history, increased risk in CT or NIPT, abnormal US findings)	for pregnant women with risk factors	for pregnant women with risk factors (e.g., high risk at CT or NIPT, maternal age, known genetic or familial condition, abnormal US findings)
Second-trimester ultra-sound (US) screening	for all pregnant women	for all pregnant women	for all pregnant women	for all pregnant women	for all pregnant women	for all pregnant women
Financing of prenatal screening/diagnostic tests (fully or partially publicly reimbursed, self-paid)						
FTS/CT	completely self-paid ("IGeL – individuelle Gesundheitsleistung")	fully publicly reimbursed	n/a (not offered anymore since 10/2021)	fully publicly reimbursed	n/a (not offered anymore since 09/2021)	fully publicly reimbursed
NIPT	currently, completely self-paid; introduction as a health insurance benefit in 2022 (criteria: increased risk from another test, high psychological burden; no detailed list of risk factors)	fully publicly reimbursed for women with increased risk (see above)	partially publicly reimbursed/co-payment of 175€ for pregnant women without risk factors; for women with increased risk: fully reimbursed	fully publicly reimbursed if done as contingent screening (see above)	fully publicly reimbursed for women with risk factors (see above)	depending on the region
AC/CVS	fully publicly reimbursed for women with risk factors	fully publicly reimbursed for women with risk factors	fully publicly reimbursed for women with risk factors	fully publicly reimbursed for women with risk factors	fully publicly reimbursed for women with risk factors	fully publicly reimbursed for women with risk factors
Second-trimester US	fully publicly reimbursed for women with risk factors/ suspicious findings	fully publicly reimbursed	fully publicly reimbursed	fully publicly reimbursed	fully publicly reimbursed	fully publicly reimbursed

	DE	CH	NL	UK	NO	IT
Setting of prenatal screening/diagnostic tests (hospitals, doctor's practice, other)						
FTS/CT	in hospitals, doctor's practices, prenatal centres (mostly outpatient)	in hospitals, doctor's practices, ultrasound centre	n/a (not offered anymore since 10/2021)	in hospitals	n/a (not offered anymore since 09/2021)	in hospitals, doctor's practices, private clinics
NIPT	in hospitals, doctor's practices, prenatal centres (mostly outpatient)	in hospitals, doctor's practices, ultrasound centre	in midwifery practices, in hospitals (women with increased risk)	in hospitals	in hospitals	in hospitals, doctor's practices, private clinics
AC/CVS	in hospitals, prenatal centres, institutes with a special qualification	in hospitals, doctor's practices (specialised in feto-maternal medicine), ultrasound centre	in hospitals (centres for prenatal diagnosis)	in hospitals	in hospitals	in hospitals, doctor's practices, private clinics
Second-trimester US	in hospitals, doctor's practices, prenatal centres (mostly outpatient)	in hospitals, doctor's practices (specific US diploma), ultrasound centre	in centres for prenatal ultrasound (often part of a midwifery practice), in hospitals	in hospitals, at community scanning clinics for low-risk women	in hospitals	in hospitals, doctor's practices, private clinics

Abbreviation: AC – amniocentesis, CH – Switzerland, CT – Combined Test, CVS – chorionic villus sampling, DE – Germany, FTS – First Trimester Screening, IT – Italy, n/a – not applicable, NIPT – non-invasive prenatal test, NL – Netherlands, NO – Norway, UK – United Kingdom, US – ultrasound

** women can choose if they want to have other findings than T21, T18 and T13 reported*

3.6 Uptake of the examinations in the selected countries (RQ4)

***Forschungsfrage 4* fokussiert auf Inanspruchnahme**

In the questionnaire, we also asked the experts for data or estimates of the percentages of pregnant women who use prenatal screening and diagnostic examinations. The numbers differ substantially.

FTS/CT

FTS/CT: 72 % bis fast 100 % in Ländern mit kostenfreiem Angebot; in NL Reduktion von 24 % auf 1 % nach NIPT-Einführung

In 2 countries (NL, NO), the FTS/CT is no longer available. In NL, uptake of FTS/CT decreased from 34% in 2016 to only 1% in 2020. Countries with free charge offers for all pregnant women have uptake estimates/data from 72% to (almost) 100% (CH, UK, IT). For Germany, uptake was estimated to be around 60%, depending on region, insurance and socioeconomic status.

NIPT

NIPT: unterschiedliche Schätzungen von 10 %-30 %; 51 % in NL

For the NIPT, most data are estimates (sometimes there are diverging estimates from different experts from the same country): they range from 15% in IT, 10%-35% in CH, 20% in NO and 30% in DE. In the Netherlands, 51% of pregnant women took the NIPT in 2020, according to the "Monitor 2020" [38]. No data is available yet for the UK.

Invasive tests (AC/CVS)

AC/CVS: 1 %-3 %

The uptake of invasive test methods was partly unknown and relatively low; estimates mainly were given as 1 to 3%.

US screening for fetal anomalies in the second trimester

US-Screening: 70 % bis fast 100 %

Data and estimates regarding the second-trimester ultrasound examination are high in all selected countries, ranging from 70% to (almost) 100%.

3.7 Information on counselling in the context of prenatal screening and diagnostics (RQ5)

Forschungsfrage 5 **fokussiert auf Beratung**

Counselling is a critical topic in the context of prenatal screening and diagnostic examinations for fetal anomalies. Therefore, we asked for specific regulations or requirements in the selected countries. This chapter summarises the collected information and gives examples from selected countries.

in allen Ländern Beratung verfügbar, Ausgestaltung heterogen

Overall, according to the expert consultation, there is counselling in connection with prenatal screening and diagnostic examinations in all 6 selected countries. However, the specific design, requirements and involved professional groups vary from country to country.

Bsp. NL: 30-minütige Beratung durch zertifizierte Berater*innen (meist Hebammen) als Teil des Screening-Programms; Qualitätssicherungsmaßnahmen

A lot of information on counselling can be found in the Netherlands. Counselling is part of the prenatal screening programme and aims to enable pregnant women to make an informed choice about whether or not to participate in the prenatal screening programme and for which tests. It can only be performed by certified obstetric counsellors (usually midwives) and includes a 30-minute pre-test counselling, supported by leaflets in several languages and online information. Several quality assurance procedures exist, e.g., a minimum number of consults per year and continuous education for the counsellors ([7], see expert information in Table A-3).

Bsp. UK: Beratung ebenfalls durch Hebammen; ausgewogene, evidenzbasierte Infos

In the UK, counselling is also carried out by midwives during the first prenatal visit. Each woman offered screening should make a personal informed choice to accept or decline a test based on accessible, accurate, and evidence-based information, covering, e.g., risks and benefits of the screening, limitations and uncertainties, potential outcomes and pregnancy options.

Bsp. DE/CH: Beratung vorwiegend durch Gynäkolog*innen; Versicherteninformation des IQWiG

In Germany and Switzerland, primarily gynaecologists/obstetricians are involved in the counselling related to prenatal testing. The NIPT will be introduced in Germany as a health insurance benefit for pregnant women with specific criteria in 2022. A prerequisite for introducing this screening test was developing patient information by the Institute for Quality and Efficiency in Health Care (IQWiG) [39].

4 Discussion

Summary of the results: Differences and similarities

Policy Brief zeigt große Heterogenität von Angebot, Regulierung und Finanzierung von PND in den 6 ausgewählten Ländern

z. B. Angebot des FTS/CT für alle oder kürzliche Abschaffung des Tests, NIPT als first-line oder second-line Screening, unterschiedl. Risiko-Cutoff des FTS/CT für NIPT, national geregelte Screening-Programme vs. regionale Unterschiede; involvierte Berufsgruppen, …

This policy brief shows that the provision, regulation and financing of prenatal screening and diagnostic examinations for fetal anomalies differ substantially across countries. This can be illustrated by several examples from the 6 selected countries (DE, CH, NL, UK, NO, IT): For example, whereas some of the countries offer FTS/CT for all pregnant women as part of their prenatal screening programmes (CH, UK, IT), others have recently stopped offering the test at all (NL, NO). Instead, since 2021, NL and NO have introduced the NIPT. However, while in NL all pregnant women can take the test as a first-line screening with a private co-payment of 175€ (NIPT for women with increased risk is fully reimbursed); in NO, it is only reimbursed for women previously identified as high-risk, i.e., as a second-line screening. In 2 other countries, the NIPT is also used as a second-line screening: In the UK, it is made available for all women with an FTS/CT result of >1:150; in CH, however, women with a risk of >1:1,000 from the FTS/CT can take the NIPT. Some countries seem to have very clear and transparent regulation of those tests (e.g., UK, NL), while in other countries, there are regional differences (IT), or it is unclear for which specific indications particular tests are publicly reimbursed (e.g., DE). There are also differences regarding the professional groups involved in prenatal screening/diagnostic tests, e.g., the counselling in this context is in some countries conducted by gynaecologists (DE, CH) and in other countries by midwives (UK, NL). This may have to do with the organisation and regulation of antenatal care in general, especially regarding the main professional groups involved: while in 3 countries, it is mainly gynaecologists who care for low-risk pregnancies (DE, CH, IT), in 3 other countries this is routinely done by midwives (NL) or midwives and general practitioners (UK, NO).

große Unterschiede auch bei NIPT-Implementierung, z. B. hinsichtlich des Jahres der Einführung

Concerning the NIPT introduction, there are also considerable differences between countries. Of all the countries analysed, the Netherlands and Switzerland were the first to introduce NIPT as a health insurance benefit. In Switzerland, the NIPT was started to be publicly reimbursed for women with increased risk due to FTS/CT results in 2015. In the Netherlands, the NIPT was made available as part of 2 scientific studies licensed by the Dutch Ministry of Health: TRIDENT-1 started in 2014 for high-risk pregnant women, and TRIDENT-2 began in 2017 for all pregnant women. Several articles have published results (e.g., [37, 40]). In the other countries, NIPT was either introduced into the national screening programme during the last year (NO, UK), or the implementation is currently ongoing (DE) or planned for the near future (IT, regional differences).

Heterogenität bei Inanspruchnahme der Tests

Uptake of examinations also varies between countries: Regarding the FTS/CT, uptake was estimated from 72% to almost 100% in countries with a universal offer for all pregnant women and free of charge. However, for example, in the Netherlands, where pregnant women could choose between FTS/CT or NIPT (both with the same private co-payment), FTS/CT uptake decreased from 34% in 2016 to only 1% in 2020 [38] and is now no longer available. Data and estimates range from 10% to 50% for NIPT uptake and from 70% to (almost) 100% for the second-trimester ultrasound examination.

trotz Heterogenität auch Gemeinsamkeiten der Länder: z. B. bei US-Screening im 2. Trimester und bei invasiven Tests

But, despite the heterogeneity, there are also some similarities between countries: In all of the 6 selected countries, the second-trimester ultrasound examination for fetal anomalies is offered for all pregnant women and also fully publicly reimbursed (though, in DE, risk factors or "suspicious findings" are prerequisite for reimbursement). However, further detailed analysis is needed to assess whether the second-trimester ultrasound screening's quality and level of detail are comparable across countries. Another similarity concerns invasive tests, which are carried out in all countries exclusively in the case of certain risk factors (e.g. increased risk due to previous screening examinations) and the costs of which are covered by the public health system.

Discussion of the findings

auch andere Studien zeigten Heterogenität der Regelungen

A recent survey on NIPT use in Europe, Australia, and the USA [2] also concluded that implementation and uptake of NIPT differ substantially across countries, leading to almost all models being "unique". The Office of Technology Assessment at the German Bundestag [3] analysed, in a report from 2019, 4 European countries (Switzerland, Denmark, UK and Netherlands) and their approaches to prenatal testing, concluding that there was a great variety in the access regulations and abortion legislation.

gemeinsame Themen z. B.: Kosten als Hindernis für gleichberechtigten Zugang, Schutz der Rechte von Menschen mit Behinderungen

Ravitsky et al. [7] analysed the implementation of NIPT in several countries. They found some common issues among countries: costs as a barrier to equitable access (if public funding is not offered), the complexity of decision-making about public funding, a shortage of appropriate resources for informed choice (trained professionals as well as comprehensive and balanced informational material) and the protection of disability rights.

mögliche Gründe für Unterschiede zwischen Ländern: z. B. gesellschaftliche Einstellung zu Behinderung und zu Schwangerschaftsabbruch, gesellschaftlicher Zugang zu Screening

Bsp. NL: Regulierung durch "Population Screening Act", PND-Inanspruchnahme geringer als in anderen Ländern

Differences between countries regarding prenatal screening and diagnostic examinations for fetal anomalies can have several reasons. For example, the public attitudes towards disability and pregnancy termination (including the corresponding legal framework) can influence the development of screening programmes. In the Netherlands, the introduction of prenatal screening has provoked a broad political and public debate. Several concerns were raised, e.g., regarding the possible routinisation of prenatal screening (undermining women's informed decision-making) or regarding the acceptance and care for children with T21 if fewer children with T21 are born as a result of the screening. However, the uptake of prenatal screening is lower in the Netherlands compared to other European countries; possible reasons include the emphasis on the right not to know about the option of screening (i.e., pregnant women are explicitly asked if they want to receive information on screening at all), the relatively positive attitudes toward having a child with T21 as well as the rather negative attitude toward termination of pregnancy [7]. In the Netherlands, the Population Screening Act regulates screening for untreatable conditions and aims at protecting citizens against the potential adverse effects of screening. When a new screening test for untreatable conditions is proposed, a governmental license is needed before the screening can be implemented. This is why the introduction of prenatal screening in the Netherlands has been careful and thoughtfully assessed, considering the potential negative effects [41].

Bsp. NO: sehr restriktiver Zugang zu PND, Regelung durch „Biotechnology Act", große Bedenken bzgl. selektivem Schwangerschaftsabbruch

In Norway, access to prenatal screening and diagnostic examinations was very restrictively regulated according to the Biotechnology Act, i.e., only a small proportion of pregnant women had access to FTS/CT and NIPT. The NIPT was approved for use in Norway in 2017, but only for women with increased risk, according to the FTS/CT results. The test was not available outside this indication; that's why some women took the test abroad [18]. Last year, the

NIPT was introduced as a health insurance benefit for pregnant women with increased risk. All other pregnant women can have the test and pay for it themselves. Norway's abortion practices can be considered liberal, but there has been a large concern about selective abortion (due to fetal malformation or chromosomal aberration) and a "sorting society" [18].

weitere Gründe für Unterschiede: z. B. öffentlicher Diskurs, Art der Beratung

However, a recent analysis of several European countries found that different abortion legislation did not seem to explain national differences regarding the uptake of prenatal screening. Also, geographic and cultural neighbouring countries such as the Netherlands and Belgium show significant differences in the uptake, although they both offer NIPT as a first-line test. The article concludes that factors such as the national public, social discourse and who performs the counselling may have a significant influence, but more research is needed to understand those differences [42].

Bsp. Dänemark: FTS/CT Angebot für alle Schwangeren, bei high-risk Ergebnis wählt Großteil invasiven Test, nur 1 % macht NIPT

Another example is Denmark, which can be summarised as a country with an intensively used, publicly funded and socially widely accepted practice of prenatal diagnostics [3]. However, it is interesting that after a high-risk result from the FTS/CT (which is offered to all women), the majority of pregnant women choose to have an invasive test and not the NIPT. In total, less than 1% of all pregnancies are tested with NIPT. Reasons for this probably include the public communication of Danish data documenting a lower than expected risk of invasive tests, as well as a system leading to faster results with more information from invasive testing and subsequent chromosomal microarray (allowing diagnosis of all microdeletion and duplication syndromes) than with NIPT (which is done "only" for T21, T18, T13 and sex in Denmark) [42].

in DE große Debatte aufgrund rezenter Aufnahme des NIPT als Kassenleistung; Kritikpunkt: Kriterien der Krankenversicherung nicht erfüllt, …

The recent decision to introduce NIPT as a statutory health insurance benefit in Germany has triggered a major debate. Numerous organisations and individuals have launched the "#noNIPT alliance against the public funding of the blood test for trisomies*". One of the points of criticism is, for example, that the NIPT has no medical benefit (because it cannot maintain, restore or improve the health of either the pregnant woman or the child) and therefore does not meet the criteria for inclusion in the benefits catalogue of the statutory health insurance[11].

… da keine therapeutischen oder präventiven Interventionen als Folge des Screenings vorhanden, somit kein medizinischer Nutzen

The NIPT, or screening for T21, T18 and T13 in general, raises so many ethical questions and concerns because it has a special position: it does not serve to promote maternal and/or child health, as do other screening tests in pregnancy, but aims to detect fetal abnormalities for which there are no therapeutic or preventive interventions. Instead, these tests aim to promote reproductive autonomy for expectant parents by enabling them to obtain information about their future child and decide whether to continue or terminate a pregnancy in case of a genetic disorder [43].

NIPT überwiegend für T21, T18 und T13; weitere Optionen bis zu Sequenzierung des gesamten Genoms verfügbar;

NIPT is primarily used for screening for T21, T18 and T13. However, test manufacturers also offer other options, such as screening for sex chromosome aneuploidies, rarer trisomies, copy number variants, and microdeletions (and even whole-genome sequencing is already carried out), but the sensitivity and positive predictive value (PPV)[12] for these conditions are significantly lower [7]. The PPV varies depending on the conditions tested and the prevalence in

[11] https://nonipt.de/ (cited 18/03/2022)

[12] Positive predictive value (PPV): the probability that people with a positive screening test result indeed do have the condition of interest; the PPV is dependent on the prevalence of the condition in the population that is tested

Sensitivität und positiver prädiktiver Wert jedoch viel geringer (abhängig von Prävalenz in getesteter Population)

the population being tested. For example, the likelihood that a 40-year-old pregnant woman who receives a high-risk NIPT result for T21 will truly have a baby with T21 is approximately 93%. In comparison, the likelihood for a 25-year-old woman is only 51% due to different baseline risks[13]. This has to be considered when deciding which pregnant women will be offered the test, and it also needs to be communicated to women/couples during pre-test counselling.

Counselling

Bericht aus DE: oft kein klares Verständnis für PND bei den Schwangeren; bei Gynäkolog*innen oft Zeitdruck, fehlende Vergütung für Beratung, Sorge um haftungsrechtliche Konsequenzen

In Germany, a report concludes that (pregnant) women often do not have a clear understanding of prenatal diagnostics, yet the majority use them. Most of them name their attending physician as the central source of information. Although most women are satisfied with the medical counselling, they see a need for improvement in that ethical, social and psychological issues should also be addressed to a greater extent. The situation of gynaecologists in Germany is reported to be characterised by time pressure, lack of remuneration for doctor-patient conversations and concerns about legal liability consequences. There is also a lack of time for further training on the new NIPT procedures, so many use manufacturer information for counselling [3].

wichtig im Zusammenhang mit Beratung: qualitativ gute, ausgewogene Informationen; ausreichend Zeit für Beratung; autonome, informierte Entscheidungsfindung; Aus- und Fortbildung für Gesundheitspersonal

Many countries and institutions emphasise the importance of accurate, balanced information for pregnant women and their partners that supports all screening choices equally, and of sufficient time to discuss any concerns with screening and the potential implications, providing an environment that enables pregnant women to make autonomous, informed choices (e.g., [19, 41, 43, 44]). High-quality counselling focusing on personal values and the freedom to choose is essential for informed decision-making. Another crucial aspect for pregnant women to make an informed decision free from pressure is the availability of high-quality care and support for people with disabilities [45]. The Nuffield Council on Bioethics, for example, recommends that accurate, balanced and non-directive information should be produced before NIPT is introduced and that all healthcare professionals involved in the screening should have compulsory high-quality education and training. Furthermore, NIPT should only be offered as part of an inclusive package of care, including, at a minimum, counselling before and after the test, as well as invasive diagnostic if needed as a follow-up [19].

Beispiele für gute Beratung z. B. aus NL und UK

oft jedoch Mangel an ausgebildeten Berater*innen und hochwertigem Informationsmaterial, v. a. bei NIPT-Durchführung im Privatsektor

Ravitsky et al. concluded that counselling appears to be well organised and funded in countries with rigorous monitoring of NIPT implementation (e.g., in NL, as part of a national scientific study) or extensive public consultation (e.g., in UK). However, many countries seem to have a shortage of trained counsellors and high-quality and neutral information material, particularly those where NIPT is offered mostly or exclusively in the private sector [7]. If countries don't implement national regulation of prenatal testing, decision-makers need to be aware that this also means that access to testing is unequal (and dependent on the individual, including the financial situation of the pregnant woman/couple) and that a shift to the private sector also implies that issues such as counselling, but also, e.g., the scope of the NIPT, are difficult to influence.

[13] NIPT/Cell Free DNA Screening Predictive Value Calculator, https://www.perinatalquality.org/vendors/nsgc/nipt/ (cited 18/03/2022)

Limitations

Fokus auf 6 ausgewählte Länder mit großer Heterogenität; weitere Modelle in anderen Ländern

This Policy Brief aimed to give a broad overview of possible approaches to prenatal screening and diagnosis of fetal anomalies, focusing on the provision, the financing, and the setting of these examinations. We selected 6 European countries that differ in various relevant criteria, covering, e.g., different health care systems, geographical locations (with a focus on neighbouring countries) and antenatal care systems. However, as the results show, the models of prenatal testing are very heterogeneous across countries. An analysis of other countries will probably bring up even more different approaches, as demonstrated with Denmark's example.

tw. gegensätzliche Antworten von Expert*innen aus gleichem Land; in diesen Fällen z. B. unklare Regelungen oder regionale Unterschiede

Apart from the country selection, which implies that we cannot give a complete overview of European country models for prenatal screening and diagnostics, another limitation of the report is that for some countries, answers from the participating experts were partly conflicting, and it was not possible to prove all answers from the experts in detail. However, inconsistent expert information could partly be explained by unclear regulations in the respective countries or by regional differences; for example, in Italy; i.e. the answers could not reflect the situation in all parts of Italy.

5 Conclusion

The overview of approaches to prenatal screening and diagnosis of fetal anomalies in 6 European countries shows that these tests' provision, financing, and setting are heterogeneous. This applies particularly to the offer of screening for T21, T18 and T13 (for all pregnant women or women with specific criteria), the choice of first-line tests (FTS/CT or NIPT), and the public reimbursement of those tests. Countries have similarities regarding the provision and financing of invasive tests and second-trimester ultrasound screening for fetal anomalies. Reasons for the differences are not yet fully understood but may include, for example, different attitudes towards disabilities and termination of pregnancy as well as different antenatal care models. Due to the many ethical aspects of this topic, a broad societal dialogue and debate with the relevant stakeholders and involved groups seem appropriate. Particular attention should be paid to information and counselling in connection with screening for fetal anomalies; this should be of high quality, balanced and non-directive and support the pregnant women/couples in making an informed decision without pressure and based on personal values. For this, appropriate quality-assured education and continuous training of the involved health care professionals are essential. To be able to provide high-quality prenatal screening and diagnostic examinations, including professional counselling, sufficient personnel resources are required. Involving professional groups other than medical doctors may need to be considered for implementation, as is done in several European countries.

Übersicht zeigt große Heterogenität bzgl. Angebot, Finanzierung und Setting

aufgrund vieler ethischer Fragen scheint breiter gesellschaftlicher Diskurs nötig

besonderes Augenmerk sollte auf gute, neutrale Beratung mit ausreichend personellen Ressourcen und qualitätsgesicherter Aus- und Fortbildung gelegt werden

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Appendix

Data extraction tables for each country

Germany

Table A-1: Summary of results, Germany

Country	Germany
Organisation of prenatal care and offer of prenatal screening/diagnostic tests	
Routine screening/preventive programme for pregnancy	Yes, "Mutterpass", regulated in the maternity guidelines [Mutterschaftsrichtlinien] of the Federal Joint Committe [Gemeinsamer Bundesausschuss, G-BA], https://www.g-ba.de/richtlinien/19/ [21]
Prenatal screening/diagnostic examinations for fetal anomalies as part of this programme?	*Yes; NIPT (planned to start 2022), amniocentesis/CVS and second-trimester US for fetal anomalies for women at risk or in cases with suspicious findings*
Routine offer for all pregnant women or women with risk factors	
■ First Trimester Screening/Combined Test	*For all pregnant women/women with risk factors*; offered on a private basis (self-paid)/obstetrician's choice*
■ NIPT	*For all pregnant women/women with risk factors*; currently offered on a private basis, but will be included in the national maternity programme in April 2022; indication: increased risk,* Scope: trisomies 21, 18 and 13; time frame: can be carried out from the 10th week of gestation [21]
■ Amniocentesis/chorionic villus sampling	*For pregnant women with increased risk (age, suspicious findings)*
■ Second-trimester ultrasound screening	*For all pregnant women/women with risk factors* (suspicious findings)*
Financing of prenatal screening/diagnostic tests	
Type of funding for the tests, criteria for full or partial public reimbursement	
■ First Trimester Screening/Combined Test	*Completely self-paid [IGeL, "indviduelle Gesundheitsleistung"]*
■ NIPT	*For now, fully self-paid; however, some insurances offer the test as additional service. Introduction planned for 2022; criteria/risk factors unclear so far ("…if the question arises in the course of medical antenatal care as to whether a fetal trisomy could be present and the uncertainty represents an unreasonable burden for the woman")* Introduction of NIPT as a health insurance benefit expected in spring 2022 [46]; criteria for public reimbursement: indication of a trisomy from other tests, or if a woman, together with her doctor, comes to the conclusion that the test is necessary in her personal situation (e.g., the possibility of a trisomy is such a burden on a woman that she wants to have this clarified) [21]
■ Amniocentesis/chorionic villus sampling	*Fully publicly reimbursed*
■ Second-trimester ultrasound screening	*Fully publicly reimbursed (for women with a referral for further examination [Feindiagnostik] because of risk factors, suspicious findings)*
Setting of prenatal screening/diagnostic tests	
Setting of tests/in hospitals or doctor's practices	
■ First Trimester Screening/Combined Test	*in hospitals, doctor's practices, prenatal centres; mostly in outpatient settings (private institutes or hospital ambulances)*
■ NIPT	*in hospitals, doctor's practices, prenatal centres; mostly in outpatient settings (special genetic education needed)*
■ Amniocentesis/chorionic villus sampling	*in hospitals, prenatal centres, institutes with special qualification (DEGUM, KV)*
■ Second-trimester ultrasound screening	*in hospitals, doctor's practices, prenatal centres; mostly in outpatient settings (private institutes or hospital ambulances)*
Data or estimates on uptake of the examinations	
■ First Trimester Screening/Combined Test	*Approx. 60%, depending on region, insurance and socioeconomic status*
■ NIPT	*Approx. 30%, depending on region, insurance and socioeconomic status*
■ Amniocentesis/chorionic villus sampling	*1-2%/<5%/<10%**
■ Second-trimester ultrasound screening	*70%/>95%*, depending on region (e.g., nearly all women in Berlin)*

Country	Germany
Information on counselling	
Provision of counselling, involved professional groups, quality specifications and/or ethical standards	*Counselling is done by mainly the obstetricians/gynaecologists (special genetic education needed), by the ones offering prenatal medicine and in some cases by the geneticists* *When abnormal results: counselling by a combination of various specialities (obstetricians/gynaecologists, human geneticist, neonatologist, and others)* A prerequisite for introducing the NIPT was the development of patient information by the Institute for Quality and Efficiency in Health Care (IQWiG) [39].

Sources: information provided in the questionnaire by 3 experts (in italic writing), [21, 39, 46]
** indicating differing information from the experts*

DEGUM – German Society for Ultrasound in Medicine [Deutsche Gesellschaft für Ultraschall in der Medizin],
KV – Association of Statutory Health Insurance Physicians [Kassenärztliche Vereinigung]

Switzerland

Table A-2: Summary of results, Switzerland

Country	Switzerland
Organisation of prenatal care and offer of prenatal screening/diagnostic tests	
Routine screening/preventive programme for pregnancy	Yes, see "Maternity benefits" [Leistungen bei Mutterschaft] regulated by the Federal Office of Public Health [Bundesamt für Gesundheit] [23]
Prenatal screening/diagnostic examinations for fetal anomalies as part of this programme?	*Yes, all of them* See Expert letter of the Swiss Society for Gynaecology and Obstetrics "Prenatal non-invasive risk assessment of fetal aneuploidies" [25]
Routine offer for all pregnant women or women with risk factors	
■ First Trimester Screening/Combined Test	*For all pregnant women*
■ NIPT	For pregnant women with increased risk (>1:1000) for trisomy 21, 18 or 13 [25] Scope: trisomies 21, 18 and 13; time frame: recommended in the period 11+0 to 13+6 weeks of gestation [25] *Available for all pregnant women (self-paid)*
■ Amniocentesis/chorionic villus sampling	For pregnant women with increased risk: e.g., risk of >1:380 in First Trimester Screening, positive NIPT, abnormal findings in ultrasound screening, family history [47]
■ Second-trimester ultrasound screening	*For all pregnant women*
Financing of prenatal screening/diagnostic tests	
Type of funding for the tests, criteria for full or partial public reimbursement	
■ First Trimester Screening/Combined Test	*Fully publicly reimbursed*, if performed in accordance with the Swiss Study Group 1st Trimester Screening Guidelines [48]
■ NIPT	*Fully publicly reimbursed for pregnant women with increased risk from the First Trimester Screening (>1:1000 for trisomy 21, 18, and 13)* Reimbursement of the costs of the NIPT for risk assessment of trisomies 21, 18 and 13 by the compulsory health insurance (under certain conditions, see above) since July 2015 [25]
■ Amniocentesis/chorionic villus sampling	*Fully publicly reimbursed for pregnant women with a risk for trisomy 21 >1:380; only with medical indication*
■ Second-trimester ultrasound screening	*Fully publicly reimbursed for all pregnant women*
Setting of prenatal screening/diagnostic tests	
Setting of tests/in hospitals or doctor's practices	
■ First Trimester Screening/Combined Test	*in hospitals, doctor's practices, ultrasound center*
■ NIPT	*in hospitals, doctor's practices, ultrasound center*
■ Amniocentesis/chorionic villus sampling	*in hospitals, doctor's practices (with specialisation in feto-maternal medicine), ultrasound center*
■ Second-trimester ultrasound screening	*in hospitals, doctor's practices (doctors need a specific diploma for ultrasonography to be reimbursed), ultrasound center*

Country	Switzerland
Data or estimates on uptake of the examinations	
■ First Trimester Screening/Combined Test	*95%/100%**
■ NIPT	*10%/35%**
■ Amniocentesis/chorionic villus sampling	*No data available/1%**
■ Second-trimester ultrasound screening	*98%/100%**
Information on counselling	
Provision of counselling, involved professional groups, quality specifications and/or ethical standards	*Counselling before ultrasound, first trimester test or NIPT is done as a prerequisite. Mostly, gynaecologists/obstetricians are doing the counselling, but also midwifes and family planning units are sometimes involved in counselling. Obstetricians who offer first trimester test (and want to be reimbursed for it) need to perform a specific course of communication in the field of prenatal diagnosis.* *Before making an amniocentesis or chorionic villus sampling the counselling is done by a feto-maternal specialist. If the result is pathologic there is a counselling made by a geneticist or by the feto-maternal specialist.*

Sources: information provided in the questionnaire by 2 experts (in italic writing), [23, 25, 47, 48]
** indicating differing information from the two experts*

Netherlands

Table A-3: Summary of results, Netherlands

Country	Netherlands
Organisation of prenatal care and offer of prenatal screening/diagnostic tests	
Routine screening/preventive programme for pregnancy	Yes, "standard for prenatal care" [KNOV-standaard Prenatale verloskundige begeleiding] from the Dutch Midwifery Association (KNOV), https://www.knov.nl/ [27] and "Standard for Integrated care during pregnancy and childbirth" [Zorgstandaard Integrale Geboortezorg] from the "College Perinatale Zorg" (a collaboration of the associations for midwifery, gynaecology, paediatrics, patients and health care insurance companies), https://www.kennisnetgeboortezorg.nl [28]
Prenatal screening/diagnostic examinations for fetal anomalies as part of this programme?	Yes, https://www.pns.nl/prenatal-screening Trisomy 21/18/13 screening and fetaly anomaly ultrasound screening coordinated by the Centre for Population Screening, https://www.rivm.nl/ *The prenatal screening program focuses on screening for Down, Edwards and Patau syndrome and structural anomalies. It offers the NIPT starting from 11 weeks, and a second trimester US scan between 18-21 weeks. In September 2021 we introduced the first trimester US scan for fetal anomalies (12-14 weeks) as part of a scientific study.* *Diagnostics are not part of the screening, but can follow screening or be indicated in high risk pregnancies.*
Routine offer for all pregnant women or women with risk factors	
■ First Trimester Screening/Combined Test	*n/a (The Combined Test is not offered anymore since October 2021, replaced by NIPT)* *A 13 weeks US scan is currently introduced as part of a nationwide scientific study (IMITAS study, https://13wekenecho.org/). All pregnant women can opt for this first trimester US. Women with an a priori increased risk for structural anomalies, younger than 16 years and with an increased risk at NIPT are excluded.*
■ NIPT	*For all pregnant women* *(Pregnant women with an a priori increased risk are referred to a prenatal diagnosis department for counselling and either NIPT or invasive testing)* The NIPT was introduced in 2014 for high-risk pregnant women (based on the Combined Test results) and in 2017 for all pregnant women within 2 scientific studies (TRIDENT-1 and TRIDENT-2, https://www.meerovernipt.nl/de-studies-trident-1-en-trident-2) Scope: whole genome (findings other than trisomies 21, 18 and 13 were reported to women on request, 78% chose to have these reported); time frame: at or after 11+0 weeks of gestation [37]
■ Amniocentesis/chorionic villus sampling	*Only performed in women with an increased risk based on NIPT, prior pregnancy or US abnormalities*
■ Second-trimester ultrasound screening	*For all pregnant women*

Country	Netherlands
Financing of prenatal screening/diagnostic tests	
Type of funding for the tests, criteria for full or partial public reimbursement	
■ First Trimester Screening/Combined Test	n/a *(no longer applicable)*
■ NIPT	*Partially publicly reimbursed/co-payment: NIPT as a screening test costs 175€ for the pregnant woman, the rest of the costs is publicly subsidized; NIPT for women with increased risk is being covered by the health insurance*
■ Amniocentesis/chorionic villus sampling	*Fully publicly reimbursed/covered by the health insurance*[14]
■ Second-trimester ultrasound screening	*Fully publicly reimbursed*
Setting of prenatal screening/diagnostic tests	
Setting of tests/in hospitals or doctor's practices	
■ First Trimester Screening/Combined Test	*n/a (no longer applicable)*
■ NIPT	*In hospitals (NIPT for women with increased risk), other setting (NIPT as screening: midwife requests NIPT, blood is drawn at lab, results are going to midwives)*
■ Amniocentesis/chorionic villus sampling	*In hospitals (selected centres for prenatal diagnosis)*
■ Second-trimester ultrasound screening	*Other: centres for prenatal ultrasound (mostly first line and part of a midwife practice, sometimes situated in hospitals) who have a contract with a regional centre for prenatal screening* *Low-level ultrasound is done by certified ultrasonographers (e.g., midwives) and regulated by government in terms of numbers (150 scans per year), education and biennial review (judgement of the images from 3 random patients). High-level ultrasound is done in hospitals primarily and is not regulated by government.*
Data or estimates on uptake of the examinations	
■ First Trimester Screening/Combined Test	*n/a (no longer applicable)* In 2020: 1%, in 2016: 34% [38]
■ NIPT	51% (2020) [38]
■ Amniocentesis/chorionic villus sampling	*Data not available (tests only available on indication)*
■ Second-trimester ultrasound screening	86% (2020) [38] (performed as part of the official screening programme by the government) *97% (estimation including also those pregnant women with a higher risk who have their 20 weeks scan not as part of the screening programme but in hospital, performed by "more qualified" professionals)*
Information on counselling	
Provision of counselling, involved professional groups, quality specifications and/or ethical standards	*Counselling is part of the prenatal screening program. Midwives perform the counselling. The aim is that pregnant women make an informed choice whether or not to participate in the prenatal screening program and for which tests. The counselling can only be done by certified obstetric counsellors (e.g., midwives), who are educated in counselling and have good knowledge on the tests and conditions that are being screened for. There are several quality assurance procedures in place for the counselling (including a minimum number of consults [at least 50 counselings per year] and continuing education courses every 2 years).* *The post test counselling is mostly done by midwives and doctors and then a referral is done to a specialised unit (e.g., prenatal diagnosis department at an university hospital), where couples receive further counselling and are offered tests on follow up by a gynaecologist.* Pregnant women and their partners are offered a 30-minute pretest counseling session by a certified provider (typically a primary care midwife); counseling is supported by a leaflet in 5 languages and online information, which is produced by the Centre for Population Screening [7]

Sources: information provided in the questionnaire by 2 experts (in italic writing), [7, 27, 28, 37, 38]

[14] In the Netherlands, hospital care is covered by health insurance, but everybody has a "eigen risico" (own risk); usually the first 400€ a year are not reimbursed, but people sometimes choose a higher "own risk" in order to have a lower monthly rate (information provided by expert via e-mail)

United Kingdom

Table A-4: Summary of results, United Kingdom (expert information relates to England only)

Country	United Kingdom
Organisation of prenatal care and offer of prenatal screening/diagnostic tests	
Routine screening/preventive programme for pregnancy	Yes, NHS Prenatal care, https://www.nhs.uk/pregnancy/your-pregnancy-care/ [31]; also see NICE Antenatal care guideline, https://www.nice.org.uk/guidance/ng201
Prenatal screening/diagnostic examinations for fetal anomalies as part of this programme?	*Yes, all of them* NHS Fetal Anomaly Screening Programme (FASP), https://www.gov.uk//guidance/fetal-anomaly-screening-programme-overview [32] Women can choose: not to have screening; to have screening for T21, T18 and T13; to have screening for T21 only; to have screening for T18 and T13 only [49]
Routine offer for all pregnant women or women with risk factors	
■ First Trimester Screening/Combined Test	*For all pregnant women*
■ NIPT	*For pregnant women with increased risk; contingent screening after Combined Test (or quadruple test) risk >1:150 (introduced in June 2021)* NIPT was added to the existing NHS screening pathway for Down's syndrome, Edwards' syndrome and Patau's syndrome as part of an evaluative rollout in June 2021. The evaluation aims to answer question raised by the UK National Screening Committee regarding the choices women make, the accuracy of NIPT in finding trisomies 18 and 13 and the number of inconclusive results [50]. Scope: trisomies 21, 18 and 13; time frame: can be offered up to 21+6 weeks of gestation [51]
■ Amniocentesis/chorionic villus sampling	*For pregnant women with the following risk factors: previous history, increased risk in Combined Test or NIPT, abnormality on ultrasound screening*
■ Second-trimester ultrasound screening	*For all pregnant women* (ultrasound scan which is performed between 18^{+0} to 20^{+6} weeks to screen for 11 physical conditions) [49]
Financing of prenatal screening/diagnostic tests	
Type of funding for the tests, criteria for full or partial public reimbursement	
■ First Trimester Screening/Combined Test	*Fully publicly reimbursed*
■ NIPT	*Fully publicly reimbursed, if done as contingent screening supported by the NHS; if accessed outside this pathway then cost is approx. £450*
■ Amniocentesis/chorionic villus sampling	*Fully publicly reimbursed*
■ Second-trimester ultrasound screening	*Fully publicly reimbursed*
Setting of prenatal screening/diagnostic tests	
Setting of tests/in hospitals or doctor's practices	
■ First Trimester Screening/Combined Test	*in hospitals*
■ NIPT	*in hospitals*
■ Amniocentesis/chorionic villus sampling	*in hospitals*
■ Second-trimester ultrasound screening	*in hospitals (low-risk women may have this provided at community scanning clinics attached to GP surgeries)*
Data or estimates on uptake of the examinations	
■ First Trimester Screening/Combined Test	*72.5-89.8% depending on region (proportion of eligible women for whom a conclusive result is available)*
■ NIPT	*Unknown (only introduced in June 2021 so minimal data on uptake)*
■ Amniocentesis/chorionic villus sampling	*(no data available on national level)*
■ Second-trimester ultrasound screening	*98.9-99.3% depending on region (proportion of pregnant women eligible for fetal anatomy ultrasound screening who are tested leading to a conclusive result within the defined timescale)*

Country	United Kingdom
Information on counselling	
Provision of counselling, involved professional groups, quality specifications and/or ethical standards	*Midwives for all women at booking – discussion of screening options. Following identification of abnormality of high risk result initial counselling by specially trained screening midwives and referral to fetal medicine where appropriate.* Each woman offered screening should make a personal informed choice to accept or decline a screening test based on accessible, accurate and evidence-based information (covering: e.g., risks and benefits of the screening, limitations and uncertainties of screening, potential outcomes of screening and pregnancy options). Every woman should receive the leaflet (available in several languages) at first contact, have a discussion with a healthcare professional about screening options and have time to think about accepting or declining screening and what the possible results might mean [49].

Sources: expert information provided in the questionnaire (in italic writing), [32, 49-51]

Norway

Table A-5: Summary of results, Norway

Country	Norway
Organisation of prenatal care and offer of prenatal screening/diagnostic tests	
Routine screening/preventive programme for pregnancy	Yes, national professional guideline "Pregnancy care" [Svangerskapsomsorgen] from the Norwegian Directorate of Health [Helsedirektoratet], https://www.helsedirektoratet.no [33]
Prenatal screening/diagnostic examinations for fetal anomalies as part of this programme?	*Yes: NIPT for trisomy 21, 18 and 13), amniocentesis/chorionic villus sampling, second trimester ultrasound screening for fetal anomalies*
Routine offer for all pregnant women or women with risk factors	
■ First Trimester Screening/Combined Test	*- (not offered at all [the combined ultrasound and biochemical test has been replaced by NIPT (+US between weeks 11+0 and 13+6) as of september 2021])* [52] It is planned that all pregnant women will be offered an ultrasound examination during the first trimester (between 11+0 and 13+6) through the national health service; this service will be made available during 2022 [44].
■ NIPT	*For pregnant women with risk factors: e.g., age >35 at term, hereditary risk, abnormal findings at ultrasound* Scope: trisomies 21, 18 and 13, time frame: recommended for 11 to 14 weeks of gestation [44]
■ Amniocentesis/chorionic villus sampling	*For pregnant women with risk factors*
■ Second-trimester ultrasound screening	*For all pregnant women (in weeks 17-19)*
Financing of prenatal screening/diagnostic tests	
Type of funding for the tests, criteria for full or partial public reimbursement	
■ First Trimester Screening/Combined Test	-
■ NIPT	*Fully publicly reimbursed for women with the above mentioned risk factors (since 2021)* For pregnant women who are not offered NIPT in the public sector, NIPT can be offered in approved private companies for a fee [33].
■ Amniocentesis/chorionic villus sampling	*Fully publicly reimbursed*
■ Second-trimester ultrasound screening	*Fully publicly reimbursed*
Setting of prenatal screening/diagnostic tests	
Setting of tests/in hospitals or doctor's practices	
■ First Trimester Screening/Combined Test	-
■ NIPT	*in hospitals*
■ Amniocentesis/chorionic villus sampling	*in hospitals*
■ Second-trimester ultrasound screening	*in hospitals*

Country	Norway
Data or estimates on uptake of the examinations	
■ First Trimester Screening/Combined Test	-
■ NIPT	*20%*
■ Amniocentesis/chorionic villus sampling	*3%*
■ Second-trimester ultrasound screening	*98%*
Information on counselling	
Provision of counselling, involved professional groups, quality specifications and/or ethical standards	*Doctors or midwives before the test, doctors if abnormal. Needs to have taken a course in counselling.* Midwives or doctors will provide pregnant women with appropriate, neutral information about fetal diagnostics during the first consultation, to enable informed decision-making. This includes information on, e.g., the risks associated with the procedures and the potential consequences [44].

Sources: expert information provided in the questionnaire (in italic writing), [33, 44, 52]

Italy

Table A-6: Summary of results, Italy

Country	Italy
Organisation of prenatal care and offer of prenatal screening/diagnostic tests	
Routine screening/preventive programme for pregnancy	Yes, according to Article 59 "Specialized outpatient assistance for pregnant women and for the protection of maternity" [Assistenza specialistica ambulatoriale per le donne in stato di gravidanza e a tutela della maternità] of "National standard levels of assistance" [Nuovi Livelli Essenziali di Assistenza], https://associazioneitalianaostetricia.it [35]
Prenatal screening/diagnostic examinations for fetal anomalies as part of this programme?	*Combined Test is available in all regions (free of charge)*; amniocentesis/CVS and second trimester US are available in all regions (free of charge).* *NIPT is not yet fully implemented even though it is proposed by the Ministry of Health as a goal for 2022; most regions are moving fast toward a universal free of charge implementation (there might be differences between regions regarding the use of NIPT as first or second line of screening). NIPT is already offered free of charge in some regions (e.g., Emilia Romagna).*[15]
Routine offer for all pregnant women or women with risk factors	
■ First Trimester Screening/Combined Test	*For all pregnant women*
■ NIPT	*Based on regional offer; e.g., in Lombardy, for pregnant women with risk factors (second-line test after a CT result of intermediate risk); e.g., in Emilia Romagna, for all pregnant women* Example Emilia Romagna: was the first region in Italy to offer the NIPT free of charge in 2020, for all pregnant women, regardless of age or risk factors. Scope: trisomies 21, 18 and 13; time frame: from the 10th week of gestation [53] The Superior Health Council [Consiglio Superiore di Sanità] of the Ministry of Health criticises in a document from 2021 the inhomogeneity between Italian regions concerning the availability of NIPT as well as misinformation and absence of counselling in some regions. It therefore recommends the inclusion of NIPT into the "National standard levels of assistance" and/or into regional pathways as a second-line test (i.e., contingent screening after CT), for the screening of trisomies 21, 18 and 13. It further gives several recommendation relating to quality assurance, specialisation of involved doctors, counselling, etc. [54]
■ Amniocentesis/chorionic villus sampling	*For pregnant women with risk factors: e.g., high risk at CT or at NIPT, maternal age, known genetic or familiar condition, abnormal early ultrasound*
■ Second-trimester ultrasound screening	*For all pregnant women*

[15] In Italy, the National healthcare system (SSN) is public and organized under the Ministry of Health, but administered on a regional basis, so there are guidelines, but some items are decided regionally. SSN offers a screening programme for pregnancy free of charge, even if the mother or the specialist can decide to add more tests, at the mother's expense. Moreover, private structures, more prevalent in some regions, are accessible to carry out screening tests, but with partial or complete payment (information provided by expert via e-mail)

Country	Italy
Financing of prenatal screening/diagnostic tests	
Type of funding for the tests, criteria for full or partial public reimbursement	
■ First Trimester Screening/Combined Test	*Fully publicly reimbursed according to [35]**
■ NIPT	*Depending on the region, e.g., Emilia Romagna region offers NIPT to all pregnant women free of charge; in other regions, partially or completely self-paid*
■ Amniocentesis/chorionic villus sampling	*Fully publicly reimbursed for women with risk factors (mentioned above)*
■ Second-trimester ultrasound screening	*Fully publicly reimbursed*
Setting of prenatal screening/diagnostic tests	
Setting of tests/in hospitals or doctor's practices	
■ First Trimester Screening/Combined Test	*in hospitals (free of charge within the national healthcare system), doctor's practices and private clinics (fully self-paid)*
■ NIPT	*in hospitals (free of charge within the national healthcare system), doctor's practices and private clinics (fully self-paid)*
■ Amniocentesis/chorionic villus sampling	*in hospitals (free of charge within the national healthcare system), doctor's practices and private clinics (fully self-paid)*
■ Second-trimester ultrasound screening	*in hospitals (free of charge within the national healthcare system), doctor's practices and private clinics (fully self-paid)*
Data or estimates on uptake of the examinations	
■ First Trimester Screening/Combined Test	*90-95%*
■ NIPT	*15% (increase after recent introduction in the national healthcare system, even if on a regional basis)*
■ Amniocentesis/chorionic villus sampling	*1-2% (decrease after new national guidelines 2017)*
■ Second-trimester ultrasound screening	*95-98%*
Information on counselling	
Provision of counselling, involved professional groups, quality specifications and/or ethical standards	*Gynaecologists and midwives explain screening programmes and implications; if an abnormality is detected, other specialists are involved: geneticist, neonatologist, psychologist, paediatric surgeon, depending on the anomaly and the gestational age*

Sources: information provided in the questionnaire by 3 experts (in italic writing), [35, 53, 54]
** indicating differing information from the two experts*

List of contacted institutions

Table A-7: List of contacted EUROCAT representatives and medical societies from the 6 selected countries

Country
Germany
EUROCAT ■ Birth Registry Mainz Model [Geburtenregister Mainzer Model] ■ Malformation Monitoring Centre Saxony-Anhalt [Fehlbildungsmonitoring Sachsen-Anhalt]
Medical societies ■ German Society for Prenatal and Obstetric Medicine [Deutsche Gesellschaft für Pränatal- und Geburtsmedizin (DGPGM)] ■ German Society for Gynaecology and Obstetrics [Deutsche Gesellschaft für Gynäkologie und Geburtshilfe (DGGG)] ■ German Society for Ultrasound in Medicine [Deutsche Gesellschaft für Ultraschall in der Medizin (DEGUM)], Section Gynaecology and Obstetrics
Switzerland
EUROCAT ■ Swiss Registry, Department of Woman-Mother-Child, Lausanne
Medical societies ■ Swiss Society for Gynaecology and Obstetrics [Schweizerische Gesellschaft für Gynäkologie und Geburtshilfe (SGGG)] ■ Swiss Society for Ultrasound in Medicine [Schweizerische Gesellschaft für Ultraschall in der Medizin (SGUM)], Section Gynaecology and Obstetrics
Netherlands
EUROCAT ■ Eurocat Northern Netherlands, University of Groningen
Medical societies ■ Dutch Society for Obstetrics and Gynaecology [Nederlandse Vereniging voor Obstetrie & Gynaecologie (NVOG)]
United Kingdom
EUROCAT ■ National Congenital Anomaly and Rare Disease Registration Service ■ Regional Maternity Survey Office, Newcastle University
Medical societies ■ Royal College of Obstetricians and Gynaecologists (RCOG) ■ British Maternal & Fetal Medicine Society (BMFMS)
Norway
EUROCAT ■ Medical Birth Registry of Norway, Bergen
Medical societies ■ Norwegian Society for Gynecology and Obstetrics [Norsk gynekologisk Forening (NGF)] ■ Norwegian Perinatal Medical Association [Norsk Perinatalmedisinsk Forening (NPF)]
Italy
EUROCAT ■ Emilia Romagna Registry of Birth Defects ■ Registry of Congenital Anomalies in the Metropolitan Area of Milan ■ Unit of Epidemiology, Pisa, Tuscany
Medical societies ■ Italian Society for Gynaecology and Obstetrics [Società Italiana di Ginecologia e Ostetricia (SIGO)] ■ Italian Society for Perinatal Medicine [Società Italiana di Medicina Perinatale (SIMP)]

Questionnaire for expert consultation

Questionnaire for the project „Regulation and financing of prenatal screening and diagnostic examinations for fetal anomalies in selected European countries" (policy brief)

This questionnaire was prepared by the Austrian Institute for Health Technology Assessment (AIHTA) and serves as (supplementary) data collection for the policy brief commissioned by the Austrian Federal Ministry of Social Affairs, Health, Care and Consumer Protection on the topic of "*Regulation and financing of prenatal screening and diagnostic examinations for fetal anomalies in selected European countries*". The project aims to research and summarise the offer and financial framework of prenatal screening and diagnostic examinations for fetal anomalies in selected European countries. The project plan can be read here.
The following tests are relevant for this project:

- First Trimester Screening/Combined Test
- Non-invasive prenatal test (NIPT)
- Amniocentesis/chorionic villus sampling
- Second-trimester ultrasound screening for fetal anomalies

Thank you in advance for your willingness to participate in this survey!
If possible and available, please provide references/relevant literature sources.
If you have any questions, please contact Mag. Inanna Reinsperger, MPH, inanna.reinsperger@aihta.at.

Name: Click here to enter text.
Country: Click here to enter text.
Institution: Click here to enter text.

1. Is there a routine screening/preventive programme for all pregnant women in your country?
   - ☐ yes, name of the programme/website: Click here to enter text.
   - ☐ no

2. Are the above-listed prenatal screening/diagnostic examinations part of this routine screening/preventive programme? If yes, which?
   Click here to enter text.

3. Which of the following prenatal screening/diagnostic examinations are routinely offered to all pregnant women or women with certain risk factors in your country (*regardless of whether the test is part of the routine screening/preventive programme or not*)?

Type of test	All pregnant women/ with risk factors	Type of risk factors/criteria	Comments, resources, …
First Trimester Screening/Combined Test	☐ all pregnant women ☐ pregnant women with risk factors ☐ other criteria	Click here to enter text.	Click here to enter text.
Non-invasive Prenatal Test (NIPT)	☐ all pregnant women ☐ pregnant women with risk factors ☐ other criteria	Click here to enter text.	Click here to enter text.
Amniocentesis/chorionic villus sampling	☐ all pregnant women ☐ pregnant women with risk factors ☐ other criteria	Click here to enter text.	Click here to enter text.
Second-trimester ultrasound screening for fetal anomalies	☐ all pregnant women ☐ pregnant women with risk factors ☐ other criteria	Click here to enter text.	Click here to enter text.

4. How are the costs for the following prenatal screening/diagnostic examinations covered? What are the criteria for full or partial public reimbursement (e.g. certain indications, risk factors, other criteria [e.g. low-income families])?

Type of test	Type of funding	Criteria for full or partial public funding	Comments, resources, …
First Trimester Screening/Combined Test	☐ fully publicly reimbursed ☐ partially publicly reimbursed/ co-payment (private/public) ☐ completely self-paid	Click here to enter text.	Click here to enter text.
Non-invasive Prenatal Test (NIPT)	☐ fully publicly reimbursed ☐ partially publicly reimbursed/ co-payment (private/public) ☐ completely self-paid	Click here to enter text.	Click here to enter text.
Amniocentesis/chorionic villus sampling	☐ fully publicly reimbursed ☐ partially publicly reimbursed/ co-payment (private/public) ☐ completely self-paid	Click here to enter text.	Click here to enter text.
Second-trimester ultrasound screening for fetal anomalies	☐ fully publicly reimbursed ☐ partially publicly reimbursed/ co-payment (private/public) ☐ completely self-paid	Click here to enter text.	Click here to enter text.

5. Where are the following prenatal screening and diagnostic tests carried out (e.g., hospital, doctor's practices)?

Type of test	Setting	Comments, resources, …
First Trimester Screening/ Combined Test	☐ in hospitals ☐ in doctor's practices ☐ other: Click here to enter text.	Click here to enter text.
Non-invasive Prenatal Test (NIPT)	☐ in hospitals ☐ in doctor's practices ☐ other: Click here to enter text.	Click here to enter text.
Amniocentesis/chorionic villus sampling	☐ in hospitals ☐ in doctor's practices ☐ other: Click here to enter text.	Click here to enter text.
Second-trimester ultrasound screening for fetal anomalies	☐ in hospitals ☐ in doctor's practices ☐ other: Click here to enter text.	Click here to enter text.

6. Are you aware of data or estimates from your country on the percentage of pregnant women who make use of the following examinations?

Type of test	Percentage of pregnant women	Comments, resources, …
First Trimester Screening/Combined Test	Click here to enter text.	Click here to enter text.
Non-invasive Prenatal Test (NIPT)	Click here to enter text.	Click here to enter text.
Amniocentesis/chorionic villus sampling	Click here to enter text.	Click here to enter text.
Second-trimester ultrasound screening for fetal anomalies	Click here to enter text.	Click here to enter text.

7. How is counselling provided in connection with prenatal diagnostics
   (before the respective examination, or in the case of an "abnormal" test result)?
   Which professional groups carry out the counselling?
   Are there quality specifications and/or ethical standards in this context?

   Click here to enter text.

8. Space for further comments, references, etc.:

   Click here to enter text.

Thank you very much for your participation!

Contact:
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Austrian Institute for
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