CENTRO ANALISI MONZA

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Quality Diagnostics

NIPT onfield

DNA fetale circolante e
Test Prenatali non invasivi

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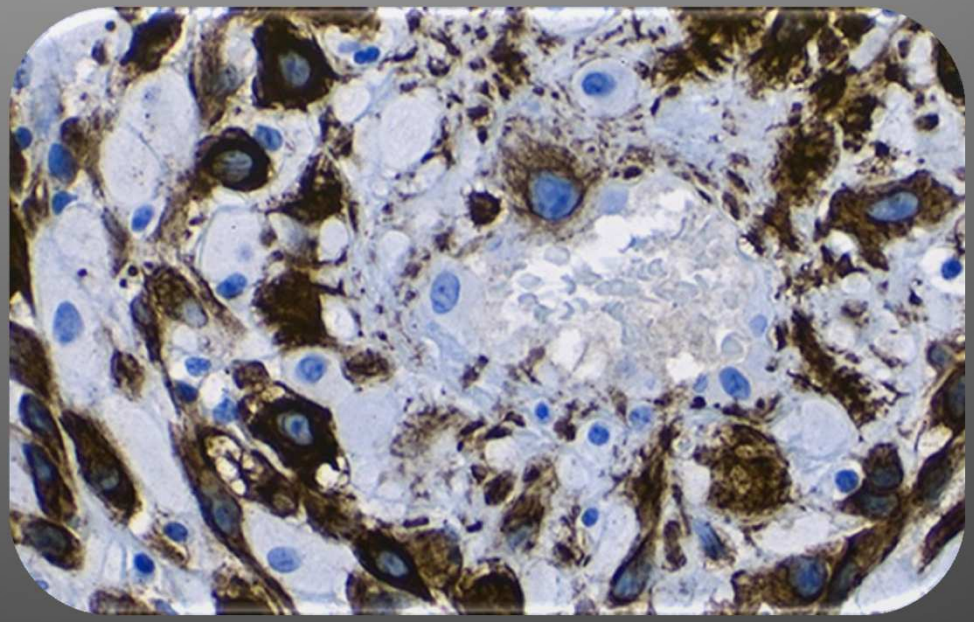
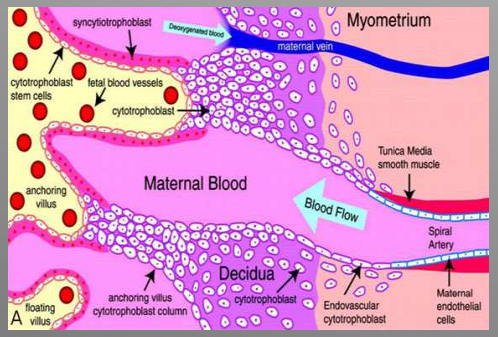
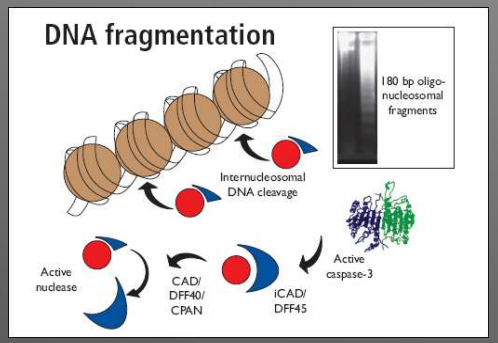
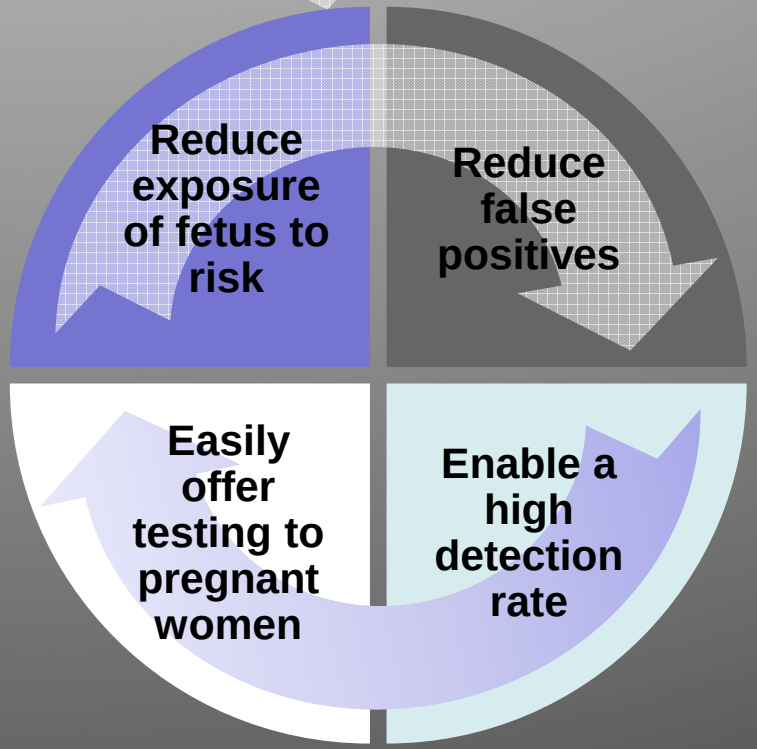


NIPT

NON INVASIVE PRENATAL TEST







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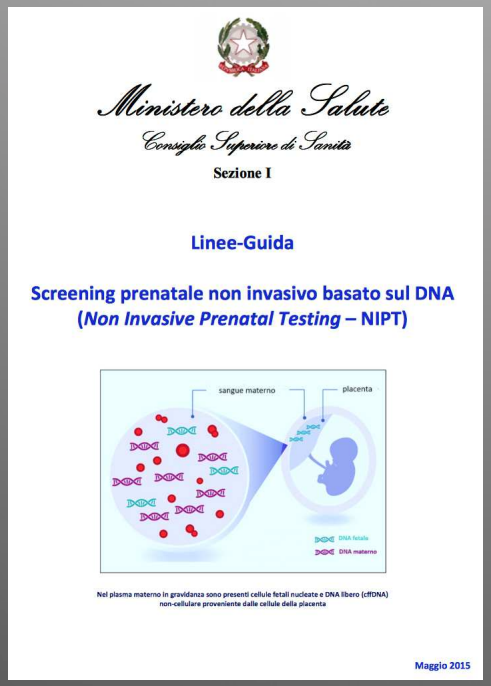

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Sezione I

Linee-Guida

Screening prenatale non invasivo basato sul DNA
(*Non Invasive Prenatal Testing* – NIPT)

Nel plasma materno in gravidanza sono presenti cellule fetali nucleate e DNA libero (cffDNA) non-cellulare proveniente dalle cellule della placenta

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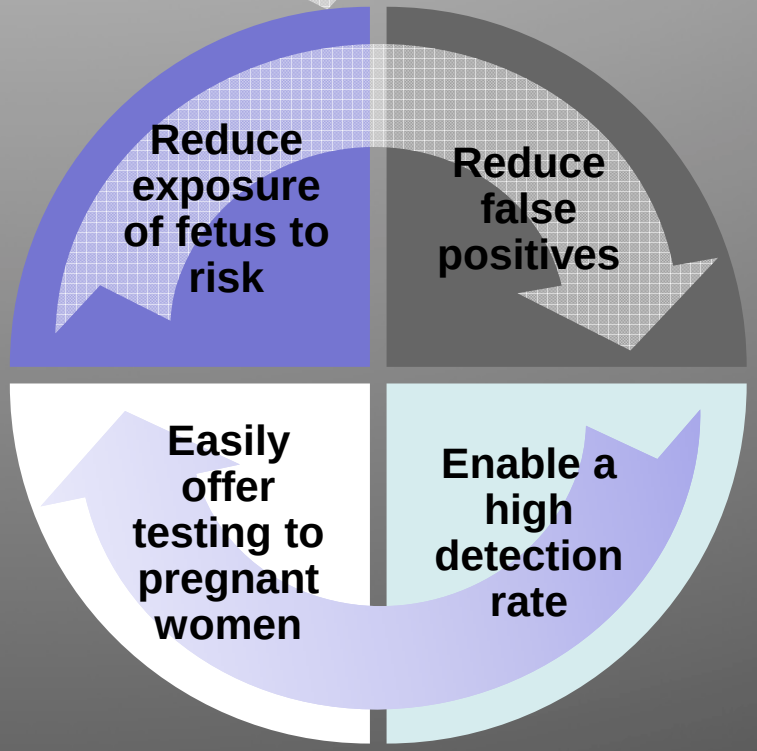


NIPT

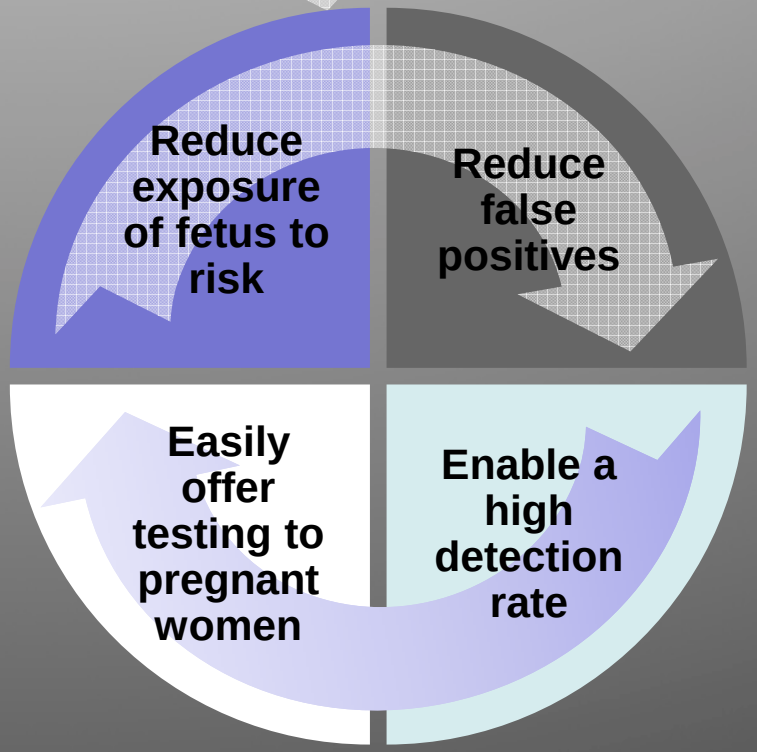
NON INVASIVE PRENATAL TEST

CONSULENZA PRE TEST

La disponibilità di varie tecniche che utilizzano il DNA fetale per la ricerca di anomalie genetiche nel corso della gravidanza rende tassativa la consulenza pre-test, che rappresenta lo strumento di elezione per informare la gestante/coppia sulle diverse opzioni disponibili.

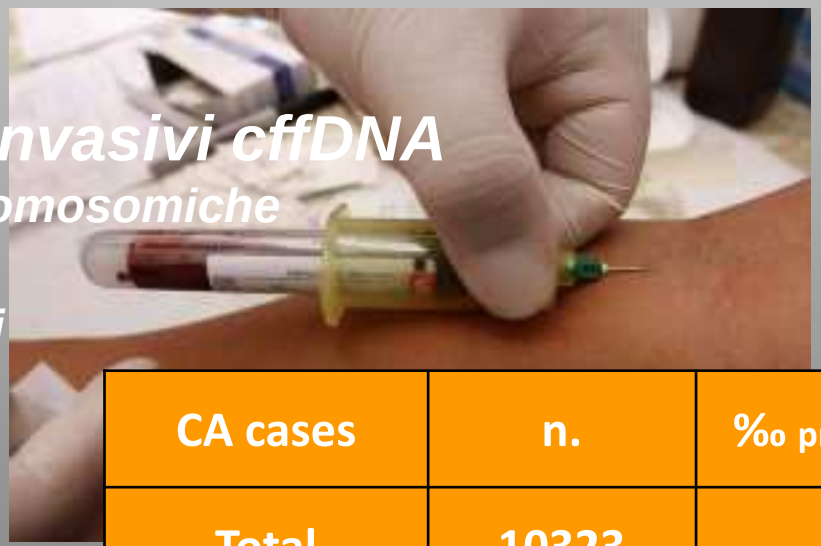
Infatti, è stato dimostrato che la comprensione delle potenzialità e dei limiti del test cfDNA/NIPT è fortemente compromessa, in assenza della consulenza.

La consulenza pre-test deve essere effettuata da uno specialista esperto di medicina fetale.

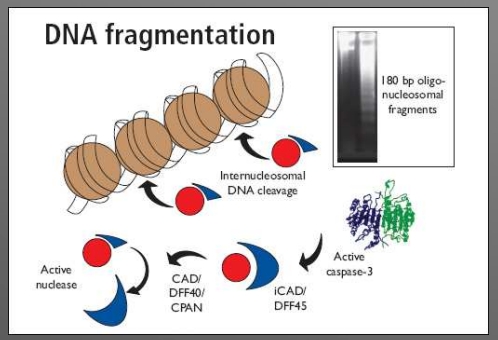


Screening non invasivi cffDNA

Rischio Anomalie Cromosomiche



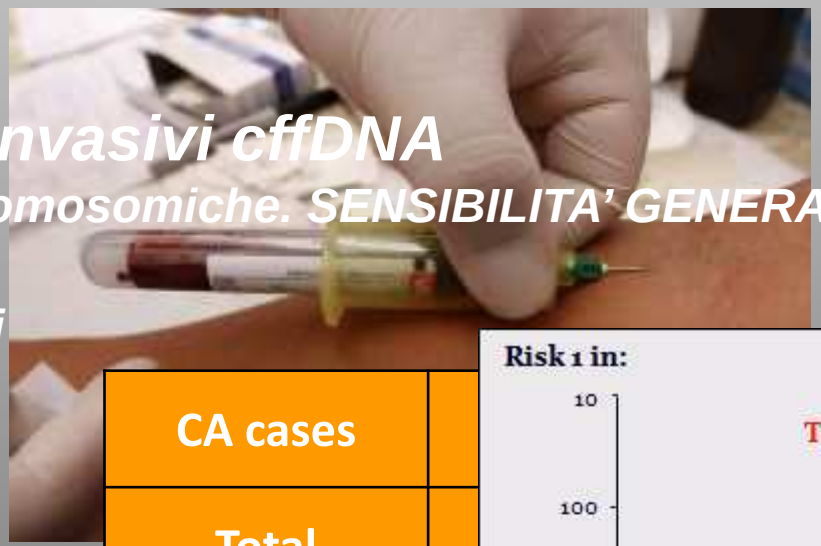
T21	*1/700 nati*
T18	*1/2000*
T13	*1/5000*
X/Yaneupl.	
RCA	



CA cases	n.	‰ prevalence	% CA
Total	10323	4,4	
T21 T18 T13	7335	3,1	71 53 - 13 - 5
X-Y trisomies	473	0,2	5
X0	778	0,33	8
RCA	1737	0,7	17

Screening non invasivi cffDNA

Rischio Anomalie Cromosomiche. SENSIBILITA' GENERALE



T21	*1/700 nati*
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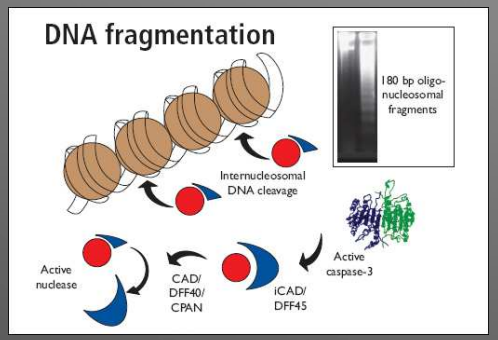
T13	*1/5000*
X/Yaneupl.	
RCA	



CA cases		% CA
Total		
T21 T18 T13		48<77
X-Y trisomies		5
X0		8
RCA		10>40

Screening non invasivi cffDNA

Rischio Anomalie Cromosomiche. SENSIBILITA' GENERALE

Fetal fraction and Expected ratio for trisomy

Fetal Fraction	Expected ratio for Trisomy
4%	1.02
10%	1.05
20%	1.10
40%	1.20

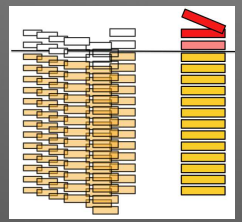
SNP

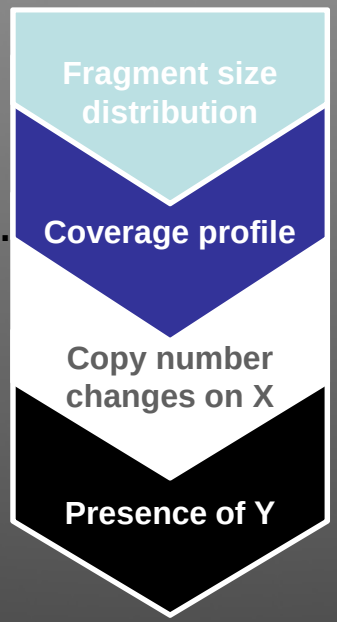
ABRSJA5517	**Maternal (buffy coat)**	A/C	G/G	C/T	A/T	A/A	A/G	C/T	C/C	A/C	A/G
	Fetal (cfDNA)					**A/G**			C/C		

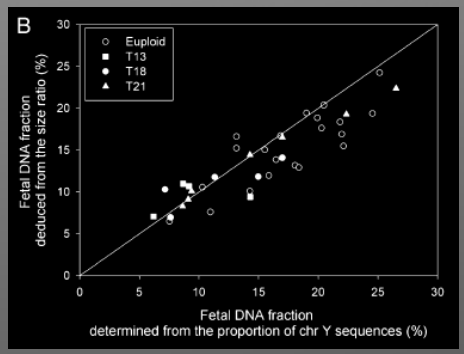
Fragment size, #X CNV & #Y

Fetale

Materno







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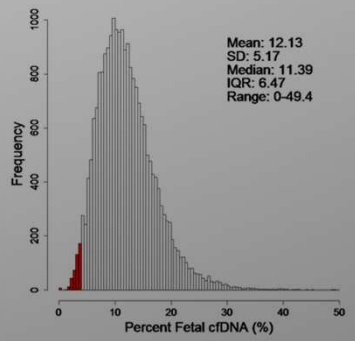

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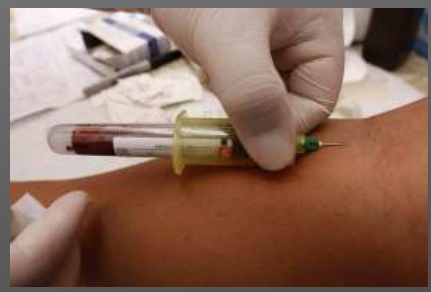
Fetal fraction and test failure

Cases	1200
Successful 1st tier	1187
Successful 2nd tier	9 (0,7%)
Low DNA	7
High variance/1 obese	2
Double fail	4 (0,3%)
Low DNA-HV / FIV ovod.	2
High Variance / obese	2

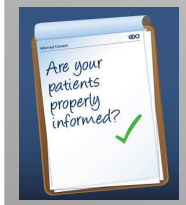
Fetal fraction and gestation weeks

Mean weeks	12,34
Mean fetal fraction	11,5%

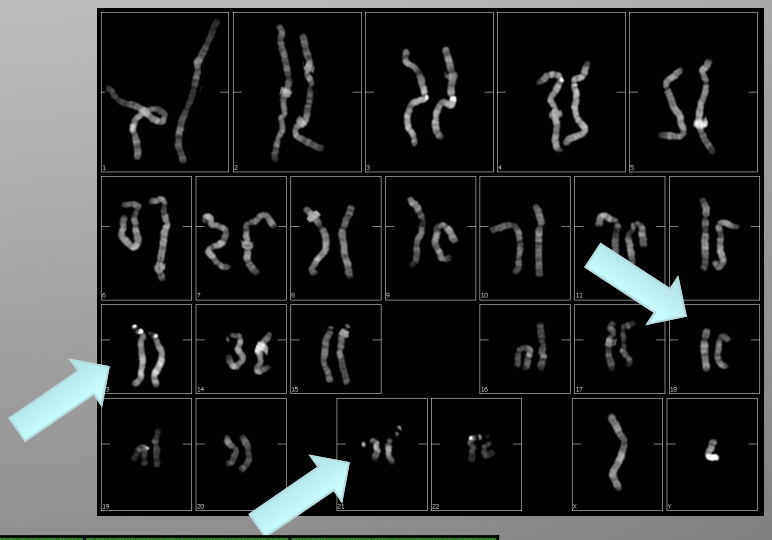


Screening non invasivi cffDNA

Rischio Anomalie Cromosomiche. SENSIBILITA' SPECIFICITA'



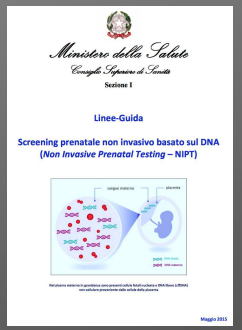
***Validation** and aneuploidy risk prediction:* **high**



Frequenza Anomalie Cromosomiche Autosomi

T21	**1/700 nati+ivg**
T18	**1/2000**
T13	**1/5000**

		Trisomy 21	Trisomy 18	Trisomy 13
CVS trophoblast	False positive rate/specificity	0.08%	0.06%	0.2%
62000 cases*	False negative Population rate False negative/sensitivity	0.02% 0.74%	0.01% 1.59%	NS 0.74%
NIPT total 2013-2015	False positive rate/specificity	0.09%	0.13%	0.13%
	False negative Population rate False neg. /detection rate	0.08% 0.8%	0.06-0.12% 3.7%	0.18-0.36% 9%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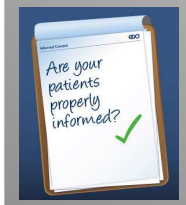
Screening non invasivi cffDNA

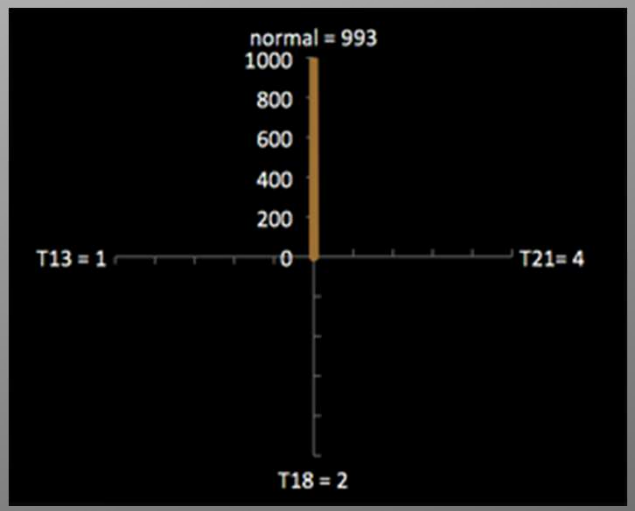
Rischio Anomalie Cromosomiche. SENSIBILITA' SPECIFICITA'



***Validation* and aneuploidy risk prediction: high**

Frequenza Anomalie Cromosomiche Autosomi

T21 1/700 nati+ivg
T18 1/2000 nati
T13 1/5000 nati



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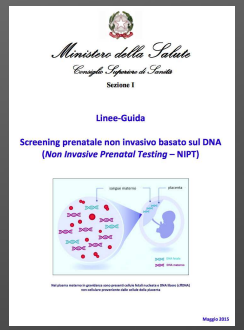
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Screening non invasivi cffDNA

Rischio Anomalie Cromosomiche. SENSIBILITA' SPECIFICITA'

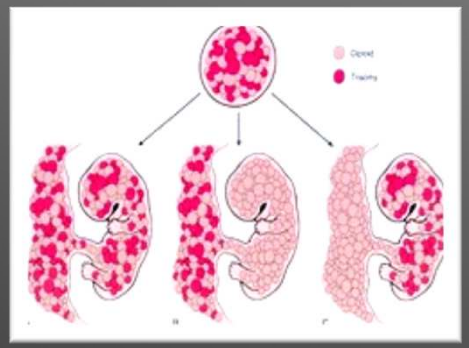
Validation** and Aneuploidy risk prediction:* ***medium

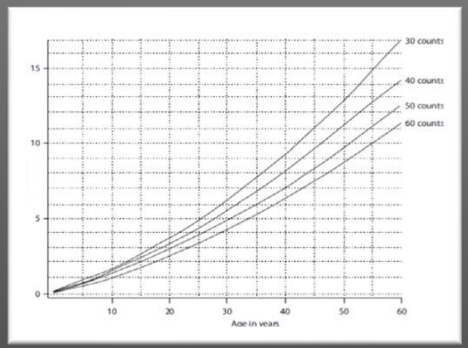
Frequenza Anomalie Cromosomiche SEX

45X

47XXX,47XXY,47XYY

65-90%





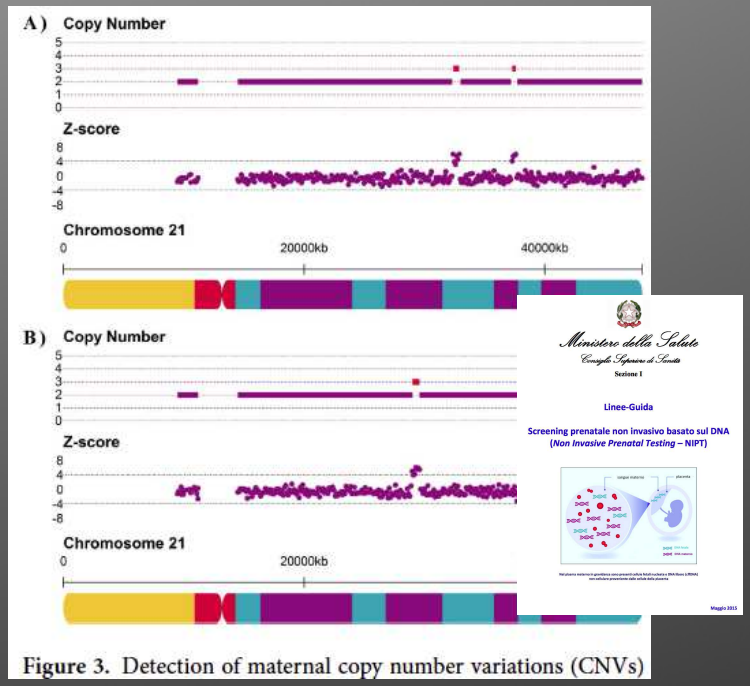


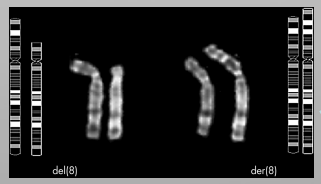
Figure 3. Detection of maternal copy number variations (CNVs)

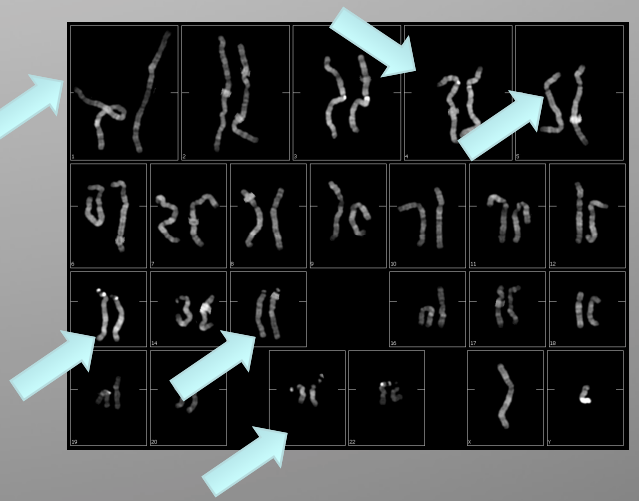
Screening non invasivi cffDNA

Rischio Anomalie Cromosomiche. SENSIBILITA' SPECIFICITA'

Validation and Aneuploidy risk prediction: low/not

validated….





Frequenza Anomalie Cromosomiche

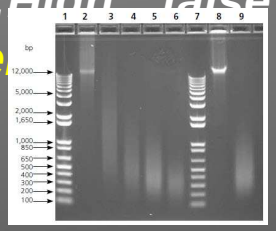
RCA Altre (15-50%) >1/1800

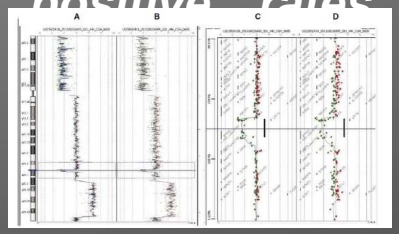
DELEZIONI > 10 Mb

…….why?

Because tested with simulated fragmentation by…. DNA sonication …… than NGS and sequencing…High false positive rates

Sonicated DNA vs……cffDNA fragme





Screening non invasivi cffDNA

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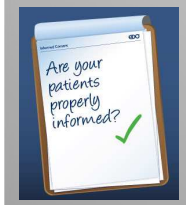
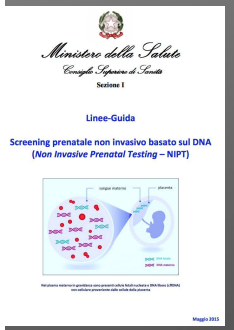


Appropriate Options for Patient Management

	Clinically relevant	Adequately validated	Accurate	Impacts clinical mgmt
Core NIPT *(T21, T18, T13)*	✓	✓	✓	✓
Invasive testing	✓	✓	✓	✓
Expanded NIPT *(microdels)*	✗	✗	✗	✗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Sezione I

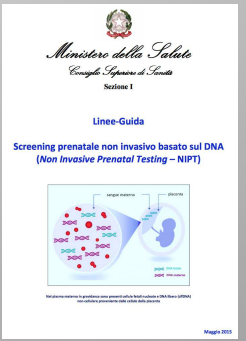
Linee-Guida

Screening prenatale non invasivo basato sul DNA
(*Non Invasive Prenatal Testing* – NIPT)

Maggio 2015

Twin pregnancies performances

Twins/multiple	
2 max	**Valore di rischio distribuito**
regular	**No sex, no identificazione feto affetto**
IVF	**No sex, no identificazione feto affetto**
Oocytes etero	**No sex, no identificazione feto affetto**
Sensitivity T21*	**93.7% (FN/tested popul. 0.6%)**
Specificity T21*	**99.8% (FPR 0.23%)**
DNA fetal fraction	**m 7,4% (12% single)**
*Gil M et al 2015	Ultrasound Obstet Gynecol 45, 249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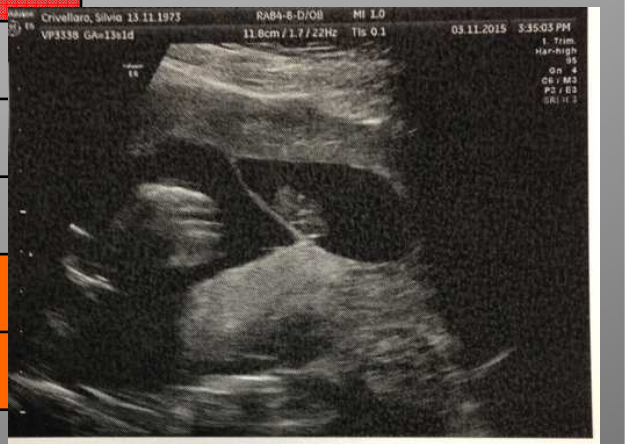
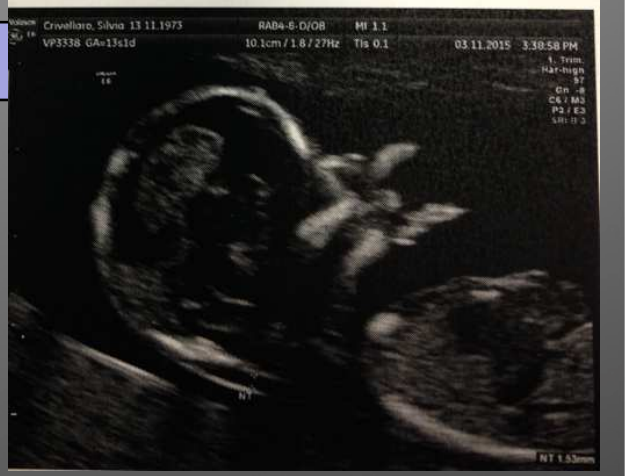
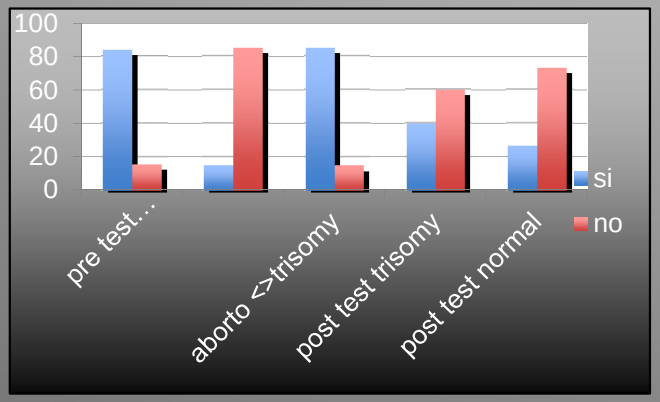


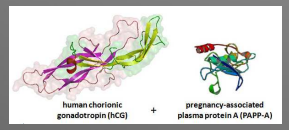


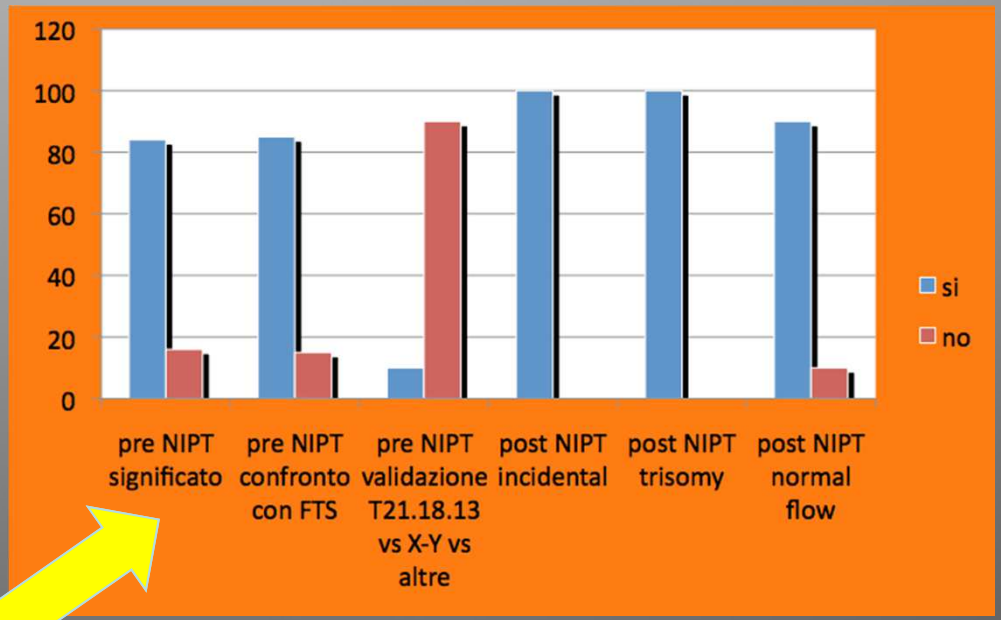
Screening non invasivi cffDNA

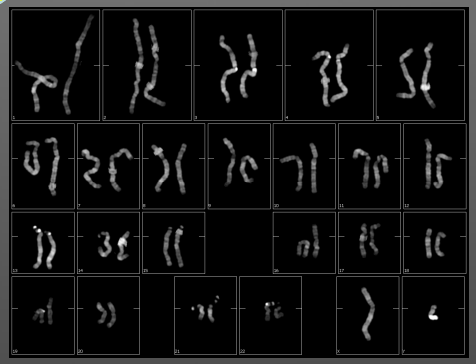
Rischio Anomalie Cromosomiche. SENSIBILITA' SPECIFICITA'

Patient information and understanding ***NIPTonfield 1000***









Screening non invasivi cffDNA

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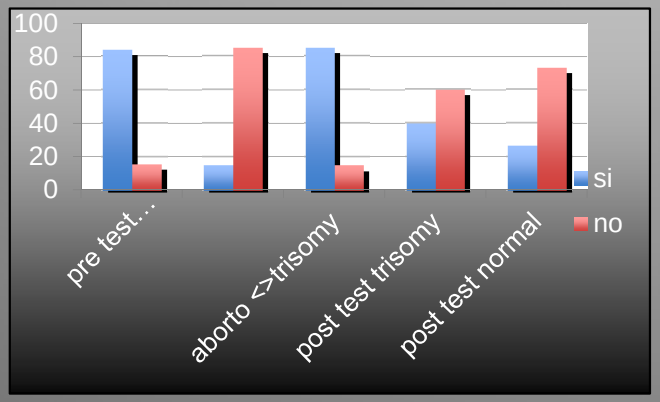

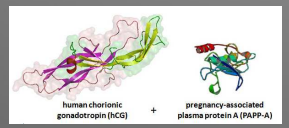

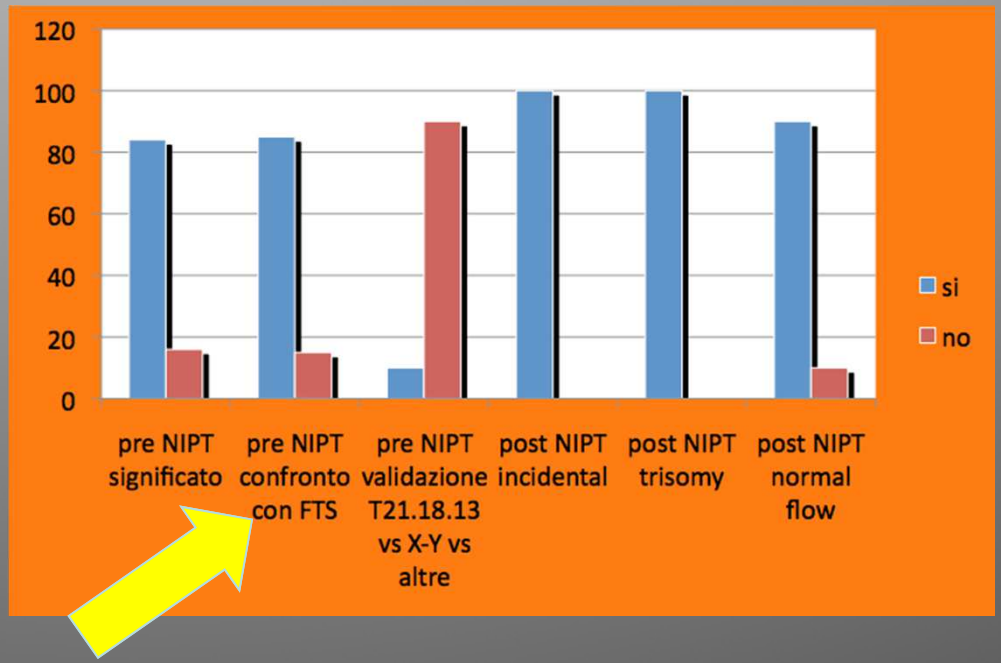

2015 NEXT STUDY 16000 parallel cases: data trisomy 21

	cffDNA	*vs*	*FTS*
DETECTION RATE	*36/36 (100%)*		*28/36 (77.8%)*
FALSE POSITIVE RATE	*9/15050 (0.06%)*		*818/15050 (5.4%)*

Screening non invasivi cffDNA

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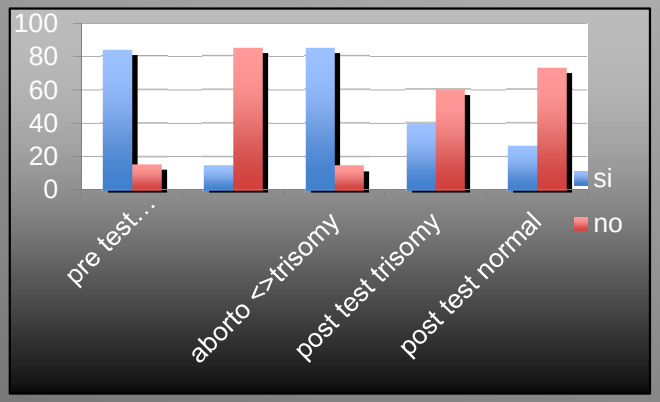
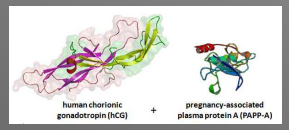
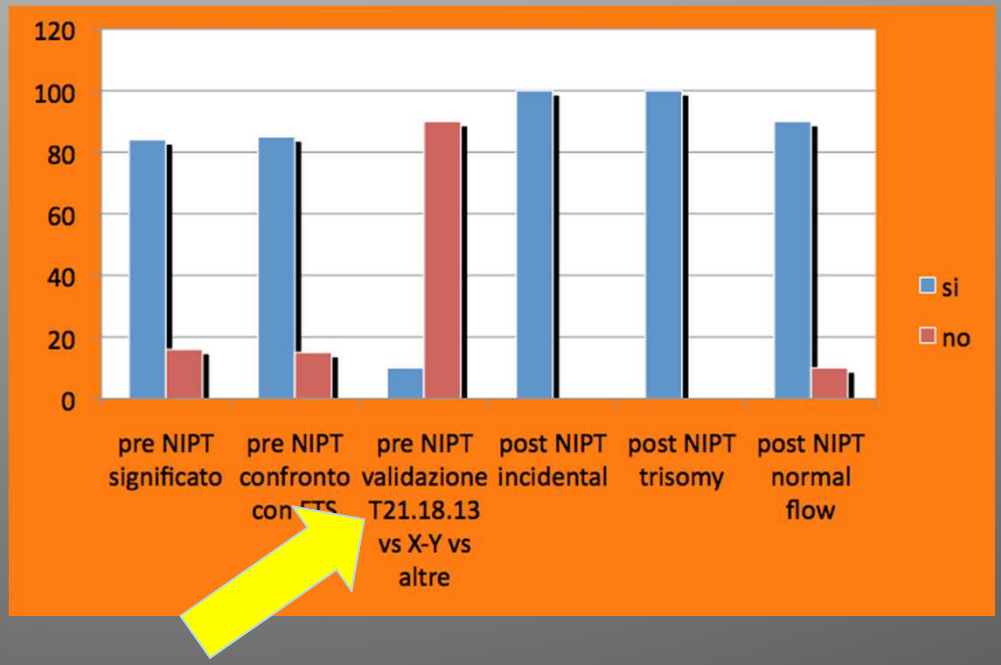
Patient information and understanding ***NIPTonfield 1000***







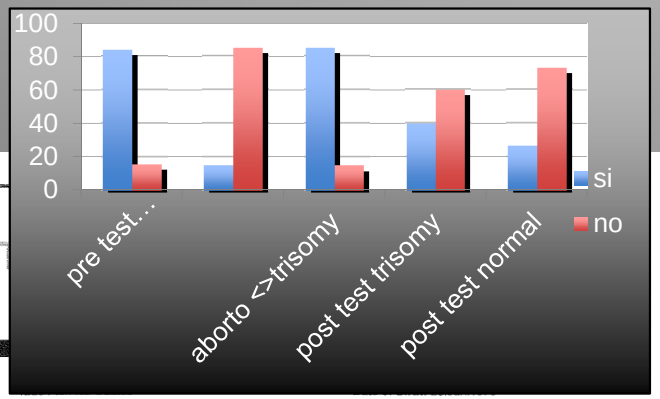
Anomalie Cromosomiche NIPT validazione

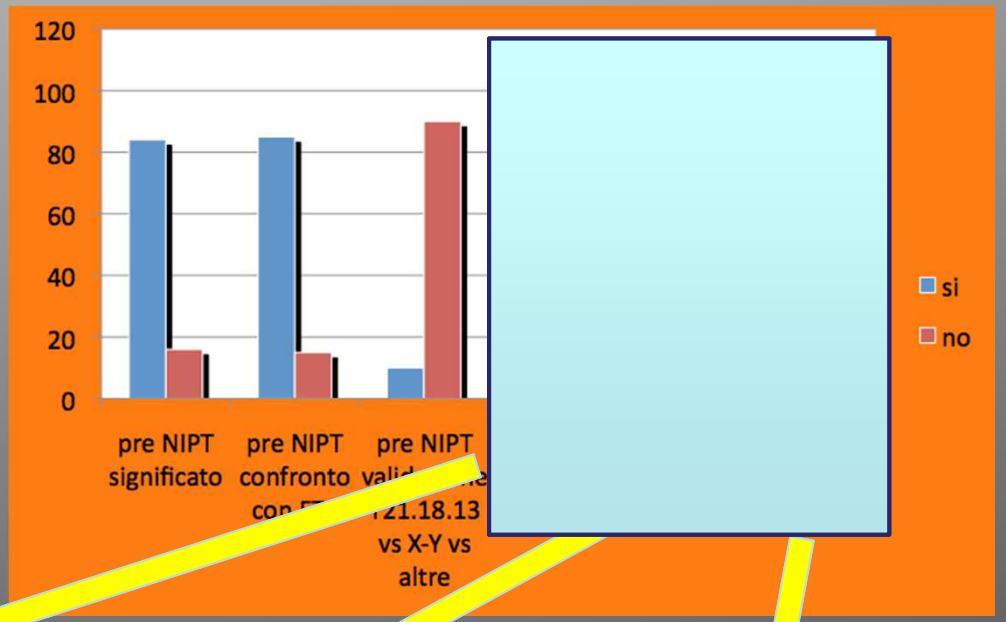
T21 T18 T13	***XXX XXY XYY X0***	***Rare Chromosome Anomalies***
>99	***60-90***	***no on-field clinical data***
Validated	***Validated***	***Not validated***

Screening non invasivi cffDNA

Rischio Anomalie Cromosomiche. SENSIBILITA' SPECIFICITA'

Patient information and understanding ***NIPTonfield 1000***





Geneva - Switzerland

Medical Record/Patient ID:
Gestational Age at Draw (weeks): 12
Indication:
Counselor:
Client Sample ID:

PRENATAL ANEUPLOIDY TEST RESULTS -- Singleton Pregnancy

RESULT	INTERPRETATION
No aneuploidy detected	Results consistent with two copies of chromosome 21
No aneuploidy detected	Results consistent with two copies of chromosome 18

SAMPLE ID

Order ID:	Sample ID:	Draw Date: 02.Mar.2015	Receipt Date:06.Mar.2015

Test Method:
Non Invasive Prenatal Test: Nucleic Acid extraction, DNA sequencing using NGS technology, and analysis of sequencing results to determine fetal aneuploidy.

Limitations of Test:

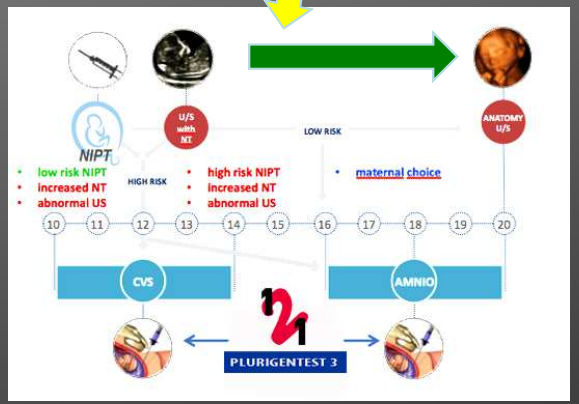
Disclaimer:

No Call Rate ≤ 0.1%

Genoma SWISS BIOTECHNOLOGY a company of esperite

TRDS2.0-1114-EN0X

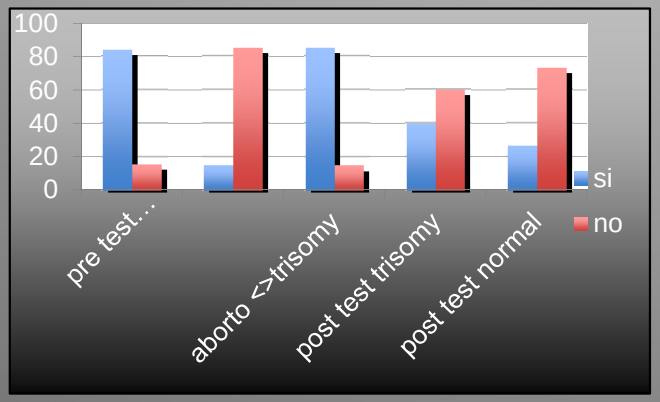
	T21	T18	T13	45X
False Positive	***0.09%***	***0.13%***	***0.13%***	***0.23%***
Population rate	***0.09%***	***0.13%***	***0.13%***	***0.23%***
Case to case (PPV)	***7/100***	***23/100***	***66/100***	***62/100***

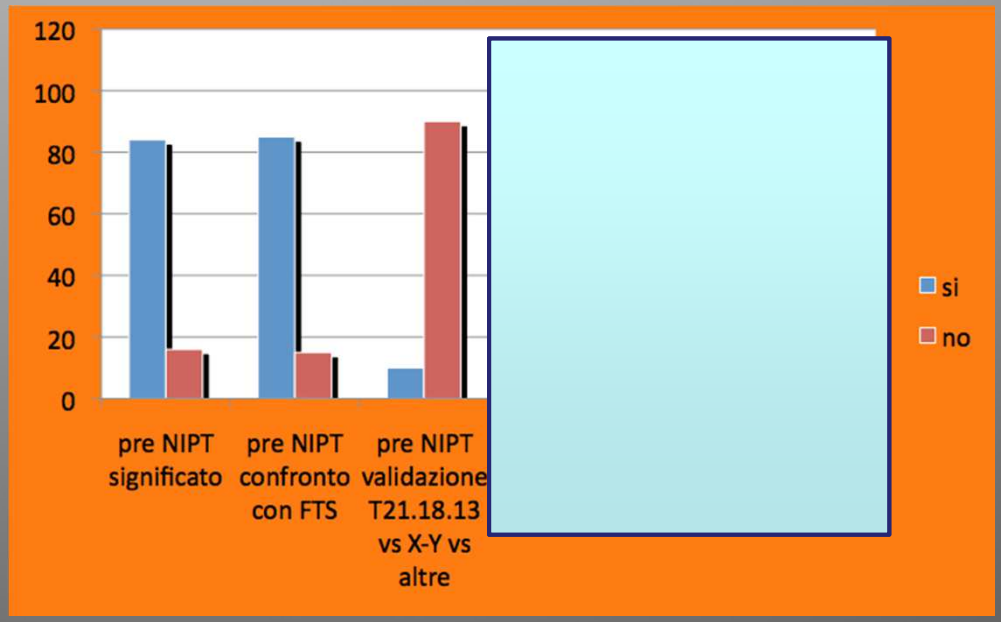


Screening non invasivi cffDNA

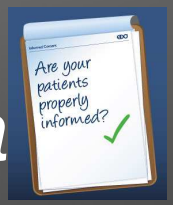
Rischio Anomalie Cromosomiche. SENSIBILITA' SPECIFICITA'

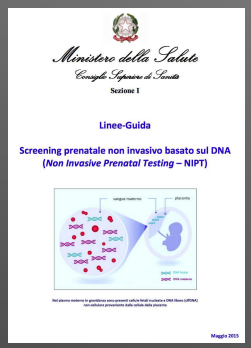
Patient information and understanding ***NIPTonfield 1000***





indice di comprensione dopo consulenza genetica pre test passa dal 25-40% al 85-100%




Ministero della Salute
Consiglio Superiore di Sanità
Sezione 1

Linee-Guida

Screening prenatale non invasivo basato sul DNA
(*Non Invasive Prenatal Testing* – NIPT)

Maggio 2015

LLGG.NIPT ***Raccomandazioni generali***

I Centri che offrono il test devono avere competenze nella diagnosi ecografica, nella diagnosi prenatale; devono avere competenze qualificate per la consulenza pre-test e post-test; devono garantire la tracciabilità del campione ed essere collegati con il laboratorio che esegue il test. Nel caso il laboratorio sia all'estero o a distanza è necessario un efficiente contatto a sostegno della interpretazione dei risultati.

NIPTonfield1000

Poliambulatori con competenze integrate.

Visita ostetrica/ecografia. Consulenza genetica pre test. NIPT e/o altre indagini. Consulenza e/o Supporto post test. Decorso ecografico.

NIPT non è per "il venditore di medicine".....(C.Santamaria)


ricerca
indagate
caratteristiche
disponibili
prendendo
fallimento
tassativa
considerando
possibilità
varie
fetale
materna
termini
disponibilità
materno
genetica
illustrare
DNA
opzioni
informare
nel
test
dell
limiti
analisi
liquido
rende
età
villi
quelli
come
circolo
referto
sui
all
origine
pre-test
sulle
dei
quando
stimata
definire
relazione
delle
per
sugli
placentare
embriologica
compresi
amniotico
conseguenti
dimostrato
necessario
elezione
anomalie
specificità
consulenza
consulenti
patologie
post-test
diverse
amniociti
affrontare
corso
cromosomiche
quelle
Infatti
alcuni
risultati
indagini
presente
assenza
riferimento
strumento
implicazioni