Prenatal Genetics gone

TM

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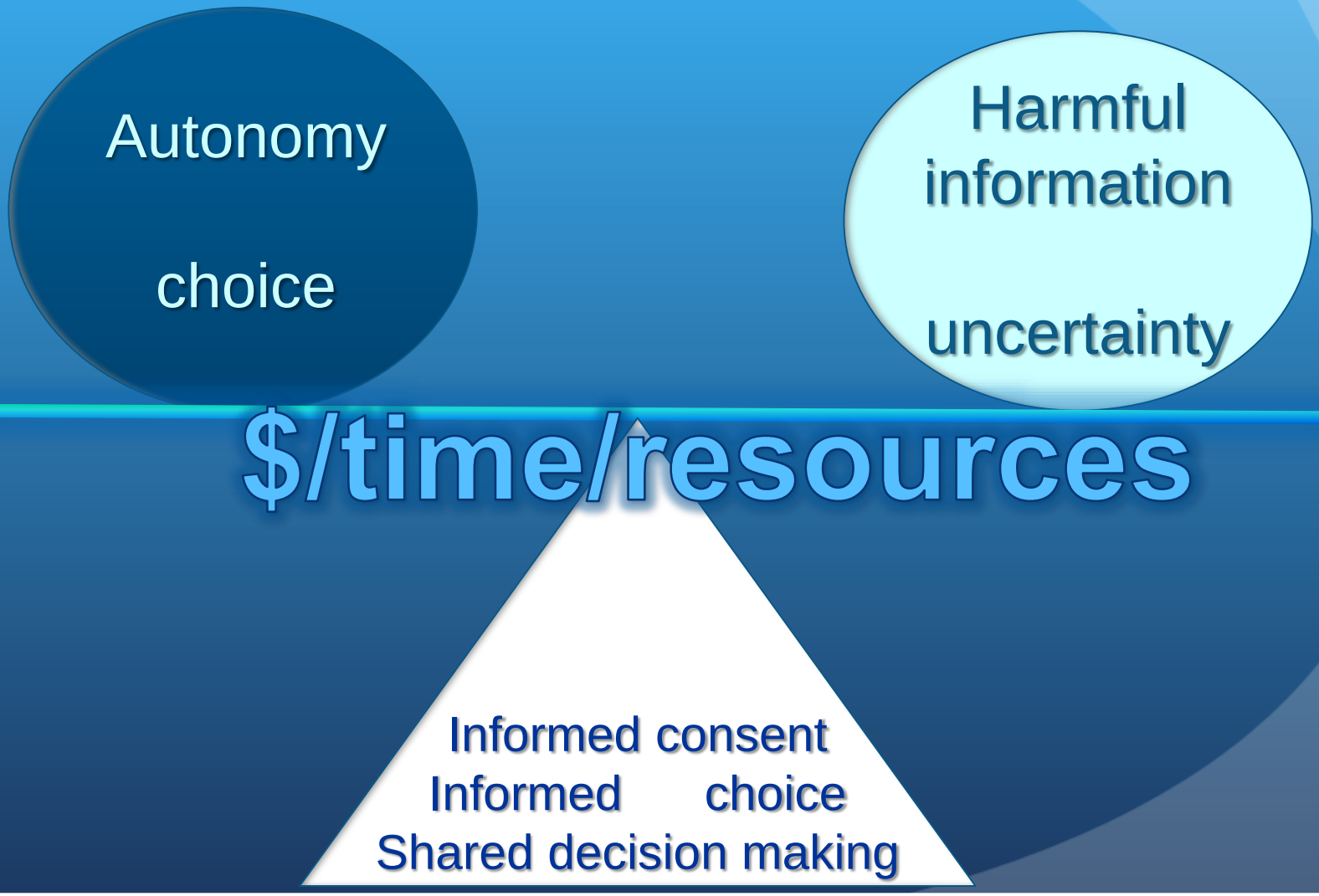
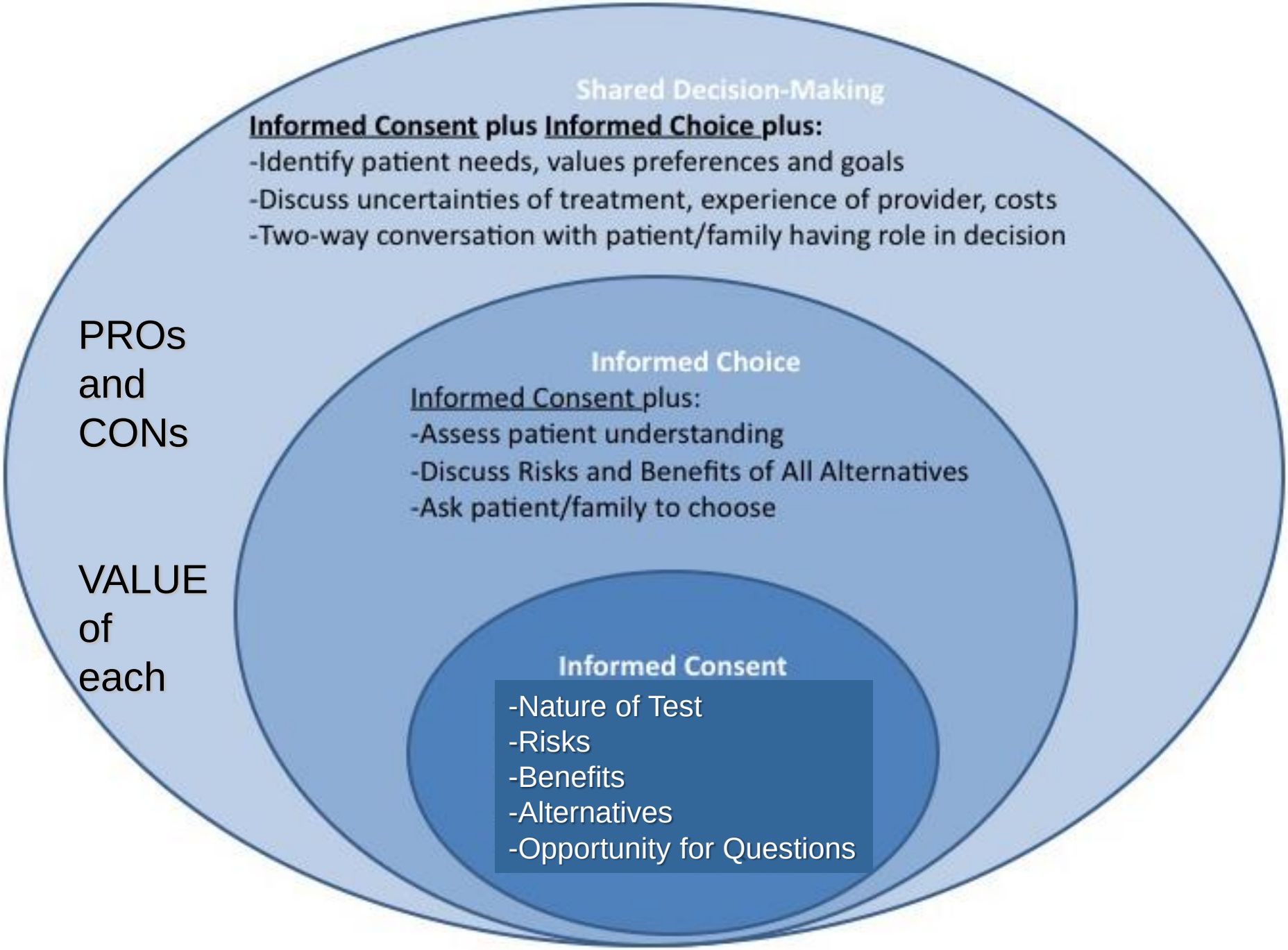
Microarray- a better test, but…

Balancing Act




What i'm about to tell you is gonna change your life forever. Are you really sure you want to know it?


Shared Decision-Making
Informed Consent plus Informed Choice plus:
-Identify patient needs, values preferences and goals
-Discuss uncertainties of treatment, experience of provider, costs
-Two-way conversation with patient/family having role in decision
PROs and CONs
VALUE of each
Informed Choice
Informed Consent plus:
-Assess patient understanding
-Discuss Risks and Benefits of All Alternatives
-Ask patient/family to choose
Informed Consent
-Nature of Test
-Risks
-Benefits
-Alternatives
-Opportunity for Questions

Variants of unknown significance

NOT a new concept for us, this is what we do

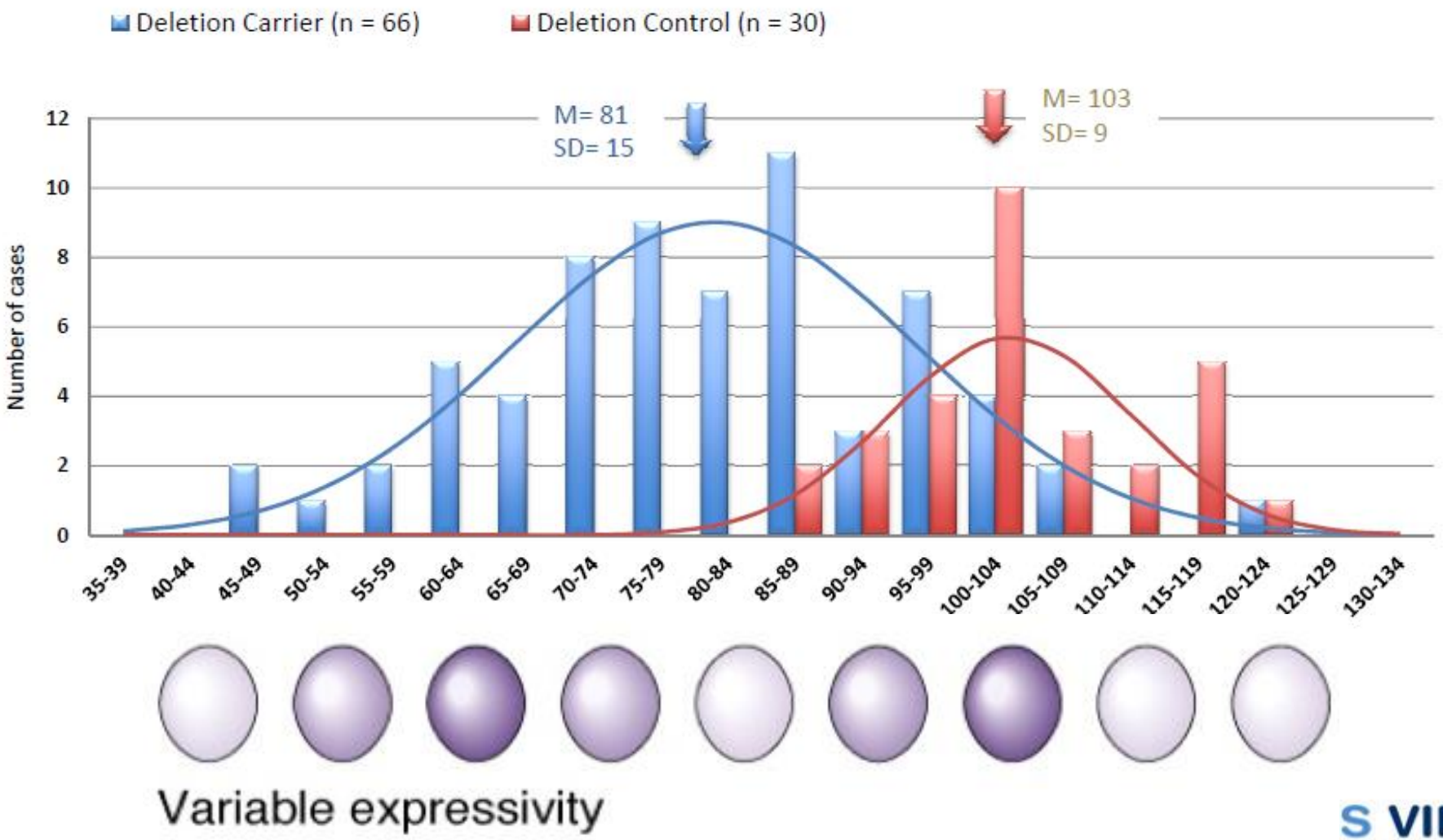
-cytogenetics (heterochromatin, markers, deNovo rearrangements, mosaicism, etc)

-prenatal ultrasound (agenesis of corpus callosum, any “apparently isolated structural finding”, cystic hygroma)…

-low PappA, high AFP, high hCG…

need to get comfortable with shades of grey

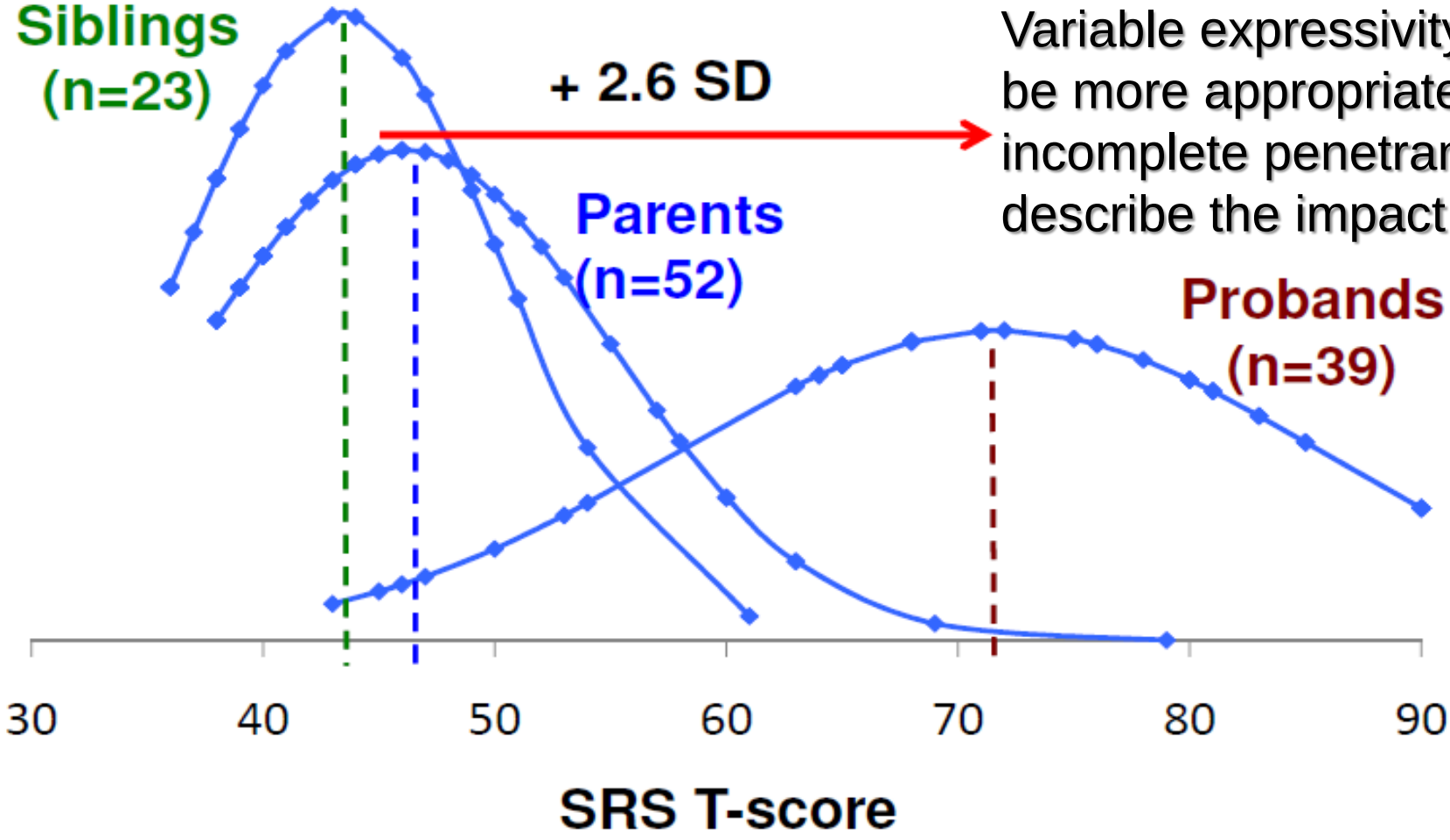
16p11.2 Child Carriers and Control Full Scale IQ



Variable expressivity

S VIP
VARIATION IN INDIVIDUALS PROJECT

SRS in the Simons VIP Cohort (de novo cases only)

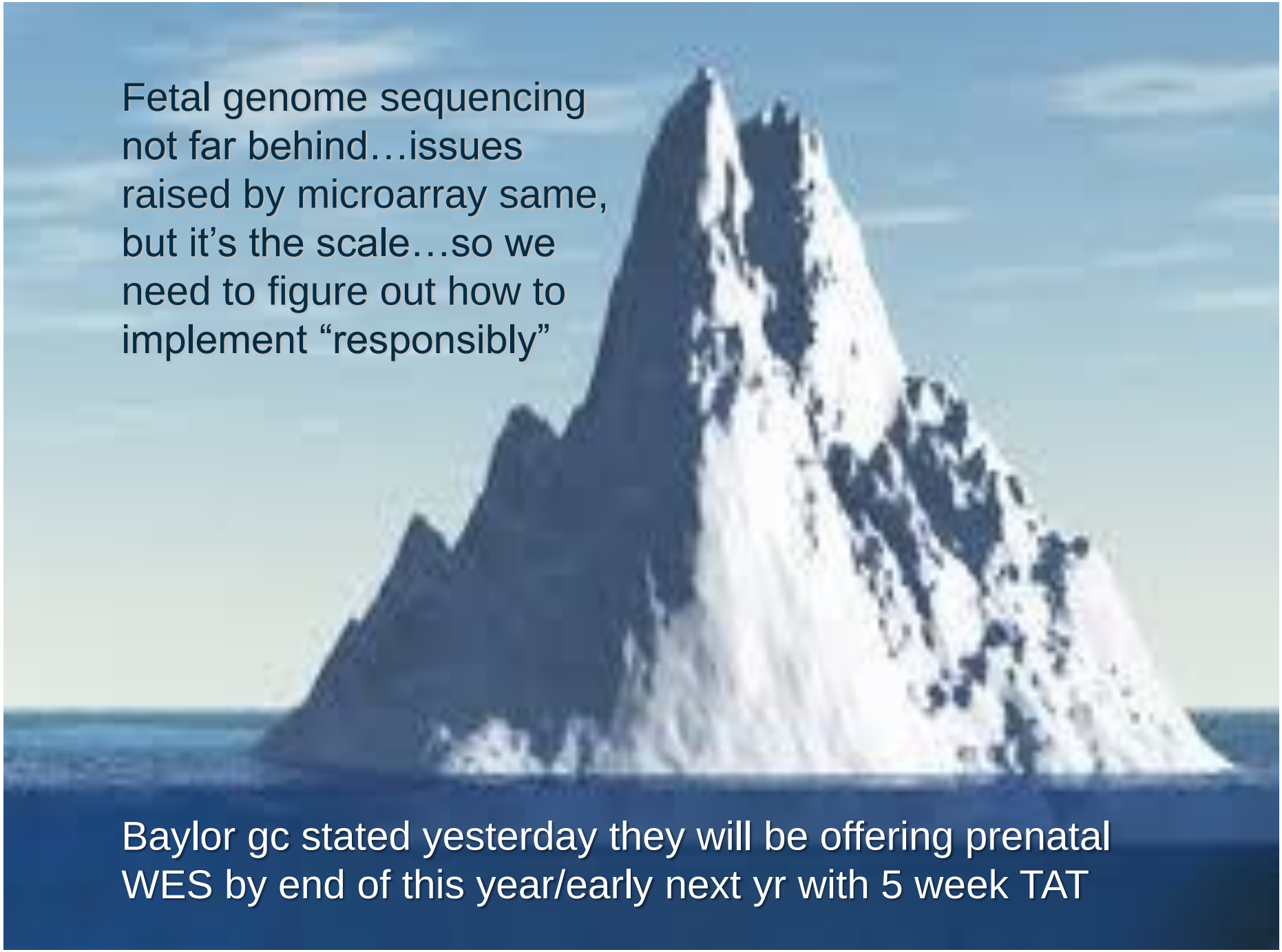


Variable expressivity may be more appropriate than incomplete penetrance to describe the impact

A. Moreno de Luca et al.

Perfect Storm

-Wapner's study 1.7% risk of CNV for "low risk" and failing VOUS rate (2.5 to 1.5 to 1%, majority to path)
-Risk of amniocentesis reduced 1/1000 and rate of invasive decreasing
-NIPT expanding into the microdel world


Fetal genome sequencing not far behind…issues raised by microarray same, but it's the scale…so we need to figure out how to implement "responsibly"
Baylor gc stated yesterday they will be offering prenatal WES by end of this year/early next yr with 5 week TAT

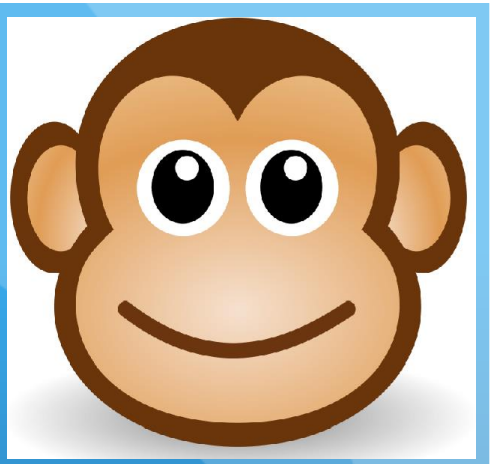
What do pregnant couples want? The preferences of pregnant couples at increased risk for Down's syndrome who are offered a choice in prenatal diagnosis between the clinical outcomes of 5 Mb and 0,5 Mb whole genome SNP array analysis

M. Knapen, S.L. van der Steen, S. Riedijk, K. Diderich, M.S. Joosten, L. Govaerts, D.V. Opstal, R.J. Galjaard, J. Visser, M.I. Srebniak, A. Tibben

Results: Ninety-six percent of the individuals wished to decide about the scope of PND and 90% were satisfied with their choice. Of the PNS group 69% would opt for 0,5 Mb array, of which 44% also opted to be informed about SL. Of the PND group 94% chose 0,5 Mb array and 68% opted to be informed of SL. The PND group chose 0,5 Mb array significantly more often than the PNS group $\chi = 18.49$, $p < 0.001$.

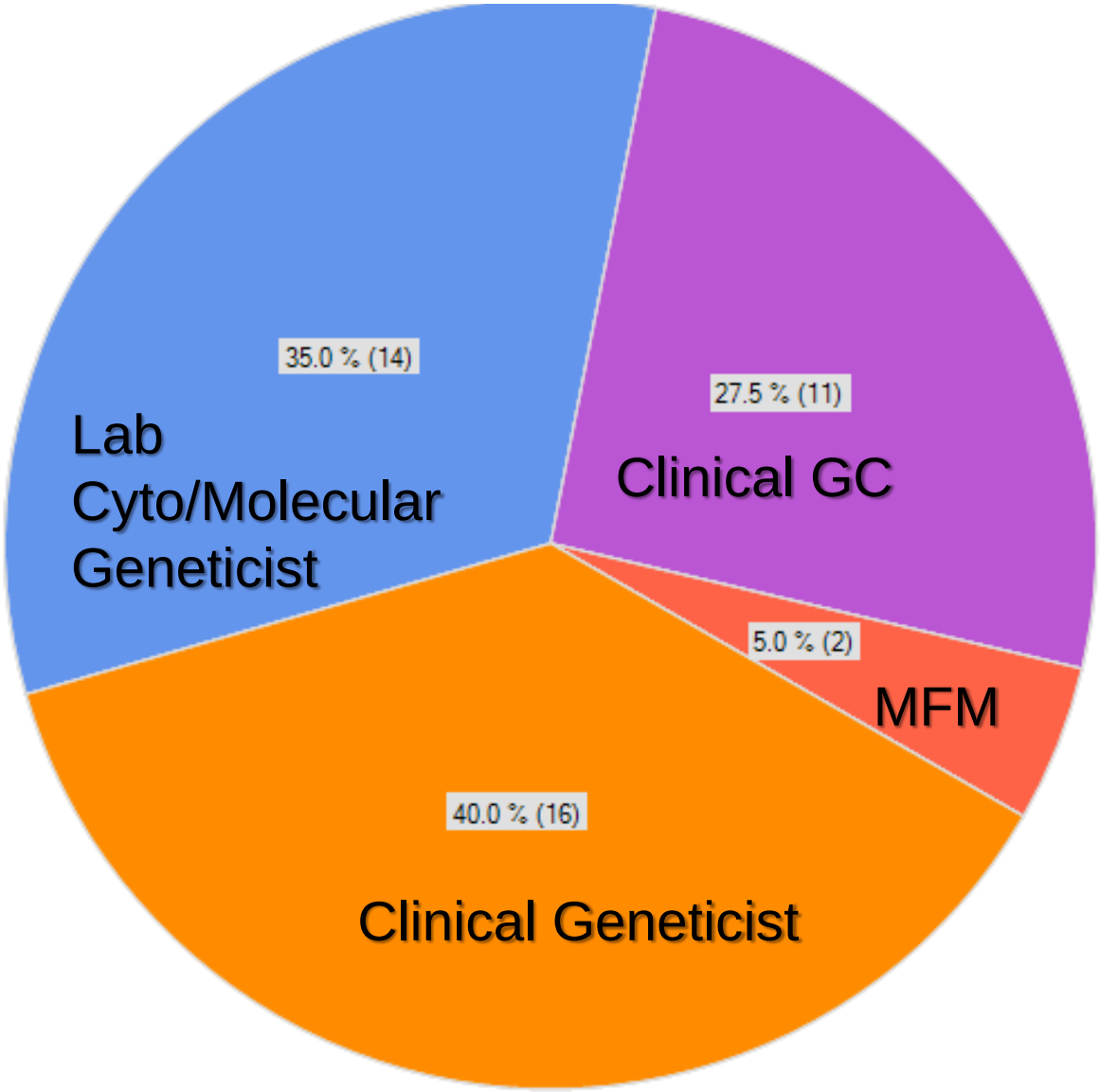
Conclusions: The first results of our study suggest that pregnant couples have a strong information need regarding PND and wish to make their own choices. Offering a choice regarding the scope of prenatal genetic testing and the disclosure of SL in the group of pregnant couples opting for PND based on an increased risk for Down's syndrome seems to be justified.

Our Survey….THANK YOU



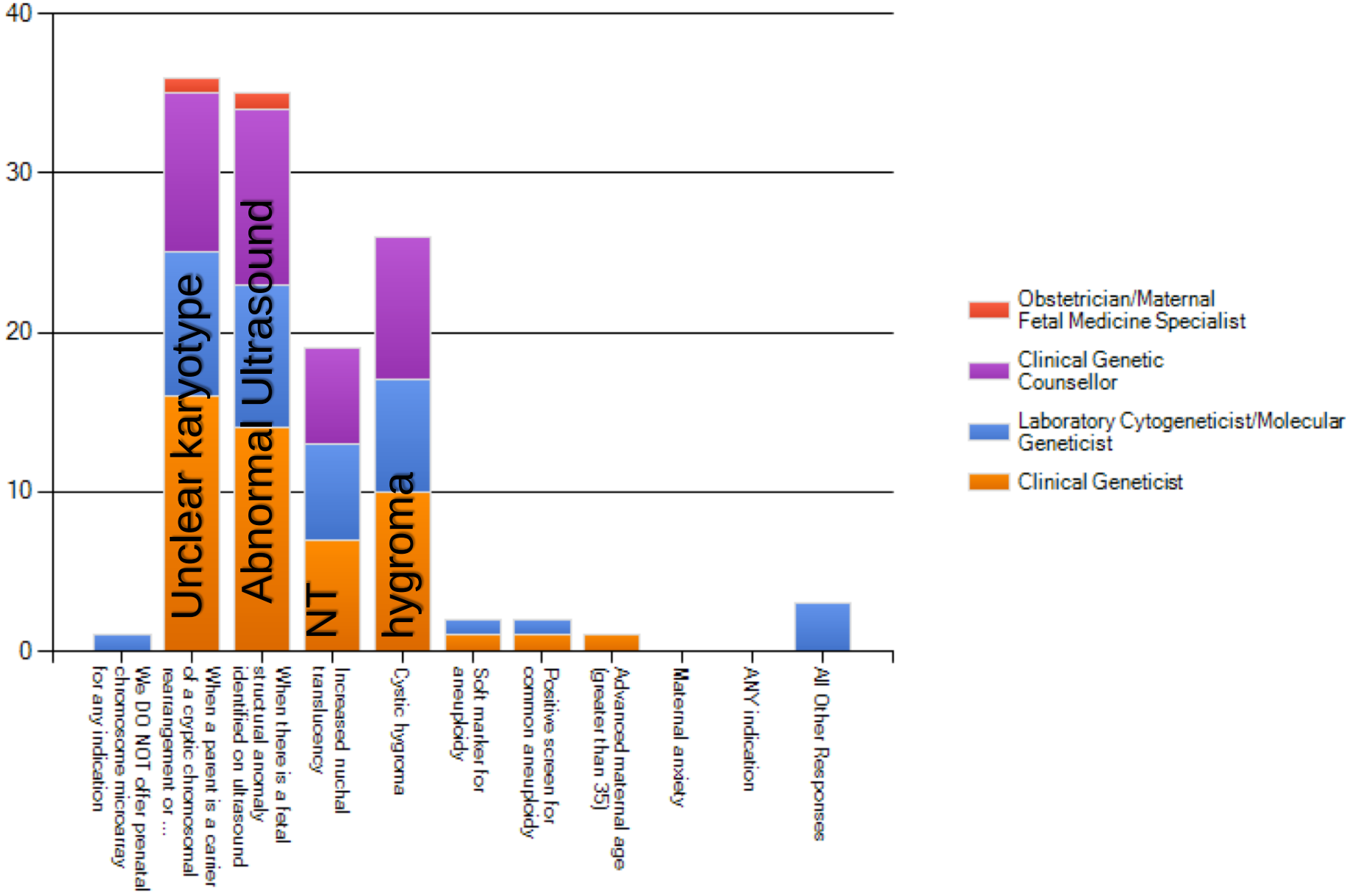
- Key points:
- Consensus
  1) want National guidelines
  2) consent form needed
  3) think women should be able to to choose some types of information to be withheld
  4)do NOT want to offer all pregnant women invasive testing
  5) but there appears to be **a shift in thinking** to expanding the use of microarray..
- Reporting issues- what to report/not, when karyotype required etc- handouts of the responses will be given to that working group to review

WHO ARE YOU anyway?

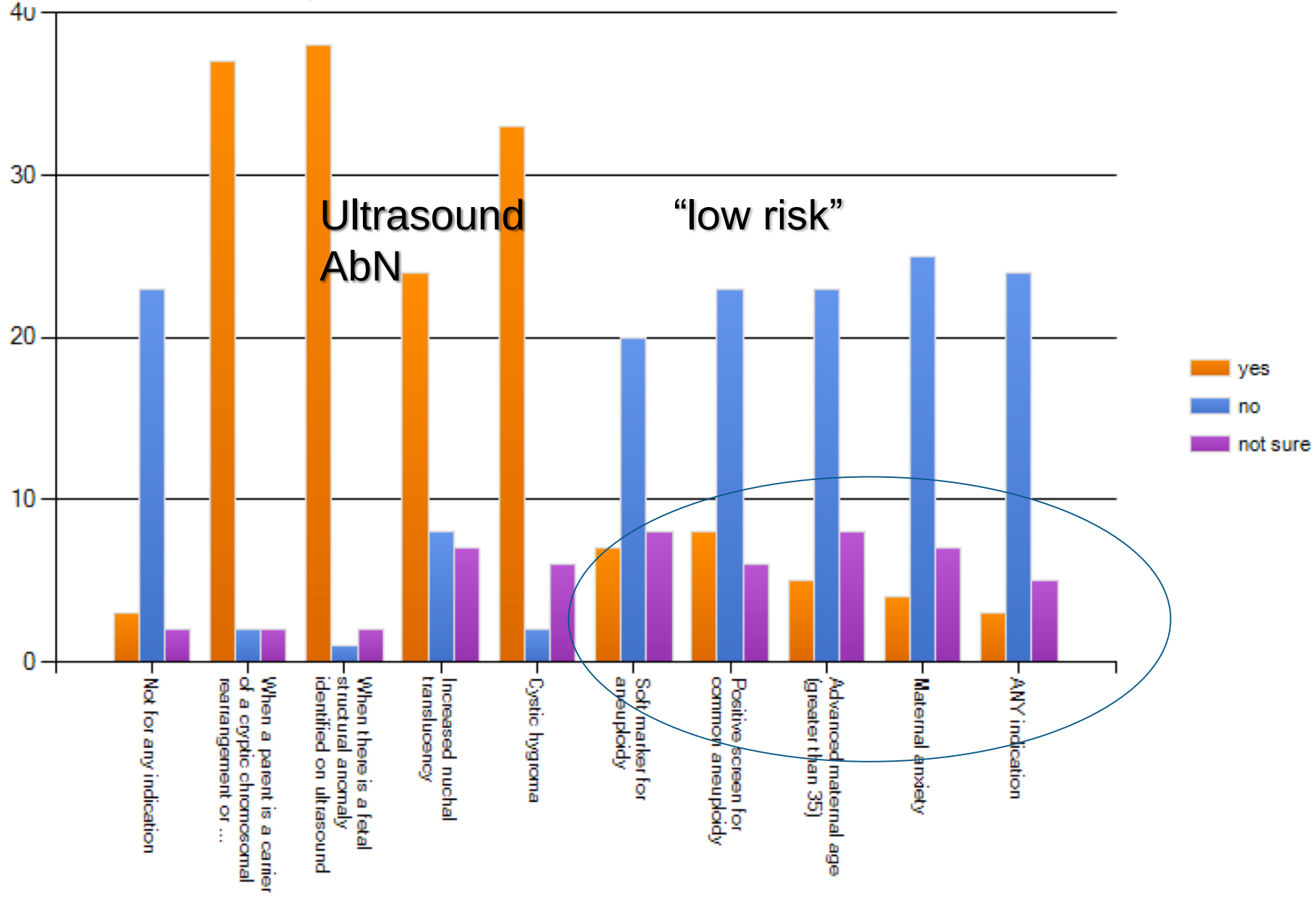


-Most of you (~51%) order prenatal CMA often (1/day or /week)
-34% less often (17%: 1 or more/month to 17% less than 1 a month)
-~15% not at all

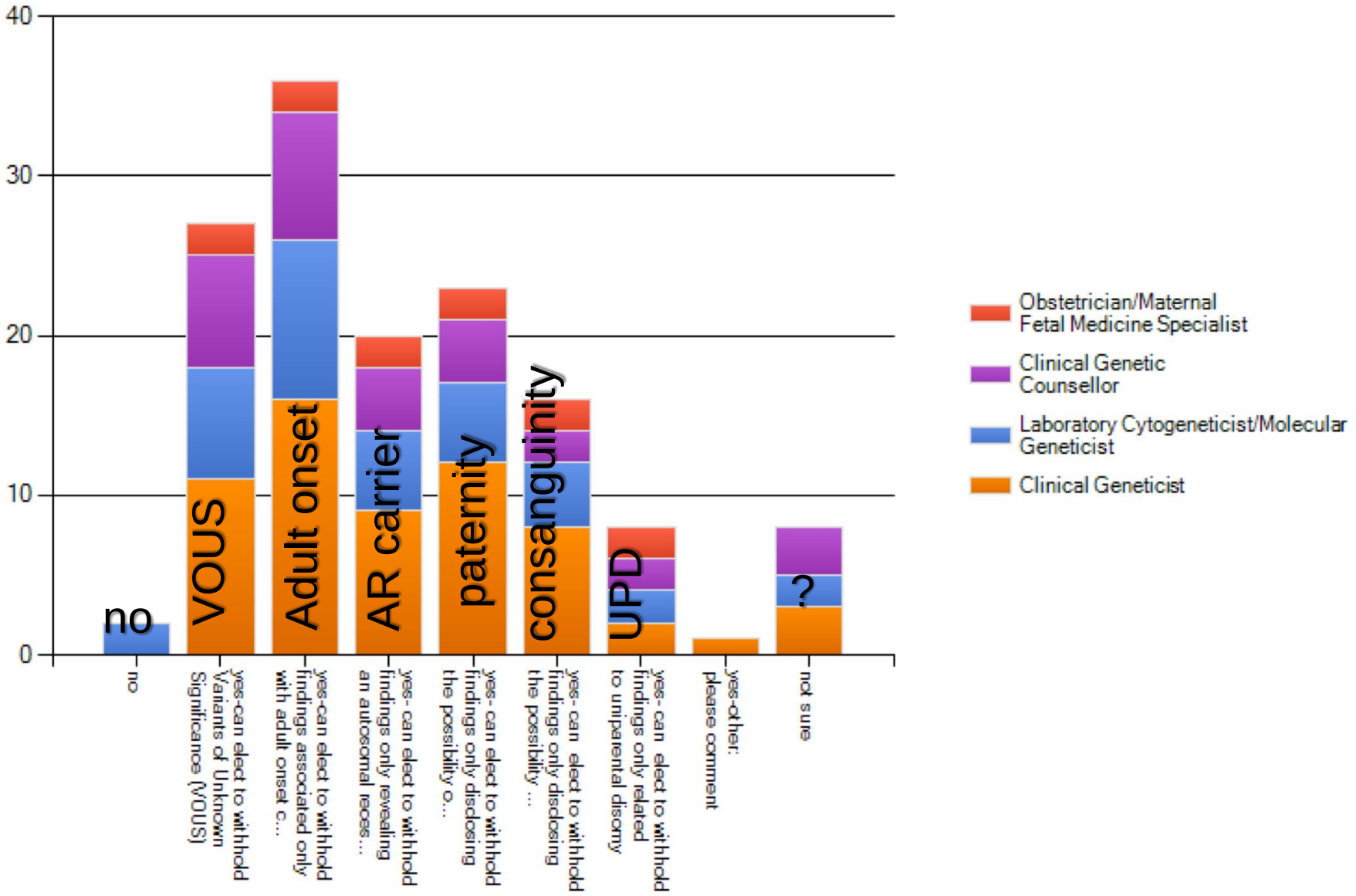
When do you currently offer CMA after normal aneuploidy screen?



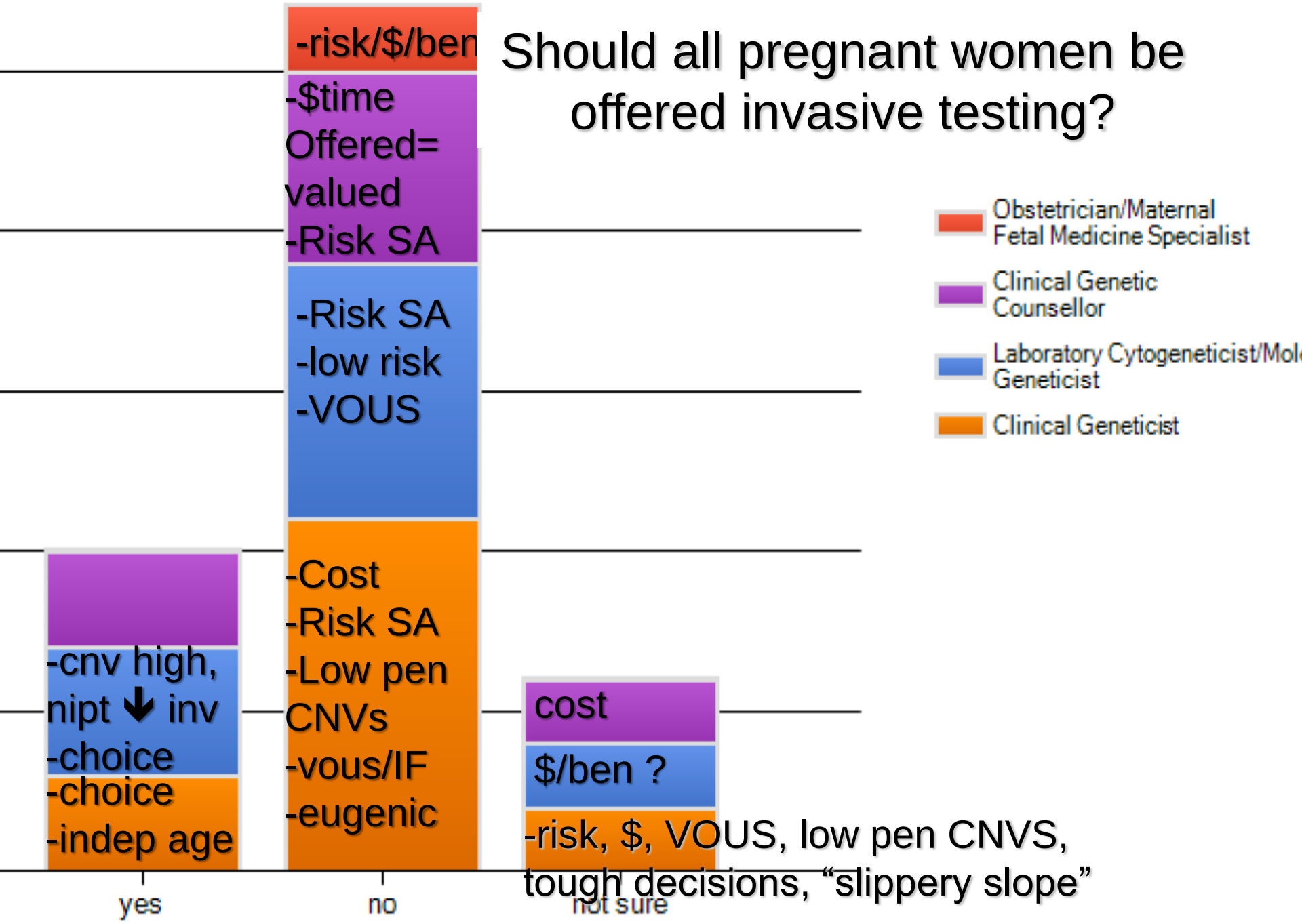
When should be order a prenatal microarray (assume aneuploidy screen normal)?



Should pts get to choose what kind of data to be reported/withheld?



Should all pregnant women be offered invasive testing?



Clinical Geneticist…Invasive for all? *unsure*

- There is an associated **risk** with the procedure and significant use of our limited **publicly funded** resources for the number of pathogenic results that would be found. The detection rate of a pathogenic CNV may be equal to the risk of the procedure, however, there will be many cases tested that are normal, or will have **incidental findings or VOUS**. This is a *slippery slope* with regards to testing each pregnancy for any potential genetic predisposition to health issues. There are a number of relatively common **CNVs with reduced penetrance** for neurocognitive issues that will be found and will put many couples through a **difficult decision** making process with **limited time** to make informed decisions.

Clinical Geneticist…unsure

- Invasive testing is a medical investigation which should be available to individuals **as medically indicated**. As health care providers, it is our **responsibility to educate** our patients as to the appropriate testing for their specific circumstances. We also have to be responsible in our utilization of health care dollars. Having said that I have made invasive testing available to women solely for anxiety, which contradicts my previous statements. That is why I am not sure!

Genetic Counsellor…Invasive for all? *unsure*

-don't think it should be offered to everyone but I think everyone has the **right to access** invasive testing. I think only offering it to people who know to ask for it is unfair yet I still don't think we should discuss it with everyone just so they know about it.

-**Cost** and impact on the **health care**

NO- **risk of SA**


go
where
I go
from
here

Together we can work it out…. Present various algorithms aimed at balancing autonomy and minimizing harms… and evaluate them…..research….research…research..


ONCE YOU UNFOLD ONE OF THESE THINGS, ITS NEVER THE SAME.
MAP OF THE HUMAN GENOME
Ethical Questions
Legal Tangles
Privacy concerns
Moral Issues
Insurance Applications
Medical Dilemmas