Prenatal screening in Czech Republic: history, present, future

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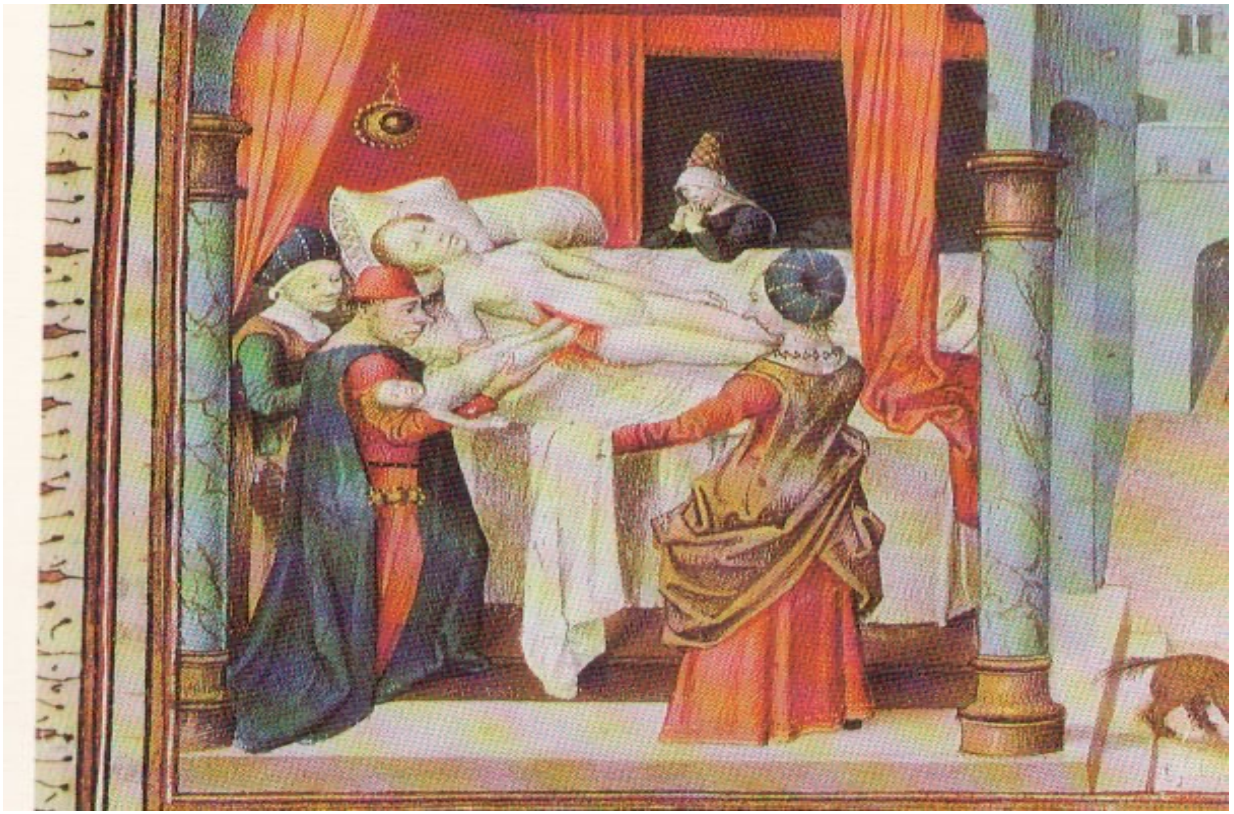
The aim of maternal-foetal care

the uncomplicated birth of a healthy baby

to a healthy mother at term



Screening of foetal aneuploidies in the CR

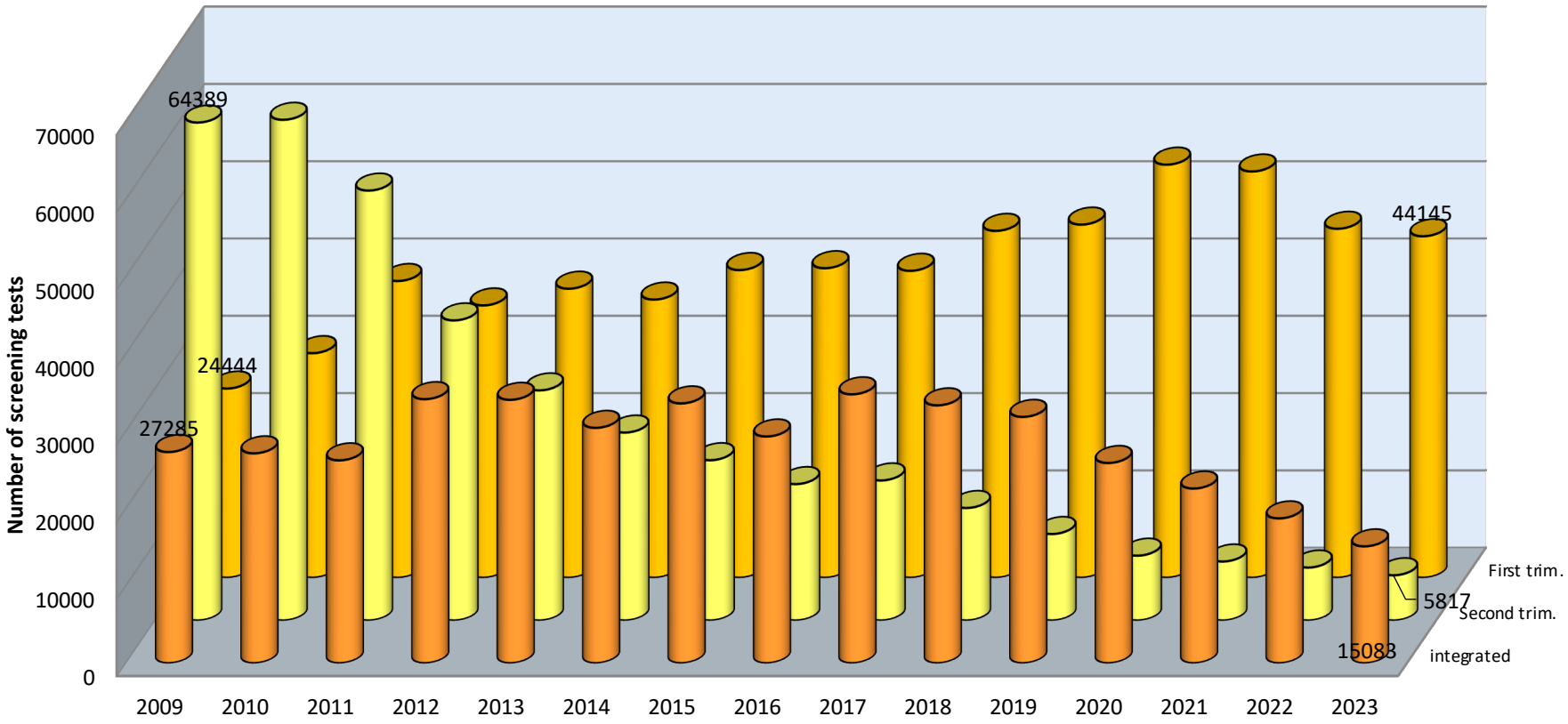
- List of laboratories performing laboratory screening of congenital malformations is kept at the Reference Laboratory for Clinical Chemistry in Prague since 2002.

- List of laboratories, data and links to external quality control are given on the website

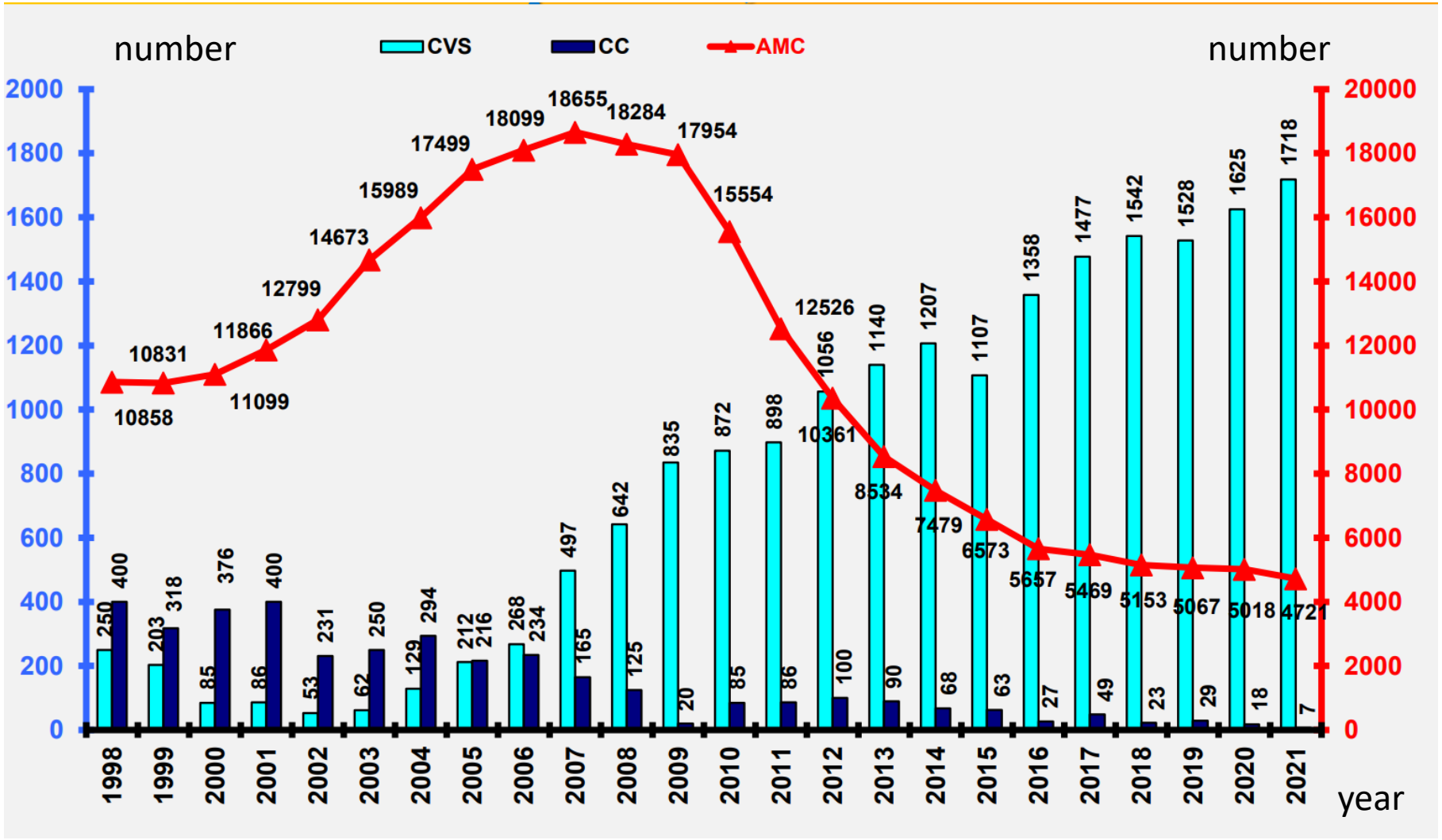
- **2023 - registered 40 laboratories.**
- **92,200 children born in 2023 in Czech Republic**

- **In the Czech Republic, NIPT is performed for direct payment and is provided to about 15-17% of pregnant women**

Screening in CR



Invasive prenatal diagnostics Czech Republic

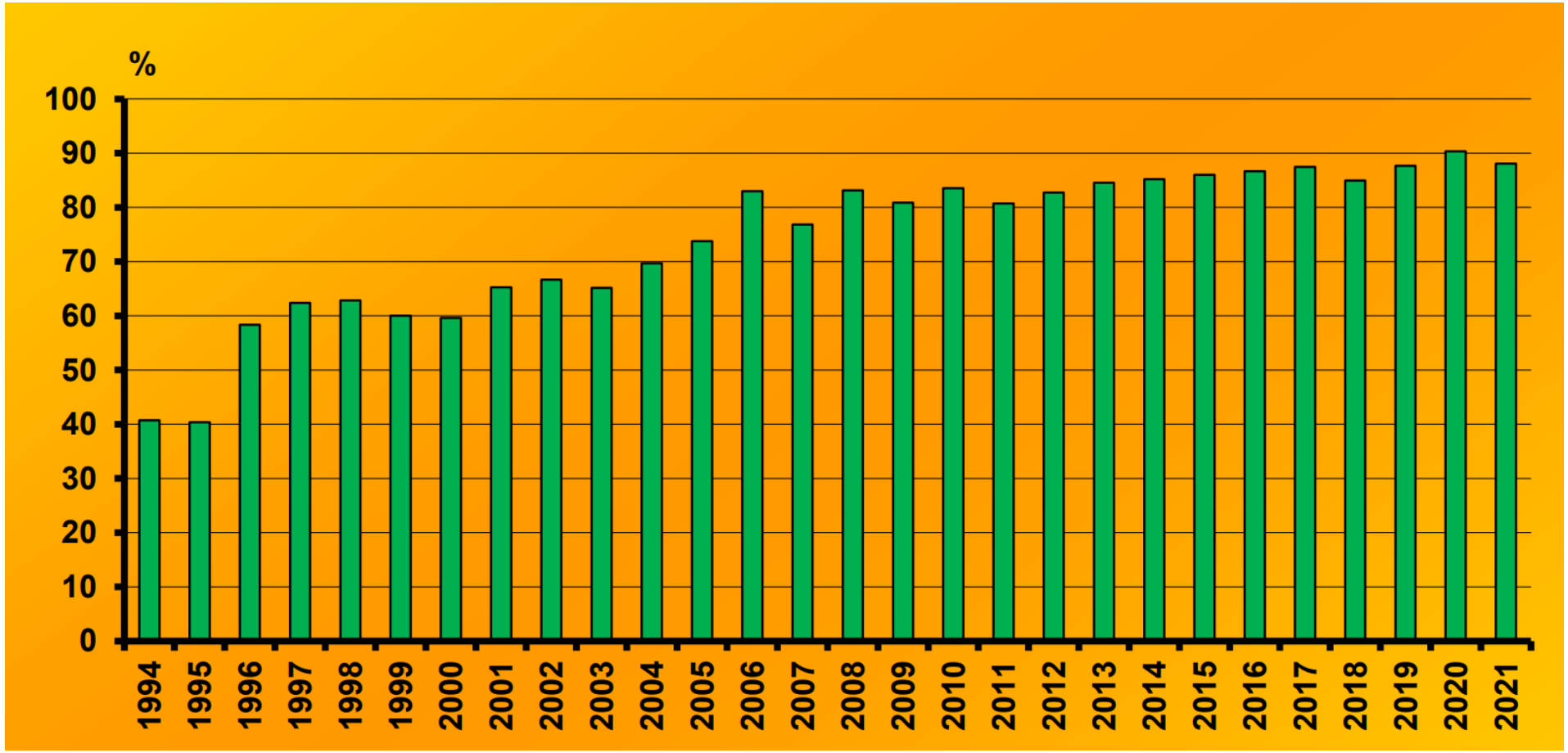


Vrozené vady

http://www.vrozene-vady.cz

Down syndrom in Czech Republic

Percentage of prenatally diagnosed and terminated cases



Vrozené vady

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NON-INVASIVE PRENATAL TESTING (NIPT)

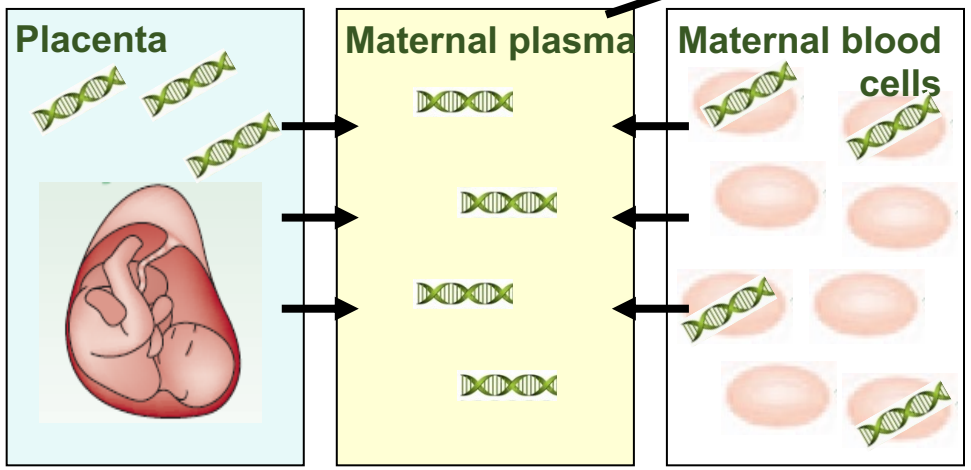
Extraction of cell free foetal nucleic acids

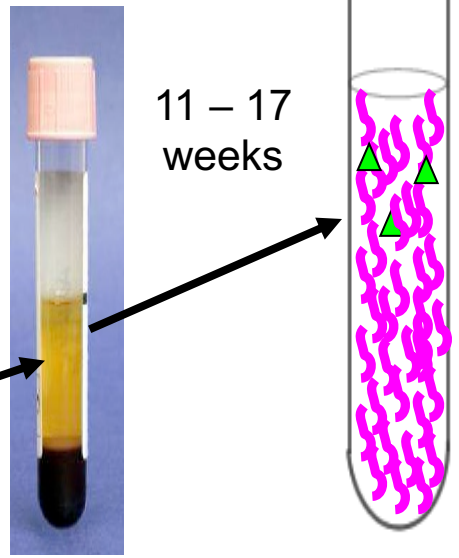
•1997 First report of free fetal DNA in maternal circulation. (Lo YMD *et al*. *Lancet* 1997;350:485-7)

•Population variation

• Low copy number of cf foetal DNA

• Background 'contamination' with cf maternal DNA (94 – 97%)





11 – 17 weeks

▲ Cell free foetal DNA (3.4%)

Cell free maternal DNA (96.6%)

Expectations and reality of NIPT I

Expectations	Reality
The test can be performed earlier than others	This is correct; it is a screening test
The test includes zero risk for the unborn baby in contrast to invasive testing, which has 1–3% abortion risk	First point is correct; however, nowadays risk of invasive testing is between 0 and 0.3% only
If we do the NIPT there is no need to do invasive testing	In case NIPT is positive an invasive confirmatory test is obligatory In case NIPT is negative but sonography normal invasive confirmatory test is recommended to exclude a placenta mosaicism
The test is based on fetal DNA	The test is based on placenta derived DNA
The test is a quick test and is easy to understand	There are many variants of the test There is a need for detailed pre-test counseling (e.g., to explain that a hidden maternal tumor may be detected) The technical details how the test works are very complicated

Expectations and reality of NIPT II

Expectations	Reality
The test is equally reliable for all kinds of genetic conditions tested	Highest reliability is available for trisomy 21; all other conditions have lower PPVs In many cases there are no PPVs available for the corresponding tested syndrome
There is a clear answer if baby will be ok	It is a screening test
The results are available very fast	It lasts 2 weeks and in 1.58–6.39% of the cases the tests needs to be repeated due to not sufficient cffDNA in maternal plasma
There is a clear answer if baby will be not ok, e.g., have trisomy 21	2% risk of placenta mosaics; false positive results are possible
It is a test which can exclude all genetic problems	Neither the “normal NIPT” nor the “expanded NIPT” can exclude all possible genetic conditions

Limitation of NIPT

- NIPT is a screening test, with positive results requiring confirmation via invasive testing (Shaw et al., 2020)
- Negative NIPT results and a fetus with sonographic findings may need further (invasive) testing (Liehr et al., 2017)
- NIPT is advertised as an assay capable of reducing the risk for invasive tests
- Today, the risk of invasive diagnostics is at 0–0.3% (Liehr et al., 2017).

- The sensitivity of NIPT for trisomy 21 is generally given as 99.3%, for trisomy 18, 97.4% and for trisomy 13, 97.4%,
- - with a specificity of 99.9% for trisomy 21 (Taylor-Phillips et al., 2016)
- The list of limitations begins with the understanding that at a maximum 50% of cases with chromosomal aberrations of the first and second trimester are detectable via NIPT

- Pregnant women must be properly informed about this when considering available testing options during pregnancy.

NIPT and world

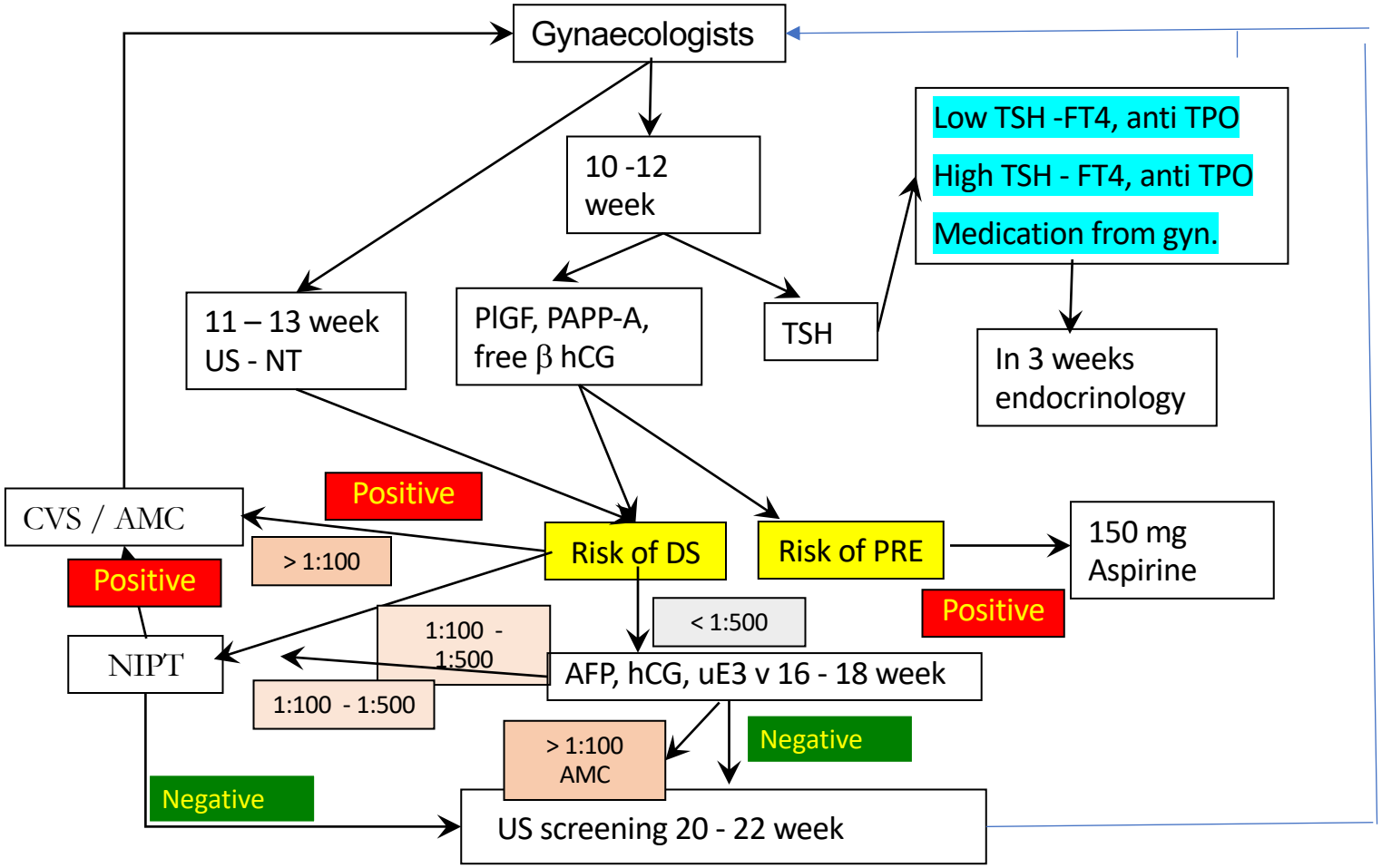
- NIPT is now available in more than 60 countries (introduction in 2011)
- The implementation of NIPT is different in Europe, Asia and the United States,
- *The Netherlands*
  - Since January 2007, a nationwide prenatal screening program has been implemented
  - The combined test (CT) in the first trimester to determine the risk for trisomy 21 and a structural ultrasound for neural tube defects in the second trimester are offered to all pregnant women
  - Since April 2017, NIPT has been offered to all pregnant people irrespective of their risk status
  - Women can still choose the first-trimester combined test first, with NIPT as a second-tier test
- *The United Kingdom*
  - The National Health Service is responsible for the screening program
  - The UK NSC recommended the use of NIPT as a second-tier test for T21, T18, and T13 in November 2015
  - The recommendation is that women who chose to take up the initial screening offer and have a higher-chance combined test result in the first trimester or in the second-trimester quadruple test (using a threshold of 1:150 from either) are eligible for the offer of NIPT.
  - This recommendation was implemented in Wales 2018, in Scotland 2020 and in England in 2021

Annu. Rev. Genom. Hum. Genet. 2021.22:309-338.

NIPT in Czech Republic

- The proposed NIPT system is not a general screening,
- It is indicated for women at risk between 1/101 and 1/500 and a negative ultrasound finding
  - It concerns about 4 - 6% of examined women, depending on their age distribution
- It is an alternative method which, in indicated cases, is not only thrifty, but also a more financially advantageous alternative
- Large centers (3 - 7 thousand screenings/year) performed NIPT in about 15% of examined women in previous years

Algorithm of prenatal screening in Czech Republic



Problems in prenatal screening for aneuploidy in CR

1/ screening as a whole is not covered by public health insurance!!!!!

2/ NOT – performance and proposal for the real amount of reimbursement for ultrasound measurement of nuchal translucency

Czech Soc of Gyn and Obst and health insurance companies

3/ READY - performance and proposal for a new performance of NIPT

- genetics , clinical biochemistry and health insurance companies

Czech Soc of Gyn and Obst has been blocked for several years

An angel with Down syndrome

Adoration of the Christ Child from the 16th century