提問回答補充

1. NIPS偽陰性比率為0.02-0.26%
2. DiGeroge syndrome的發生率1/3000-6000
3. 抗凝血劑會造成fetal fraction降低，intermediate risk上升，但Aspirin的影響較小 (2024 AJOG Raj Shree et al)

早孕期進階檢查

非侵入性產前染色體基因檢查 NIPS篇

2024/04/14 台中榮總婦女醫學部 林俐伶

台灣婦產科醫學會「產前進階照護 」 教育訓練課程


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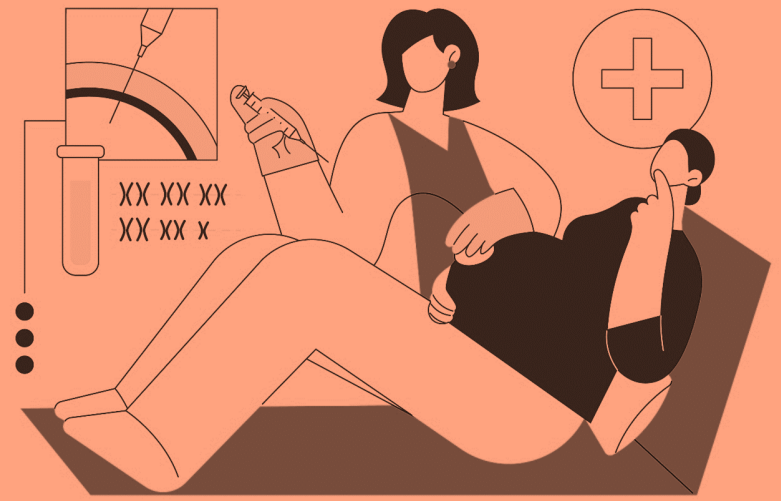
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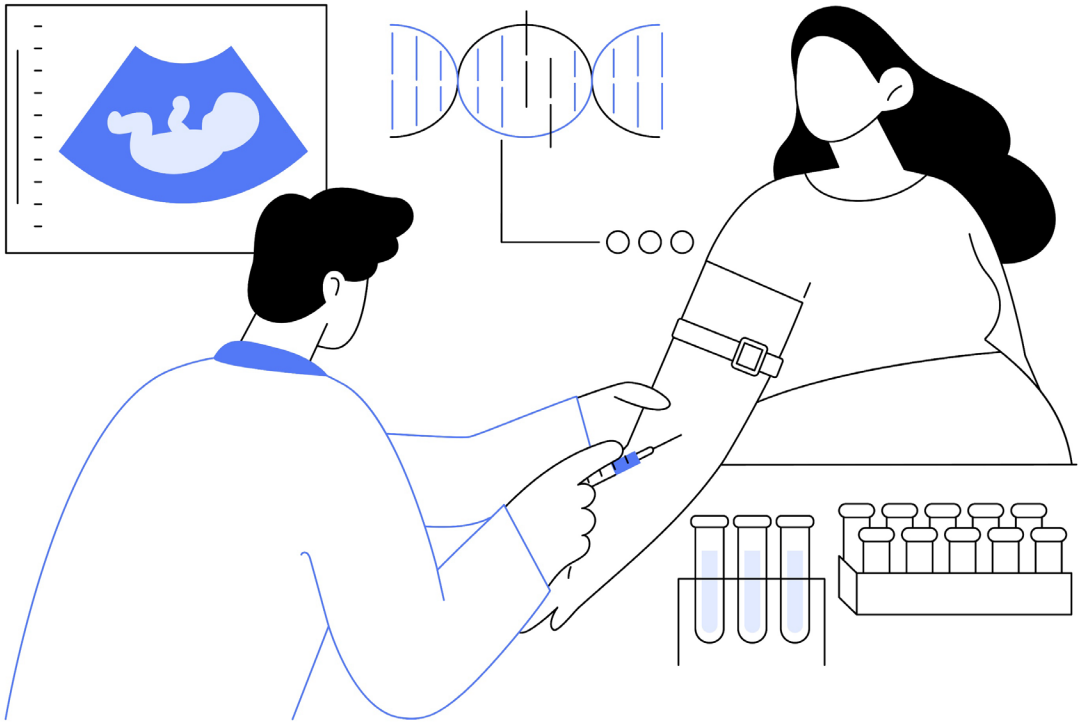
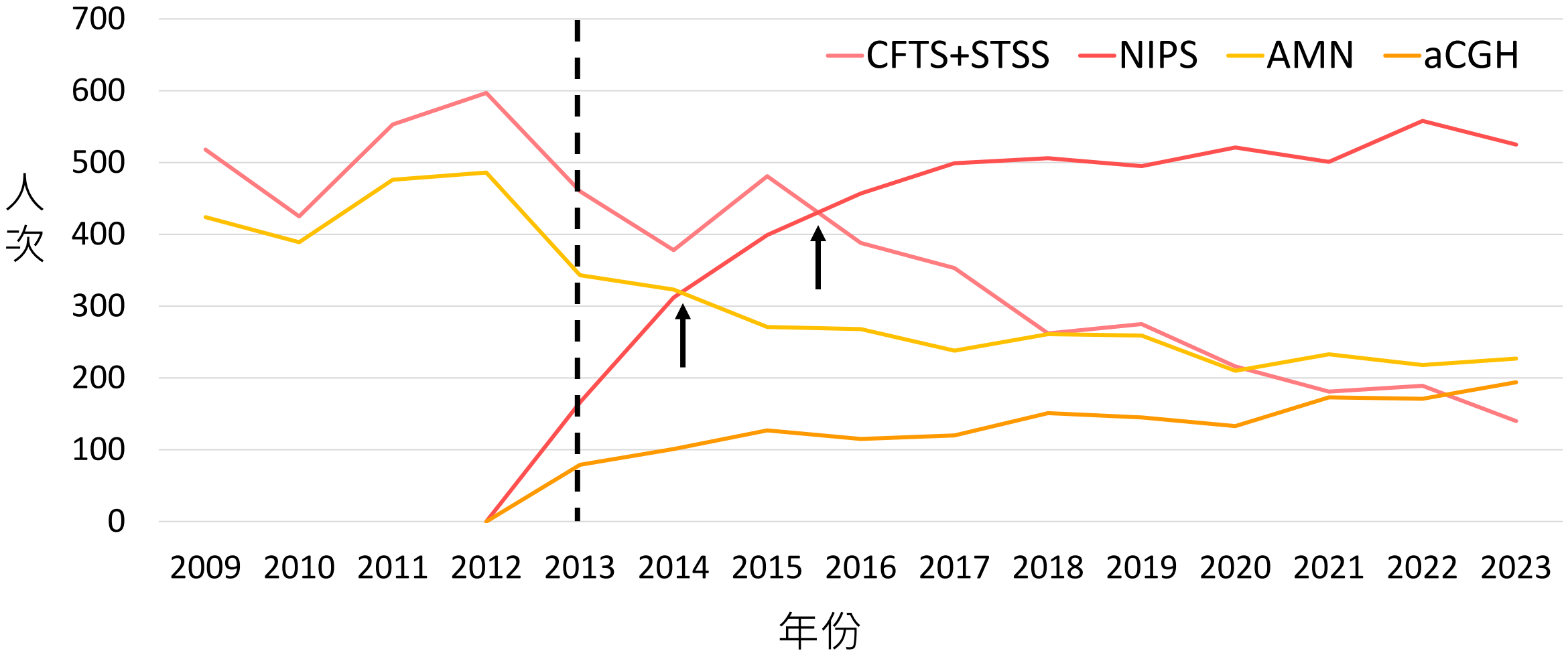


The impact of NIPS

台中榮總 產前篩檢與診斷工具使用概況



TCVGH data

OBSTETRICS

Impact of noninvasive prenatal testing in regionally dispersed medical centers in the United States

Lawrence D. Platt, MD; Mary Beth Janicki, MD; Tracy Prosen, MD; James D. Goldberg, MD; Joseph Adashek, MD; Reinaldo Figueroa, MD; John Rodis, MD; Wayne Liao, PhD; Amy J. Sehnert, MD; Holly L. Snyder, MS; Steven L. Warsof, MD

TABLE 4

Annual invasive testing volume prior to and after introduction of NIPT

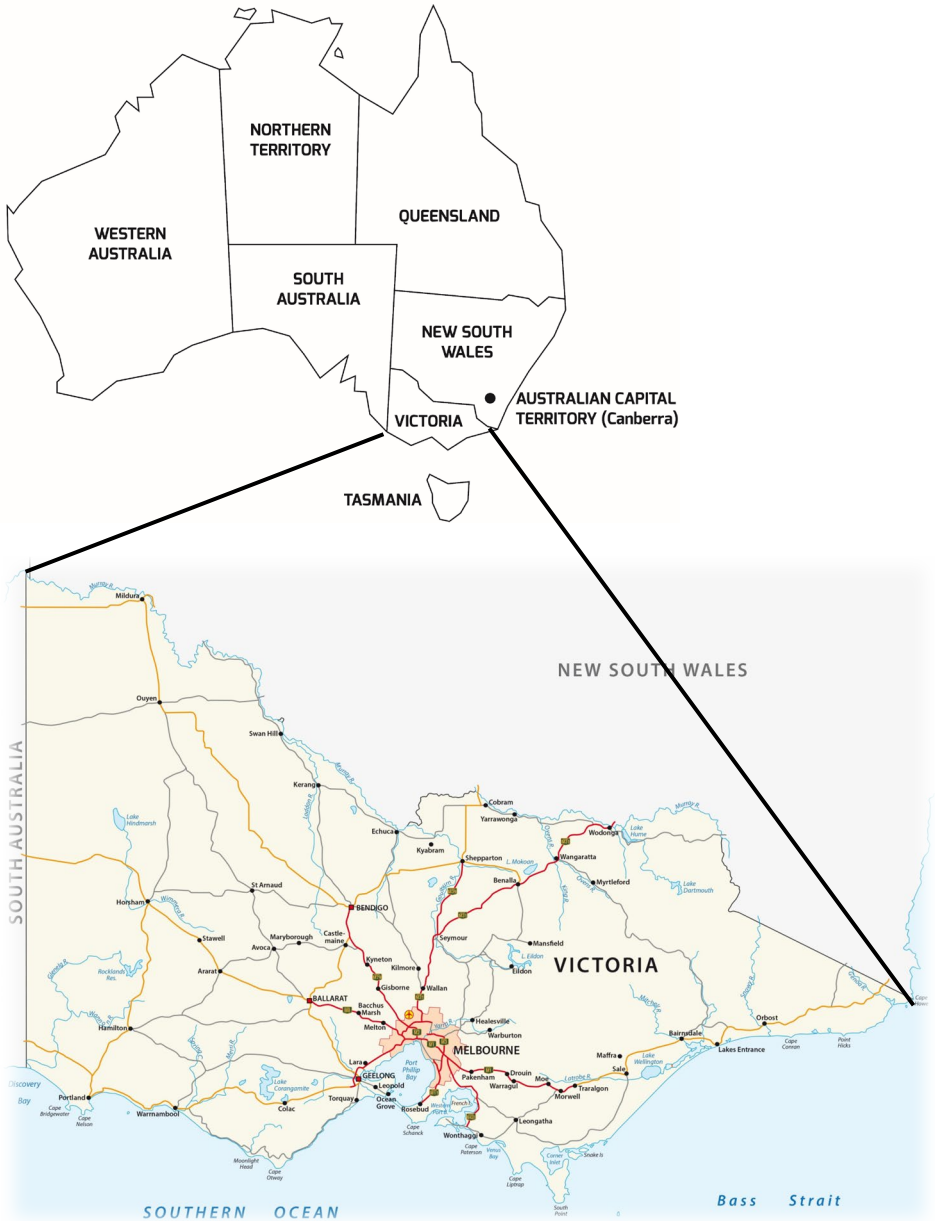
Site	Amnio rates prior to NIPT, n/year	Amnio rates after NIPT, n/year	Percent change, %	CVS rates prior to NIPT n/year	CVS rates after NIPT n/year	Percent change
West	1034	764	−26.1	1064	798	−25.0
A[a]	216	165	−23.6	33	16	−51.5
B[b]	367	280	−23.7	750	541	−27.9
C[a]	451	319	−29.3	281	241	−14.2
East	292	161	−44.9	89	43	−51.6
D[b]	82	41	−50.0	19	19	0.0
F[a]	210	120	−42.9	70	24	−65.7
Midwest	205	149	−27.3	120	120	0.0
E[c]	205	149	−27.3	120	120	0.0

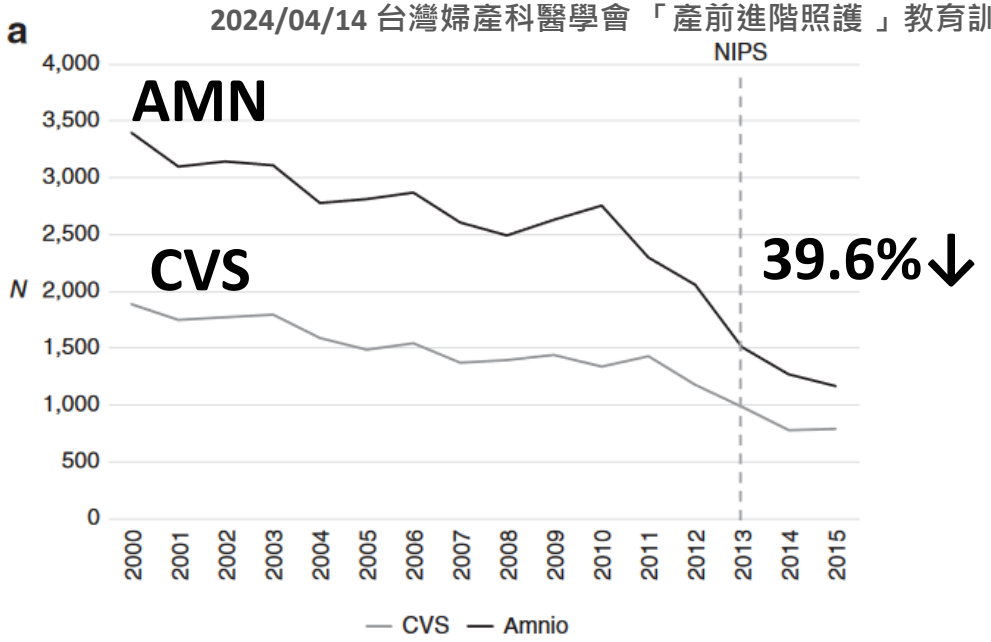
CVS, chorionic villus sampling; *NIPT*, noninvasive prenatal testing.

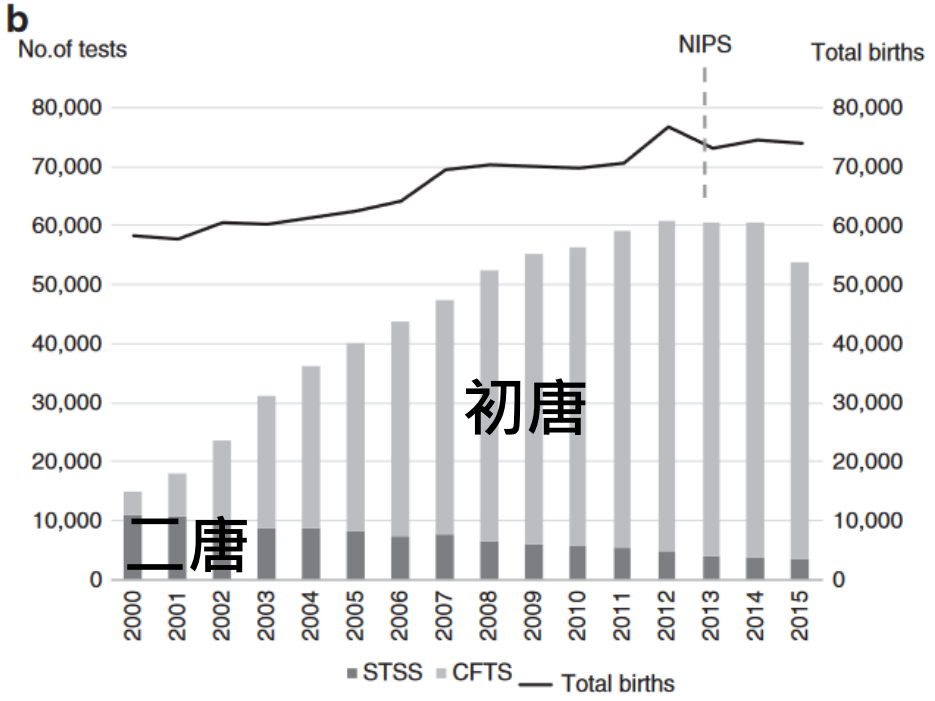
[a] Data based on billing statistics; [b] Data based on internal physician database; [c] Data based on sample accessioning from internal cytogenetics laboratory for all prenatal diagnosis samples.

Platt. Noninvasive prenatal testing, regionally dispersed implementation. Am J Obstet Gynecol 2014.

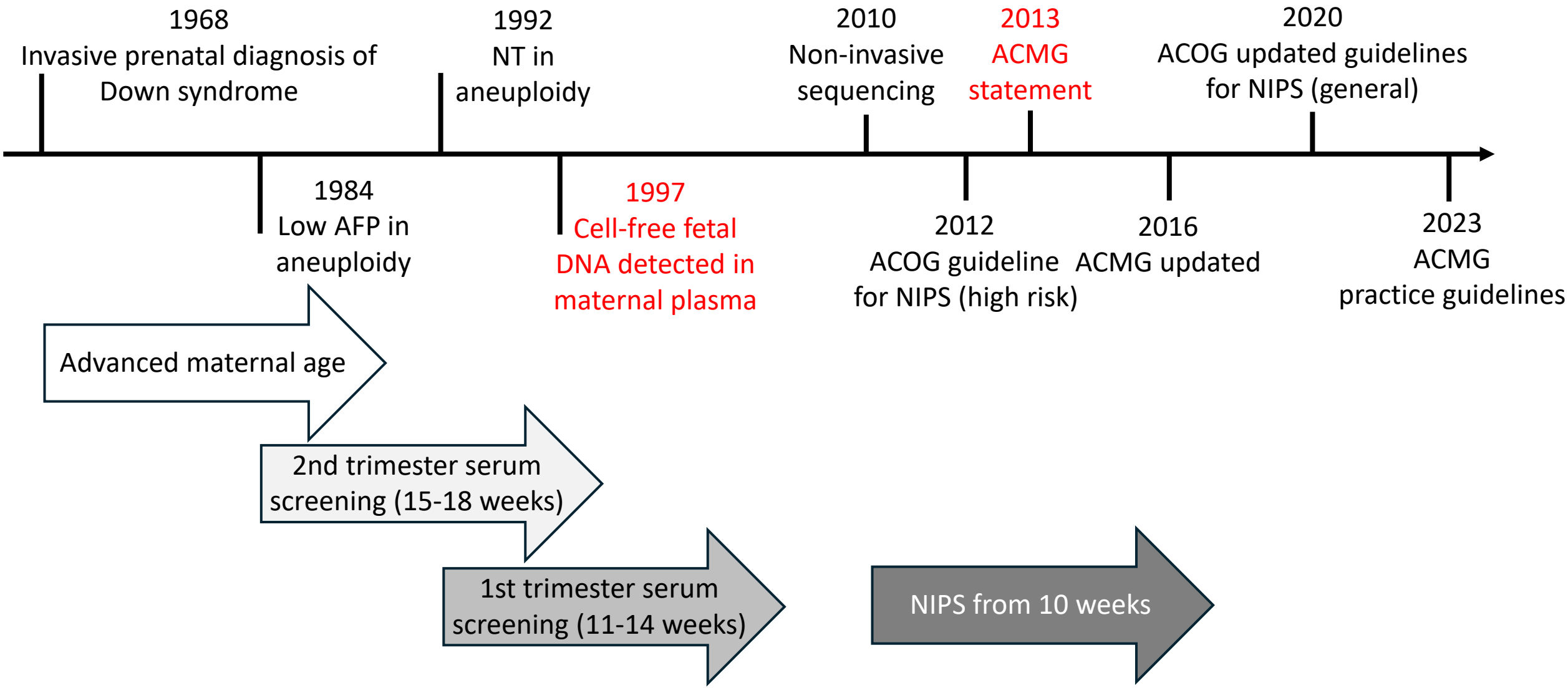
Platt LD et al. *Am J Obstet Gynecol*. 2014







Hui L et al. Population-based impact of noninvasive prenatal screening on screening and diagnostic testing for fetal aneuploidy. *Genet Med*. 2017



Hui L. Noninvasive Approaches to Prenatal Diagnosis: Historical Perspective and Future Directions. *Methods Mol Biol*. 2019
Benoy ME. The impact of insurance on equitable access to non-invasive prenatal screening (NIPT): private insurance may not pay. *J Community Genet*. 2021

ACOG The American College of Obstetricians and Gynecologists

Society for Maternal-Fetal Medicine High-risk pregnancy experts

ACOG PRACTICE BULLETIN

Clinical Management Guidelines for Obstetrician–Gynecologists

NUMBER 226 *(Replaces Practice Bulletin 163, May 2016, Reaffirmed 2018)*

Committee on Practice Bulletins—Obstetrics, Committee on Genetics, and Society for Maternal-Fetal Medicine. This Practice Bulletin was developed by the American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics and Committee on Genetics, and the Society for Maternal-Fetal Medicine in collaboration with Nancy C. Rose, MD, and Anjali J. Kaimal, MD, MAS with the assistance of Lorraine Dugoff, MD and Mary E. Norton, MD on behalf of the Society for Maternal-Fetal Medicine.

Screening for Fetal Chromosomal Abnormalities

Genetics in Medicine (2023) 25, 100336

ELSEVIER

Genetics in Medicine

An Official Journal of the ACMG

www.journals.elsevier.com/genetics-in-medicine

ACMG PRACTICE GUIDELINE

Noninvasive prenatal screening (NIPS) for fetal chromosome abnormalities in a general-risk population: An evidence-based clinical guideline of the American College of Medical Genetics and Genomics (ACMG)

"**Cell-free DNA is the most sensitive and specific screening test** for **common fetal aneuploidies**."

"**ACMG strongly recommended** NIPS for all pregnant individuals over traditional screening for **common trisomy (in singleton and twin pregnancies)** and **SCAs (singleton pregnancies)**."

"Nevertheless, it has the potential for false positive and false negative results. Furthermore, it is not equivalent to diagnostic testing."

ACOG Practice Bulletin, Number 226. *Obstet Gynecol*. 2020
Dungan JS, Klugman S, Darilek S, et al. ACMG practice guideline. 2023

The interpretation of NIPS results

	Disorder	No Disorder
Positive Test Result	True Positive (TP)	False Positive (FP) **Unnecessary test**
Negative Test Result	False Negative (FN) **Residual risk**	True Negative (TN)

Sensitivity = TP/(TP+FN) **Detection rate**
Specificity = TN/(TN+FP)
PPV = TP/(TP+FP)
NPV = TN/(FN+TN)

Carvajal DN, Rowe PC. Sensitivity, specificity, predictive values, and likelihood ratios. *Pediatr Rev*. 2010

Ultrasound Obstet Gynecol 2015; **45**: 249–266
Published online 1 February 2015 in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.14791

Analysis of cell-free DNA in maternal blood in screening for fetal aneuploidies: updated meta-analysis

M. M. GIL*, M. S. QUEZADA*, R. REVELLO*, R. AKOLEKAR*† and K. H. NICOLAIDES*†

**Harris Birthright Research Centre for Fetal Medicine, King's College Hospital, London, UK; †Fetal Medicine Unit, Medway Maritime Hospital, Gillingham, Kent, UK*

	Detection rate (DR)	False positive rate (FPR)
Trisomy 21	**99.2%**	**0.09%**
Trisomy 18	96.3%	0.13%
Trisomy 13	91.0%	0.13%
Monosomy X	90.3%	0.23%
Other sex chromosome aneuploidies	93.0%	0.14%
Trisomy 21 (twins)	93.7%	0.23%

Gil MM, Nicolaides KH et al. *Ultrasound Obstet Gynecol*. 2015

Condition	Sensitivity (%)	95% CI	Specificity (%)	95% CI	PPV (%)	95% CI
Trisomy 21	98.80	97.81–99.34	99.96	99.92–99.98	91.78	88.43–94.23
Trisomy 18	98.83	95.45–99.71	99.93	99.83–99.97	65.77	45.29–81.68
Trisomy 13	100	0–100	99.96	99.92–99.98	37.23	26.08–49.93

Condition	Sensitivity (%)	95% CI	Specificity (%)	95% CI	PPV (%)	95% CI
Monosomy X	97.68	84.25–99.70	99.84	99.67–99.92	29.52	22.72–37.36
47,XXX	100	0.0–100	99.97	99.96–99.98	53.95	40.58–66.77
47,XXY	99.25	78.13–99.98	99.99	99.98–99.99	74.05	59.47–84.73
47,XYY	100	0.0–100	99.99	99.99–100)	74.45	58.40–85.81
Overall SCAs	99.63	94.83–99.98	99.80	99.69–99.88	43.13	37.92–48.50

Hui L, Ellis K, Mayen D, et al. Position statement from the ISPD. *Prenat Diagn*. 2023

Table 2 Diagnostic yield for major chromosome abnormalities by indication for testing (2013–2015)

	2013	2014	2015	Combined rate 2013–15
High-risk NIPS	82.8% (24/29)	64.3% (72/112)	64.6% (148/229)	65.9% (244/370)
Known parental rearrangement	7.9% (3/38)	37.8% (14/37)	34.9% (15/43)	27.1% (32/118)
Ultrasound abnormalities	20.9% (116/554)	22.9% (137/597)	19.0% (130/685)	20.9% (383/1,836)
High-risk CFTS	21.3% (203/954)	20.5% (160/781)	18.9% (115/608)	20.4% (478/2,343)
Prior pregnancy with chromosomal abnormality	2.8% (2/71)	5.6% (3/53)	8.1%% (4/49)	5.2% (9/173)
High-risk second-trimester screening	6.1% (7/115)	2.9% (4/139)	5.2% (5/96)	4.6% (16/350)
Advanced maternal age alone	6.8% (26/382)	1.1% (2/175)	3.3% (3/92)	4.8% (31/649)
Other	0.9% (1/112)	5.7% (5/88)	3.3% (3/91)	3.1% (9/291)

CFTS, combined first-trimester screening; NIPS, noninvasive prenatal screening.
Some cases had more than one indication coded; hence, column totals may not sum to total number of tests performed by year. Testing for single-gene disorders is not included in this table.

Hui L et al. Population-based impact of noninvasive prenatal screening on screening and diagnostic testing for fetal aneuploidy. *Genet Med*. 2017

False P	False N
Confined placenta mosaicism Maternal mosaicism Maternal malignancy Vanished twins	True fetal mosaicism Incorrect clinical annotation Lower fetal fraction

65% No explanation!

Hartwig TS, Ambye L, Sørensen S, Jørgensen FS. Discordant non-invasive prenatal testing (NIPT) - a systematic review. *Prenat Diagn*. 2017

DOI: 10.1002/pd.4659 PRENATAL DIAGNOS

ORIGINAL ARTICLE

The type of feto-placental aneuploidy detected by cfDNA testing may influence the choice of confirmatory diagnostic procedure†

Francesca Romana Grati[1]*, Komal Bajaj[2], Francesca Malvestiti[1], Cristina Agrati[1], Beatrice Grimi[1], Barbara Malvestiti[1], Eva Pompilii[1], Federico Maggi[1], Susan Gross[2,3], Giuseppe Simoni[1] and Jose Carlos P. Ferreira[2,4]

[1]Toma Advanced Biomedical Assays, Busto Arsizio, Varese, Italy
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*Correspondence to: Francesca Romana Grati. E-mail: fgrati@tomalab.com
†The data reported in this paper was presented at the 14th World Congress in Fetal Medicine, held between the 21st and the 25th of June of 2015 in Crete, Gree

Table 1 Categories of feto-placental mosaicisms based on the tissue distribution

Mosaic type	Cytotrophoblast (direct preparation)	Mesenchyme (long-term culture)	Amniocytes
CPM 1	Abn	N	N
CPM 2	N	Abn	N
CPM 3	Abn	Abn	N
TFM 4	Abn	N	Abn
TFM 5	N	Abn	Abn
TFM 6	Abn	Abn	Abn

CPM, confined placental mosaicism; TFM, true fetal mosaicism; Abn, abnormal; n, normal.

Table 2 Estimated likelihoods for which a CVS performed after high-risk cfDNA result would require a follow-up amniocentesis because of the diagnosis of mosaicism on CVS

Likelihood			Trisomy 21	Trisomy 18	Trisomy 13	Monosomy X
			Ratio (raw data); %; 1/x (95% CI)			
Prediction of mosaic CVS result after HR-cfDNA testing result	Probability of requiring a secondary amniocentesis (=probability of mosaicism on CVS sample)	CPM1 + CPM3 + TFM4 + TFM6/ Total – (CPM2 + TFM5)	18/1043; 2%; 1/58 (1/91;1/27)	14/345; 4%; 1/25 (1/41;1/15)	27/124; 22%; 1/5 (1/6;1/3)	66/112; 59%; 1/2 (1/2;1/1)
	Probability of both CVS cytotrophoblast and mesenchyme being abnormal if mosaicism is detected	(CPM3 + TFM6)/(CPM1 + CPM3 + TFM4 + TFM6)	9/18; 50%; 1/2 (1/3;1/1)	5/14; 36%; 1/3 (1/6;1/2)	7/27; 26%; 1/4 (1/8;1/2)	21/66; 32%; 1/3 (1/5;1/2)
	Probability of CVS cytotrophoblast only being abnormal if mosaicism is detected (1-previous)	(CPM1 + TFM4)/(CPM1 + CPM3 + TFM4 + TFM6)	9/18; 50%; 1/2 (1/3;1/1)	9/14; 64%; 1/2 (1/3;1/1)	20/27; 74%; 1/1 (1/2;1/1)	45/66; 68%; 1/1 (1/2;1/1)
Prediction of fetal confirmation after mosaic CVS	Probability of amniocytes showing abnormal cells if any type of mosaicism is detected on CVS	(TFM4 + TFM6)/(CPM1 + CPM3 + TFM4 + TFM6)	8/18; 44%; 1/2 (1/4;1/2)	2/14; 14%; 1/7 (1/25;1/3)	1/27; 4%; 1/27 (1/152;1/5)	17/66 26% 1/4 (1/6;1/3)
	Probability of amniocytes being abnormal if both, CVS cytotrophoblast and mesenchyme, are abnormal	TFM6/(CPM3 + TFM6)	7/9; 78%; 1/1 (1/2;1/1)	2/5; 40%; 1/3 (1/9;1/1)	0/7; NA; NA	10/21; 48%; 1/2 (1/4;1/1)
	Probability of amniocentesis being abnormal if only CVS cytotrophoblast is abnormal	TFM4/(CPM1 + TFM4)	1/9; 11%; 1/9 (1/50;1/2)	0/9; NA; NA	1/20; 5%; 1/20 (1/113;1/4)	7/45; 16%; 1/6 (1/13;1/3)

CPM, confined placental mosaicism; TFM, true fetal mosaicism; CVS, chorionic villous sample; HR-cfDNA testing, high risk cell free DNA testing; NA, not available.

Grati FR, Bajaj K, Malvestiti F, et al. *Prenat Diagn*. 2015

Table 2. Contribution of an abnormal ChrX maternal karyotype in a prospective study of 187 discordant SCAs.

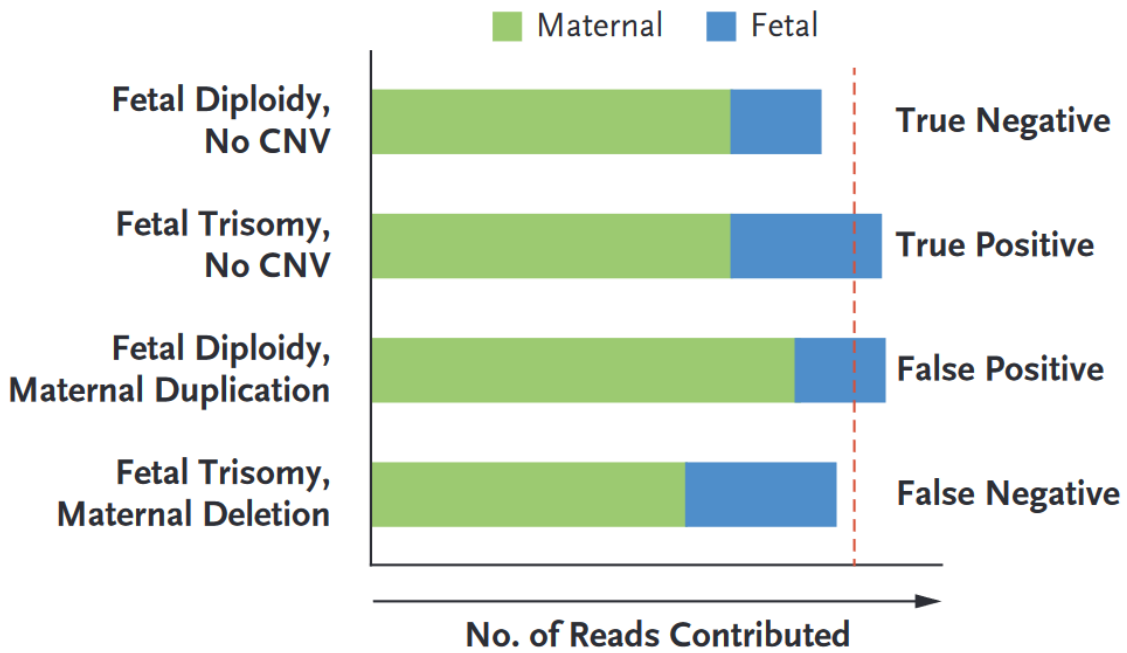
Clinical	NIPT findings	NIPT ChrX gain	NIPT ChrX loss	Total
NIPT follow-up	Abnormal NIPT for SCA, n	63	124	187
	Normal maternal karyotype, n	57	114	171
	Altered maternal karyotype, n	6	10	16
	Maternal mosaicism rate	9.52%	8.06%	8.56%

The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

Copy-Number Variation and False Positive Prenatal Aneuploidy Screening Results

Matthew W. Snyder, M.S., LaVone E. Simmons, M.D., Jacob O. Kitzman, Ph.D., Bradley P. Coe, Ph.D., Jessica M. Henson, B.S., Riza M. Daza, B.S., Evan E. Eichler, Ph.D., Jay Shendure, M.D., Ph.D., and Hilary S. Gammill, M.D.



Snyder MW, Simmons LE, Kitzman JO, et al. Copy-number variation and false positive prenatal aneuploidy screening results. *N Engl J Med*. 2015;
Kingsley C, Wang E, Oliphant A. Copy-Number Variation and False Positive Results of Prenatal Screening. *N Engl J Med*. 2015
van den Boom D, Ehrich M, Kim SK. Copy-Number Variation and False Positive Results of Prenatal Screening. *N Engl J Med*. 2015
Wang Y et al. Maternal mosaicism is a significant contributor to discordant sex chromosomal aneuploidies associated with noninvasive prenatal testing. *Clin Chem*. 2014

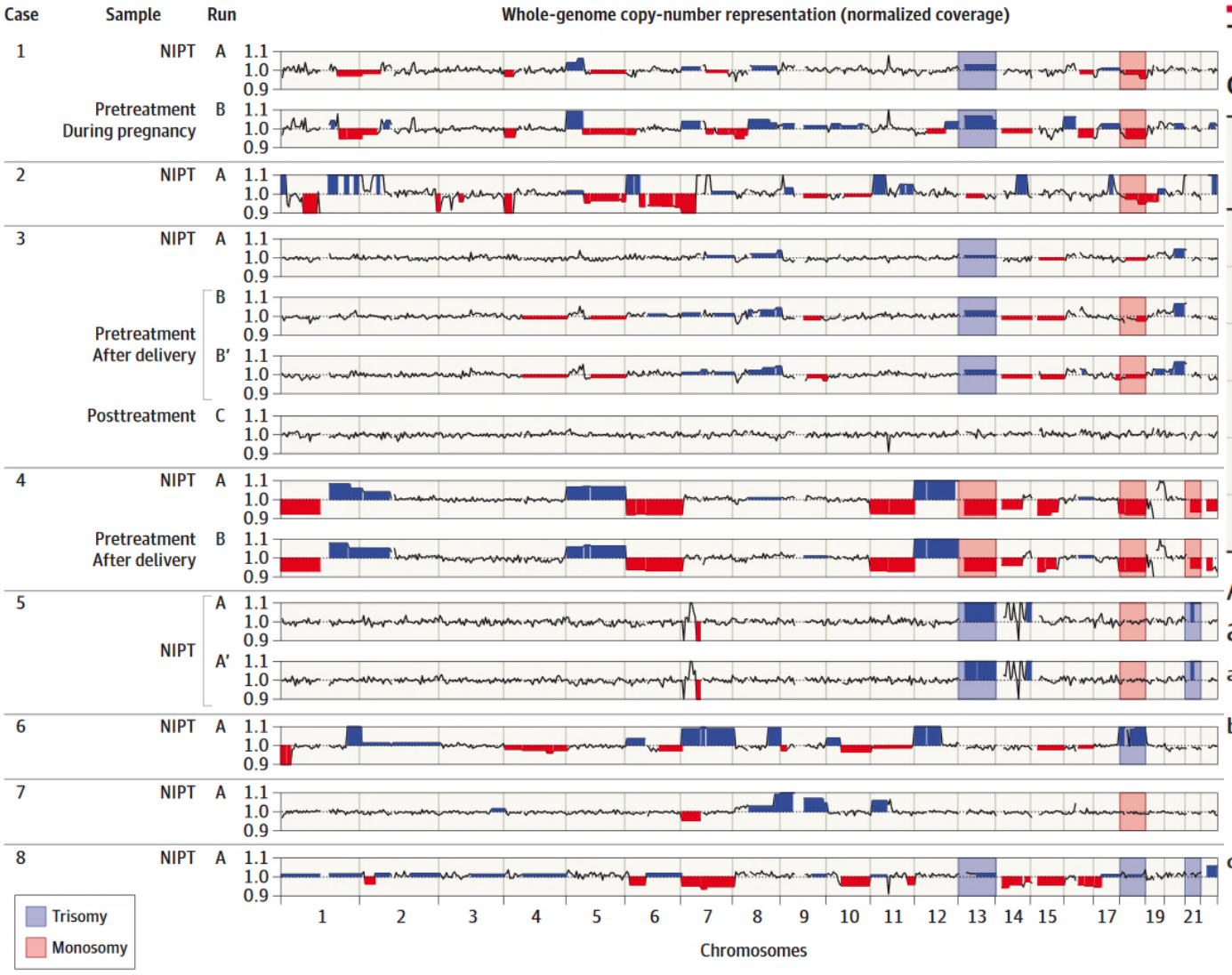


Table 2. Association of Maternal Cancers With Different Types of Aneuploidies Detected at Noninvasive Prenatal Testing

Type of Aneuploidy Detected by NIPT	Total No. of Samples	No. of Known Maternal Cancers (%) [95% CI]
Single trisomy[a]	2650	2 (0.08) [0-0.27]
Single SCA[b]	950	0 (0) [0-0.39]
Single trisomy + SCA	30	0 (0) [0-11.5]
Single monosomy	88	1 (1.14) [0-6.1]
Multiple aneuploidy[c]	39	7 (17.9) [7.5-33.5]
Total abnormal NIPT	3757	10 (0.26) [0.12-0.48]

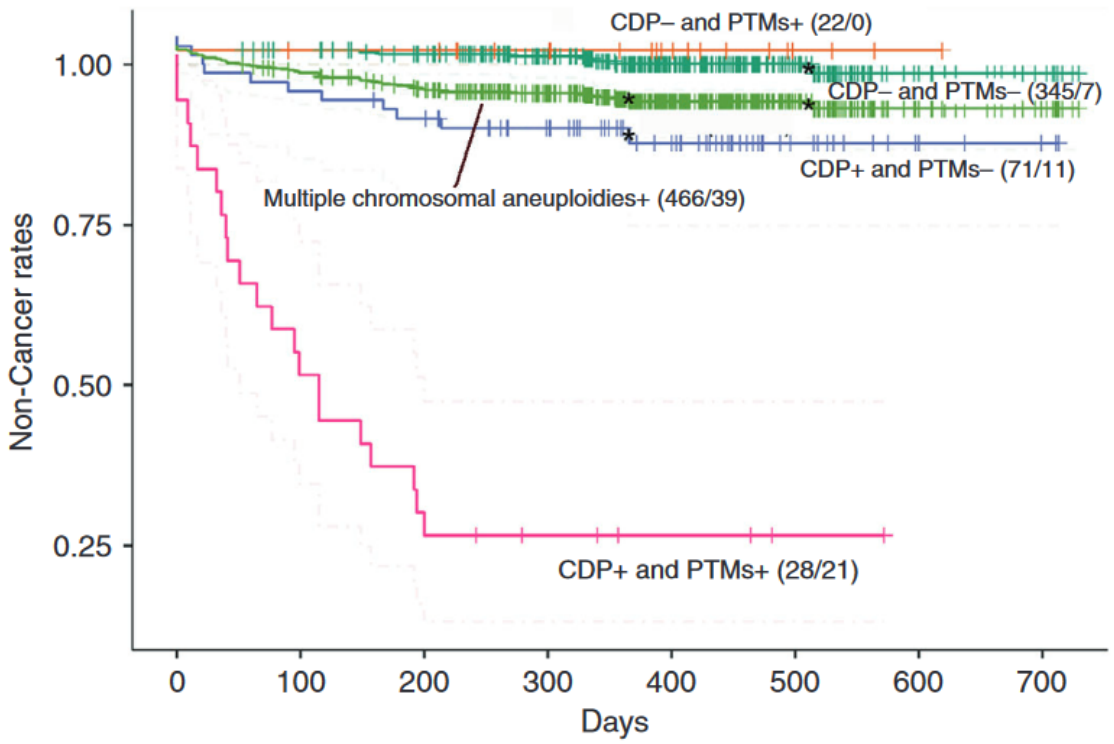
Abbreviations: NIPT, noninvasive prenatal testing; SCA, sex chromosome abnormality.

[a] Single trisomy refers specifically to trisomy of chromosomes 13, 18, or 21.

[b] Single SCA refers to the presence of 1 of the sex chromosome aneuploidies: Turner syndrome (monosomy X), Klinefelter syndrome (XXY), XYY syndrome, or trisomy X (XXX).

[c] The multiple aneuploidy category includes every other combination of autosomal and/or sex chromosome aneuploidy except single trisomy and SCA as noted in the Table.

Bianchi DW, Chudova D, Sehnert AJ, et al. Noninvasive Prenatal Testing and Incidental Detection of Occult Maternal Malignancies. *JAMA*. 2015
Snyder HL, Curnow KJ, Bhatt S, Bianchi DW. *Prenat Diagn*. 2016



Number of non-cancer participants by time

Multiple chromosomal aneuploidies+	466	438	413	347	227	91	26	9
CDP+ and PTMs+	28	14	8	5	3	1	0	0
CDP+ and PTMs–	71	65	61	49	34	13	5	2
CDP– and PTMs+	22	21	21	17	10	3	1	0
CDP– and PTMs–	345	338	323	276	180	74	20	7

Box 1. Stepwise Evaluation of the Patient With More Than One Aneuploidy Detected on Cell-Free DNA

1. Discuss results with performing laboratory
   ↓
2. History and physical examination with laboratory evaluation
   - Complete blood count with peripheral smear
   - Metabolic panel
   - Pap test
   - Fecal occult blood

   ↓
3. Chest radiograph
   ↓
4. Magnetic resonance image of the chest, abdomen, and pelvis
   ↓
5. Consider annual complete blood count for surveillance

PPV 7.6%
PPV 75%

Carlson LM, Hardisty E, Coombs CC, Vora NL. Maternal Malignancy Evaluation After Discordant Cell-Free DNA Results. *Obstet Gynecol*. 2018
Ji X, Li J, Huang Y, et al. Identifying occult maternal malignancies from 1.93 million pregnant women undergoing noninvasive prenatal screening tests. *Genet Med*. 2019

DOI: 10.1002/pd.4119 PRENATAL DIAGNOSIS

ORIGINAL ARTICLE

Gestational age and maternal weight effects on fetal cell-free DNA in maternal plasma

Eric Wang*, Annette Batey, Craig Struble, Thomas Musci, Ken Song and Arnold Oliphant

Ariosa Diagnostics, San Jose, CA, USA
*Correspondence to: Eric Wang. E-mail: ewang@ariosadx.com

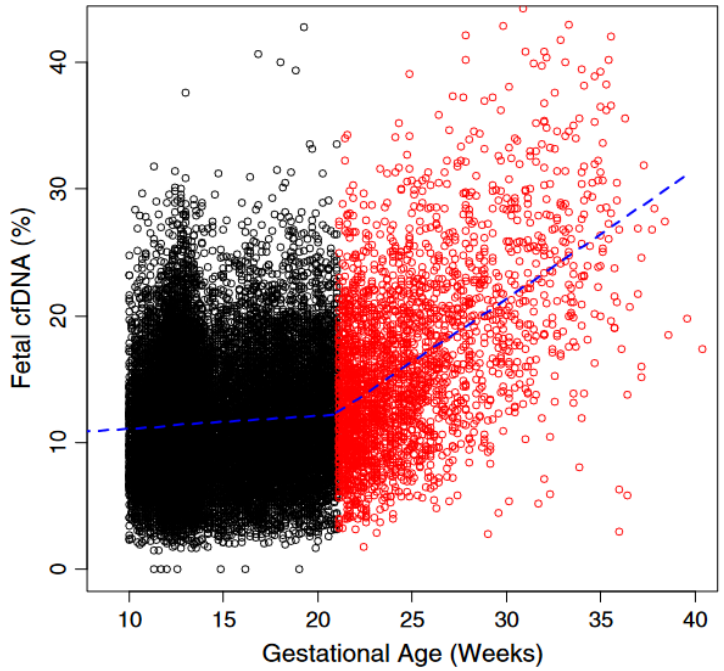
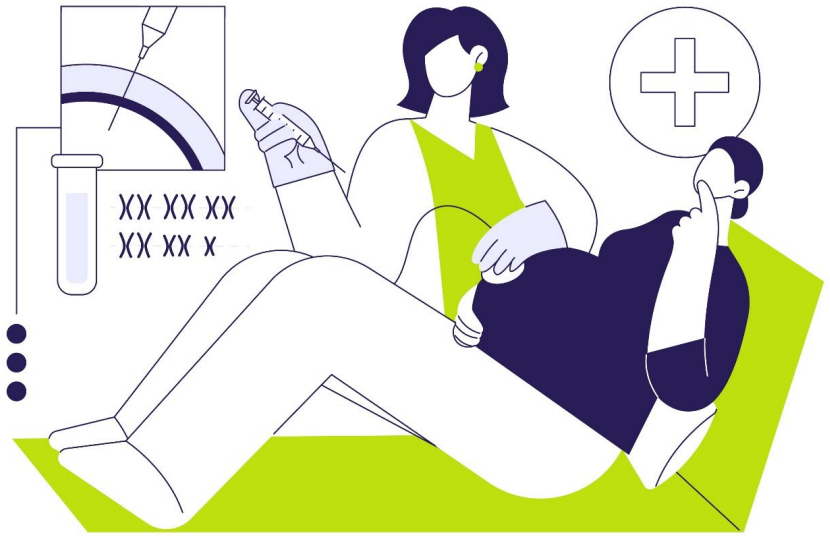


Figure 2 Relationship between percentage of fetal cfDNA and gestational age. Fetal cfDNA percentage for 22 384 pregnancies is plotted with respect to gestational age (weeks). At 10 weeks 0 days to 10 weeks 6 days gestation, the median fetal cfDNA percentage was 10.2%. Between 10 and 21 weeks gestation (black open circles), fetal cfDNA increased at 0.10% per week ($p < 0.0001$; blue dash

Table 1 Proportion of pregnancies with ≥4% fetal cell-free DNA on first blood draw

Maternal weight bin (kg)	*n*	Pregnancies with ≥4% fetal cell-free DNA (%)
<50	809	99.8
≥50 < 60	4825	99.6
≥60 < 70	6224	99.2
≥70 < 80	4313	98.8
≥80 < 90	2574	98.2
≥90 < 100	1608	96.3
≥100 < 110	921	93.9
≥110 < 120	508	89.8
≥120 < 130	298	87.9
≥130 < 140	172	81.4
≥140	132	71.2

Wang E, Batey A, Struble C, Musci T, Song K, Oliphant A. Gestational age and maternal weight effects on fetal cell-free DNA in maternal plasma. *Prenat Diagn*. 2013



What to do after positive NIPS results?

Received: 9 March 2022 | Revised: 21 June 2022 | Accepted: 10 August 2022

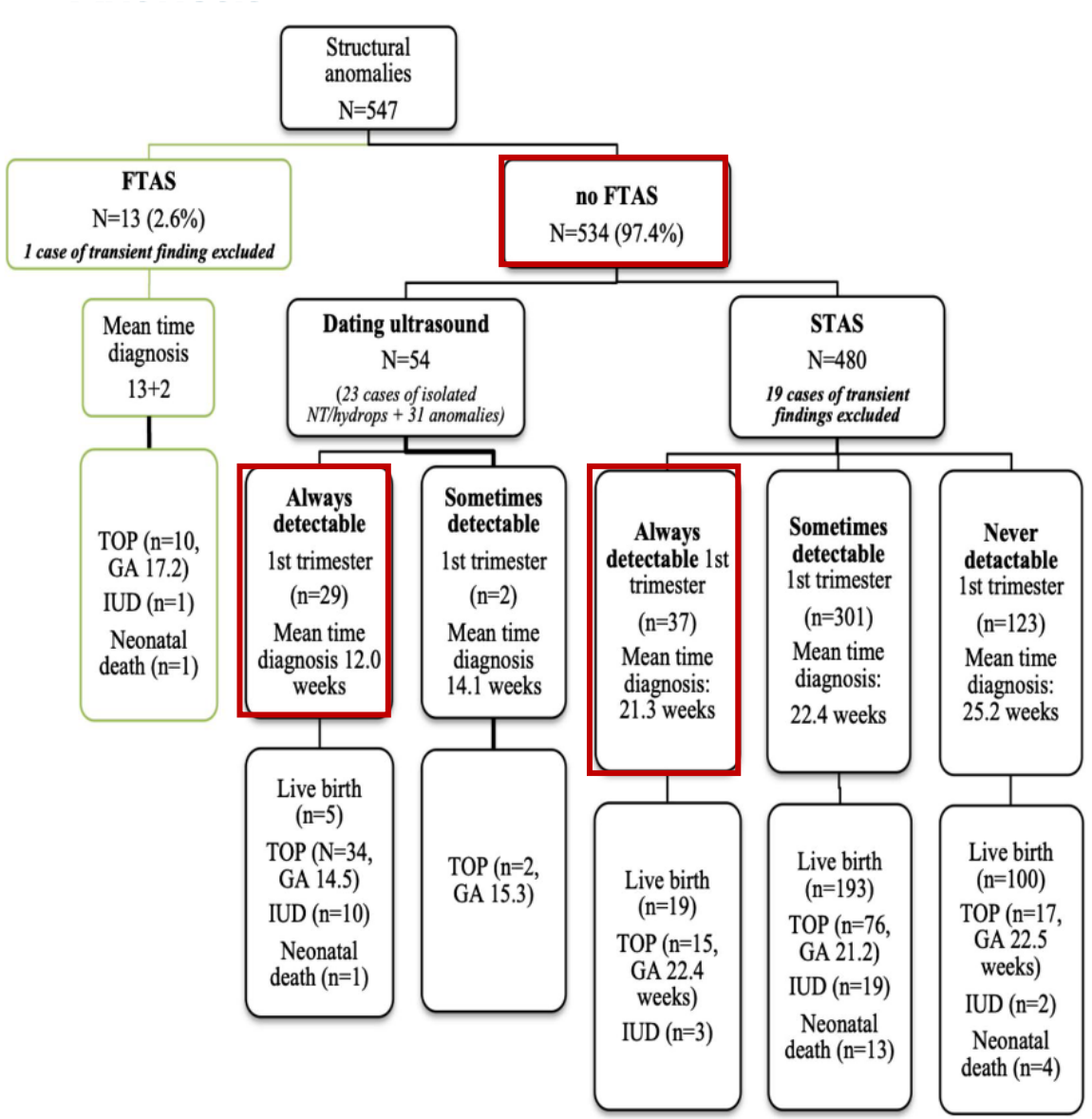
DOI: 10.1002/pd.6224

ORIGINAL ARTICLE

PRENATAL DIAGNOSIS WILEY

Timing of diagnosis of fetal structural abnormalities after the introduction of universal cell-free DNA in the absence of first-trimester anatomical screening

Francesca Bardi[1] | Anne Marie Beekhuis[1] | Marian K. Bakker[1] | Ayten Elvan-Taşpınar[1] | Caterina Maddalena Bilardo[2]



Bardi F et al. *Prenat Diagn*. 2022

NIPS (45,X) **PPV 30%**

NIPS (45,X)+USG(+) **PPV 85%**

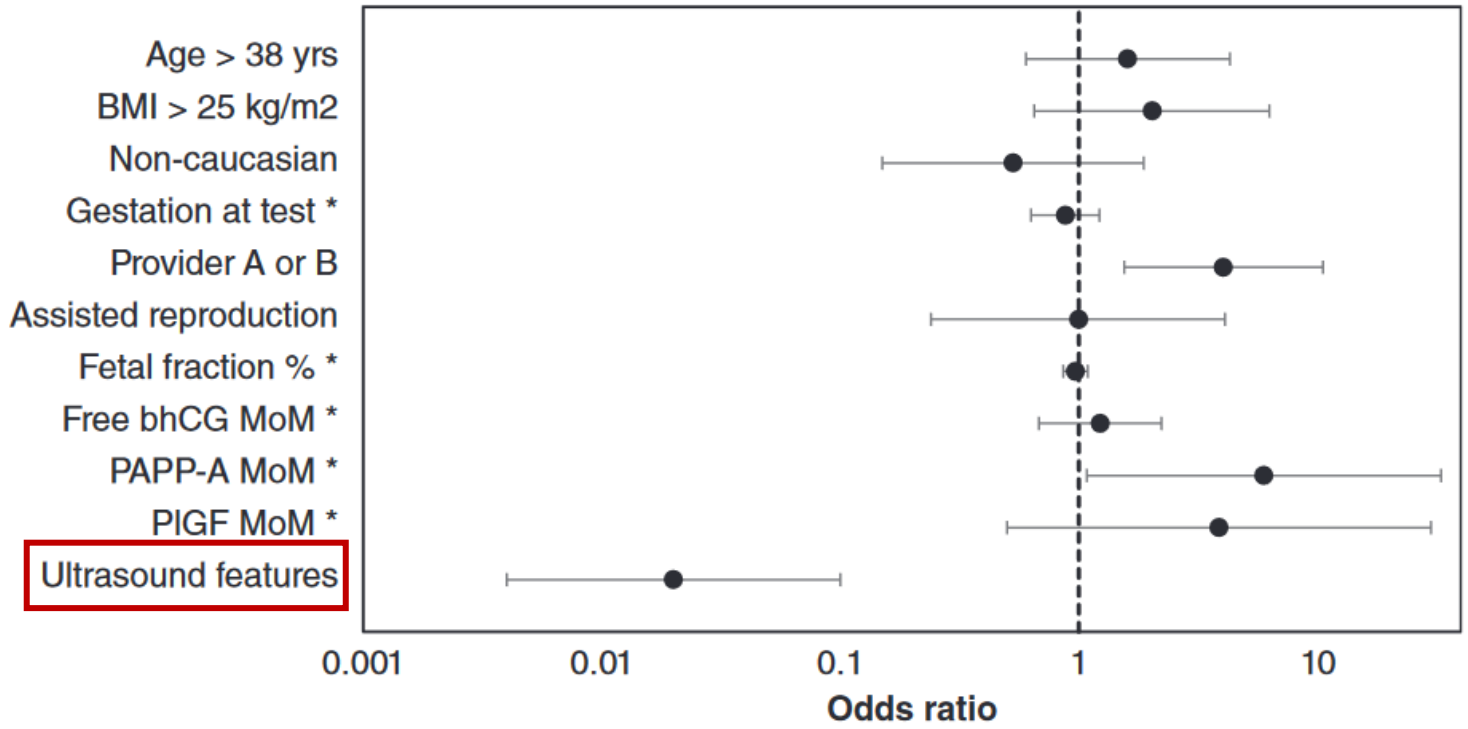
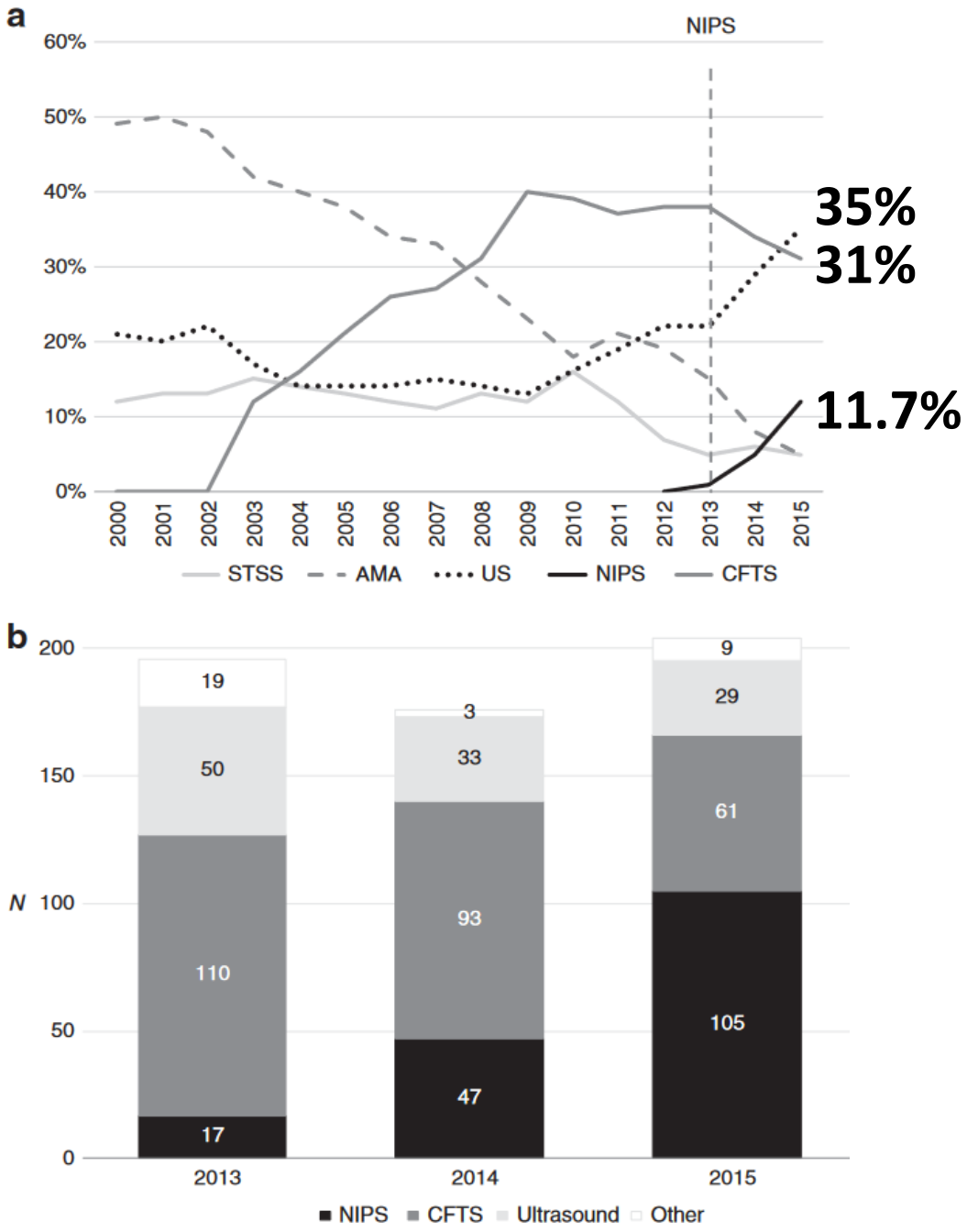


FIGURE 2 Effect size (odds ratio and 95% confidence intervals) of predictor variables and probability of a false-positive result. *Effect size determined as a continuous variable as no clear dichotomisation point was obtained

Sandow R et al. Increasing maternal age is not a significant cause of false-positive results for monosomy X in non-invasive prenatal testing. *Prenat Diagn*. 2020

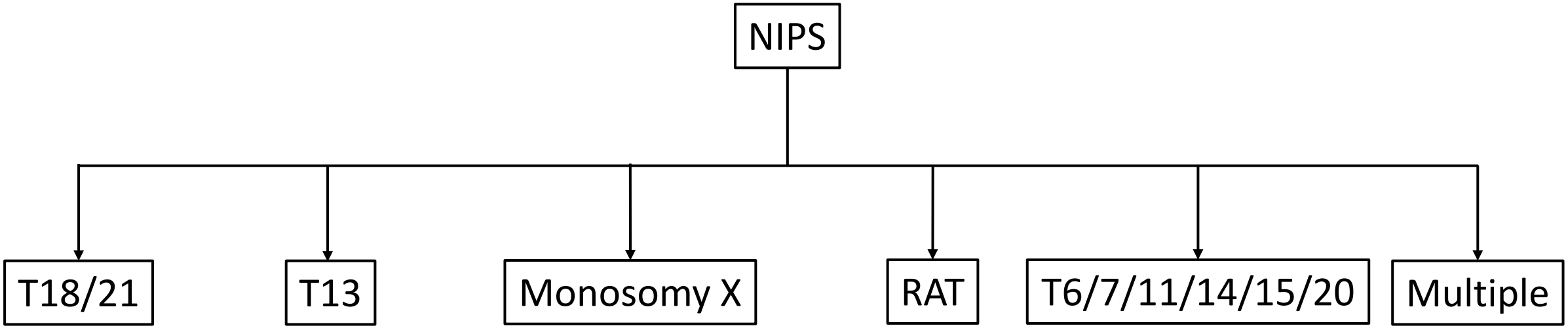


NIPS high risk

USG abnormal

CFTS high risk

Hui L et al. Population-based impact of noninvasive prenatal screening on screening and diagnostic testing for fetal aneuploidy. *Genet Med*. 2017



Created by Liliane Lin. Adapted from Mardy et al. Table2.

TABLE 2 Suggested management of cell free DNA results in pregnancy

Chromosome	Category	Suggested invasive procedure	Other considerations
Trisomy 1, 2, 3, 4, 5, 7, 8, 9, 10, 12, 16, 17, 19, 22	Rare autosomal trisomy	Normal 1st trimester ultrasound: amniocentesisAbnormal 1st trimester ultrasound: CVS	3rd trimester growth scan (especially in trisomy 16)
Trisomy 6, 7, 11, 14, 15, 20	Rare autosomal trisomy, imprinted genes	CVS, followed by amniocentesis if abnormal	If fetus unaffected, consider methylation studies
Trisomy 13	Common aneuploidy, high rate of CPM	Normal 1st trimester ultrasound: amniocentesisAbnormal 1st trimester ultrasound: CVS	Amniocentesis if mosaicism on CVS
Trisomy 18, 21	Common aneuploidy, low rate of CPM	CVS	Amniocentesis if mosaicism on CVS
Monosomy X	Common aneuploidy, high rate of CPM	Normal 1st trimester ultrasound: amniocentesisAbnormal 1st trimester ultrasound: CVS	If unaffected fetus, consider maternal karyotype for mosaic Turner syndrome
Multiple aneuploidies	Risk of maternal malignancy	Normal 1st trimester ultrasound: amniocentesisAbnormal 1st trimester ultrasound: CVS	If unaffected fetus, consider work up for maternal malignancy

Abbreviation: CVS, chorionic villous sampling.

Mardy AH, Norton ME. Diagnostic testing after positive results on cell free DNA screening: CVS or Amnio?. *Prenat Diagn*. 2021

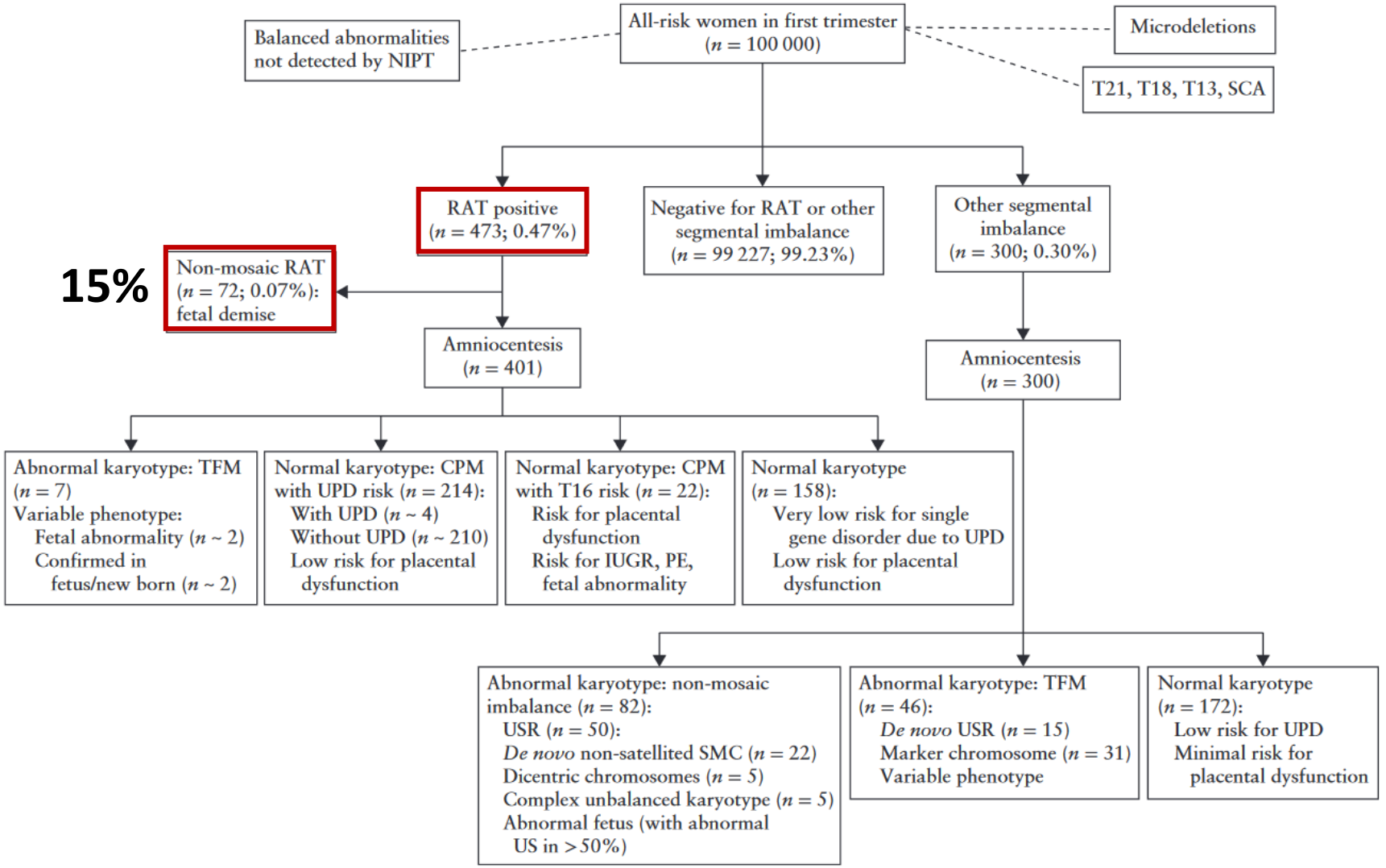


Figure 1 Expected performance of genome-wide non-invasive prenatal testing (NIPT) in 100 000 women in the first trimester. Cytogenetically visible imbalances that are included in current NIPT standard protocols (i.e. trisomies 21, 18 and 13 (T21, T18, T13), sex chromosome abnormalities (SCA) and microdeletions) and also balanced structural rearrangements not detectable by NIPT are not considered in the

Benn P, Grati FR. Genome-wide non-invasive prenatal screening for all cytogenetically visible imbalances. *Ultrasound Obstet Gynecol*. 2018

Table 3 Summary of all association studies between CPMs and outcomes

Outcome	CPM (RATs excluding T16) $N = 94$	CPM (tetraploidy only) $N = 18$	CPM (T16 only) $N = 12$	Controls $N = 468$	Significant associations
Binary outcome variables (X^2)	# Abnormal outcome/total (%)			# Abnormal outcome/ total (%)	
	P value[a]				
Birthweight percentile <3rd	3/87 (3.4%)	0/17	3/11 (27.3%)	13/401 (3.2%)	T16 only
	P 1.0	*P* 0.672	P **0.007**		
FGR	7/92 (7.6%)	2/17 (11.8%)	2/12 (16.7%)	10/428 (2.3%)	RATs (excluding t16) T16 only
	P **0.018**	*P* 0.072	P **0.039**		
NICU admission (excluding FGR)	5/84 (6%)	1/18 (5.6%)	1/10 (10%)	8/420 (1.9%)	RATs (excluding T16)
	P **0.049**	*P* 0.317	*P* 0.192		
HD	6/92 (6.5%)	1/18 (5.6%)	1/12 (8.3%)	20/428 (4.7%)	None
	P 0.60	*P* 1.0	*P* 1.0		
Spontaneous PTD	4/81 (4.9%)	0/16 (0%)	2/9 (22.2%)	11/403 (2.7%)	T16 only
	P 0.48	*P* 1.0	P **0.029**		
Quantitative outcome variables (Mann–Whitney rank-sum test)	***N* (median, IQR, 25th–75th percentile)**			***N* (median, IQR, 25th–75th percentile)**	
	***P* value[a]**				
Birthweight percentile	$N = 87$ (49, 52, 26–78)	$N = 17$ (44, 37, 25–63)	$N = 11$ (35, 89, 2–91)	$N = 401$ (55, 50, 31–81)	None
	P 0.257	*P* 0.186	*P* 0.181		
Apgar score at 5 minutes	$N = 87$ (10, 1, 9–10)	$N = 17$ (9, 1, 9–10)	$N = 11$ (9, 0, 9–9)	$N = 408$ (10, 1, 9–10)	T16 only
	P 0.477	*P* 0.120	P **0.006**		

[a]*P* values compare the CPM group versus controls.

FGR risk↑

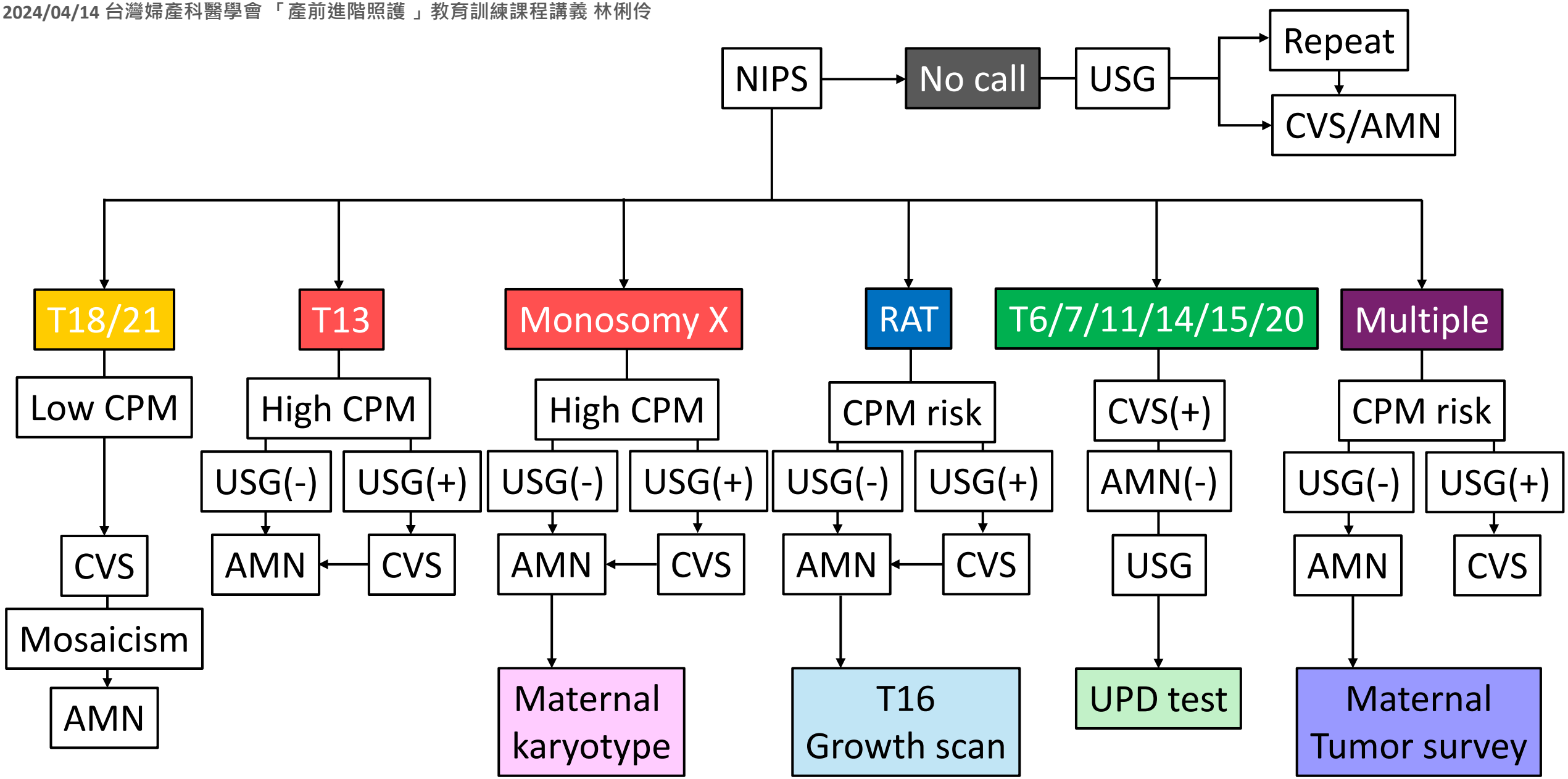
Preterm risk↑

OR 11.2

OR 8.4

OR 10.2

Grati FR et al. Outcomes in pregnancies with a confined placental mosaicism and implications for prenatal screening using cell-free DNA. *Genet Med*. 2020



Created by Liliane Lin. Adapted from Mardy et al. Table2.

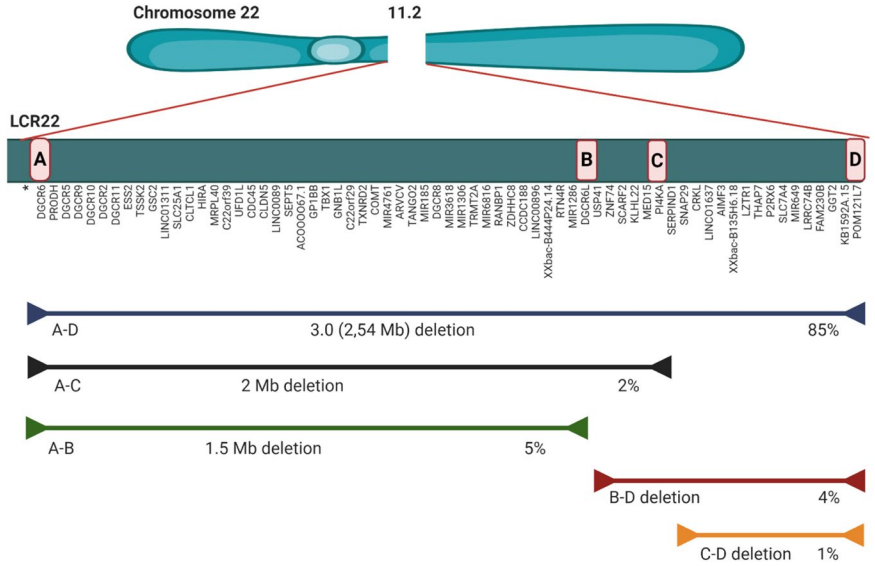
NIPS future and implementation

ACMG guidelines do **not** recommend NIPS for genome-wide RAT and CNV screening.

However, ACMG suggests NIPS for **22q11.2 deletion syndrome** be offered to all pregnant individuals.

Reference	Sensitivity%	Specificity%	Positive Predictive Value (PPV)%	Negative Predictive Value (NPV)%
Dar et al., 2022 [26]	83.3	99.8	52.6	99.9
Lin et al., 2021 [28]	100	99.9	53.9	99.9
Bevilacqua et al., 2021 [29]	69.6 *	100 *	100 *	98 *

Design, sample acquisition, methods, and ability to detect nested 22q11.2 deletions differ for each study (see text for details). * Enriched cohort with ultrasound scan abnormalities of CHD and 6.3% prevalence of 22q11.2DS, and thus high PPV.



Dungan JS, Klugman S, Darilek S, et al. ACMG guideline. 2023
Blagowidow N, Nowakowska B, Schindewolf E, et al. Prenatal Screening and Diagnostic Considerations for 22q11.2 Microdeletions. *Genes (Basel)*. 2023

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RESEARCH NOTE

PRENATAL DIAGNOSIS WILEY

nanoNIPT: Short-fragment nanopore sequencing of cell-free DNA for non-invasive prenatal testing of fetal aneuploidies and sex chromosome aberrations

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frontiers | Frontiers in Genetics

TYPE Original Research
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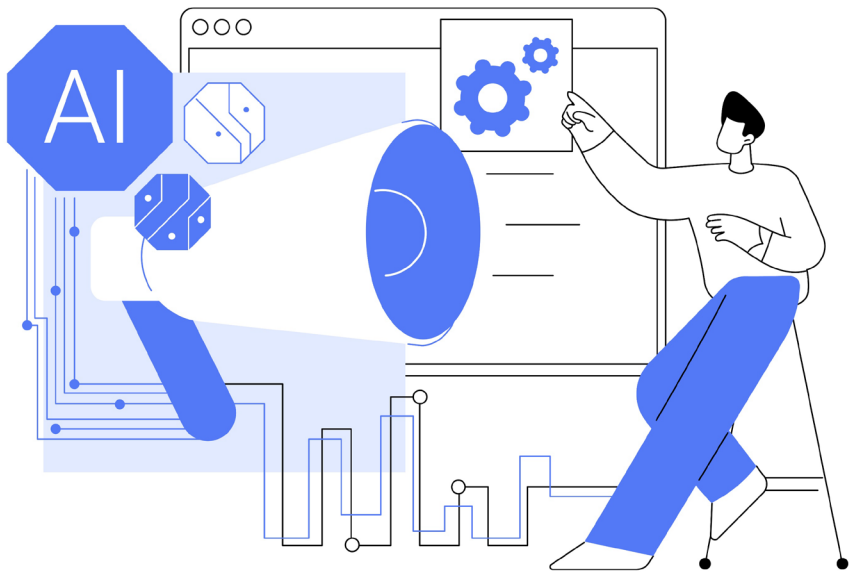

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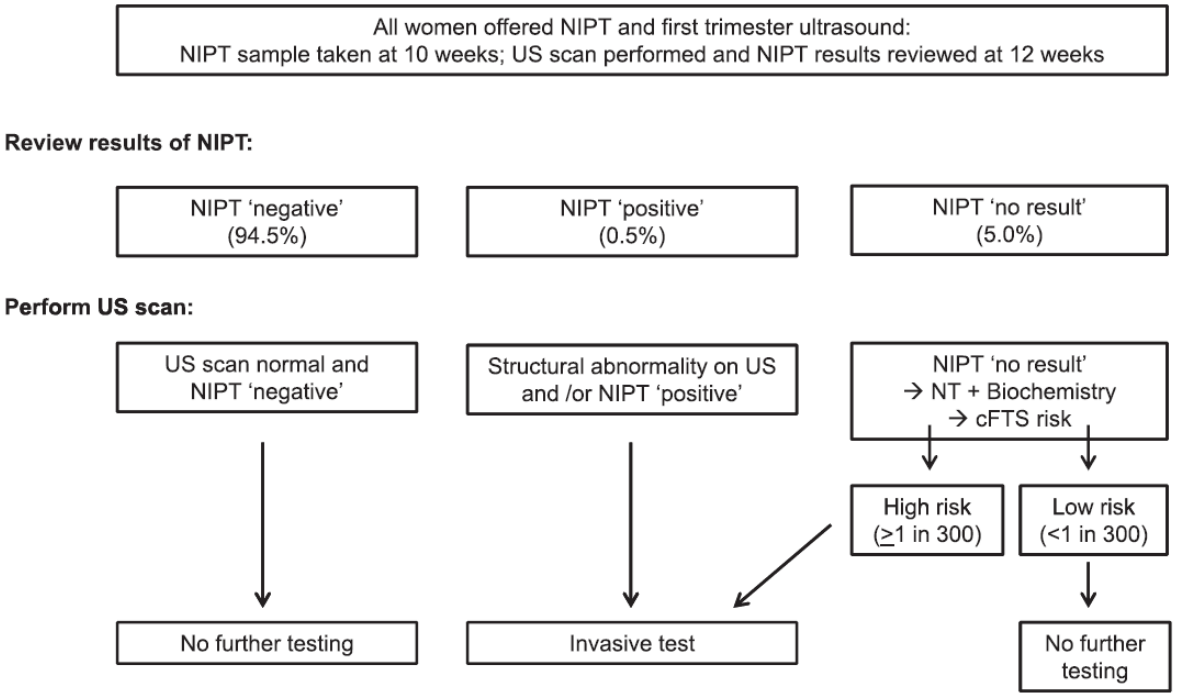
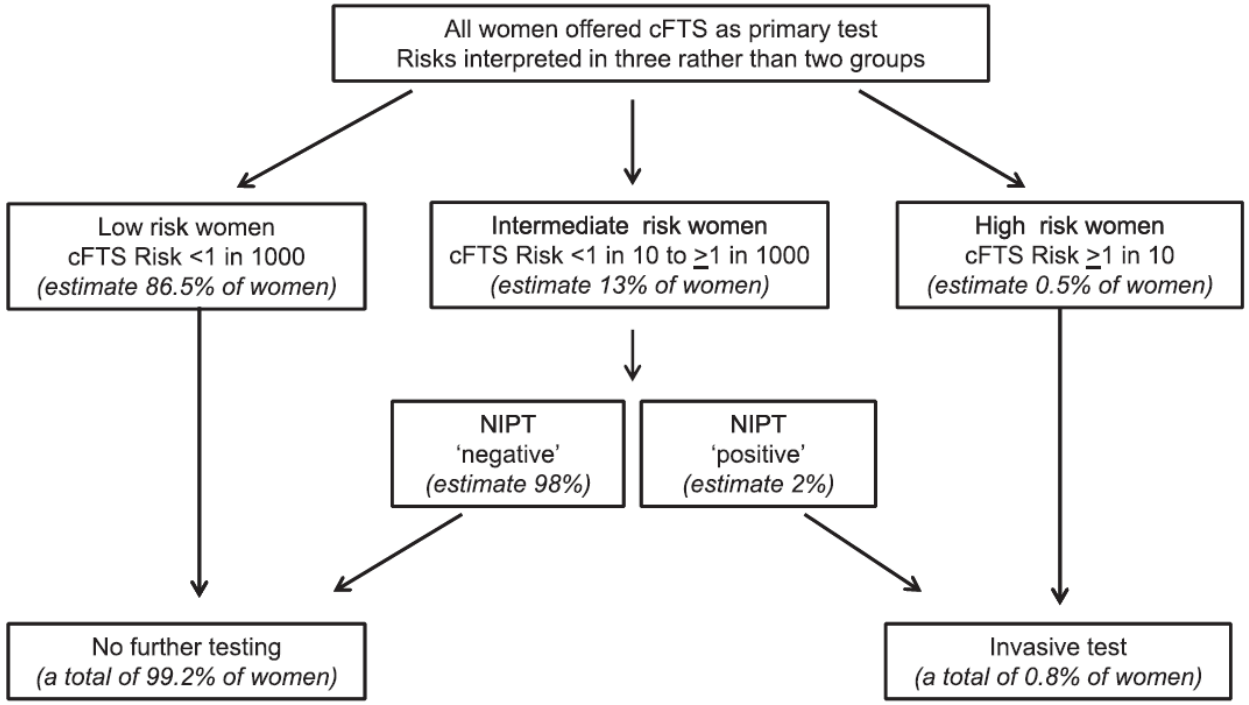
Development and performance evaluation of an artificial intelligence algorithm using cell-free DNA fragment distance for non-invasive prenatal testing (aiD-NIPT)

Junnam Lee[1,2†], Sae-Mi Lee[1†], Jin Mo Ahn[1], Tae-Rim Lee[1], Wan Kim[1], Eun-Hae Cho[1*] and Chang-Seok Ki[1*]

Primary screening



Contingent screening



Hui L, Hyett J. Noninvasive prenatal testing for trisomy 21: challenges for implementation in Australia. *Aust N Z J Obstet Gynaecol*. 2013

	Funded origin	Tier of testing	USD	Ongoing trial
Australia	Self-funded	Both	300-365	
Netherlands	Public-funded	1st tier 2nd tier (option)	205	TRIDENT-2 (GW)
UK	Public-funded	2nd tier	263-395	
USA	Partially covered	2nd tier		
Canada	Public-funded (partial)	2nd tier	380-420	PEGASUS-2 (1st tier)
Germany	Partially covered	Case by case		
Italy	Partially covered	2nd tier	197-329	
China	Partially covered	2nd tier	130-380	Pilot study (1st tier)
Hong Kong	Public-funded	2nd tier	700-1000 (2011)	
Japan	Self-funded	2nd tier	1054-1252	
India	Self-funded	Uncertain	130-160	
Israel	Self-funded	Uncertain		
Taiwan	Self-funded	Both	468-856	

Ravitsky V, Roy MC, Haidar H, et al. The Emergence and Global Spread of Noninvasive Prenatal Testing. *Annu Rev Genomics Hum Genet*. 2021

NIPS is the best screening tool for Down syndrome so far.

The value of early ultrasound for structural survey should be recognized.

Always be aware of false positives and negatives.

Thanks for your attention

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媽寶影像工作室