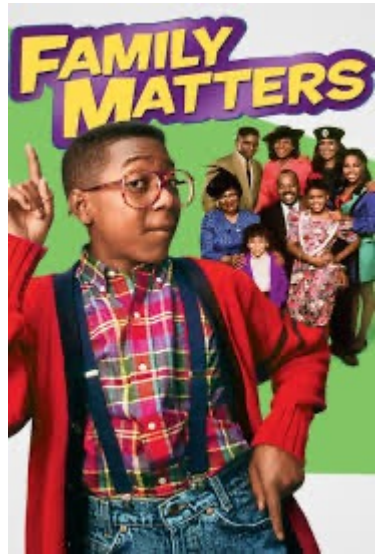




Family matters: Reproductive options and testing during pregnancy in case of a genetic disease

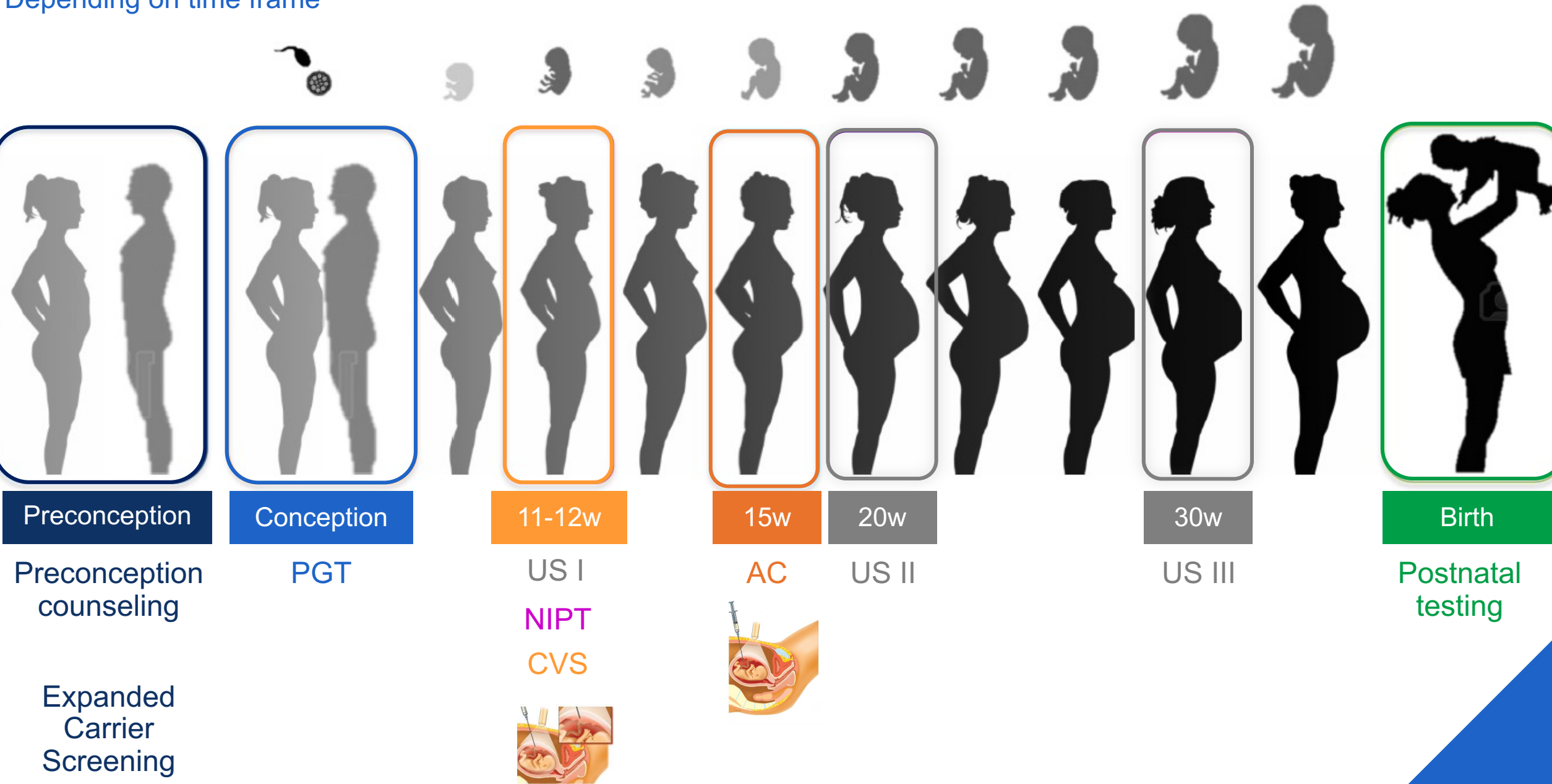
Dr. Candy Kumps
Centrum voor medische genetica

Reproductive options in case of genetic disease

- ▶ Prenatal testing (w/out termination of pregnancy)
- ▶ IVF-PGT
- ▶ Gamete donation
- ▶ Adoption
- ▶ No children
- ▶ Risk acceptance

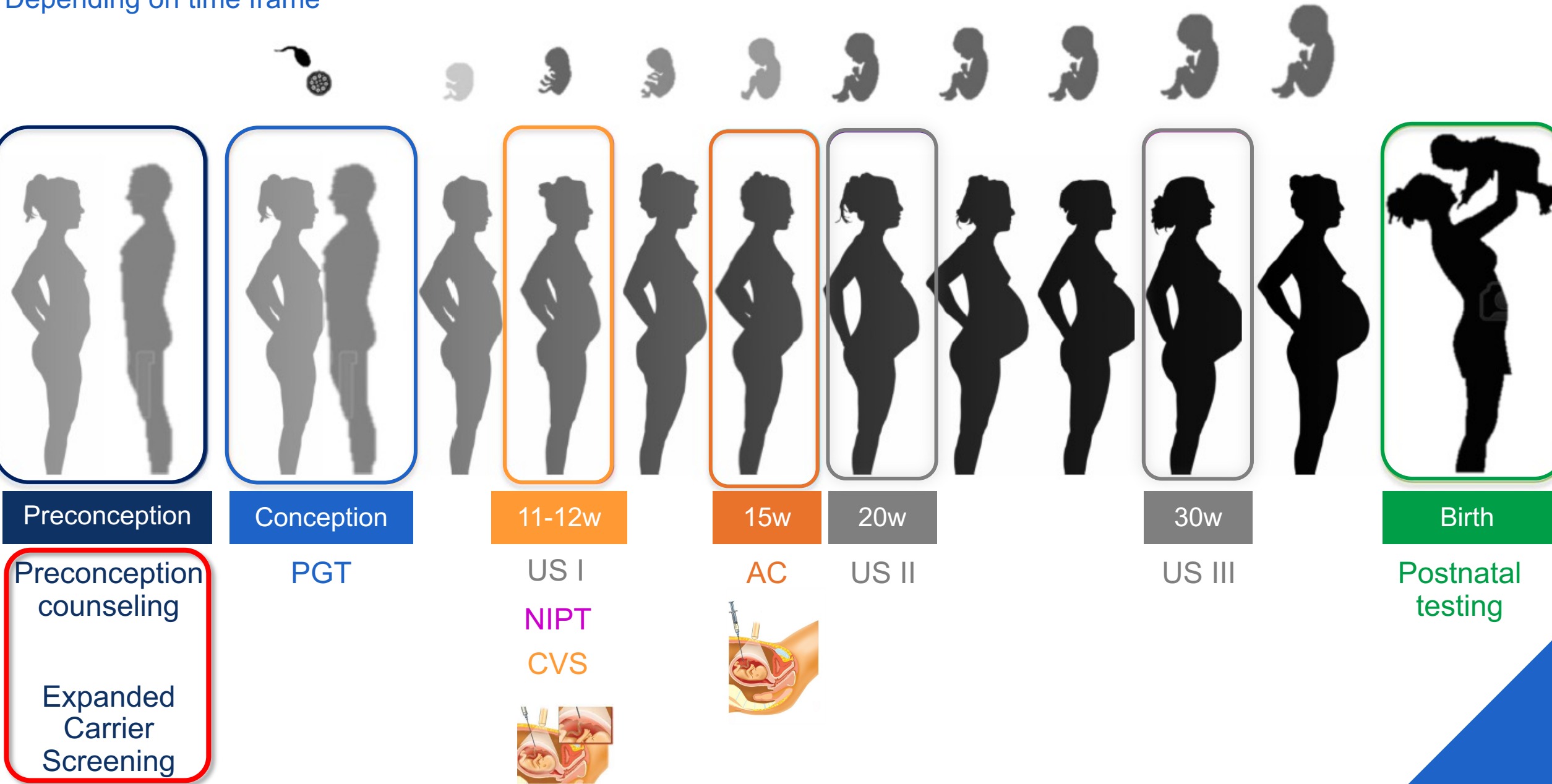
Reproductive options

Depending on time frame



Reproductive options

Depending on time frame



BeGECS – Expanded carrier screening

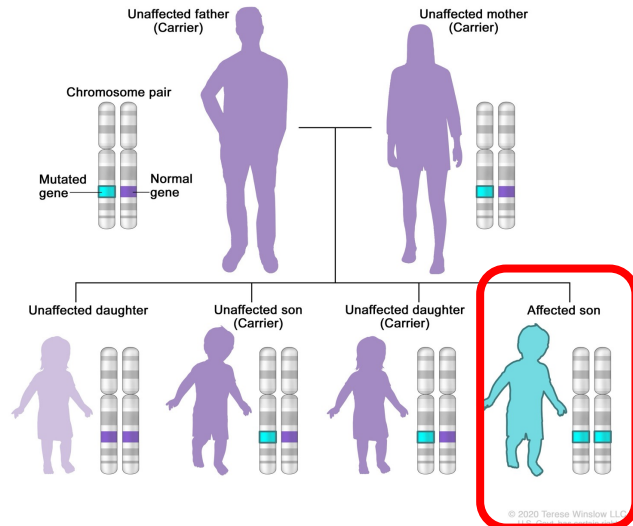
Couple test

Autosomal recessive disease

- Identify (unaffected) carriers of a genetic defect in the same gene



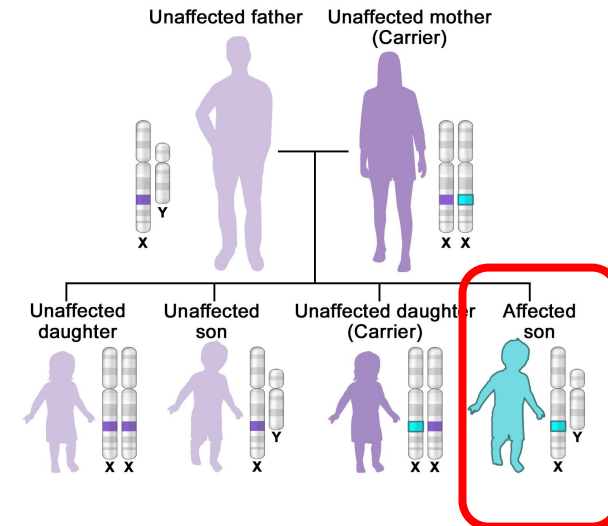
ARPKD
PKHD1



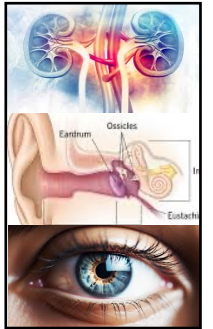
**Risk of 25% for
an affected child**

X-linked disease

- Identify (unaffected) carriers of an X-linked disease



**Risk of 50% for
an affected son**



Alport
COL4A5

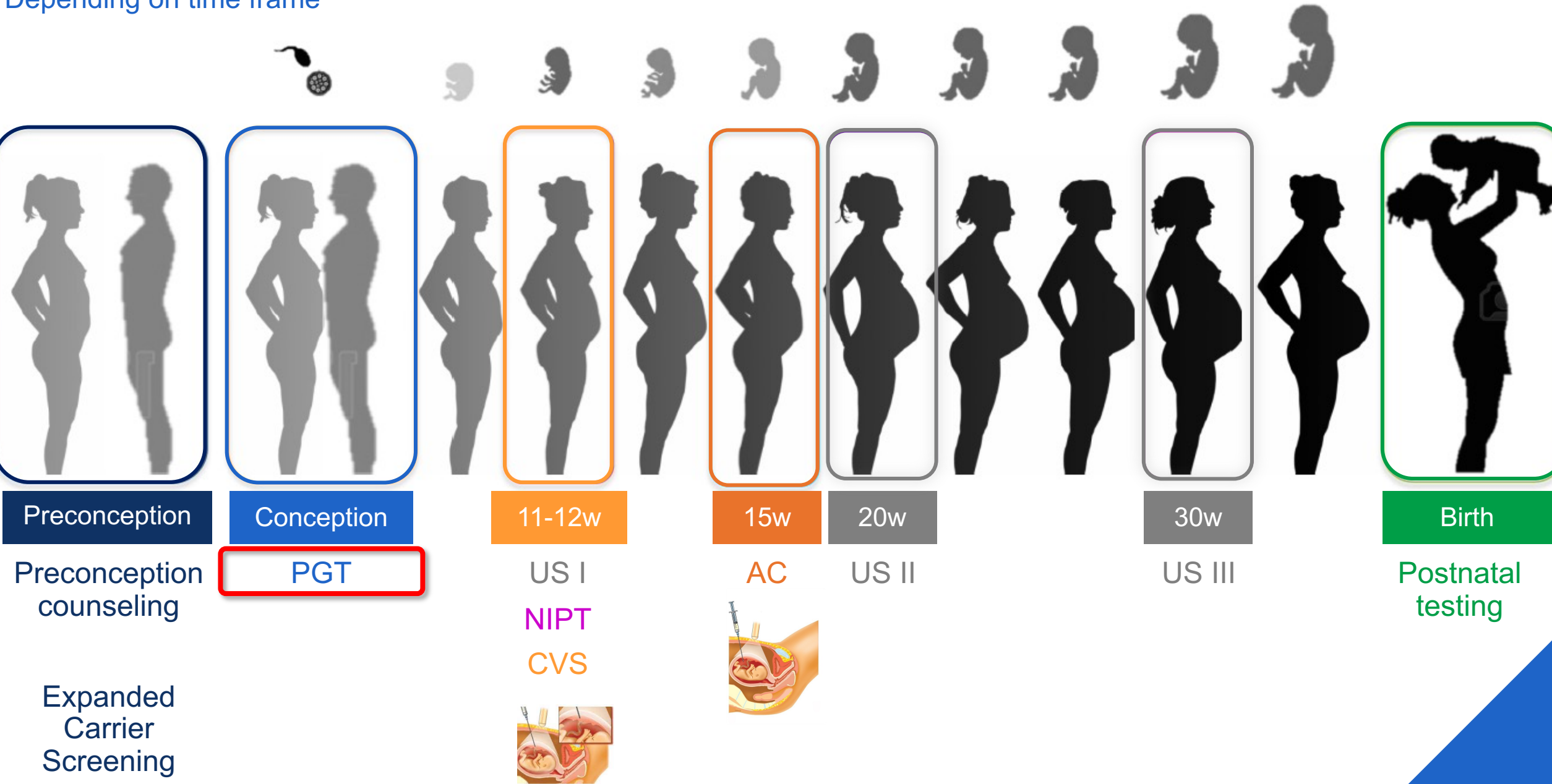
BeGECS – Expanded carrier screening

Couple test

- ▶ **Goal:** Reduce occurrence of severe recessive/X-linked disorders
- ▶ **2017:** Positive advice “Hoge Gezondheidsraad” concerning expanded carrier screening
- ▶ **>2019:** BeGECS
- ▶ **1700** genetic diseases
- ▶ **Yield:** ~3-5%
- ▶ **Turn around time:** 3 months
- ▶ **Cost:** 1500 euro
 - ▶ Neutraal ziekenfonds: 125 euro reimbursement per person

Reproductive options

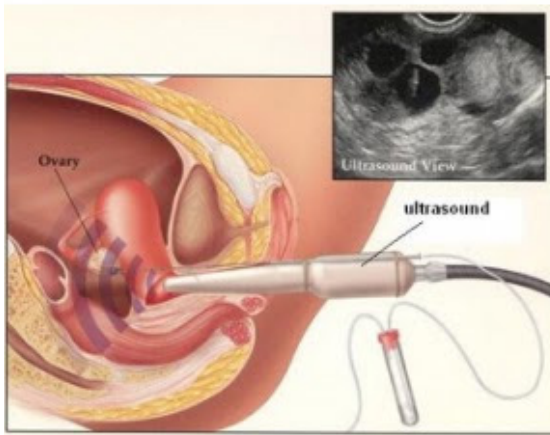
Depending on time frame



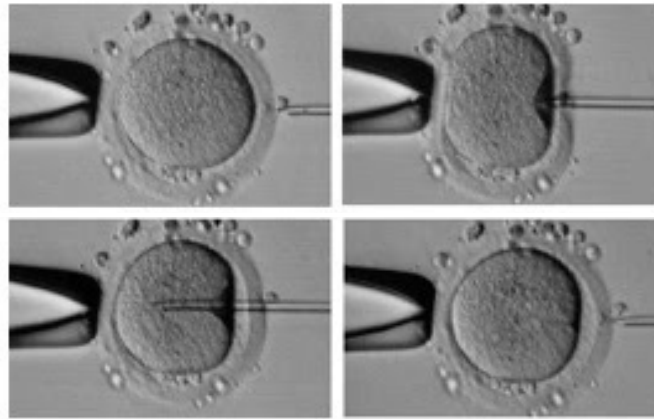
Pre-implantation genetic testing (PGT)

- ▶ For couples whose future children are *at risk* for a genetic disease
- ▶ If no PND with pregnancy interruption is desirable

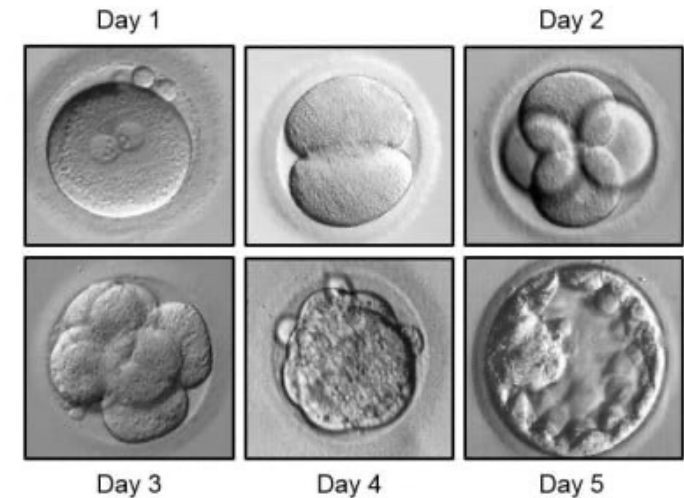
IVF



Hormone stimulation
Oocyte retrieval



Intracytoplasmic sperm
injection (ICSI)



Embryo development
Embryo biopsy

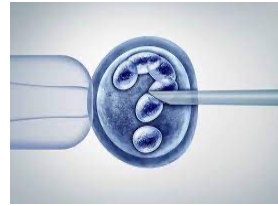
PGT: Indications

- ▶ **Co-PGT-M** (haplotyping)
 - ▶ Monogenic conditions with (likely) pathogenic variant (AR, AD, XL)
 - ▶ Additional: genome wide screening for large chromosomal abnormalities
- ▶ **PGT-SR** (low resolution sequencing)
 - ▶ Structural/imbalanced chromosomal rearrangements
 - ▶ Additional: genome wide screening for large chromosomal abnormalities
- ▶ **PGT-A** (rare)
 - ▶ Aneuploidy screening (chromosomal)
 - ▶ Shorten time to pregnancy by transfer of an euploid embryo
 - ▶ Eg. Older age, recurrent miscarriage, implantation failure

ADPKD
ARPKD
Alport (COL4A5)

t(12;20)(q24;q13)
t(14;21)

PGT: Trajectory in case of a known genetic defect



Start PGT

3 months

3 weeks

4-6 weeks

Embryo
transfer

5-6 months

- ▶ Genetic counselling
- ▶ Fine tuning test
- ▶ Genetic screening in couple
 - ▶ Standard (FraX, SMA, CFTR, karyotyping)
 - ▶ BeGECS (1700 genes – AR, XL)
- ▶ Counselling at fertility department

- ▶ Oocyte stimulation & pick up
- ▶ IVF-ICSI
- ▶ Embryo biopsy
- ▶ Embryo freezing

- ▶ Embryo testing

Success rate for live birth after transfer: ~40%

PGT: Costs

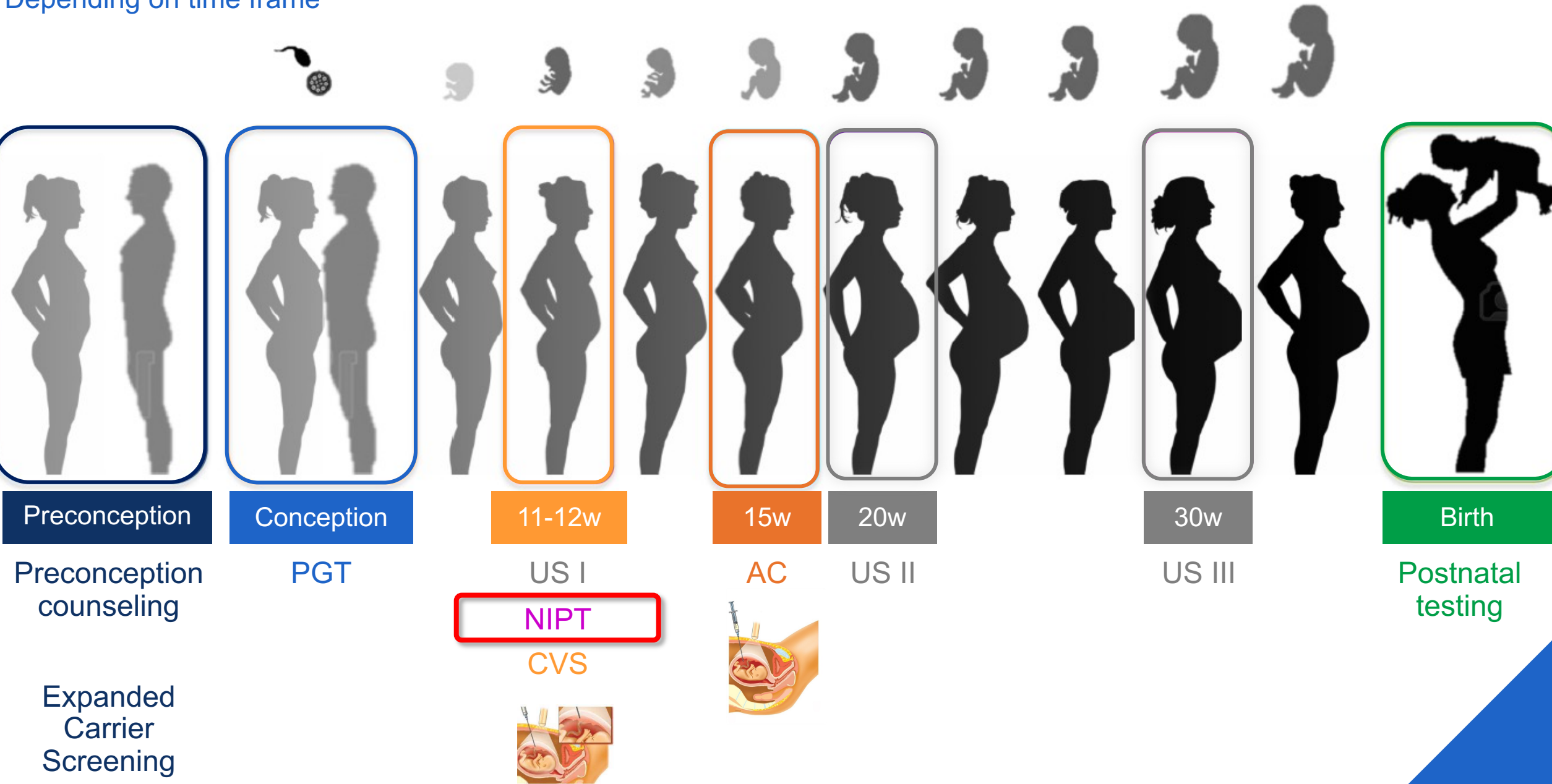
▶ Consultatie genetica beide partners	€ 93,38
▶ Karyotype beide partners	€ 664,00
▶ Dragerschapsonderzoek	
▶ Mucoviscidose beide partners	€ 349,24 (eventueel eerst ♂)
▶ Spinale musculaire atrofie ♀	€ 402,08
▶ Fragile X syndroom ♀	€ 174,62
▶ coPGT-M: oppuntstelling test	€ 2 297,60
▶ PGT analyse (per IVF cyclus)	€ 1 723,20
▶ Totale kostprijs	€ 5 629,50/ 5704,12 – € 6206,20
▶ Belgische patiënten	
▶ Remgeld / analyse	€ 8,68
▶ Remgeld consultatie beide partners	€ 24

Cost for patient +/- € 1000

6 cycles reimbursed

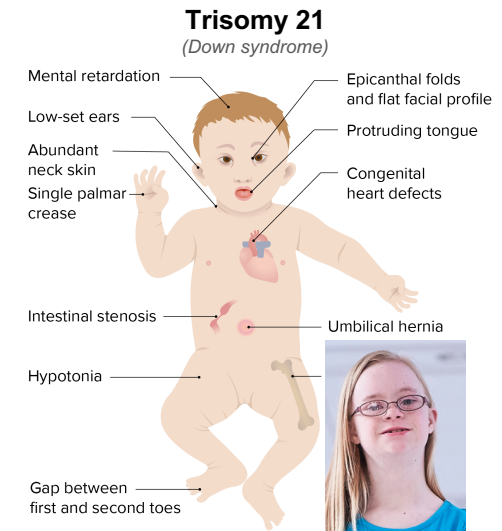
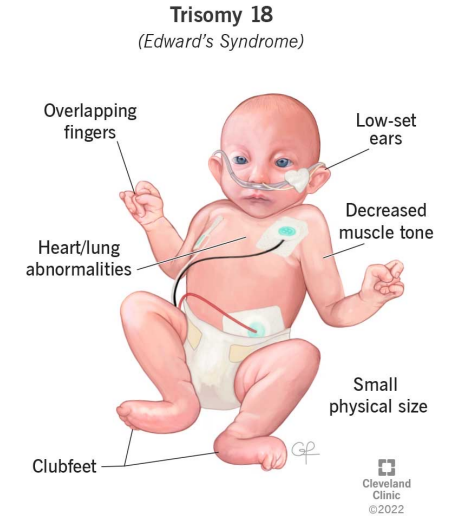
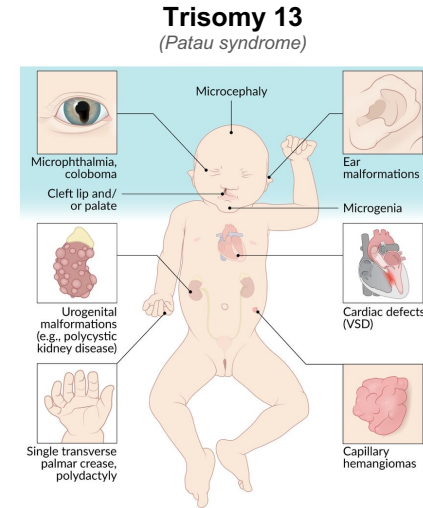
Reproductive options

Depending on time frame



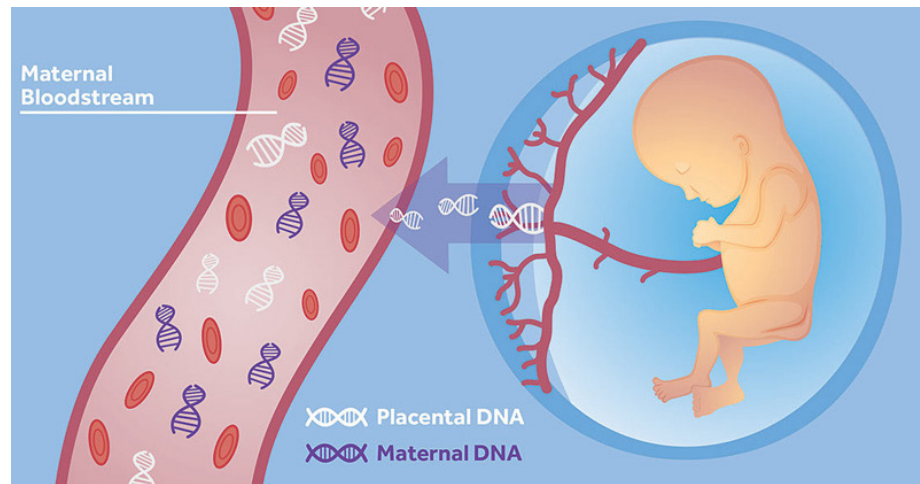
NIPT

- ▶ NIPT = **screening test** for low risk pregnancies
- ▶ GOAL = screening for **T13 – T18 – T21**
- ▶ **Sex determination possible**, not primary goal
- ▶ **Sex chromosome abnormalities (?)** (XO, XXY)
- ▶ Confirmation with **invasive diagnostics** necessary



NIPT

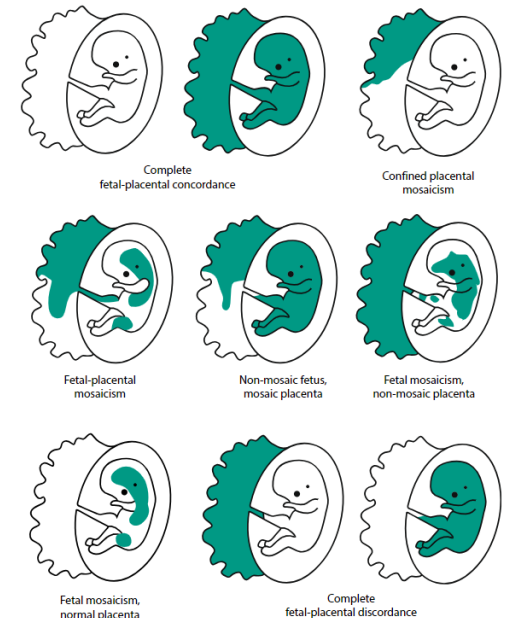
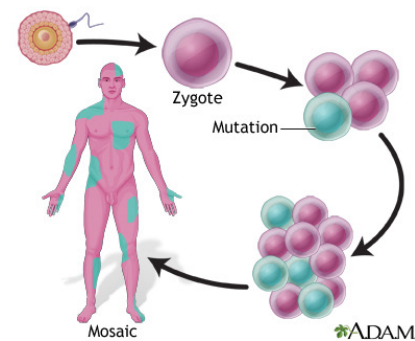
From 11-12 weeks



Cell free DNA
mother
placenta (foetal fraction)

- ~sensitivity
- ~specificity
- ~positive predictive value
- ~negative predictive value

Mosaicism



Invasive prenatal testing

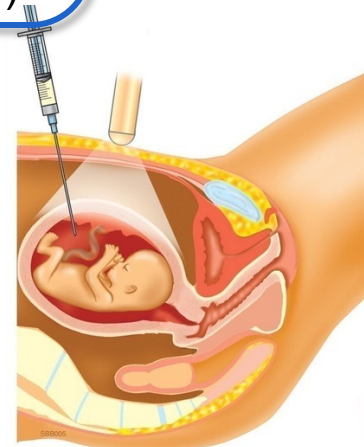
CVS (Chorion Villi Sampling)

- ▶ 11-12w
- ▶ Transvaginal/abdominal
- ▶ Placenta

AC (Amniocentesis)

- ▶ >15w
- ▶ Transabdominal
- ▶ Amniocytes (fetal cells)

- ▶ Risk miscarriage: 1/400
- ▶ Genetic tests: CNV/exome/...
- ▶ Diagnostic with US abnormalities/
known genetic risk
- ▶ TOP (termination of pregnancy)



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Volg ons op



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complex diseases

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Bone Disorders (ERN BOND)