Ethical Concerns about Prenatal Whole Genome Sequencing: A Study with Hong Kong Obstetric Professionals

Huso Yi and Olivia Ngan

CUHK Centre for Bioethics
Faculty of Medicine
The Chinese University of Hong Kong

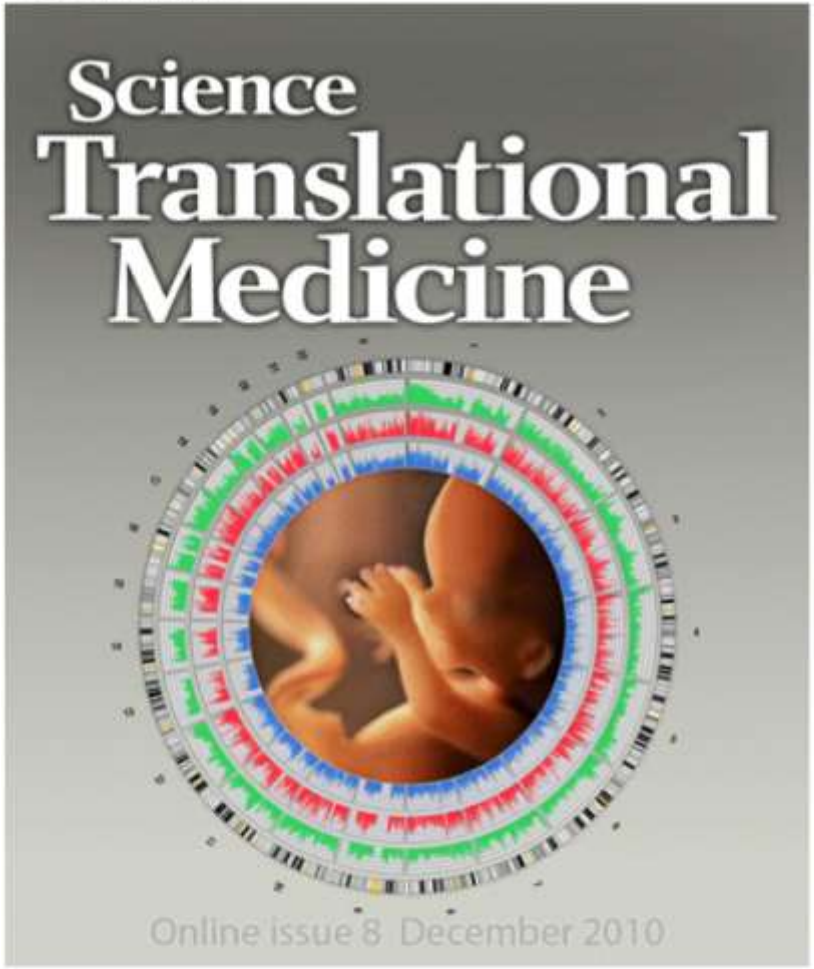
CUHK Centre for Bioethics Launch Conference
10 January 2015

CUHK Centre for Bioethics Launch Conference

Building Bioethics Capacity in Hong Kong: Ethical Dimensions of Policy for Ageing and Genetics

Conference Hall, 2/F, Central Government Offices
2 Tim Mei Avenue, Tamar, Hong Kong
9 and 10 January 2015

Cover image



RESEARCH ARTICLE

PRENATAL DIAGNOSIS

Maternal Plasma DNA Sequencing Reveals the Genome-Wide Genetic and Mutational Profile of the Fetus

Y. M. Dennis Lo,[1,2]* K. C. Allen Chan,[1,2] Hao Sun,[1,2] Eric Z. Chen,[1,2] Peiyong Jiang,[1,2] Fiona M. F. Lun,[1,2] Yama W. Zheng,[1,2] Tak Y. Leung,[3] Tze K. Lau,[3] Charles R. Cantor,[4] Rossa W. K. Chiu[1,2]

(Published 8 December 2010; Volume 2 Issue 61 61ra91)

ONLINE COVER Scanning Fetal DNA. During pregnancy, a fetus releases its DNA as short fragments into the blood of its mother. In this issue, Lo *et al.* report that by sequencing billions of DNA molecules from the plasma of a pregnant woman they were able to assemble the full genome of the fetus prenatally and noninvasively and identify a mutation in the fetal DNA for the inherited blood disease β-thalassemia. The outermost ring of this week's cover image depicts human chromosomes arranged in a circle. The green, red, and blue rings show the sequence composition (GC content) and the extent of sequencing for total (mainly maternally-derived) DNA and fetal-specific DNA in maternal plasma, respectively. [CREDIT: PHOTOGRAPH OF FETUS/SCIENCE PHOTO LIBRARY; SCHEMATIC ADAPTED FROM FIGURE 2B IN LO *ET AL.* BY ALLEN CHAN AND LEONG WOO YAN]

Genomic Snapshots in Utero

Prof. **Dennis Y.M. Lo**, Li Ka Shing Professor of Medicine and Professor of Chemical Pathology at CUHK,

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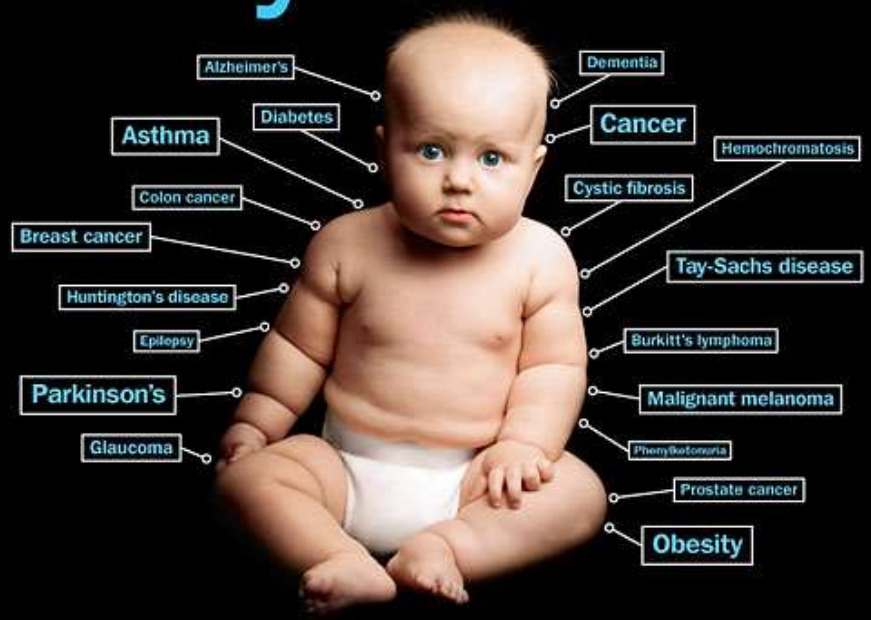

New genetic tests can point to risks—but not always a cure

BY BONNIE ROCHMAN

www.time.com

Prenatal **Whole Genome** *Sequencing*

JUST BECAUSE WE CAN, SHOULD WE?

BY GREER DONLEY, SARA CHANDROS HULL, AND BENJAMIN E. BERKMAN

With whole genome sequencing set to become the preferred method of prenatal screening, we need to pay more attention to the massive amount of information it will deliver to parents—and the fact that we don't yet understand what most of it means.

Prenatal **Whole Genome** *Sequencing*

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Whole genome sequencing is quickly becoming more affordable and accessible, with the prospect of personal genome sequencing for under $1,000 now widely said to be in sight.[1] The ethical issues raised by the use of this technology in the research context have received some significant attention, but little has been written on its use in the clinical context, and most of this analysis has been futuristic forecasting.[2] This is problematic, given the speed with which whole genome sequencing technology is likely to be incorporated into clinical care. This paper explores one particular subset of these issues: the implications of adopting this technology in the prenatal context without a good understanding of when and how it is useful. This way of adopting whole genome sequencing would be what Benjamin Wilfond and Kathleen Nolan call *ecemporaneous*, where the independent market, professional practice, and legal and consumer forces determine utilization. Conversely, in the *evidentiary* model, new technologies are adopted after an examination of the underlying normative considerations that arise from their use. An extemporaneous adoption of new technologies, Wilfond and Nolan argue, can lead to harmful consequences that could be circumvented if reasonable deliberation occurs at the onset of the technology's incorporation into clinical care.[3]

Prenatal whole genome sequencing differs from current prenatal genetic testing practice in a number of ethically relevant ways. Most notably, whole

Greer Donley, Sara Chandros Hull, and Benjamin E. Berkman, "Prenatal Whole Genome Sequencing: Just Because We Can, Should We?" *Hastings Center Report* 42, no. 4 (2012): 28-40. DOI: 10.1002/hast.50

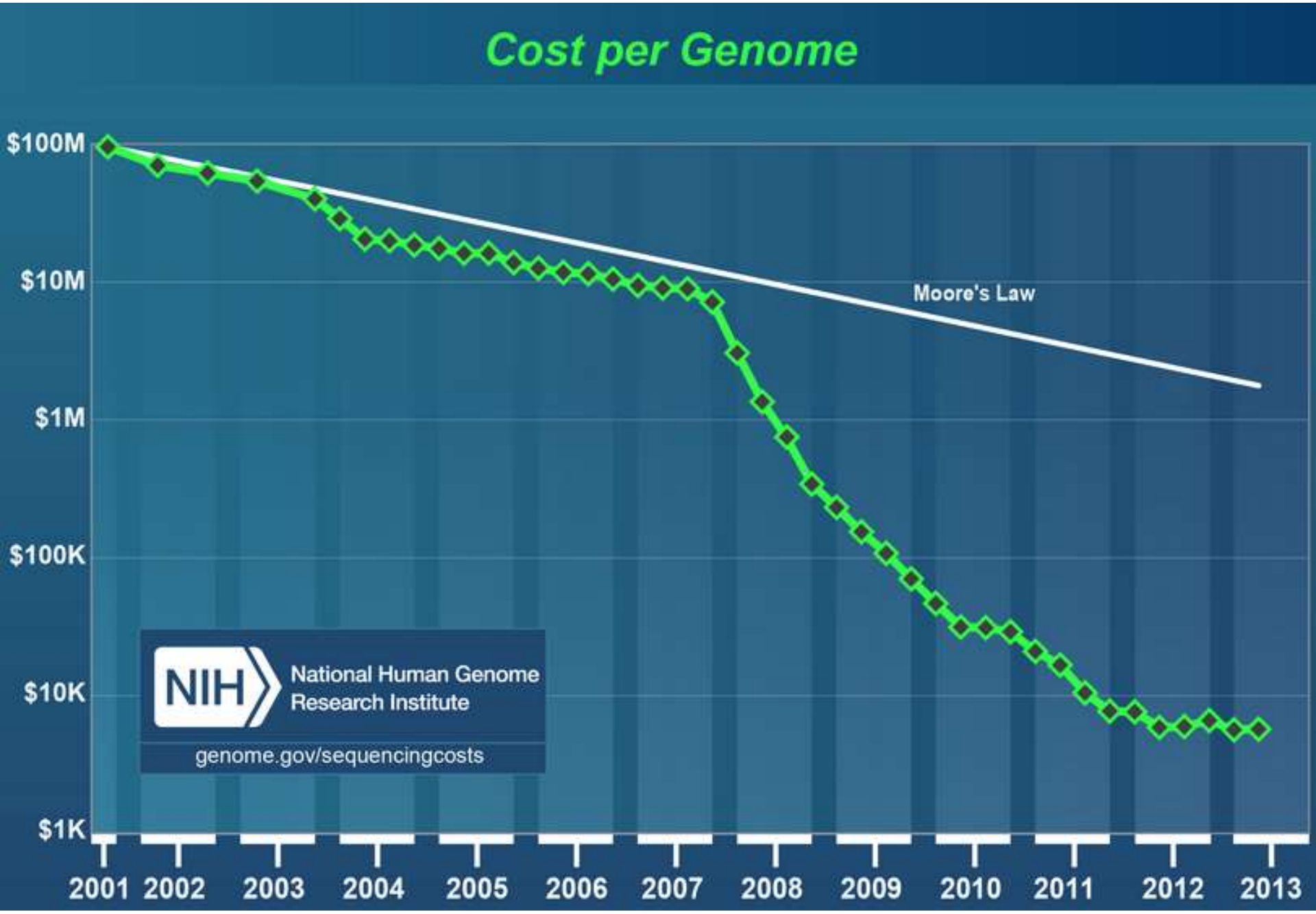
Cost per Genome
$100M
$10M
$1M
$100K
$10K
$1K
Moore's Law
NIH
National Human Genome Research Institute
genome.gov/sequencingcosts
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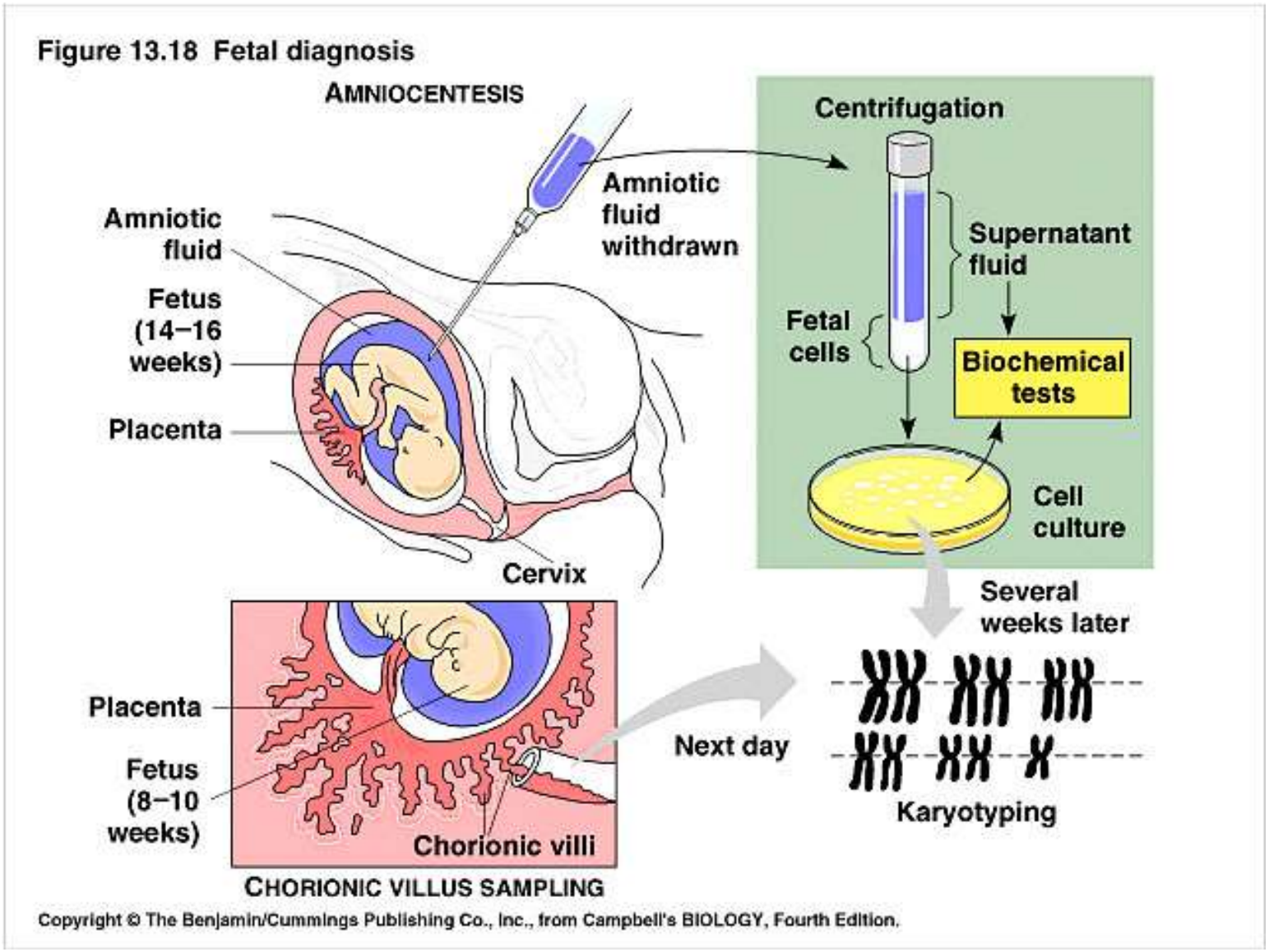
ILLUSTRATION BY GAVIN POTENZA

Get ready for the flood of fetal gene screening

Knowing May Pose Risk

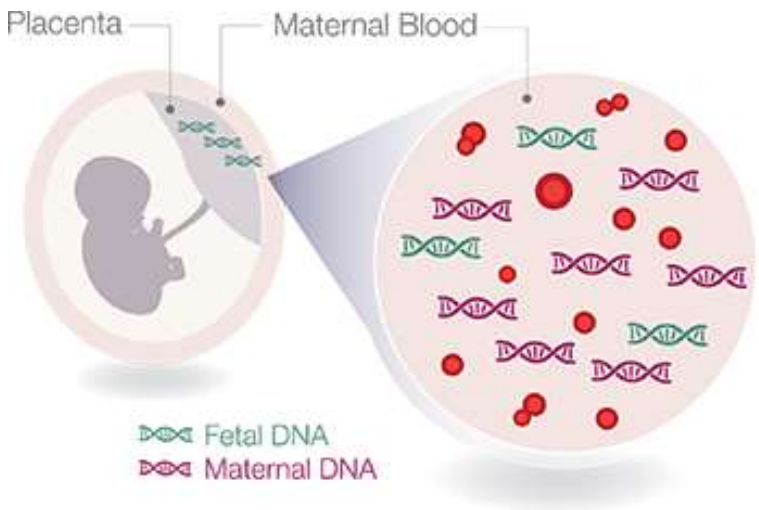


THE LANCET

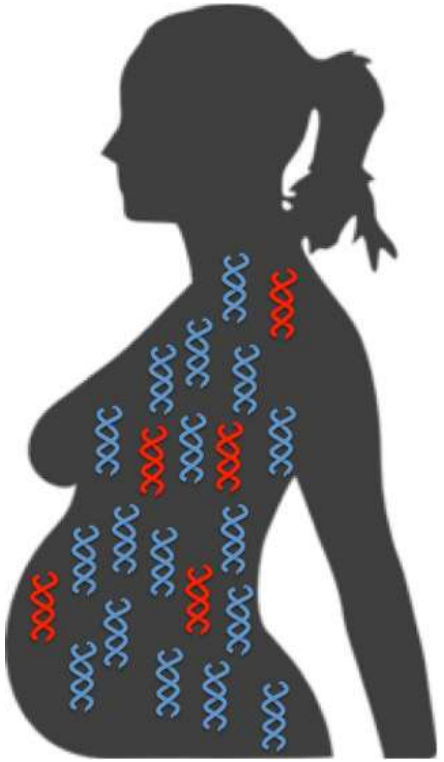
Early report

Presence of fetal DNA in maternal plasma and serum

Y M Dennis Lo, Noemi Corbetta, Paul F Chamberlain, Vik Rai, Ian L Sargent, Christopher W G Redman, James S Wainscoat



Cell-free fetal DNA in maternal circulation



Lo YM et al. Presence of fetal DNA in maternal plasma and serum. Lancet. 1997 16;350(9076):485-7.

Cell-Free Fetal DNA Sequencing NIPT

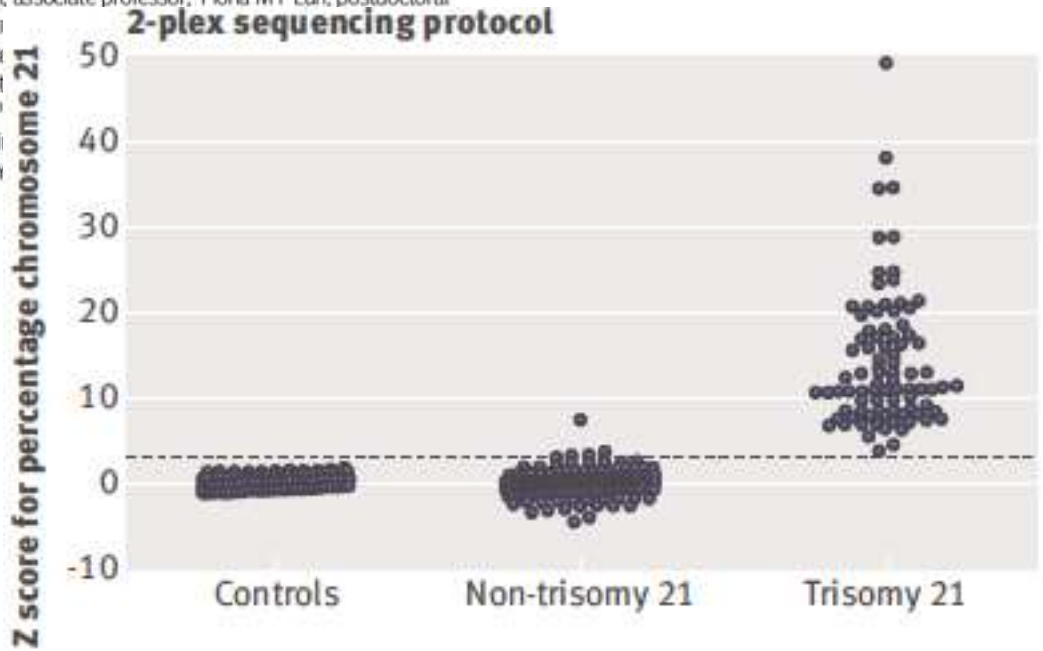
Clinical validity to detect trisomy 21 over 99.1% sensitivity.

BMJ

RESEARCH

Non-invasive prenatal assessment of trisomy 21 by multiplexed maternal plasma DNA sequencing: large scale validity study

Rossa W K Chiu, professor,[1] Ranjit Akolekar, clinical research fellow,[3] Yama W L Zheng, student,[1] Tak Y Leung, professor,[2] Hao Sun, assistant professor,[1] K C Allen Chan, associate professor,[1] Fiona M F Lun, postdoctoral fellow,[1] Attie T J I Go, professor,[4] Elizabeth T Lau, depart[1] William W K To, consultant,[6] Wing C Leung, consultant,[7] R[a] consultant,[9] Helena Lam, consultant,[10] Yu Y Kung, obstet Vugt, professor,[4] Ryoko Minekawa, postdoctoral fellow,[3] associate professor,[5] Jun Wang, professor,[12] associate di Tze K Lau, professor,[2] Kypros H Nicolaides, professor,[3] Y



Clinical Advantages

- 10th week onwards
- No Miscarriage Risk
- False-positive rate: 0.1%
- High prediction with definitive result (Positive or Negative)

- No clinical skill required
- Can be done remotely

Knowing Without Taking Risk?

- Yes, by procedure
- Maybe …
- And, what else?
- No procedural risk
- But, conceptual risk?

safeT21 is a non-invasive prenatal DNA test developed for the screening of fetal chromosomal abnormalities, such as Down syndrome, Edwards syndrome (trisomy 18) and Patau syndrome (trisomy 13). The test is based on proprietary technologies developed at The Chinese University of Hong Kong. During pregnancy, the unborn child releases some of its DNA into the blood circulation of its mother. safeT21 is a test that measures the amount of DNA molecules from chromosomes 21, 18, 13 and others in the blood samples of pregnant women.

An abnormally increased amount of chromosome 21 DNA molecules in a pregnant woman¡¦s blood sample is suggestive of Down syndrome. Large-scale clinical studies have shown that the safeT21 test can detect 99.1% of Down syndrome fetuses. The test has a false-positive rate of 0.1%.

Trisomy 18 is associated with abnormally increased amounts of chromosome 18 DNA molecules in the pregnant woman¡¦s blood sample. The safeT21 test can detect >99.9% of trisomy 18 fetuses and has a false-positive rate of 0.4%.

Trisomy 13 is associated with abnormally increased amounts of chromosome 13 DNA molecules in the pregnant woman¡¦s blood sample. The test can detect 91.7% of trisomy 13 fetuses and has a false-positive rate of 0.3%.

Additional chromosomal abnormalities, including 45 X0, 47 XXY, 47 XXX, 47 XYY, trisomy 16, trisomy 22 and some microdeletions, will also be reported when detected.

Since there is a chance of false-positive results (meaning that not all positive test results are caused by chromosomal abnormalities of the fetus), positive test results should be confirmed by amniocentesis or chorionic villus sampling. On the other hand, **a normal result does not fully exclude Down syndrome, trisomy 18 or trisomy 13 or other chromosomal abnormalities**.

The diagnostic accuracy of the safeT21 test as described above is based on the requirement of the tested baby contributing adequate amounts of DNA into the maternal plasma sample. For twin pregnancies, current technologies can only measure the total amount of DNA contributed by BOTH babies in maternal plasma. For **identical twins**, the diagnosis should be as accurate as for a singleton fetus.

For **non-identical twins**, adequate amounts of DNA in maternal plasma are required from each twin baby. **The diagnostic accuracy relies on the assumption that each non-identical twin baby contributed at least the minimum required amount of DNA into maternal plasma. If one of the babies contributed less than the minimum requirement, there is a risk of false-negative results**. For **reduced or vanished twins**, the non-viable fetus(es) may continue to contribute DNA into the mother¡¦s circulation. Hence, conventional prenatal confirmation needs to be performed for the viable fetus(es) if the safeT21 test reports chromosomal abnormalities.

It should also be noted that ~1% of test requests (single fetus and twin pregnancies), despite all reasonable efforts, results may not be reportable. Such occurrences could be caused by factors such as an unusually low amount of fetal DNA in the blood sample. When a **non-reportable result** is issued, the laboratory fees will be refunded or one may choose to repeat the test at no additional cost.

For enquiries:

- **In person**: The Chinese University of Hong Kong Fetal Medicine Unit Office, Room 20, 2/F, Li Ka Shing Specialist Out-patient Clinic South Wing, Prince of Wales Hospital
- **By phone**: Call The Chinese University of Hong Kong Fetal Medicine Unit Office at 2632-4219 (Please leave your name, telephone number and specify your request)
Our colleague will call back and make appointment with you as soon as possible.
- **Online**: Make an appointment via internet

Charge
HKD $8,000

NIPT in the US

	Natera's *Panorama*	Verinata's *verifi*	Sequenom's *MaterniT21 PLUS*	Ariosa's *Harmony*
Trisomies tested	13, 18, 21	13, 18, 21, sex chromosomes	13, 18, 21, sex chromosomes	13, 18, 21
Monosomy tested	X	X	X	
Genetic testing method	Single nucleotide polymorphism	Massively parallel sequencing	Massively parallel sequencing	Chromosome-selective sequencing
Sensitivity	92-99%	87-99%	92%-99%	80-99%
Accuracy	100%	100%	>99%	>99%
Earliest gestational age	9 weeks	10 weeks	10 weeks	10 weeks
Price	$1,495	$1,500	$2,762	$795

Source: Nature Medicine

Harmony™ PRENATAL TEST

MATERNIT21™ PLUS

panorama™ prenatal test

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NIPT in the World

BerryGenomics

华大基因 BGI

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The Advantages Of The NIFTY™ Test

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Non-invasive with no risk of miscarriage

Accurate.

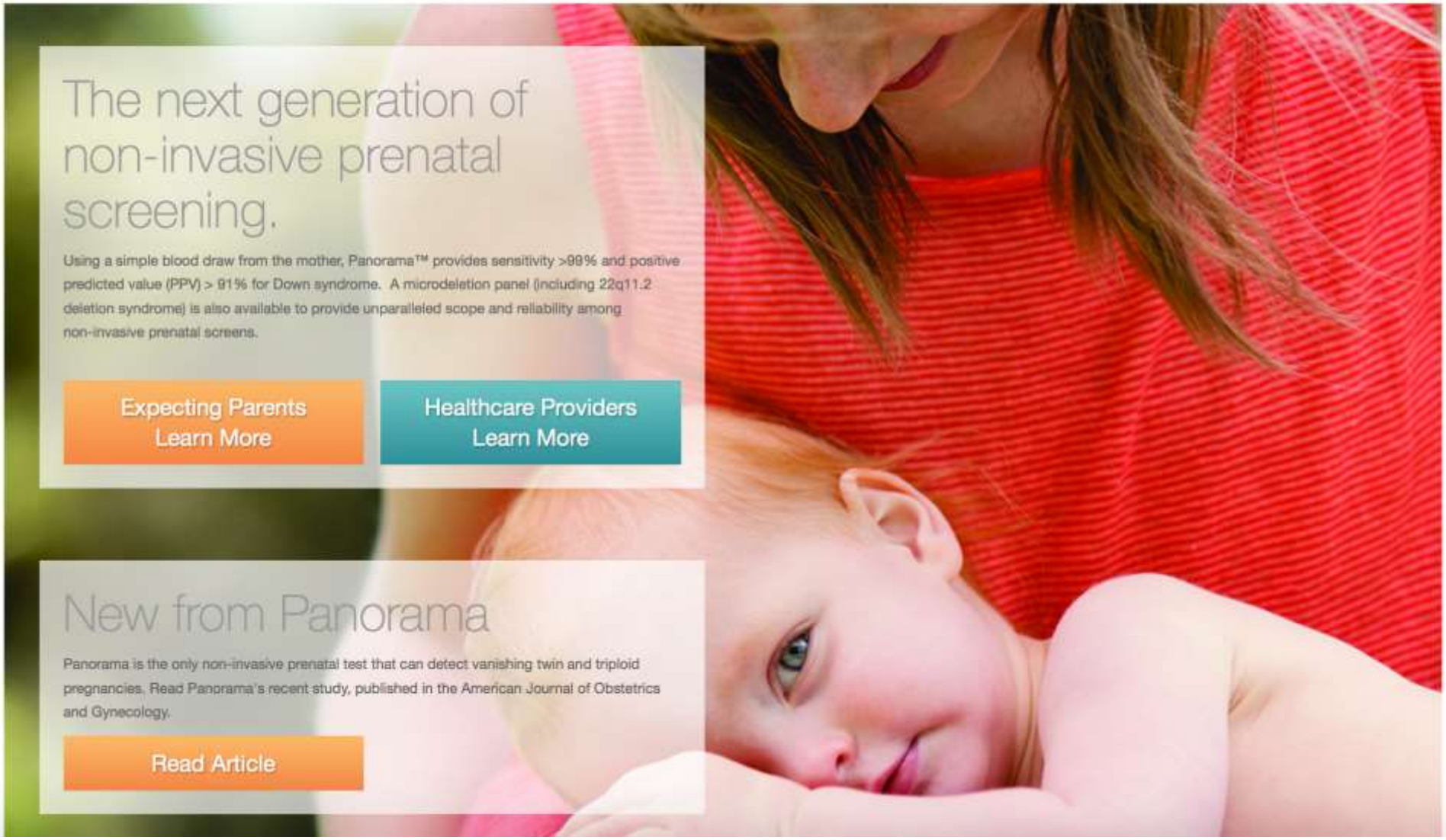
99.9% sensitivity for detection of trisomy conditions such as Down syndrome.

Simple.

Test from a small 10 ml maternal blood sample as early as week 10 of pregnancy

Trusted.

Over 350,000 tests conducted worldwide with a false positive rate of just 0.1%.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Healthcare Providers Learn More
New from Panorama
Panorama is the only non-invasive prenatal test that can detect vanishing twin and triploid pregnancies. Read Panorama's recent study, published in the American Journal of Obstetrics and Gynecology.
Read Article

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Natera is driven by a passion for elevating the science and utility of prenatal testing.

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Non-Invasive Prenatal Testing

Panorama™ is the most accurate and comprehensive non-invasive prenatal screening test in the industry — and now detects triploidy.

Genetic Carrier Screening

Horizon™ is a simple blood test that determines whether a person is a carrier for genetic disorders.

PGD/PGS Testing

Spectrum™ pre-implantation genetic testing (PGD) doubles the rate of successful implantation.

Miscarriage Testing

Anora™ miscarriage testing (products of conception testing) helps you and your patients understand why a miscarriage occurred.

Prenatal Paternity Testing

Natera's non-invasive paternity test safely establishes paternity before a baby is born.

Non-Invasive Prenatal Testing (NIPT) Market Expected to Reach USD 3.62 Billion Globally in 2019: Transparency Market Research

Share 8+1

NEW YORK, January 6, 2014 /PRNewswire/ --

According to a new market report published by Transparency Market Research, **"Non-Invasive Prenatal Testing (NIPT) Market (MaterniT21 PLUS, verifi, Harmony, Panorama, NIFTY, PrenaTest and BambniTest) - Global Industry Analysis, Size, Share, Growth, Trends and Forecast, 2013 - 2019,"** the global NIPT market was valued at USD 0.22 billion in 2012 and is expected to grow at a CAGR of 37.6% from 2013 to 2019, to reach an estimated value of USD 3.62 billion in 2019.

More by this Source

Global A2P SMS Market Expecte
Reach USD 70.32 Billion in 2020:
Transparency Market Research
Oct 22, 2014, 12:30 ET

China $8 Billion Potential NIPT Market Stopped By FDA

6 comments

Apr 6, 2014 12:56 PM | about stocks: ILMN

China Cracks Down on DNA Testing (Mar 4, 2014)

Prenatal testing is the most popular in the nascent business of genetic testing in China. A Chinese securities analyst estimates its market to be worth 50 billion yuan ($8 billion) a year, based on the number of expected births and a testing fee of 3000 yuan ($480) each. A more realistic figure might be about 480 million yuan (US$77 million), the amount spent by the 160,000 women who have taken the tests since they were made available in China. In the United States, the comparable market is estimated to be worth upward of $1.3 billion a year.

China approves DNA-sequencing devices to detect genetic defects in unborn babies

Controversial testing products for prenatal detection of birth defects get the green light

Angela Meng
angela.meng@scmp.com

PUBLISHED : Thursday, 03 July, 2014, 4:56pm
UPDATED : Friday, 04 July, 2014, 5:35pm

Many pregnant women have called for diagnostic procedures that can detect genetic diseases in foetuses. Photo: AFP

The mainland has lifted the controversial ban on medical diagnostic products that can help detect birth defects in unborn children.

The China Food and Drug Administration (CFDA) on Monday approved the registration of genomics company BGI's sequencers - which help map out the sequence of a person's genetic code, which in turn determine traits such as eye colour and skin colour or even the propensity to certain diseases.

The medical devices, called second-generation gene sequencing diagnostic products, are used for non-invasive tests on the foetus to detect genetic diseases such as Down's syndrome.

The CFDA also approved diagnostic kits for "high-risk" pregnant women, such as those older than 35.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 27, 2014 VOL. 370 NO. 9

DNA Sequencing versus Standard Prenatal Aneuploidy Screening

Diana W. Bianchi, M.D., R. Lamar Parker, M.D., Jeffrey Wentworth, M.D., Rajeevi Madankumar, M.D., Craig Saffer, M.D., Anita F. Das, Ph.D., Joseph A. Craig, M.D., Darya I. Chudova, Ph.D., Patricia L. Devers, M.S., C.G.C., Keith W. Jones, Ph.D., Kelly Oliver, B.S., Richard P. Rava, Ph.D., and Amy J. Sehnert, M.D., for the CARE Study Group*

Royal College of Obstetricians & Gynaecologists

Non-invasive Prenatal Testing for Chromosomal Abnormality using Maternal Plasma DNA

Scientific Impact Paper No. 15
March 2014

Matthew Herper
Forbes Staff

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I cover science and medicine, and believe this is biology's century.
full bio →

PHARMA & HEALTHCARE 2/26/2014 @ 1:12PM | 16,975 views

The Market For DNA-Sequencing-Based Down Syndrome Tests Could Exceed $6 Billion

On Wednesday night the New England Journal of Medicine published a study showing that a new, DNA-sequencing based blood test provides a dramatic improvement in accuracy at screening for Down syndrome and a second, deadly disorder. That could open up a $6 billion market to the biotechnology companies that are already marketing these tests.

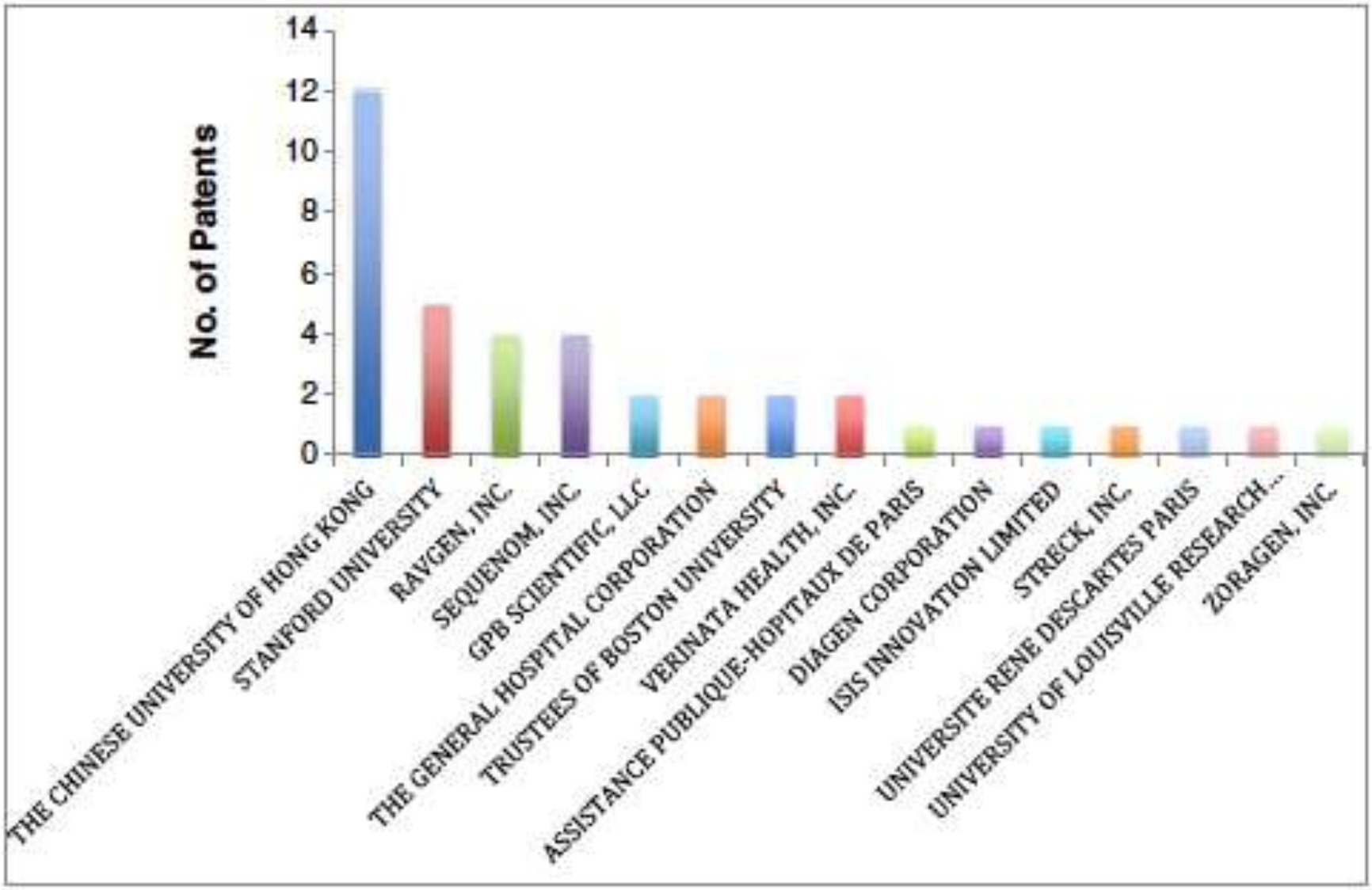
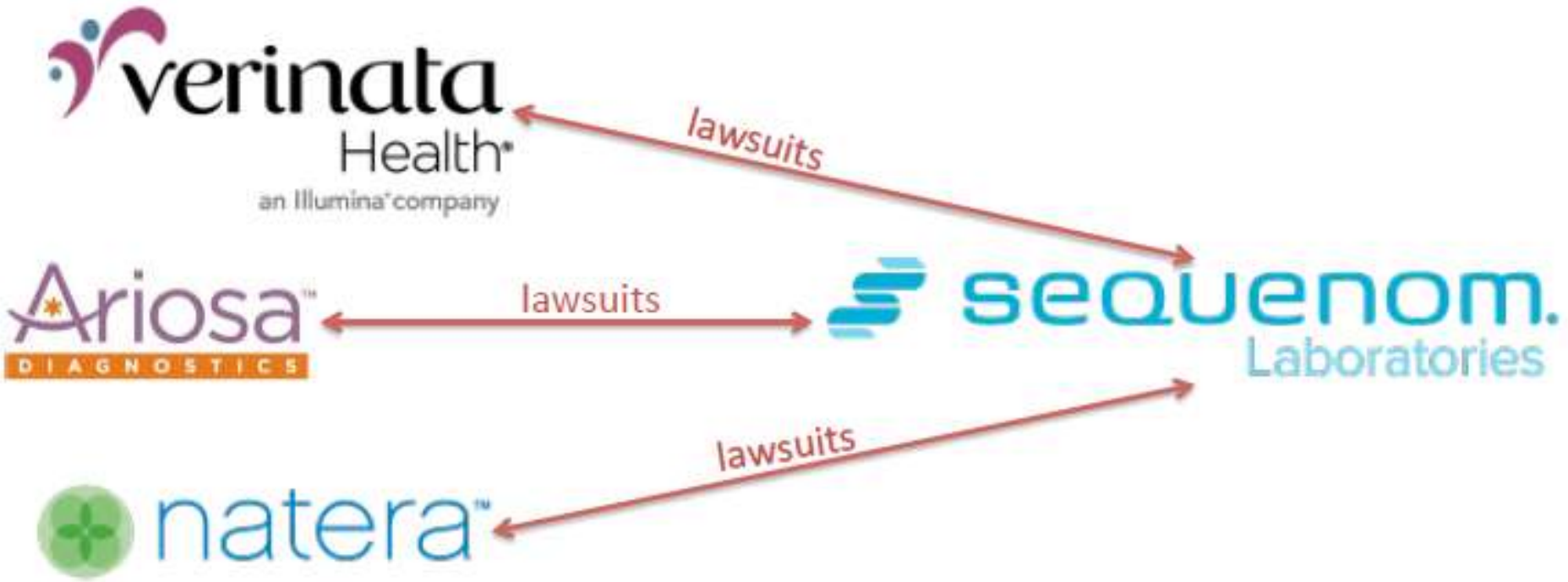


Figure 1 Patent landscape of cffDNA-based noninvasive prenatal testing in the United States.

Agarwal A et al. Commercial landscape of noninvasive prenatal testing in the United States. Prenat Diagn. 2013 Jun;33(6):521-31.

Intellectual Properties



“With a dominant and growing IP estate, we expect that Sequenom, to the exclusion of others, may have the freedom to decide which of many technologies to employ in the commercialization of noninvasive prenatal genetic testing.”

Sayres L at al. the public interest? Science Translaonal Medicin e2012;4(144):144fs23

Expanding Panels

- Single gene disorders
- Sickle Cell Disease
- Cystic Fibrosis
- Thalessemia
- Achondroplasia

Expanding Panels

- 22q deletion syndrome (DiGeorge)
- 5p (Cri-du-chat)
- 15q (Prader-Willi/Angelman)
- 1p (1p36 deletion)
- Trisomy 16
- Trisomy 22

Photo: CMAJ

Photo: Wikipedia

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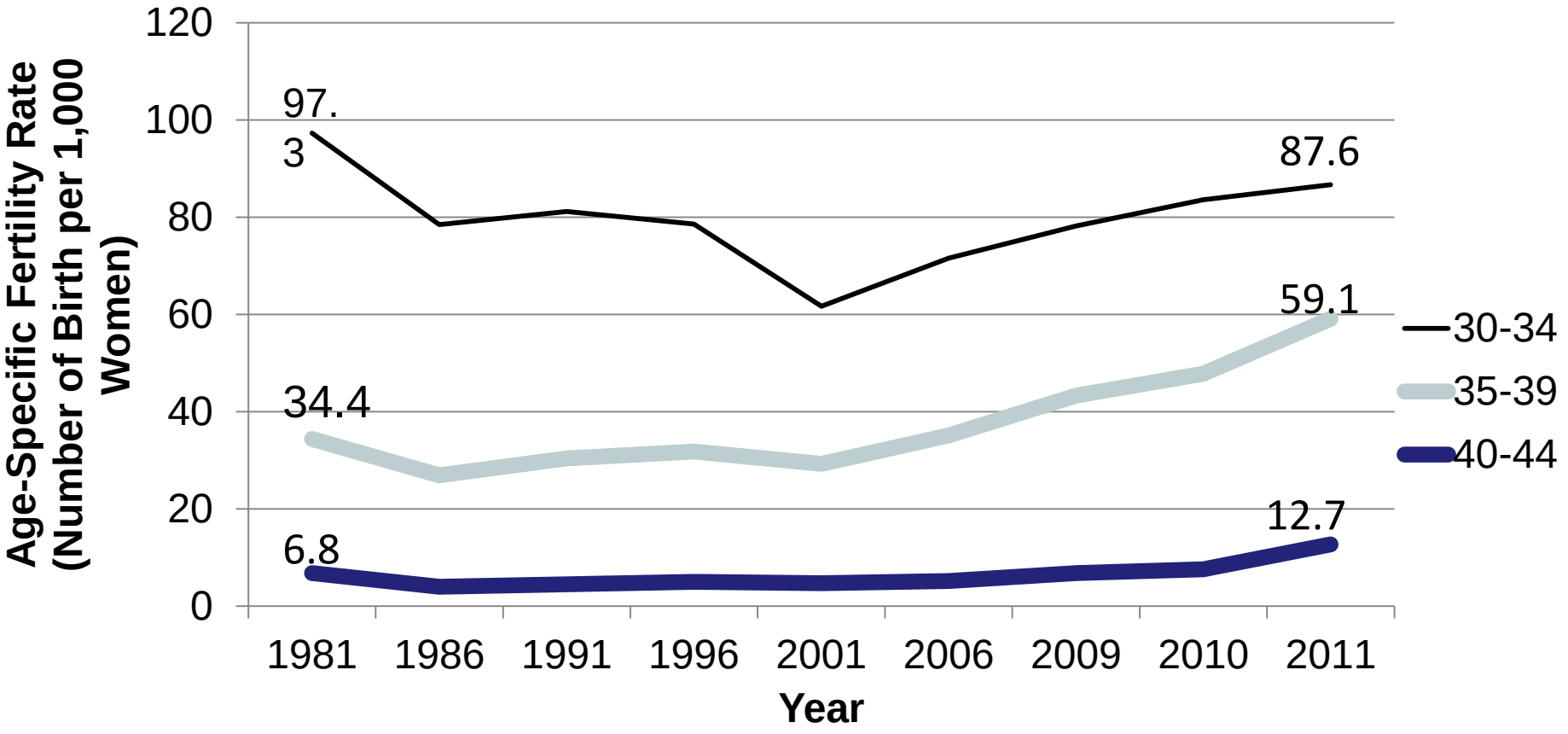
World Down Syndrome Day

otype: 47,XY,+21

Emerging NIPT Technologies

Age-specified Fertility Rate in Hong Kong



Hong Kong Census and Statistics Department , 2011

PRENATAL DIAGNOSIS
Prenat Diagn 2010; **30**: 702–703.
Published online in Wiley InterScience
(www.interscience.wiley.com) **DOI:** 10.1002/pd.2516

30th Anniversary Issue of Prenatal Diagnosis

HORIZON SCANNING

Noninvasive prenatal diagnosis in 2020

Y. M. Dennis Lo[1,2]*

[1]*Centre for Research into Circulating Fetal Nucleic Acids, Li Ka Shing Institute of Health Sciences, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, New Territories, Hong Kong SAR, China*
[2]*Department of Chemical Pathology, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, New Territories, Hong Kong SAR, China*

KEY WORDS: chromosomal aneuploidy; monogenic disease; plasma DNA; next-generation sequencing; massively parallel sequencing; genomics

Aging
Aged…?

Here is an average breakdown of the costs:

- Medications: $2,500-$5,000
- **Monitoring and Doctor's Appointments:** $3,000-$5,000
- **Retrieval:** $3,000-$7,000
- Egg Storage: $600-$1000 per year

Though there are no guarantees that you will have success once you are ready to become pregnant, it is nice to know that you have your younger eggs waiting for you once the time comes. Infertility in women over 35 is mostly due to the age of a woman's eggs, not the age of the intended mother. Costs associated with egg freezing are an insurance policy into your future. With EggBanxx, you can save off of the direct cost charged by a clinic and you can finance the treatment. Consult us first to see what you can save.

ACMG POLICY STATEMENT | Genetics inMedicine

ACMG statement on noninvasive prenatal screening for fetal aneuploidy

Noninvasive assessment of the fetal genome is now possible using next-generation sequencing technologies. The isolation of fetal DNA fragments from maternal circulation in sufficient quantity and sizes, together with proprietary bioinformatics tools, now allows patients the option of noninvasive fetal aneuploidy screening. However, obstetric care providers must become familiar with the advantages and disadvantages of the utilization of this approach as analysis of cell-free fetal DNA moves into clinical practice. Once informed, clinicians can provide efficient pretest and posttest counseling with the goal of avoiding patient harm. It is in the public's best interest that test results contain key elements and that laboratories adhere to established quality control and proficiency testing standards. The analysis of cell-free fetal DNA in maternal circulation for fetal aneuploidy screening is likely the first of major steps toward the eventual application of whole fetal genome/whole fetal exome sequencing.

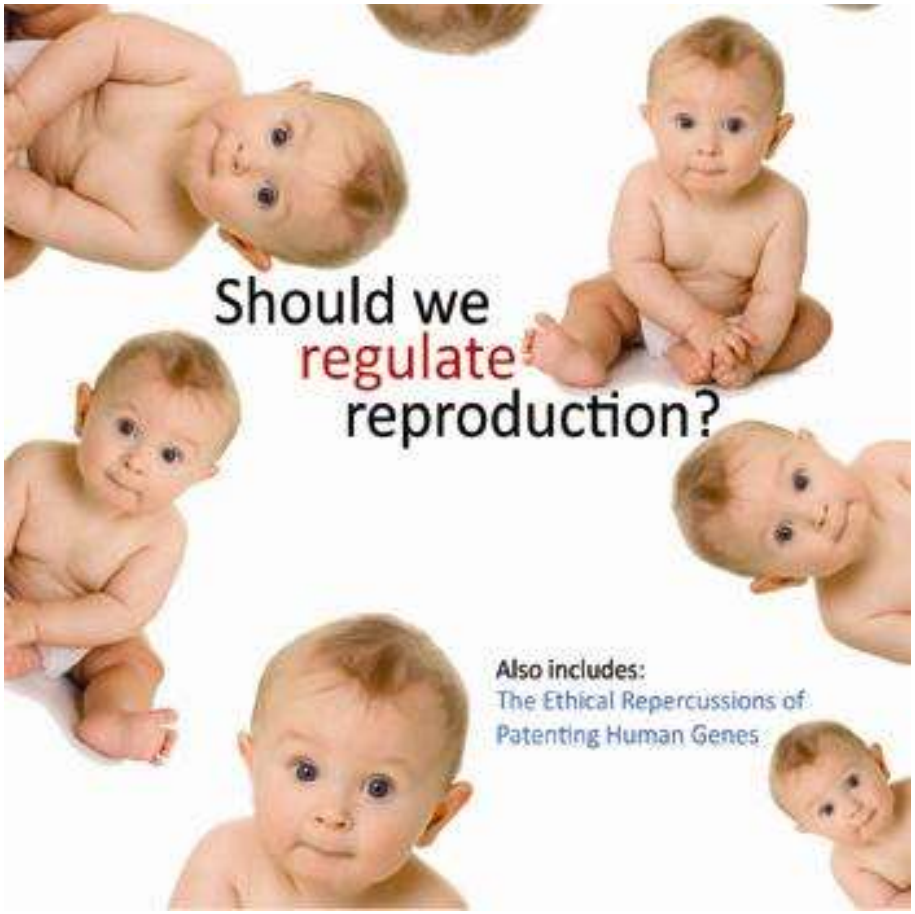
Genet Med 2013:15(5):395–398

Key Words: cell-free fetal DNA; noninvasive prenatal testing; prenatal genetic screening

Prenatal DNA Sequencing

Reading the DNA of fetuses is the next frontier of the genome revolution. Do you really want to know the genetic destiny of your unborn child?

The Executive: *Illumina CEO Jay Flatley is looking to pregnancy as a new market for DNA sequencing.*


Should we
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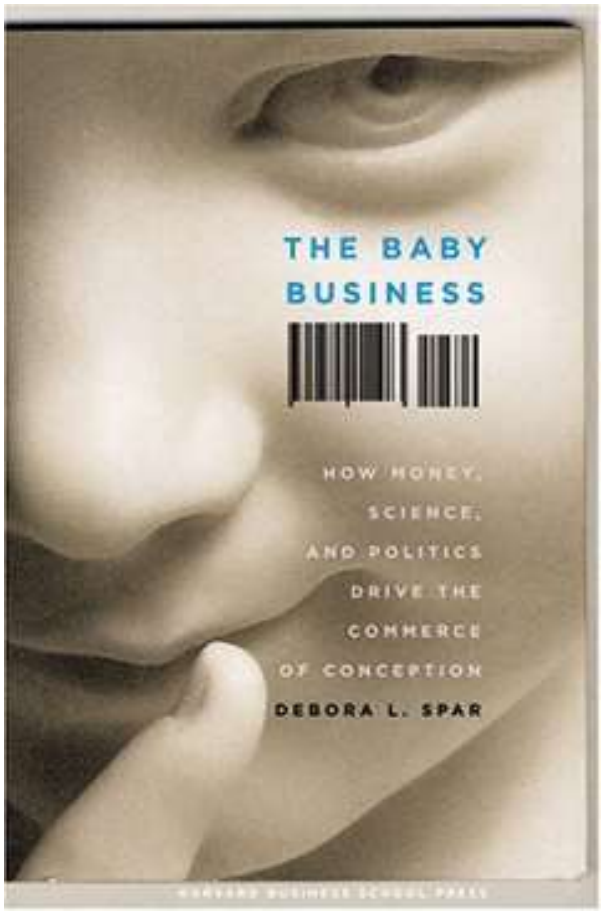
reproduction?
Also includes:
The Ethical Repercussions of
Patenting Human Genes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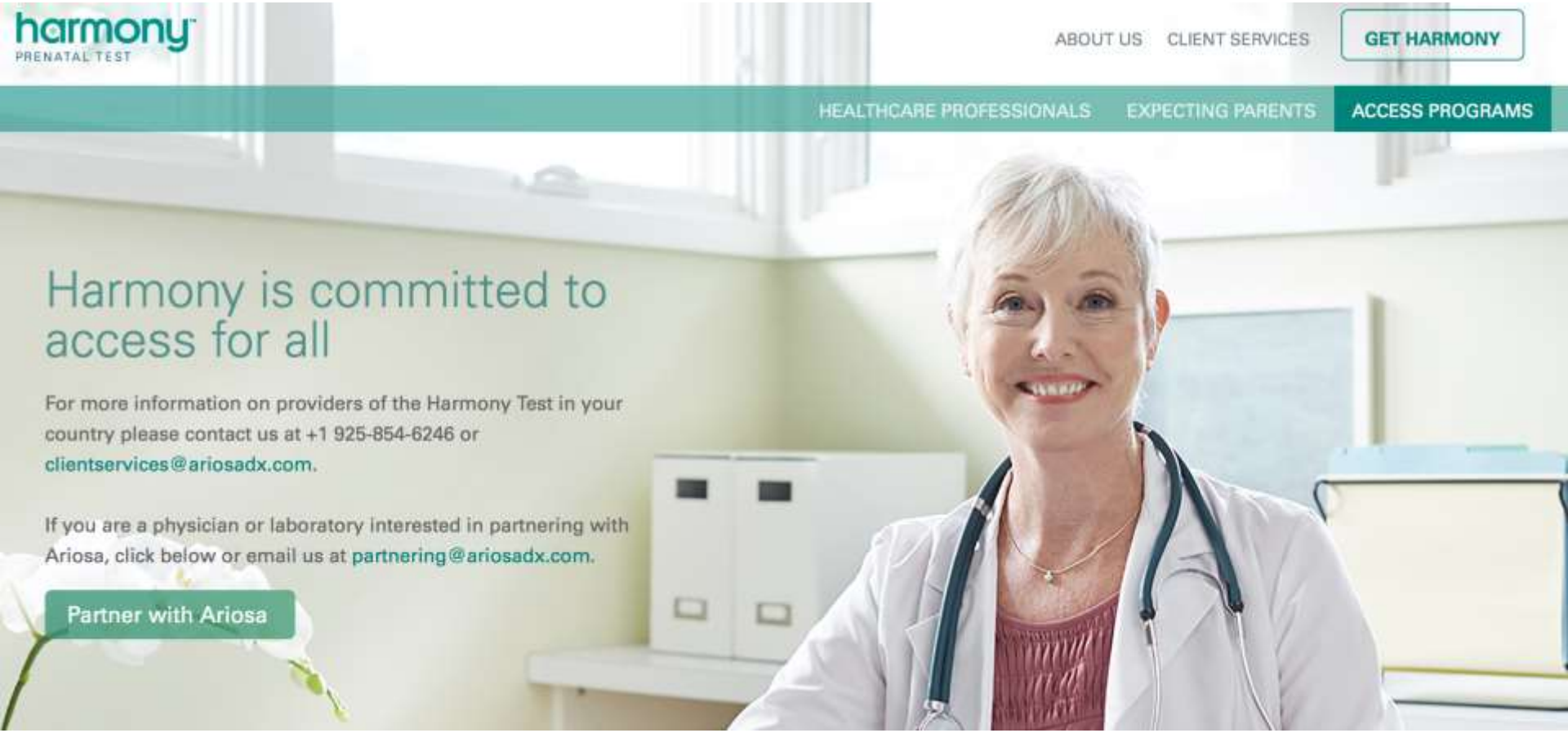
My Genes, My Child, My Way.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Mums-to-be in rush for fetus sex tests

Pregnant mainland women flock to Hong Kong for a low-risk procedure that reveals whether they are having a boy in time for termination

He Huifeng
huifeng.he@scmp.com

PUBLISHED : Tuesday, 02 October, 2012, 12:00am
UPDATED : Tuesday, 02 October, 2012, 4:49am

GLOBAL TIMES
DISCOVER CHINA, DISCOVER THE WORLD

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Mothers-to-be go gender-shopping in Hong Kong

By Yan Shuang Source:Global Times Published: 2012-8-28 1:25:03

Simply typing "fetus sex identification" into Chinese search engines results in hundreds of results advertising these services, with most of the agencies advertised operating out of Shenzhen, Guangdong Province, near the Hong Kong border.

Sex-selective abortions are illegal on the Chinese mainland, largely due to long-standing preferences for baby boys. To prevent these abortions, it's also illegal to use technology to detect the sex of a fetus.

However, mothers-to-be can pay between 5,500 to 5,800 yuan ($865 to $912) then agencies will either take them to see Hong Kong doctors or send their blood to Hong Kong testing centers, which then identify the sex of the fetus.

Zhejiang man arrested for arranging sex tests in Hong Kong for pregnant mainland women

Suspect allegedly sent blood from fetuses to clinics in city, where sex testing is legal

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The mainland bans sex tests for fear it will lead parents to selectively abort their unborn child in favour of having a boy. Photo: Reuters

Zhejiang authorities have arrested the owner of a clinic who allegedly helped pregnant women find out the sex of their fetuses by sending their blood samples to Hong Kong for tests.

The arrest of Chen Jiguo, 35, came as part of the authorities' crackdown on selective abortion after the relaxation of the one-child policy. Chen had allegedly worked with a Hong Kong woman since March last year to take blood from pregnant women's veins for tests on their fetuses' sex.

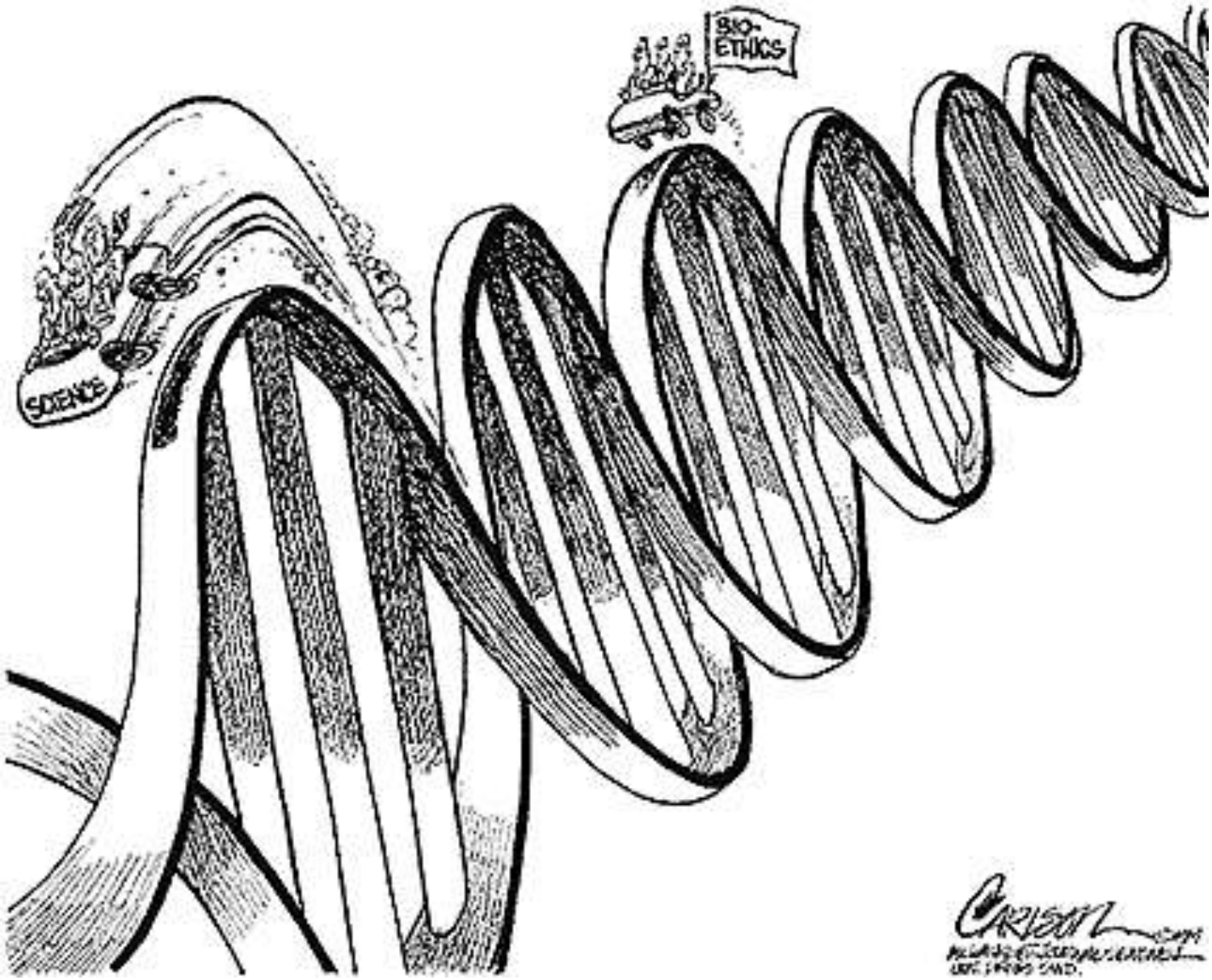
He had allegedly arranged such tests for nearly 300 women by the time he was caught in February. Some of the women arranged adoptions after finding out that they were carrying girls.

"We have attached great importance to cracking down on those who illegally check fetuses' sex and undergo or perform selective abortions ever since the central government allowed couples with at least one single-child parent to

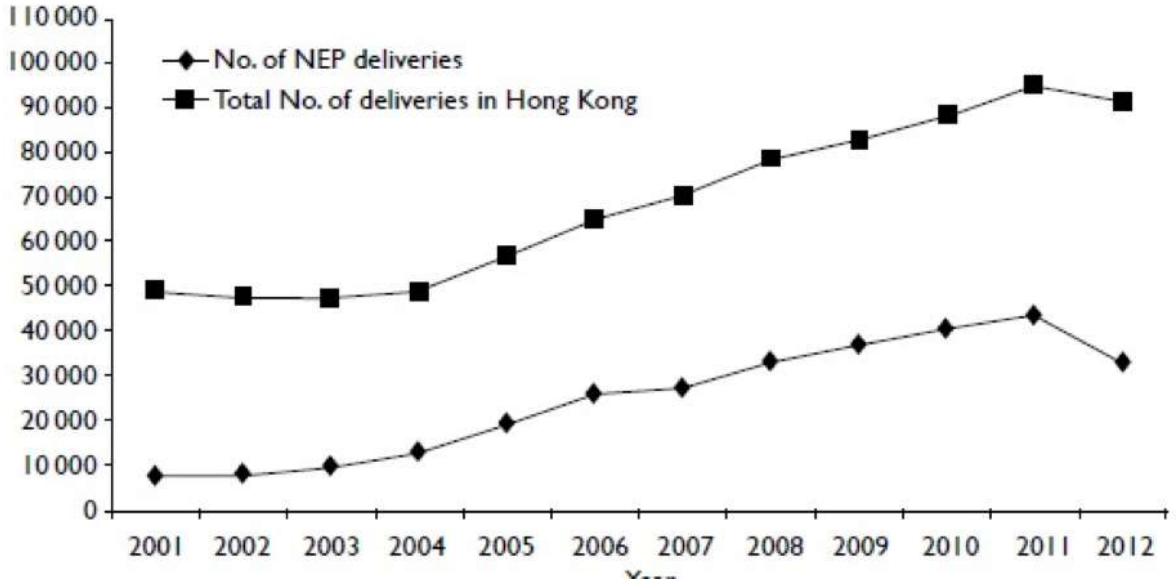
Ethical Concerns

- Autonomy and Informed decision making
- Normalizing attitude of termination of pregnancy (TOP)
- Permissibly legalizing TOP due to disability or any undesired conditions
- Quality Assurance
- Accessibility and affordability
- Justice and Fairness
- Social-cultural values and norms
- Treatment vs. enhancement - eugenics
- Disability and neuro-diversity

- And more and more


BIO-
ETHICS
SCIENCE


"I have a dream, we have a dream that we are going to sequence every living thing on Earth, that we are going to sequence everybody in the world."
by the chair of BGI in DNA Dreaming, 2013


110 000
100 000
90 000
80 000
70 000
60 000
50 000
40 000
30 000
20 000
10 000
0
No. of NEP deliveries
Total No. of deliveries in Hong Kong
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012

Prenatal **Whole Genome** *Sequencing*

JUST BECAUSE WE CAN, SHOULD WE?

BY GREER DONLEY, SARA CHANDROS HULL, AND BENJAMIN E. BERKMAN

With whole genome sequencing set to become the preferred method of prenatal screening, we need to pay more attention to the massive amount of information it will deliver to parents—and the fact that we don't yet understand what most of it means.

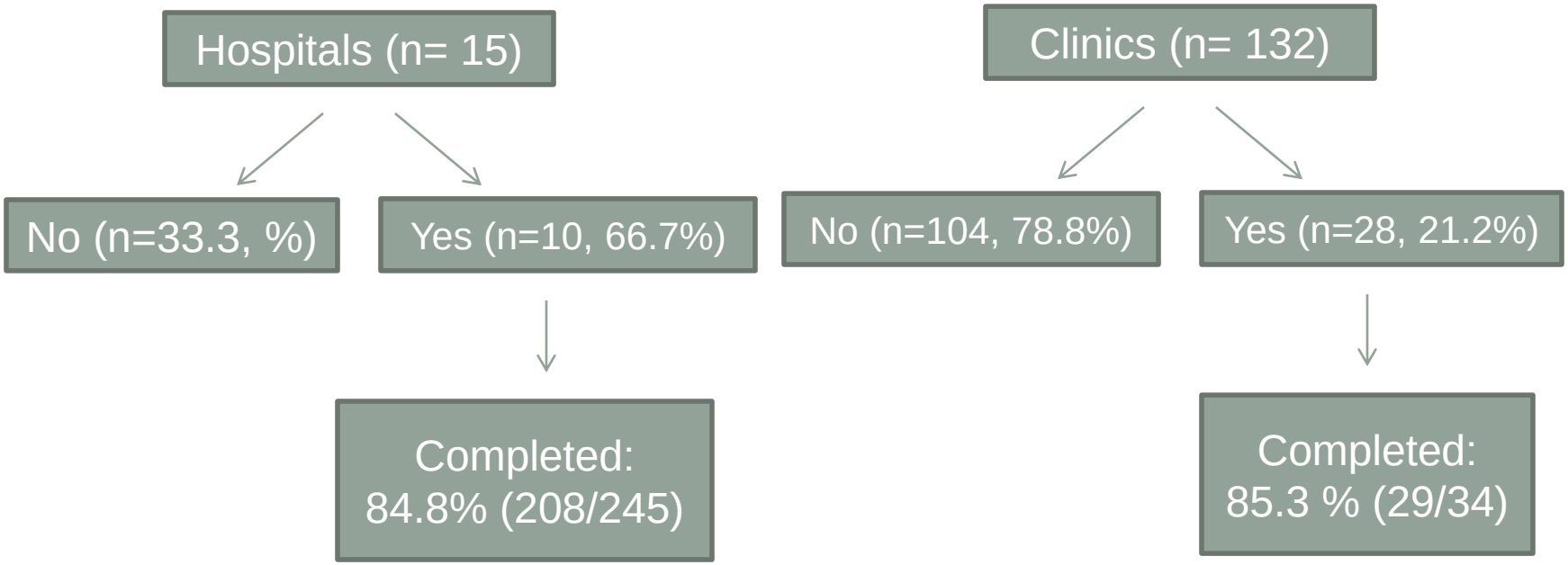
Table 1.
Potential Prenatal Testing Categories

Type of information	*Does it inform reproductive decision-making for current pregnancy?*	*Might the future child have an interest in not knowing the information?*	*Could it provide immediate benefit to the future child?*
Variants of unknown significance (genetic variations whose association with disease risk is unknown)	*No*	*Yes*	*No*
Nonmedical genetic markers (genetic variations that have no health-related significance)	*No*	*Yes*	*No*
Carrier status (possession of genetic variations that do not cause illness in the carrier but might contribute to illness in the carrier's offspring)	*No*	*Yes*	*No*
Susceptibility genes (genes with variants that indicate increased likelihood for developing a condition)	*Sometimes*	*Yes*	*No*
Late onset genetic conditions (highly penetrant genetic conditions that display no symptoms until late in life)	*Sometimes*	*Yes*	*No*
Medical conditions found by current prenatal genetic tests (conditions with 100 percent penetrance that seriously affect health and quality of life throughout the life cycle)	*Yes*	*NA*	*Sometimes*

Response Rate (n=327)

- **Overall Response Rate:** 53.6% (327/610)
- **Mail-in Survey**
  - Response Rate: 27.2% (90/331)
  - A previous study, conducted by Dept O&G, CUHK surveyed the same population, yielded a similar response rate of 32% (YM Chan et al, 2010)

- **In-person Survey**



Participants Characteristics (n=327)

- **Age:** 39.1 (S.D= 12.1; Range= 20-78)

- **Gender**
  - Male 13.5%
  - Female 86.5%

- **Highest Education**
  - Secondary/ Associate Degree 21.4%
  - University 67.0%
  - Master or above 11.6%

- **Profession**
  - Obstetricians 28%
  - Midwives 70%

- **Place of Work**
  - Private 58.4%
  - Public 41.6%

- **Employment Status**
  - Full-time 91.7%
  - Part-time 8.3%

- **Religion**
  - Buddhist 6.1%
  - Christian 27.2%
  - Catholic 8.6%
  - None 58.1%

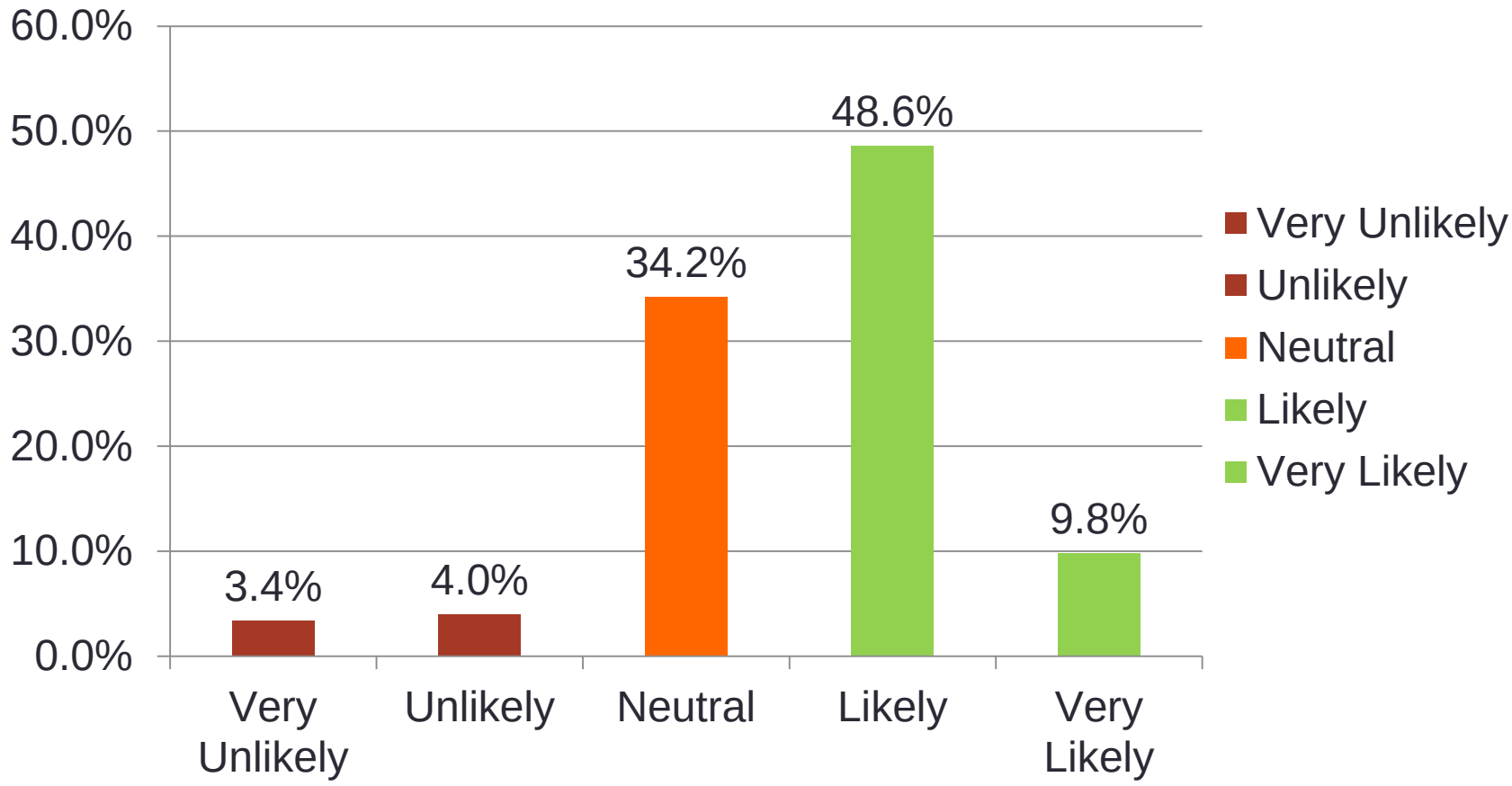
- **Years of Practice:** 12.5 (S.D 11.1, Range 1-55)

Non-invasive Prenatal Whole Genome Sequencing

- **Carrier Status**
  - e.g, colour blindness, cystic fibrosis, haemophilia
- **Condition of late onset**
  - A disease that might be developed in later life
  - e.g Huntington disease, Alzheimer
- **Susceptible genes**
  - Diseases involve complex interactions among many genes, in addition to environmental influences.
  - e.g, Cancers, Autism, Diabetes

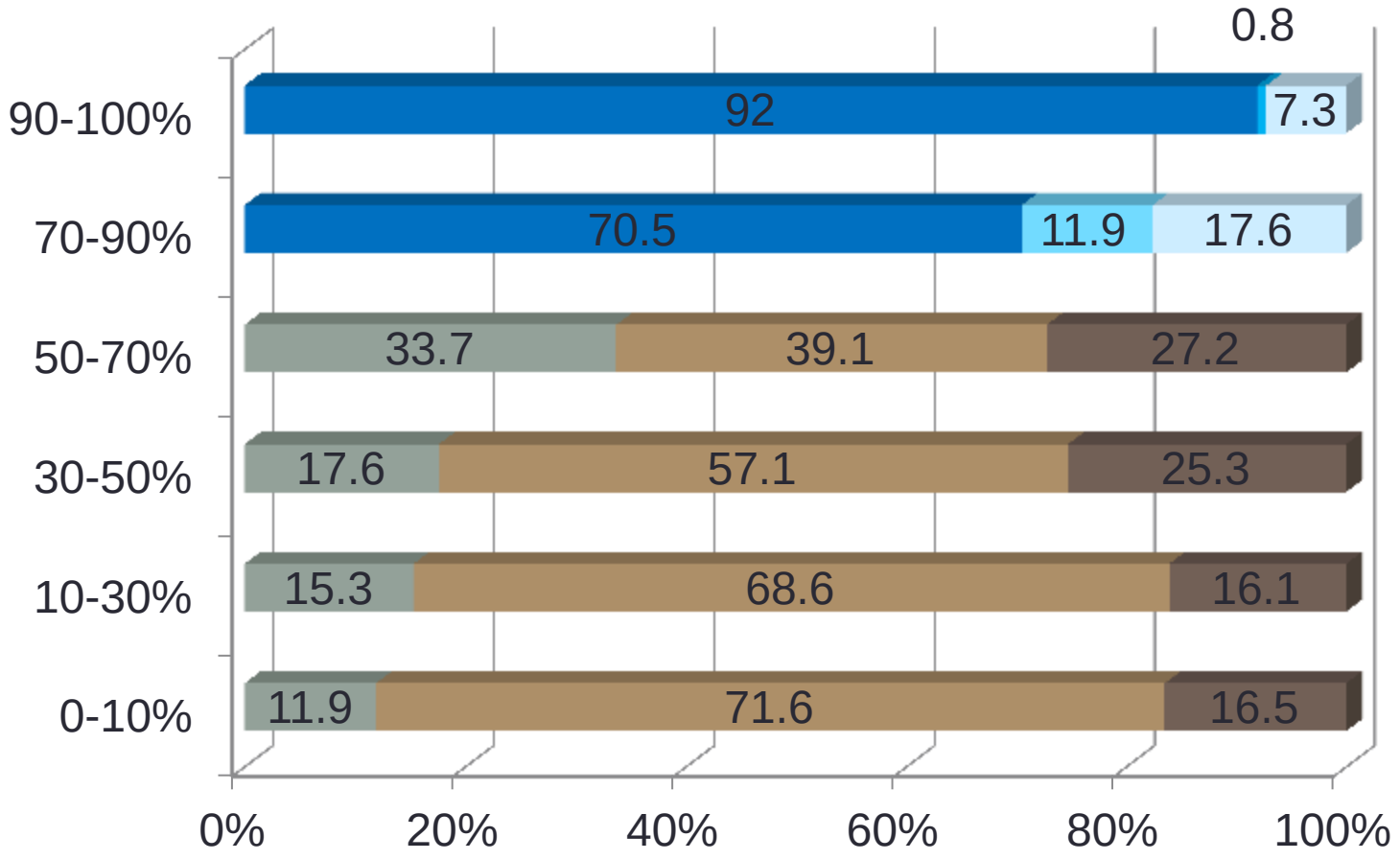
Non-invasive Prenatal Whole Genome Sequencing

If non-invasive prenatal whole genome sequencing is available in antenatal services, how like would you offer the test to women?



Non-invasive Prenatal Whole Genome Sequencing

If the prediction rates of diseases/ traits of fetus are as follows, would you consider informing pregnant women about the result?

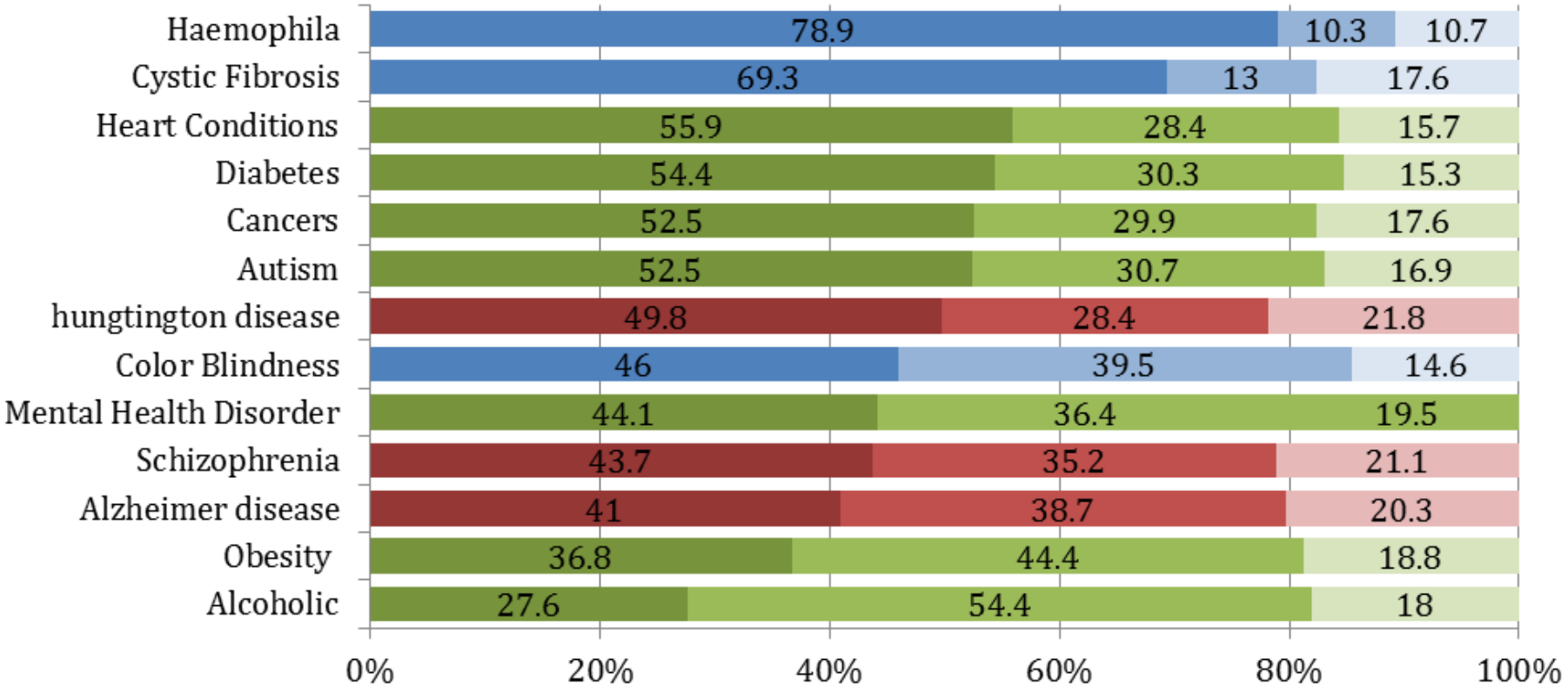


Yes → No → Not Sure

Non-invasive Prenatal Whole Genome Sequencing

Carrier Status	Late- onset Conditions	Susceptibility

Do you think knowing the following diseases/ traits of fetus is beneficial to the future child?

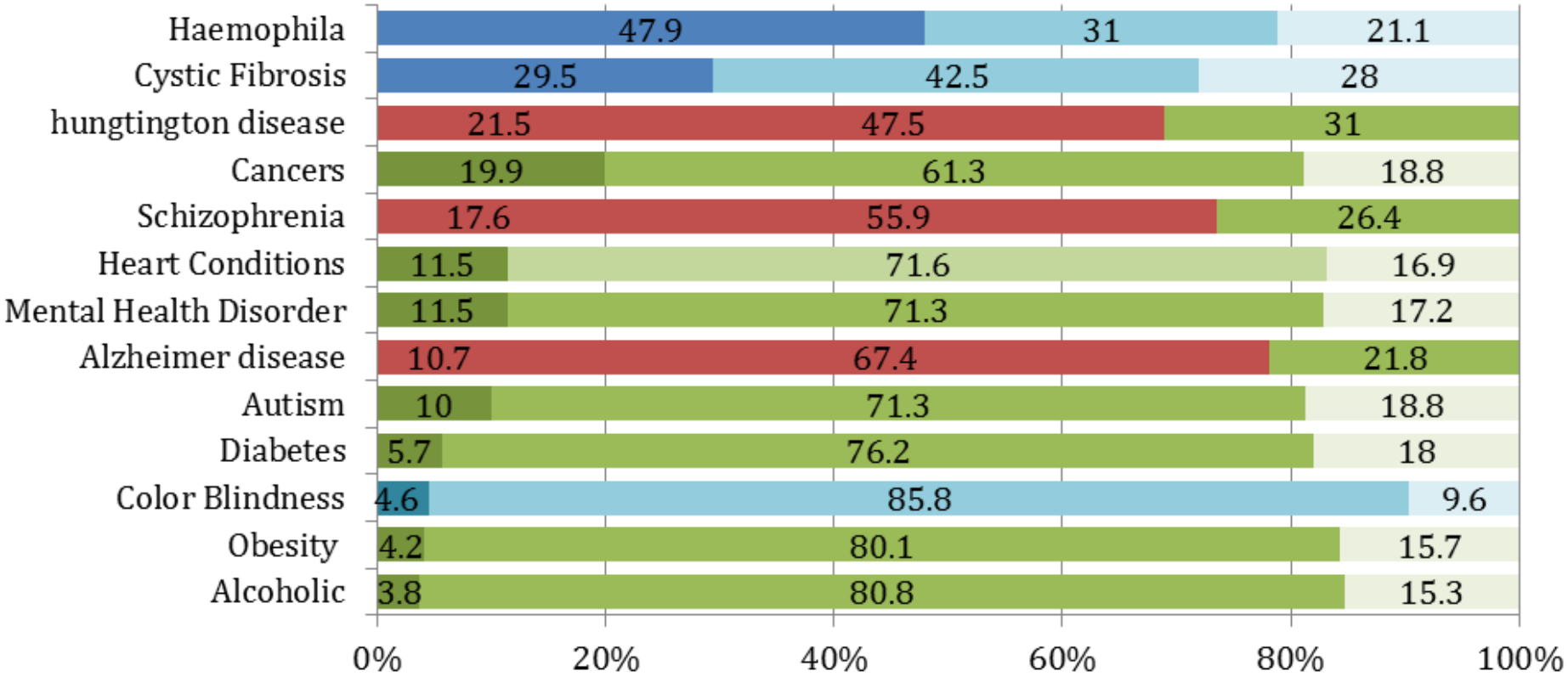


Yes → No → Not Sure

Non-invasive Prenatal Whole Genome Sequencing

Carrier Status	Late- onset Conditions	Susceptibility

Do you think it is permissible to terminate babies due to the following diseases/ traits?

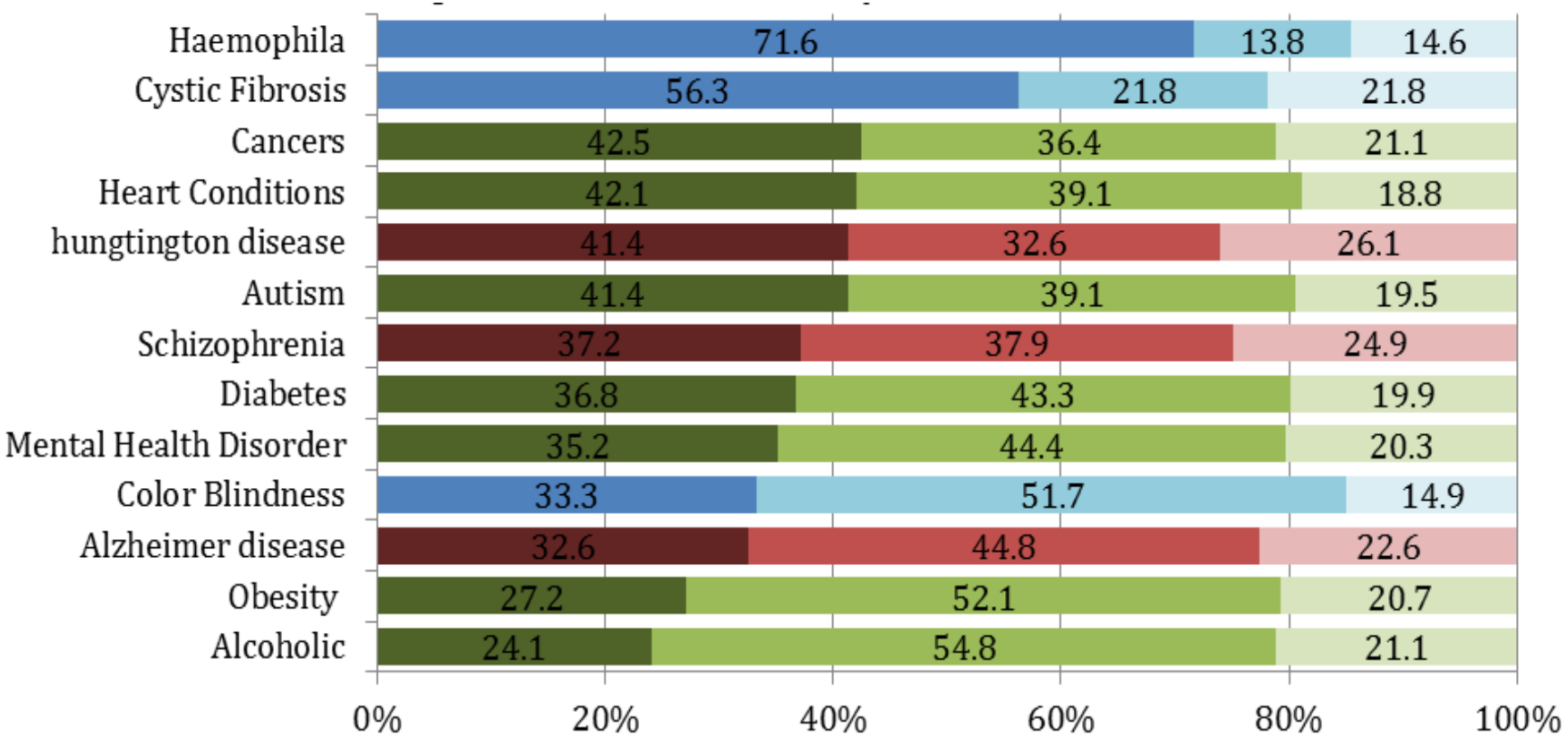


Yes → No → Not Sure

Non-invasive Prenatal Whole Genome Sequencing

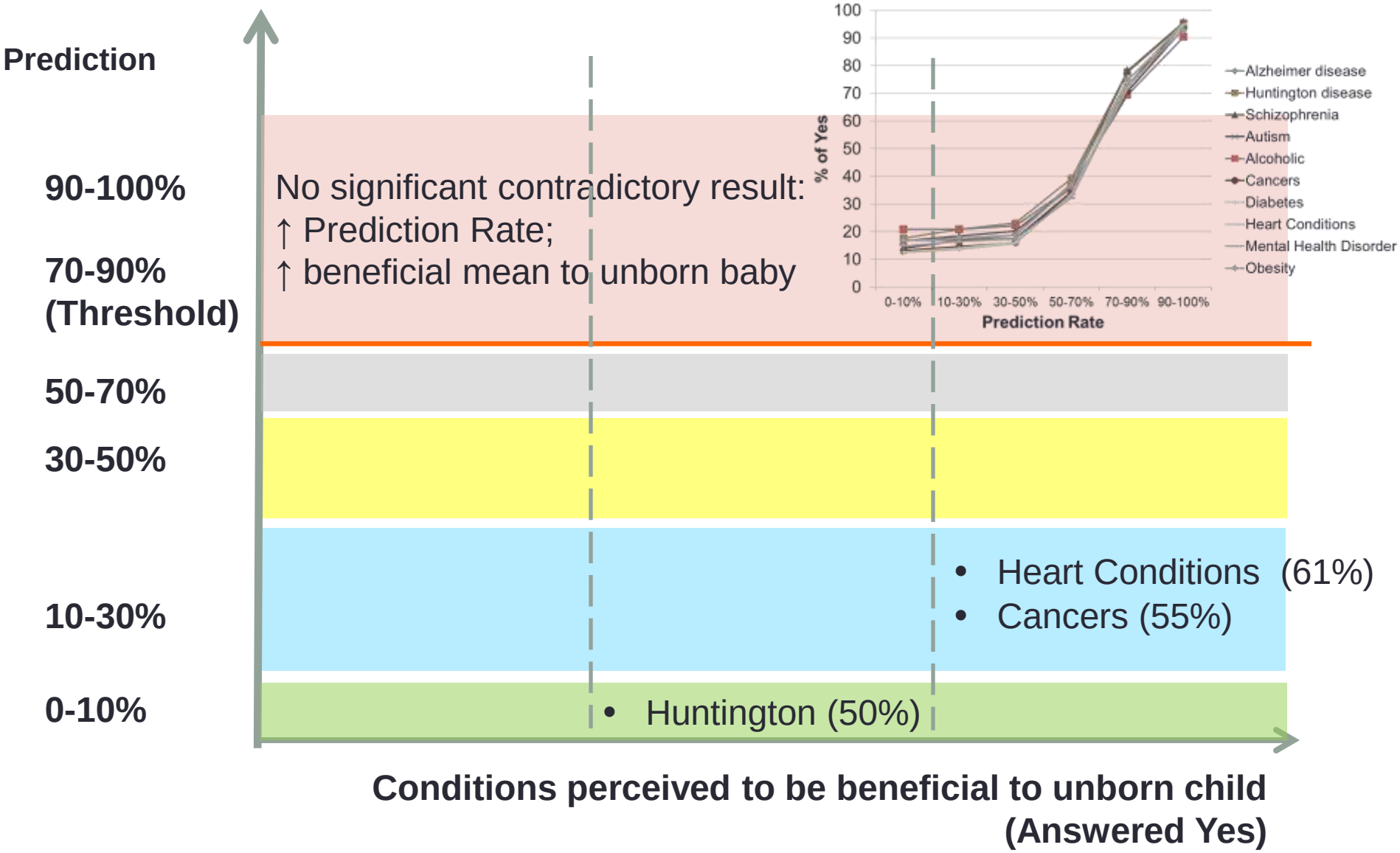
Carrier Status	Late- onset Conditions	Susceptibility

Would you promote the test assessing the following disease/ traits in prenatal care services at your clinic site?

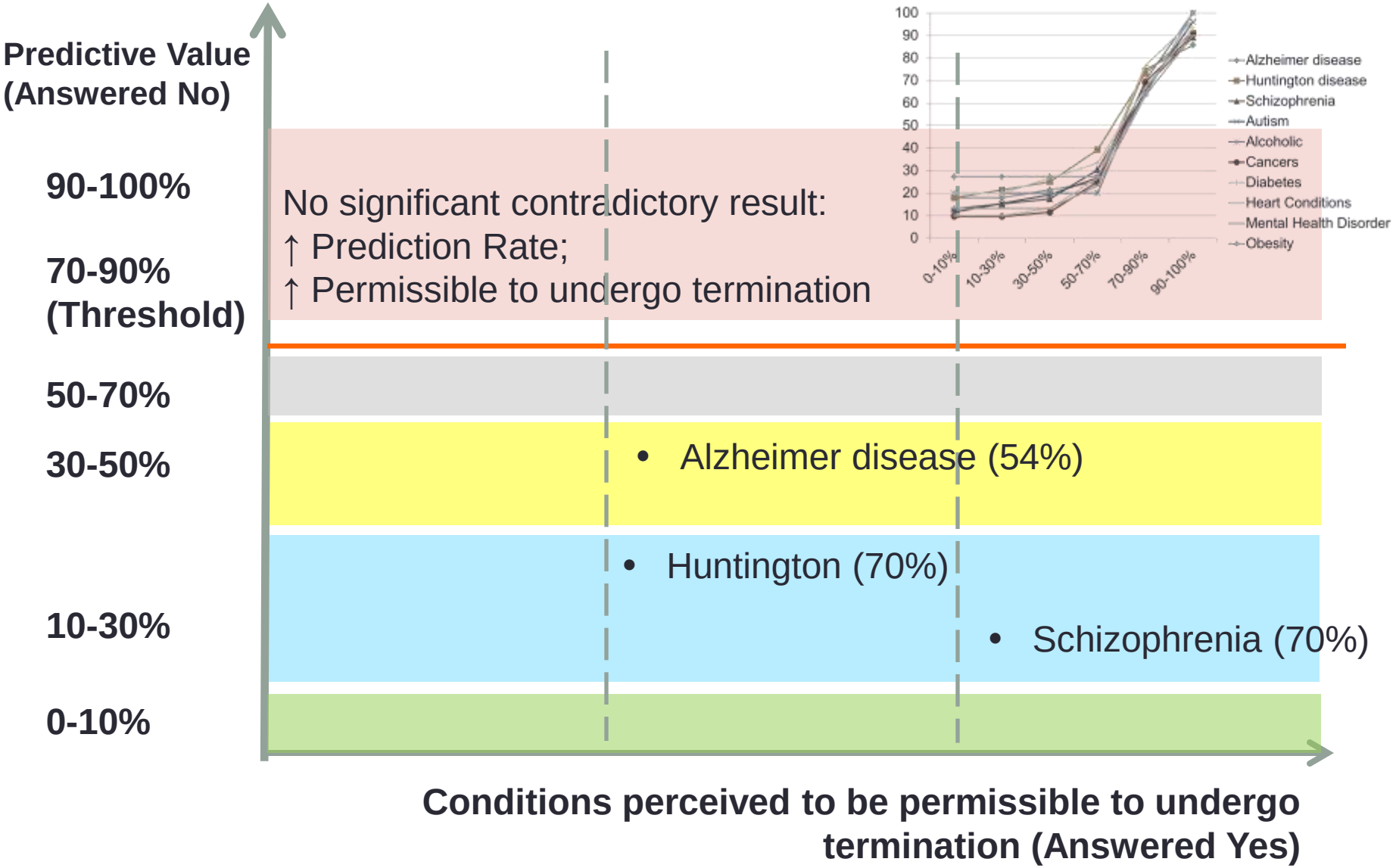


Yes → No → Not Sure

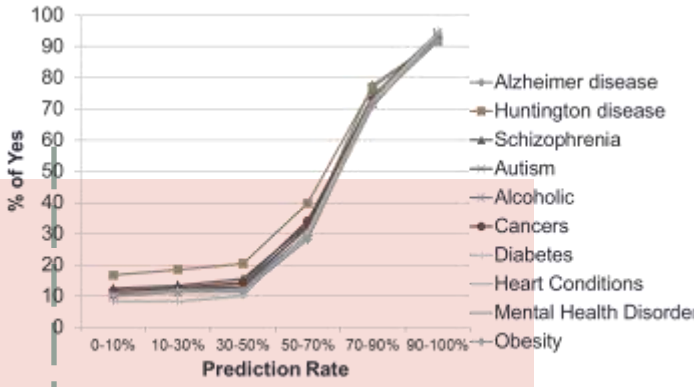
Relationship of prediction rate and perceived beneficial of PWGS to unborn child



Relationship of prediction rate and perceived of permission to undergo pregnancy termination



Relationship of prediction rate and intended interested in test promotion



Prediction

90-100%

70-90%
(Threshold)

50-70%

30-50%

10-30%

0-10%

No significant contradictory result:
↑ Prediction Rate;
↑ Intention to provide test services

- Alzheimer disease (10.6%)
- Diabetes (80%)
- Heart Conditions (80%)

Intention to provide test services (Answered Yes)

Too much information

“Prenatal whole genome sequencing screen could check all or selected interested genes. Patient are able to pick, like dim sum sheet, checking all the conditions they wish to know. However, it will be a problem if one checks all that apply, as it is uncertain how general patients, layman, can handle too much information”

DISEASE PANEL 1

CARDIOVASCULAR SYSTEM

Coronary Heart Disease	Sudden Cardiac Death	Stroke	Abdominal Aortic Aneurysm
Venous Thromboembolism	Intracranial Aneurysm	Hypertension	Atrial Fibrillation
Peripheral Artery Disease	Sick Sinus Syndrome	Responses to Cardiac Drugs	

METABOLISM

Diabetes Mellitus	Cholesterol & Lipids	Gout	Responses to Metabolic Drugs

ATOPY

Asthma	Allergic Rhinitis	Eczema

NEUROLOGY

Alzheimer's Disease	Parkinson's Disease	Multiple Sclerosis	Amyotrophic Lateral Sclerosis
Progressive Supranuclear Palsy	Migraine	Cluster Headache	

HEARING & SIGHT

Otosclerosis	Macular Degeneration	Glaucoma

LIVER

Non-Alcoholic Fatty Liver	Primary Biliary Cirrhosis	Gallstone

KIDNEY

Chronic Kidney Failure	Glomerulonephritis (3 types)	Kidney Stones	Polycystic Kidney Diseases

GASTROINTESTINAL TRACT

Crohn's Disease	Ulcerative Colitis	Celiac Disease

MUSCLE, JOINT & BONE

Limb Girdle Muscular Dystrophy	Essential Tremor	Tardive Dyskinesia	Restless Leg Syndrome
Tourette's Disease	Osteoarthritis	Paget's Disease of Bone	Lumbar Disc Degeneration

LUNG

Sarcoidosis	Chronic Obstructive Pulmonary Disease	

AUTOIMMUE DISEASES

Systemic Lupus Erythematosus	Rheumatoid Arthritis	Ankylosing Spondylitis	Alopecia Areata
Hypothyroidism	Scleroderma	Sjögren's Syndrome	Behçet's Disease

MENTAL HEALTH

Schizophrenia	Bipolar Disorder	Narcolepsy	Obsessive-Compulsive Disorder
Responses to Mental Drugs			

INFECTION

Hepatitis B Virus	Tuberculosis	Malaria	HIV & Drugs

HAEMATOLOGY

Beta Thalassaemia	Haemochromatosis

SKIN

Keloid	Vitiligo	Psoriasis

DISEASE PANEL 2

CARDIOVASCULAR SYSTEM			
Coronary Heart Disease	Stroke	Hypertension	Intracranial Aneurysm
METABOLISM	Diabetes Mellitus		
ATOPY	Asthma	Eczema	
NEUROLOGY	Alzheimer's Disease	Parkinson's Disease	
KIDNEY	Nephrotic Syndrome	Kidney Stones	
MENTAL HEALTH	Schizophrenia	Bipolar Disorder	
JOINT & BONE	Osteoarthritis	Lumbar Disc Degeneration	
AUTOIMMUE DISEASES		Rheumatoid Arthritis	Systemic Lupus Erythematosus

MY BODY PANEL

LIFESTYLE				
Alcohol Reactions	Alcohol Dependence	Nicotine Dependence	Caffeine Reactions	
Control of Eating	Dietary Fat & Weight Gain	Response to Mediterranean Diet		Sugar Crave
Muscle Type	Endurance Exercise	Ligament Strength	Exercise & Weight Loss	
Learning	Memory	Non-Verbal & Performance IQ		
RISKS				
Anaesthesia Reactions	HIV and Drugs	Heroin Dependence & Naltrexone		
Fructose Intolerance	Lactose Intolerance			
BODY				
Baldness	Non-ABO Blood Group	Senses – Odor, Pain & Taste	Male Infertility	Hair Thickness
Freckle & Mole	Body Mass Index (BMI)	Waist Circumference	Longevity	

CANCER PANEL Table 7

Lung (3 Types)	Small Cell	Non-Small Cell	Pleuropulmonary Blastoma	
Colorectal (2 Types)	Carcinoma	Adenomatous Polyposis		
Breast				
Stomach				
Gut (3 Types)	Jejunal Hamartoma	Juvenile Polyposis	Gastrointestinal Stromal Tumor	
Liver (4 Types)	Hepatocellular Carcinoma	Adenoma	Cholangiocarcinoma	Hepatoblastoma
Pancreas (2 Types)	Ductal Carcinoma	Islet Cell Carcinoma		
Nasopharynx				
Larynx				
Acute Leukemia (11 Types)	ALL	ALL B-Cell	Down's Syndrome ALL	ALL Pre-B-Cell
	ALL T-Cell	ALL Prolymphocytic T-Cell	AML	CML Blastic Transformation
	Fanconi's Anaemia AML	AML Megakaryocytic	Down's Syndrome AML Megakaryocytic	
Chronic Leukemia (7 Types)	CLL	CLL B-Cell	CLL T-Cell	CLL Prolymphocytic T-Cell
	CML	CMML	JMML	
Lymphoma (13 Types)	ALCL	Burkitt's	DLCL	Follicular
	Hodgkin's / Non-Hodgkin's	Intestinal T-Cell	Primary Mediastinal T-Cell	Marginal Zone
	MLCLS	MALT	Nasal NK T-Cell	Peripheral T-Cell
Skin (6 Types)	Squamous Cell	Basal Cell	Melanoma	Cylindroma
	Fibrofolliculoma	Trichofolcoma		
Central Nervous System (8 Types)	Ganglioneuroblastoma	Glioblastoma	GBM	Glioma
	Medulloblastoma	Meningioma	Pilocytic Astrocytoma	Pituitary Adenoma
Testes				
Prostate				
Ovary (3 Types)	Carcinoma	Clear Cell	Granulosa Cell	
Uterus (3 Types)	Endometrial Carcinoma	Endometrial Stromal	Fibroid	
Kidney (5 Types)	Renal Cell Carcinoma	Clear Cell	Malignant Rhabdoid	Papillary Carcinoma
	Wilms Tumor			
Bladder				
Head & Neck (3 Types)	Myoepithelioma	Squamous Cell Carcinoma	Multiple Ossifying Jaw Fibroma	
Eye (2 Types)	Rothrobblastoma	Uveal Melanoma		
Bone (2 Types)	Aneurysmal Bone Cysts	Exostosis		
Thyroid (5 Types)	Follicular	Medullary	Microfollicular	Toxic Adenoma
	Papillary	Adenoma		
Parathyroid				
Neurological (4 Types)	Acoustic Neurons	Neuroblastoma	Neurofibroma	Paraganglioma
Sarcoma (16 Types)	Alveolar Soft Part	Angiosarcoma	Angiomatoid Fibrous Histocytoma	
	Clear Cell	Ewing's Sarcoma	Dermatofibrosarcoma Protuberans	
	Fibromyxoid	Congenital Fibrosarcoma	Desmoplastic Small Round Cell	
	Liposarcoma	Osteosarcoma	Extraskeletal Myxoid Chondrosarcoma	
	Synovial	Rhabdomyosarcoma	Alveolar Rhabdomyosarcoma	Soft Tissue Sarcoma
Other Glands (5 Types)	Adrenocortical	Pheochromocytoma	Salivary Adenoid Cystic	Salivary Adenoma
	Salivary Mucoepidermoid			
Other Haematological (5 Types)	Multiple Myeloma	Mastocytosis	Idiopathic Hypereosinophilic Syndrome	
	Myelodysplastic Syndrome	Myeloproliferative Syndrome		
Other Solid Tumor (5 Types)	Carcinoid	Dermoid	Midline Carcinoma of Children and the Young	
	Lipoma	Haemangioma	Hamartoma	
Responses to Cancer Drug	Toxicity to 5-Fluorouracil			

CHILD HEALTH PANEL

BEHAVIOR

ADHD	Dyslexia		Eating Behavior	
Nicotine Dependence	Heroin Dependence			

METABOLISM

Diabetes Mellitus, type 1	G6PD Deficiency	Fructose Intolerance	Lactose Intolerance	
Gluten Hypersensitivity	Childhood Obesity			

ATOPY

Asthma	Allergic Rhinitis	Eczema		

INTELLIGENCE

Breast-Feeding & IQ	Non-Verbal & Performance IQ	Learning Abilities	Memory	Language

SPORTS TALENTS

Endurance	Muscle Power	Ligament Strength	Responses to Training

HEALTH

Weight	Senses -- Odor, Pain & Taste	Freckle & Mole	Idiopathic Scoliosis of Adolescent Girls
Near/Far-Sightedness	Hypospadias		

MY LADY GENES PANEL

OBSTETRICS & GYNAECOLOGY

Endometriosis	Polycystic Ovary Syndrome	Uterine Fibroid	Pre-eclampsia (HELLP)
Placental Abruption	Neural Tube Defect of Fetus	Intrahepatic Cholestasis of Pregnancy	
Gestational Diabetes	Birth Weight of Fetus	Menopause	Reactions to Oral Contraceptives
Sex Hormone and Reactions to Replacement Therapy			

SKIN HEALTH

Eczema	Keloid	Vitiligo	Psoriasis
Freckle & Mole	Hair Thickness		

WEIGHT

Control of Eating	Dietary Fat & Weight Gain	Response to Mediterranean Diet	
Sugar Crave	Exercise & Weight Loss	Body Mass Index (BMI)	Waist Circumference
Obesity			

Unnecessary termination of pregnancy to prevent anxiety.

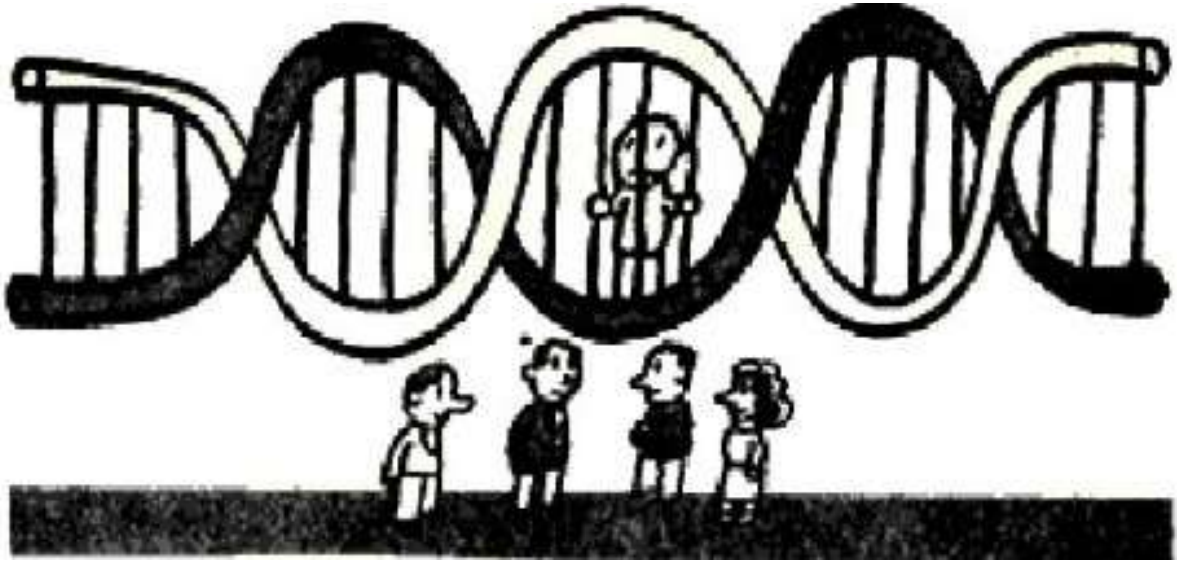
"It's would be a great pressure if one plans to abort a baby based on whatever genes (conditions) screened. If mothers choose not to abort the baby after screening while knowing the chance of developing symptoms in later life, mothers would be very anxious. Therefore, it is better not to know."

Lack of Therapeutic Intervention

“The difference from knowing and not knowing is giving one ability to take preventive measures. There is lack of preventive measure to be taken for some conditions, such as Alzheimer disease. They need to bear known conditions in long-term. I do not see it necessary”

Genetic Discrimination

"With prenatal testing, we not only discriminate people with *abnormalities* after delivery, but also started discriminate/exclude the baby at conception, preventing them from arriving in the world. The issues will be escalated further with whole genome sequencing."



HARVARD gazette

New test for Down syndrome

Symposium outlines promising, less-invasive diagnosis method

October 9, 2013

By Alvin Powell, Harvard Staff Writer

Kris Snibbe/Harvard Staff Photographer

The new test, according to Diana Bianchi, executive director of Tufts Medical Center's Mother Infant Research Institute, misses only a very small fraction of Down cases, meaning that fewer women would need amniocentesis.

A new, noninvasive screening test for Down syndrome would allow some women with high-risk pregnancies to avoid amniocentesis and in the future may provide detection early enough for treatment to improve some babies' cognitive function, a Tufts University neonatal genetics expert told a symposium at Harvard Medical School on Tuesday.

Genetic expert Diana Bianchi misrepresents new eugenic test for Down syndrome

Saturday October 12, 2013 *by Mike* *24 Comments*
Diana Bianchi, discrimination, Down syndrome, Eugenics, Genetic Screening

This week the Harvard Gazette published an article on the "new test for Down syndrome". It contained the usual offensive language about our community. It contains the usual misleading information about screening. It introduces a new Trojan horse of a "future treatment" to defend harmful current practice. All in a brief, typically medical focussed, article that uses smoke and mirrors to defend Down syndrome birth prevention programs.

The article reports on a presentation by Diana Bianchi, executive director of Tufts Medical Center's Mother Infant Research Institute at the Harvard Medical School. She has a long record of being involved in developing and promoting birth prevention measures against the Down syndrome community. The Tufts Medical Center represent themselves as *"an internationally-respected academic medical center – a teaching hospital where we pride ourselves not only in the sophistication of the care we provide but the compassionate way in which we provide it.'* The Harvard Medical School themselves has, as a Core Commitment, the noble *"Service to Humanity"*. Unfortunately we see little compassion or service to humanity in the article. One is left wondering how many people with Down syndrome Bianchi knows and loves.

Saving Downs on Facebook

Hot topics on the Saving Downs blog

Adoption | Alberto Giubilini | ALRANZ | Autism | Bill Gavin | Close Up Down syndrome | CRPD | Diana Bianchi | discrimination | Down syndrome | Dr Deidre Little


DECEMBER 24, 2012
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Epilepsy
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Dementia
Cancer
Hemochromatosis
Cystic fibrosis
Tay-Sachs disease
Burkitt's lymphoma
Malignant melanoma
PhenylKetonuria
Prostate cancer
Obesity
New genetic tests can point to risks— but not always a cure
BY BONNIE ROCHMAN
www.time.com


TIME
THE ANGELINA EFFECT
Angelina Jolie's double mastectomy puts genetic testing in the spotlight. What her choice reveals about calculating risk, cost and peace of mind
BY JEFFREY KLUGER & ALICE PARK

GOOD SCIENCE

BAD SCIENCE

BABY BLESSING OR BRAVE NEW WORLD?

Within a pregnant mother's blood is her unborn child's full genetic sequence. Soon, say geneticists, the question will no longer be how to get at it, but how to use it to understand the baby's future behaviour and health — and how to cope with the thorny ethical issues that will inevitably ensue.

The key to this new form of prenatal diagnosis lies in the fragments of DNA that float freely through every person's bloodstream. In pregnant women, around 15% of that DNA comes from the fetus, according to Dennis Lo, a pathologist at the Chinese University of Hong Kong, who is working to develop fetal genetic screening with Sequenom, a biotechnology company based in San Diego, California.

BY GEOFF BRUMFIEL

WHO ARE AT STAKE?

WHAT VALUES ARE AT STAKE?