

**Processes of Technology
Diffusion and
Implementation Around
Prenatal Screening in
Europe**



Jane Sandall, King's College, London
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Social and Organisational Implications of One Stop First Trimester Prenatal Screening

Jane Sandall

King's College,

Gillian Lewando-Hundt

Warwick University

Bob Heyman

City University

Kevin Spencer

Harold Wood NHS Trust

Clare Williams

King's College

Laura Pitson

King's College

Maria Tsouroufli

Warwick University

Rachel Grellier

Warwick University

Downs Syndrome in Europe

Analysis of data from 24 EUROCAT registries, covering 8.3 million births 1980-99.

Since 1980, the proportion of births to mothers of 35 years of age and over has risen.

By 1995-99, the proportion of "older" mothers varied between regions from 10% to 25%, and the total prevalence (including terminations of pregnancy) of Down Syndrome varied from 1 to 3 per 1,000 births.

The proportion of cases of Down Syndrome which were prenatally diagnosed followed by termination of pregnancy in 1995-99 varied from 0% - 77%.

European Screening Policy

Country	1st	2nd	PND	TOP
Croatia Funding not stated	NT+Blood	Triple	>35, father >45	yes
Denmark 2005	NT+Blood	?Triple	High risk, FH, >35	yes
France	All NT Free	Bio	High risk, FH, >38 Free	yes
Germany	NT Pay	Triple	>35 Free	yes
Ireland	No	On request Pay	On request Pay	no
Netherlands	NT Free > 36	Triple Free over 36	High risk, FH, >36 Free	yes
Norway	USS > 38 Free		>38, FH Free	yes
Sweden	None		>35, FH Free	yes
Switzerland	All Blood + NT Free	Blood NTD	High risk, >35, FH Free	yes
UK 2004	All Blood + NT	Blood	High risk, >35, FH Free	yes

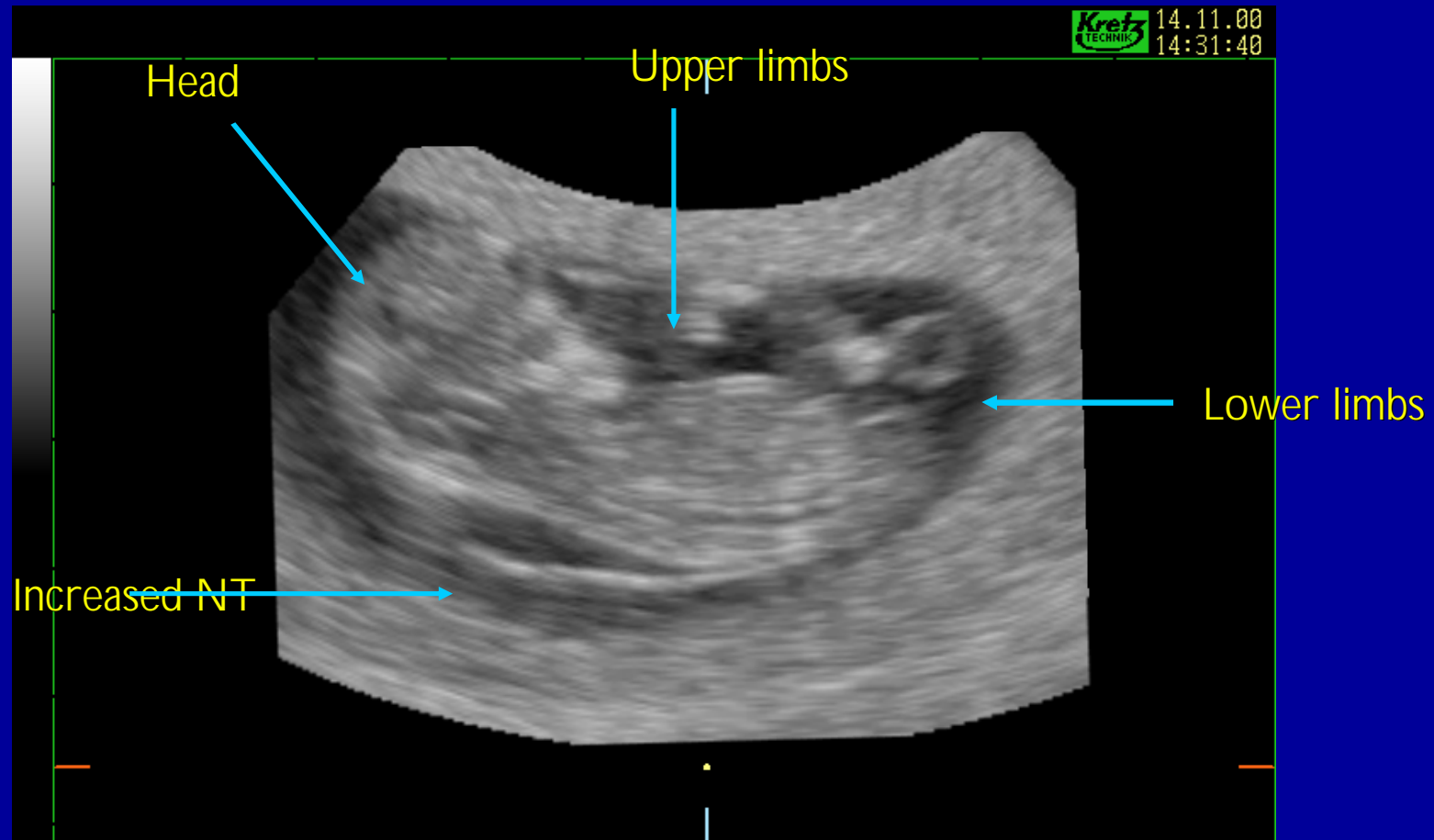
Prenatal Screening Policies in Europe, Eurocat 2005

UK National Policy

'The aim of screening for fetal anomalies is to identify specific structural malformations. This allows the parents to plan appropriate care during pregnancy and childbirth or for the parents to be offered other reproductive choices.... The woman's right to accept or decline the test should be made clear'

Antenatal Care: Routine care for the healthy pregnant woman, NICE October 2003

Prenatal Screening Practice in UK



Broader Issues

- Whether/how women make selective use of technologies
- Inequalities of access
- Broader ethical and public policy implications
- Women's understanding of risk language
- Routinisation and informed decision-making
- Raising anxiety

New Issues Raised by 1st Trimester Prenatal Screening

Offered to all women rather than those at risk

Requires redesign of care to ensure informed consent

Creates uncertainty rather than certainty

Benefits

- Avoids PND in older women unless necessary thus reduce risk of fetal loss
- Increases equity of access when offered to all women

Should provide an informed choice to all women

Harms

- 5% women will screen high risk of whom 5% true positive thus risk of raised anxiety and fetal loss with PND
- Routine offer may reduce ability to opt out
- Negative message to society re DS

Prenatal Screening Technology Assessment in UK

Trials

Reviews

Implementation and organisational
studies

Acceptability

Economic

Project Aims to Improve Understanding Of:

- Impact of new screening technologies on social management of pregnancy, service delivery and professional roles
- Participants broader responses to new reproductive technologies, and views about routinisation of screening
- Perceptions of self, the fetus, and of management of reproductive risk
- Lay and professional understanding of complex information, and influences on decision-making

Design

- Antenatal and postnatal survey of 993 and 656 women respectively
- Observation of 45 clinic sessions in hospital and community
- Interviews with 24 health professionals and a cohort of 27 women and some partners on a range of screening pathways
- Analysis of 90 audio-taped consultations

Research Setting

Two sites

Innovative one stop – one of few NHS sites in UK

First trimester screening at a one-stop clinic at 12-13 weeks, NT ultrasound scan and blood test and result within 1 hour

Standard two stop

Second trimester screening at 15-20 weeks, result back within 1 week

Spencer et al (2003)BJOG,110:281-6.

OSCAR - A 1st Trimester One Stop Clinic for Assessment of Risk for fetal anomalies

- One stop clinics have developed over the past decade in several clinical areas ranging from breast cancer screening, menopausal clinics, oncology assessment, cardiovascular risk clinics and one stop surgical clinics.
- These services all have in common the integration of a range of clinical and diagnostic services that allow for a better use of clinical time and improved diagnostic efficiency.
- They aim to maximise patient satisfaction by reducing the number of patient visits; minimising patient travel costs, anxiety and stress

Point-of-Care screening for Chromosomal Anomalies in the First Trimester of Pregnancy.
Spencer K, Clin Chem 2002; 48: 403-404

Evidence & Innovations Leading to Development of OSCAR

- Ultrasound markers of chromosomal anomalies - fetal nuchal translucency thickness at 11-14 weeks.
- Maternal serum Biochemical markers of chromosomal anomalies - free b-hCG & PAPP-A at 10-14 weeks.
- Development of new rapid assay technology for biochemical marker measurement leading to Point of Care testing.

Kryptor Analyser

Nobel Prize winning chemistry

- **Small bench top analyser - clinic based**
- **Rapid assay times (19 mins)**
- Kinetic reading - leading to automatic rediluting of high samples within 4 minutes
- **Precise** - cv less than 3% between day
- **Continuous sample access** - stat capability
- Small sample (<50ul) and reagent (<150ul) volumes.
- **User friendly**
- **Other manufacturers now developing POC systems for Prenatal Screening.**

Jean-Marie Lehn; Nobel Laureate in Chemistry 1987

Point of Care 1st Trimester Platforms

Kryptor



access
for

Delfia Express

Key Milestones in the Development of OSCAR

- 1987 - Jean-Marie Lehn becomes Nobel Laureate in Chemistry for the development of the caged Kryptate molecules used in the Kryptor TRACE technology.
- 1988 – CIS (French Company) part fund the Down's Screening Research program of Dr Spencer.
- 1988 – CIS licences the Kryptate technology with the view to developing a new immunoassay analyser system.
- 1991 – Free β -hCG identified as a Second Trimester Down's marker by Dr Spencer

Key Milestones in the Development of OSCAR

- 1991- PAPP-A identified as a potential First Trimester Down's marker by Dr Brambati.
- 1991 - BHR Hospitals introduce early (12wk) dating scan with early GP referral.
- 1992 – Nuchal Translucency identified as a potential First Trimester Down's marker by Kypros Nicolaides.
- 1992 – Free β -hCG identified as a potential First Trimester Down's marker by Dr Spencer.
- 1993 – Early prototype and concept of Kryptor first discussed.

Key Milestones in the Development of OSCAR

- 1994 – First studies indicating clinical effectiveness of PAPP-A & Free β -hCG as a First Trimester marker – Dr Spencer.
- 1995 – Fetal Medicine Foundation (FMF) set up by Kypros Nicolaides to promote training, certification and audit of NT measurement.
- 1995 – OSCAR concept conceived by Dr Spencer.
- 1995 – Kryptor development program begun for Free β -hCG and PAPP-A
- 1995/6 – First studies combining NT with Free β -hCG – Nicolaides & Spencer

Key Milestones in the Development of OSCAR

- 1996 – FMF multicentre prospective NT study starts – BHR a participating centre.
- 1996/7 - First retrospective clinical studies performed using Kryptor combining biochemistry & NT in BHR.
- 1997 – Business case presented to BHR Trust to set up OSCAR clinic.
- 1998 – Approval for OSCAR, live 1st June 1998.
- 1999 – Second OSCAR centre set up in Harley Street.
- 1999 – CIS announces a stop to the Kryptor development program unless a buyer is found for its Immunodiagnostics business.

Key Milestones in the Development of OSCAR

- 2000 – Brahms of Germany takes over the marketing of Kryptor. CIS R&D facility makes management buy out enabling production and development of Kryptor to continue in a new company (Cezanne) part owned by Brahms.
- 2004 – PerkinElmer launches a ME2 Kryptor platform aimed at Point of Care testing for Down's screening.
- 2005 – Over 250 Kryptor systems placed World Wide, 70% involved in Prenatal Screening.
- 2005 – Some 20 OSCAR clinics established World Wide.



The Fetal
Medicine Foundation

Third World Congress in Fetal Medicine 20-21 June 2004 - Limassol

- Downs screening at 11-14 weeks
- Diploma in fetal medicine
- World congress
- Research & developments
- Training courses
- Certificates of competence
- Books
- FMF news update



The Fetal Medicine Foundation is a Registered Charity that promotes research and training in fetal medicine.



FMF QUALITY SYSTEM

NT	BIOCHEM	SOFTWARE
STANDARD	STANDARD	STANDARD
TRAINING	APPROVED SYSTEMS	USES FMF ALGORITHM
ASSESSMENT	EQA	APPROVED SYSTEMS
CERTIFICATION	LAB CERTIFICATION	LINKED TO CERTIFICATION
ONGOING AUDIT	ONGOING AUDIT	AUDIT & UPDATE

Processes of technology innovation

Limits to evidence

Impact of professionals

Networks and networking

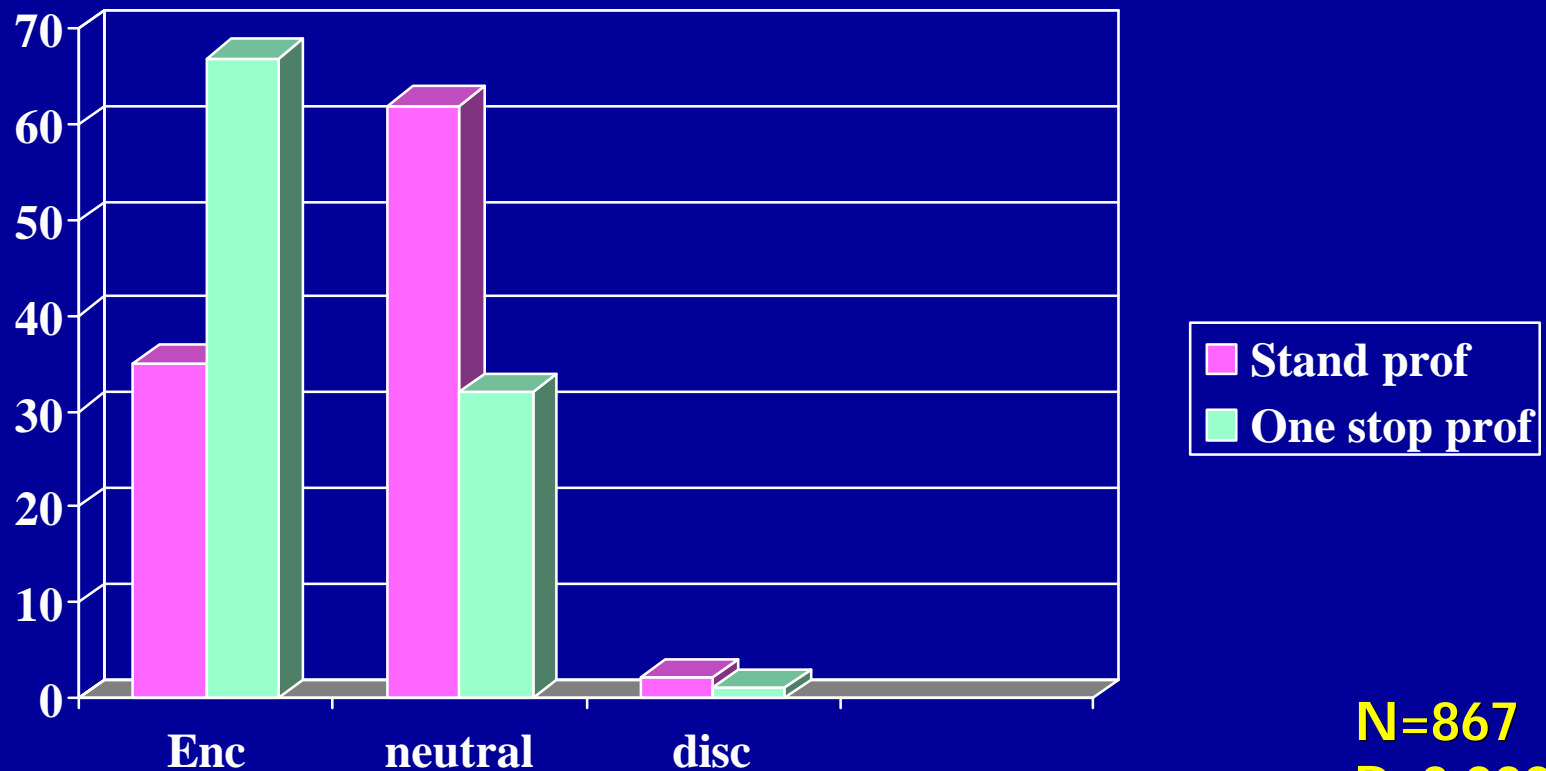
Communities of practice

Funding system

Consumer agency

Professional influence

What was the attitude of doctors and midwives to you having a screening test for Down's syndrome?



N=867
P=0.000

What do women value?

Most women in both sites said fast results and knowing results early were very important

75% of all women were prepared to pay for earlier screening in a future pregnancy

79% of women said that combined screening at about 12 weeks was their option

55% of women had decided whether or not to have screening before being offered any

Technology, Routinisation and Informed decision-making

19% women said screening not fully discussed

DS as a condition and post screening options rarely discussed

27 % women in IHT site never made up mind and went along with offer

45% women in IHT site offered as part of routine care and it was assumed that they would accept

67% women in IHT site reported professionals encouraging

Implications

Pathways from innovation to national policy

Funding counts

Gaps in technology assessment

Importance of professional attitudes in the clinic

Influence of user demand

Investigating unintended consequences at implementation phase

Ignore organisation and delivery of IHT at your peril!

Dissemination

On Being At Higher Risk: A Qualitative Study Of Prenatal Screening For Chromosomal Anomalies, Heyman, B. Lewando-Hundt, G. Sandall, J. Spencer, K. Williams, C. under review *Social Science and Medicine*.

Women as 'moral pioneers'?: experiences of first trimester antenatal screening', Williams, C. Sandall, J. Lewando Hundt, G. Grellier, R. Heyman, B, Spencer, K. in press *Social Science and Medicine*

Constraints on informed choice in a one-stop first trimester prenatal screening for Down's syndrome: a cross-sectional survey of women's experiences, Sandall, J. Pitson, L. Williams, C. Lewando Hundt, G., Heyman, B. Spencer, K. under review *BJOG*

Wellcome People Production Award, Social, ethical and cultural impacts of genetic prenatal screening technologies on experience and personhood: synthesising Biochemistry and Ultrasound technologies with Live Performance, Visual and Aural Media.

http://www.kcl.ac.uk/nmvc/research/project/moreinfo.php?id=11&the_group=1