The Danish PNS program

Including NIPT - but not yet PE

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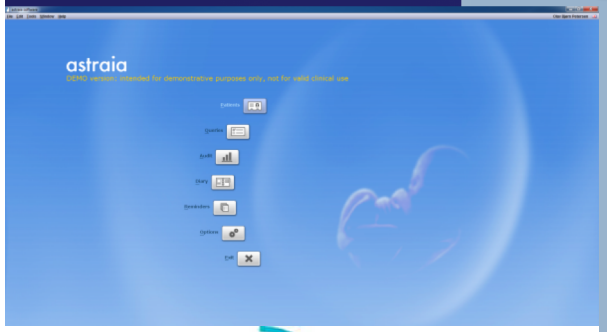
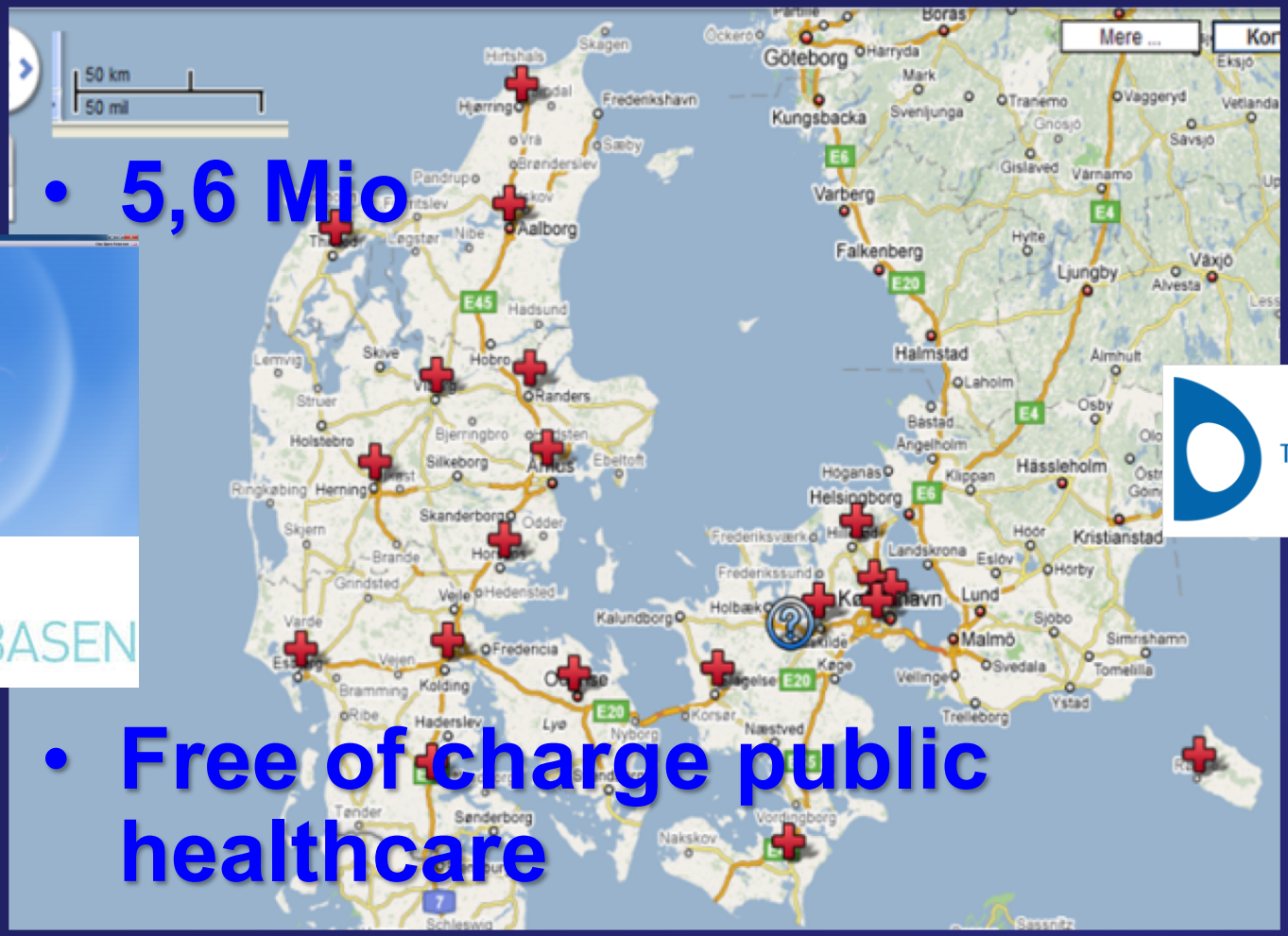
Danish prenatal healthcare



FØTO DATABASEN



- 5,6 Mio
- Free of charge public healthcare

The Fetal Medicine Foundation

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National guideline 2004
Updated 2017

RETNINGSLINJER FOR
FOSTERDIAGNOSTIK

- prænatal information, risikovurdering, rådgivning og diagnostik

2004

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Danish PNS 2018 - purpose

- A better start for the child with special needs:
  - The professionals can be prepared – ”born at the right place, with the right people available at - and after delivery”
  - The parents can be prepared for a child with special needs
- NOT specific Down Syndrome screening

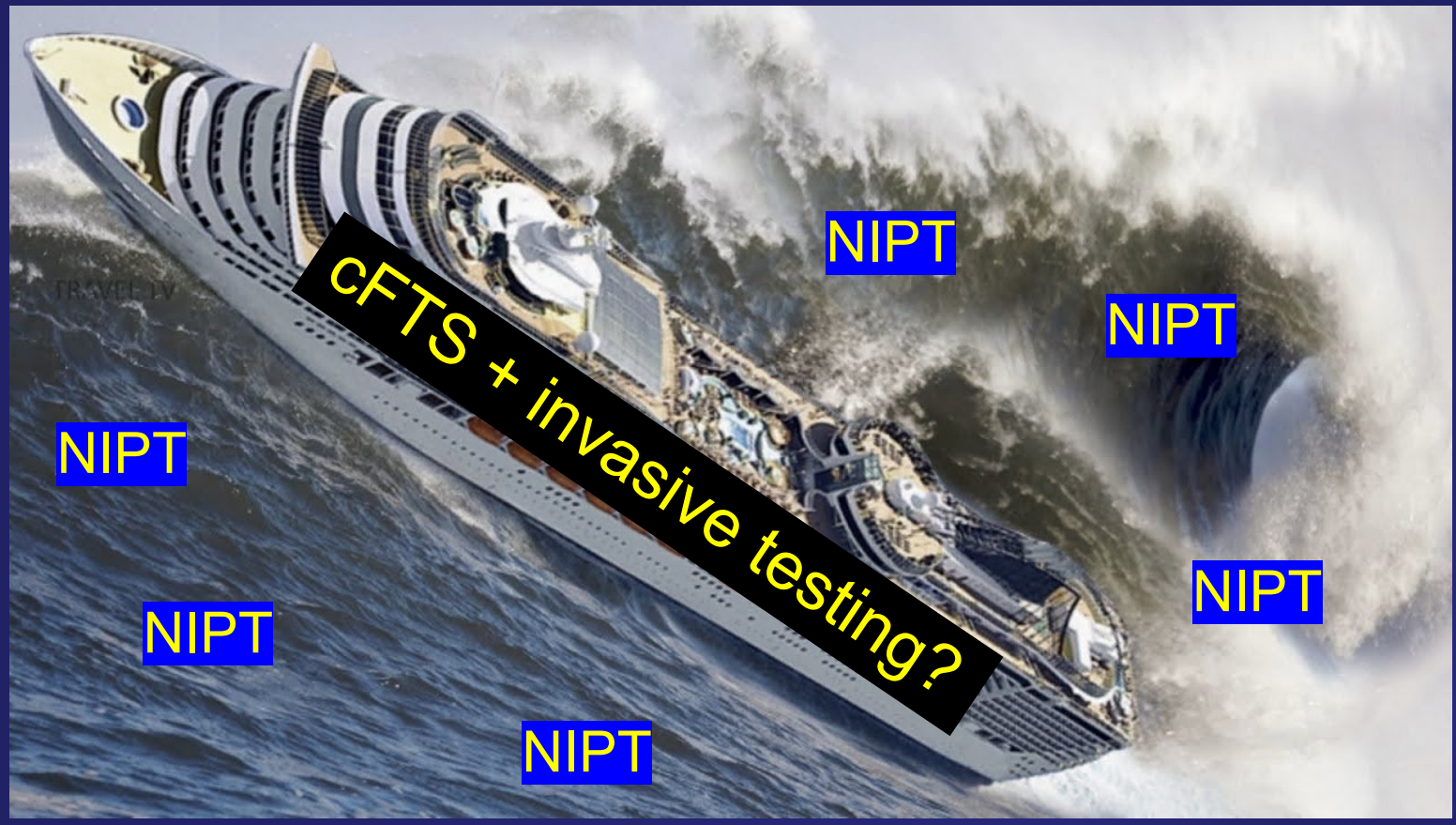
Danish PNS 2018 - Context

- Support reproductive autonomy:
  - Support couples decisions in agreement with their belief, culture and ethics
  - Continuing pregnancy or TOP are equal alternatives in case of severe disease

Danish PNS 2018 - Context

- Free of charge offer to all women of:
  - 1st Trimester scan
  - Risk assessment for chromosomal anomalies
  - 2nd Trimester scan

The NIPT wave?



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Atypical abnormal chromosomal anomalies – important?

Does atypicals matters?

Original Research

Chromosome Abnormalities Detected by Current Prenatal Screening and Noninvasive Prenatal Testing

(Obstet Gynecol 2014;124:979–86)
DOI: 10.1097/AOG.0000000000000452

Mary E. Norton, MD, Laura L. Jelliffe-Pawlowski, PhD, and Robert J. Currier, PhD

- 17% atypical likely missed by NIPT

Ultrasound Obstet Gynecol 2014; 43: 265–271
Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/uog.13270

Potential diagnostic consequences of applying non-invasive prenatal testing: population-based study from a country with existing first-trimester screening

O. B. PETERSEN*#, I. VOGEL†#, C. EKELUND‡, J. HYETT§, A. TABOR ‡, the Danish Fetal Medicine Study Group and the Danish Clinical Genetics Study Group

- 23% atypical likely missed by NIPT
- Prevalence atypical:
  - Total population: 0.14%
  - PAPP-A<0,2 MoM= 4.2%
  - Free ß-hCG<0,2 MoM=7.1%
  - Free ß-hCG >5 MoM=0.5%

Does atypicals matters?

Ultrasound Obstet Gynecol 2018; 51: 487–492
Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/uog.18979

Prenatal diagnostic testing and atypical chromosome abnormalities following combined first-trimester screening: implications for contingent models of non-invasive prenatal testing

A. LINDQUIST[1,2,3], A. POULTON[1], J. HALLIDAY[1,4] and L. HUI[1,2,3]

Prevalence atypical:

- PAPP-A<0.2 MoM= 6.9%
- Free ß-hCG <0.2 MoM=5.2%

Does atypicals matters?

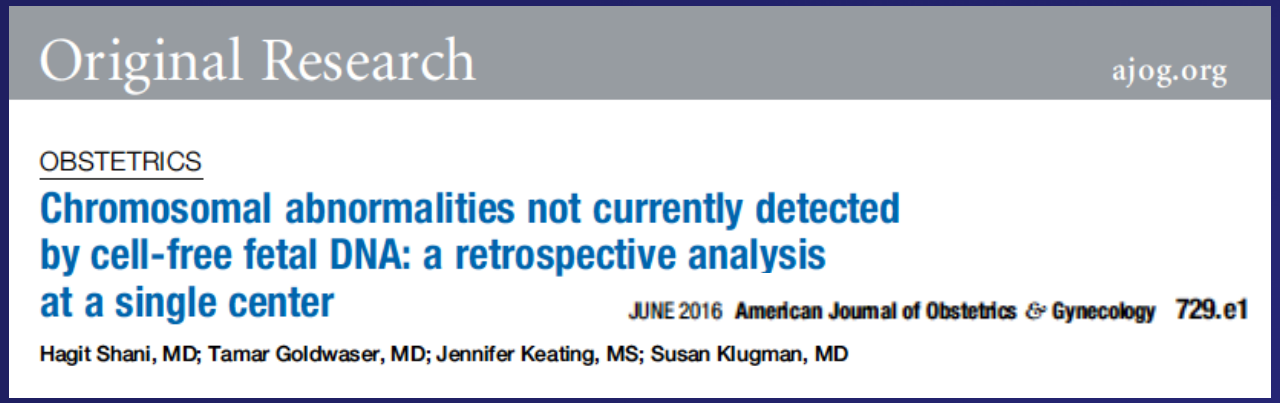
Ultrasound Obstet Gynecol 2018; **51**: 445–452
Published online in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.17533

Frequency of submicroscopic chromosomal aberrations in pregnancies without increased risk for structural chromosomal aberrations: systematic review and meta-analysis

M. I. SREBNIAK[1], M. JOOSTEN[1], M. F. C. M. KNAPEN[2,3], L. R. ARENDS[4,5], M. POLAK[4], S. VAN VEEN[1], A. T. J. I. GO[2] and D. VAN OPSTAL[1]

MA (years)	*Risk for Down syndrome (Hook et al.[5], minimal prevalence)*	*Risk for clinically relevant microscopic chromosomal aberrations (Hook et al.[5])*	*Risk for pathogenic submicroscopic aberrations associated with syndromic early-onset disorders (this review)*	*Risk for all chromosomal aberrations (both microscopic and submicroscopic)*
20	1:2000	1:555	1:270	1:179
30	1:1111	1:384	1:270	1:159
35	1:400	1:178	1:270	1:108
40	1:117	1:63	1:270	1:51
45	1:35	1:19	1:270	1:17

Does testtype matters?



Original Research ajog.org

OBSTETRICS

Chromosomal abnormalities not currently detected by cell-free fetal DNA: a retrospective analysis at a single center

JUNE 2016 American Journal of Obstetrics & Gynecology 729.e1

Hagit Shani, MD; Tamar Goldwaser, MD; Jennifer Keating, MS; Susan Klugman, MD

- 45% atypical likely missed by NIPT

Danish PNS 2018

GP *informs* about the prenatal program

- + Double test (w 9-10)
- + Referral for 1st Trim ULS
  - CRL/EDD + gross anomalies
  - +/- cFTS risk assessment

- + 2nd trim ULS

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@ cFTS high risk

- T21 risk >1:300
- T18/13 risk >1:150
- Offered
  - Invasive test (CVS), or
  - NIPT (as non-equal screening test)

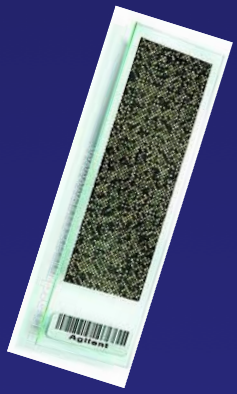
@ cFTS high risk (new)

- *Single factors*:
  - NT ≥ 3.5 mm, or
  - Free β-hCG ≥ 5 MoM, or
  - Free β-hCG or PAPP-A < 0.2 MoM, or
  - Maternal age ≥ 45 year
- Offered invasive test (CVS) with CMA
  - Or NIPT as a non-equal option

National guideline on CMA

CMA recommended as the first line prenatal invasive genetic analysis

- Unless..
- PCR?



FØTO-Sandbjerg guideline 2018

Titel
Prænatal kromosom mikroarray analyse (CMA)

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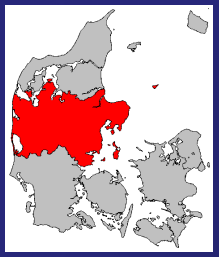
Results, 1 year experience

”Isolated” T21 Risk > 1:300, n=575

Ultrasound Obstet Gynecol 2018
Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/uog.17548

Chromosomal microarray as primary diagnostic genomic tool for pregnancies at increased risk within a population-based combined first-trimester screening program

I. VOGEL[1,2,3], O. B. PETERSEN[2,4], R. CHRISTENSEN[1,3], J. HYETT[5], S. LOU[2,6] and E. M. VESTERGAARD[1,2,3]



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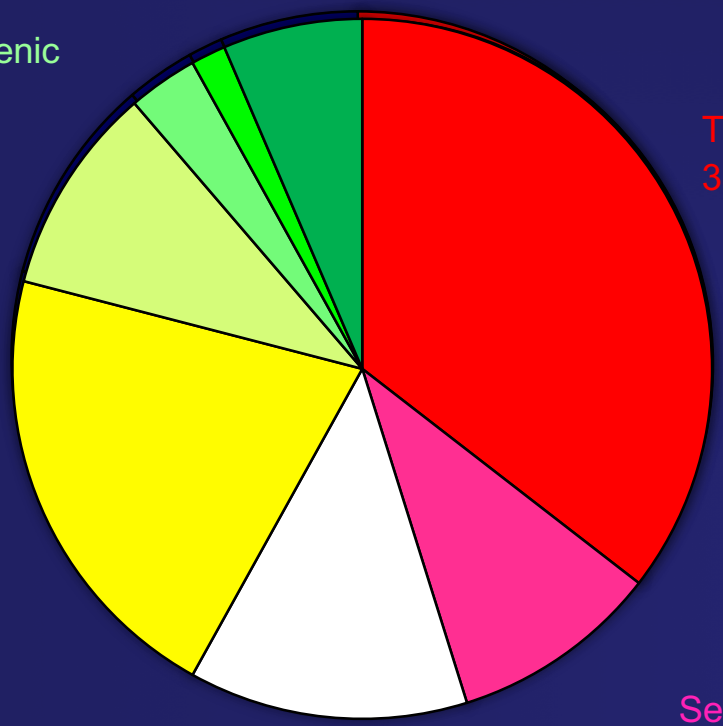
51 Abnormal using CMA

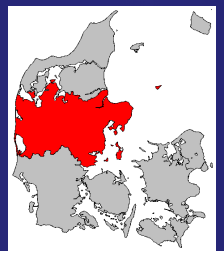


T21 Risk > 1:300, n=575

180k array-CGH

Detectable also by

- NIPT
- Cytogenetic karyotype
- CMA



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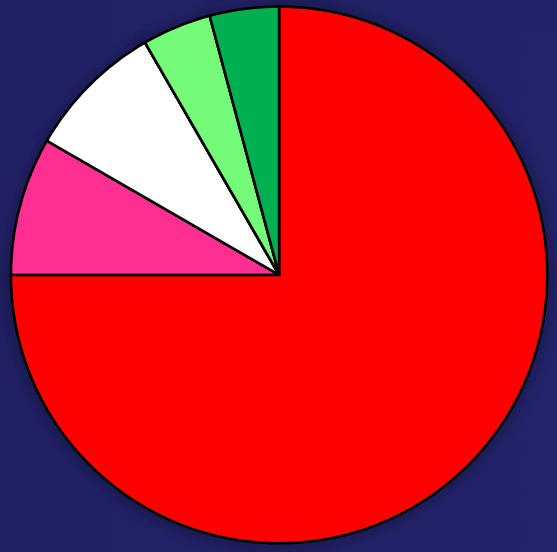
Distribution of abnormal CMA's

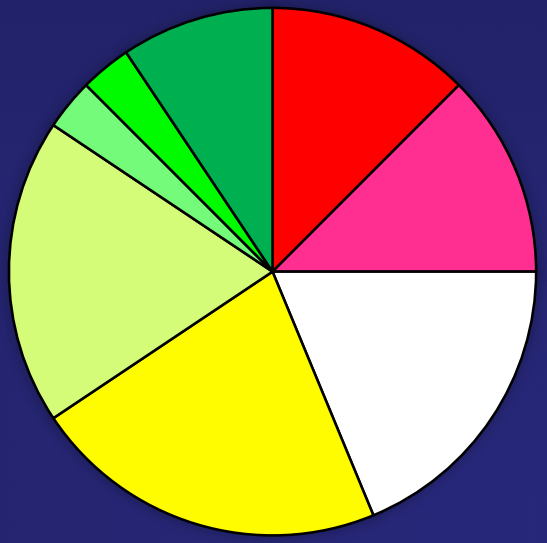
T21 Risk > 1:300, n=575

Risk > 1:50,
N=23



•**NIPT could detect 87%**

Risk 1:50-1:300
N=28



•**NIPT could detect 28%**

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Contingency: CVS only >1:50 +NIPT 1:50 to 1:300??

Would have missed 93% of the pathogenic, susceptibility and likely pathogenic CNVs

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1st trimester screening for PE in DK?

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Screening for pre-eclampsia in the first trimester

A Danish Multicenter Study

- Purpose:
  - To examine the performance of screening for pre-eclampsia in the first trimester of pregnancy in an unselected Danish population
  - To evaluate the attitude among pregnant women towards this screening

Screening for pre-eclampsia in the first trimester

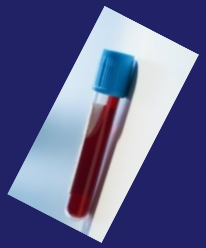
A Danish Multicenter Study

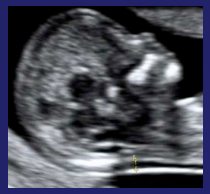
- Method:
  - We plan to include 8300 pregnant women in five University Hospitals
  - 300 women will be invited to participate in a questionnaire study

Screening for pre-eclampsia in the first trimester

A Danish Multicenter Study

•Current cFTS



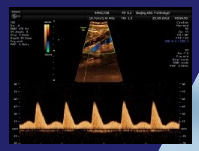


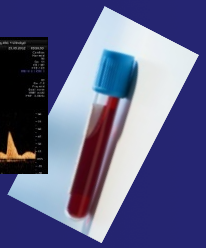
•week 9 •week 12 •week 40

•Risk assessment calculation

•+/- PE

•+ PE screening





•Inclusion starts in 2019

•9 month inclusion period

•Results in 2020

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Conclusion

cFTS identifies (a proportion of) women @ risk of atypical chromosomal anomalies

Increased diagnostic yield by CVS+CMA

1st Trim screening for PE: Awaiting DK validation study

Thanks

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Charlotte Ekelund
Karin Sundberg

And many more!!

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