PRENATAL SCREENING FOR DOWN SYNDROME, TRISOMY 18 AND OPEN NEURAL TUBE DEFECTS

Prenatal screening estimates the fetal risk of Down syndrome, trisomy 18, and open neural tube defects. The results will assist in determining the need for further diagnostic testing.

The screening tests offered will vary according to the gestational age at the time of presentation, maternal age at the time of delivery, and singleton versus twin gestation.

Table 1: Tests available through the BC Prenatal Genetic Screening Program

Test Name	Markers / Measurements	Possible Timeframe	Best Timeframe
Serum Integrated Prenatal Screen (SIPS) blood test #1	PAPP-A	9 – 13^{+6} wks	10 – 11^{+6} wks
SIPS blood test #2	AFP uE3 hCG Inhibin-A	14 – 20^{+6} wks	15 – 16 wks
Integrated Prenatal Screen (IPS)	Same as SIPS (blood test #1 & #2) with addition of NT ultrasound[1]	See SIPS for blood tests 11 – 13^{+6} wks	See SIPS for blood tests 12 – 13^{+3} wks
Quad blood screen	Same as SIPS blood test #2	14 – 20^{+6} wks	15 – 16 wks
Non-Invasive Prenatal Testing (NIPT)	Cell-free DNA in maternal blood	10 weeks and onwards	varies by indication

[1] If an NT ultrasound is performed, a separate first trimester dating ultrasound is not necessary if LMP is certain.

Resources

- BC Prenatal Genetic Screening Program; guideline and related patient teaching resources; www.bcprenatalscreening.ca
- Perinatal Services BC; T 604-877-2121; www.perinatalservicesbc.ca
- Canadian Down Syndrome Society; T (800) 883-5608; E info@cdss.ca; www.cdss.ca
- Down Syndrome Research Foundation (Canada); T 604-444-3773 or toll-free in Canada at 1-888-464-DSRF; www.dsrf.org
- Lower Mainland Down Syndrome Society (Canada); T 604-591-2722; www.lmdss.com
- Society of Obstetricians and Gynaecologists, Clinical Practice Guidelines (Canada); www.sogc.org/guidelines
- Spina Bifida and Hydrocephalus Association of BC; T 604-878-7000; E info@sbhabc.org; www.sbhabc.org
- Support Organization For Trisomy 18, 13 and Related Disorders (SOFT; US); www.trisomy.org

Genetic counselling services (Medical Genetics)

Victoria: T 250-727-4461 Fax for referrals: 250-727-4295
Vancouver: T 604-875-2157 Fax for referrals: 604-875-3484

Questions about prenatal screening in BC

Prenatal Biochemistry Laboratory: T 604-875-2331
(8:00 am – 4:00 pm, Monday – Friday)

BC Prenatal Genetic Screening Program

Perinatal Services BC
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Table 2: Screening options available through the BC Prenatal Genetic Screening Program

Characteristics of woman	Gestational Age at the First Prenatal Visit		
	≤ 13^{+6} weeks	14 – 20^{+6} weeks	≥ 21 weeks (no prior screening)
< 35 years	• SIPS (if patient is HIV+ & NT is available, IPS)	• Quad	• Detailed ultrasound
35 – 39 years	• IPS; or • If NT not available, SIPS	• Quad	• Detailed ultrasound; and • Amnio
40+ years	• IPS; or • If NT not available, SIPS; or • CVS or Amnio without prior screening	• Quad; or • Amnio without prior screening	• Detailed ultrasound; and • Amnio
Personal / family history that increases risk of fetus with Down syndrome, trisomy 18, or trisomy 13	• NIPT; or • CVS or Amnio without prior screening	• NIPT; or • Amnio without prior screening	• Detailed ultrasound; and • NIPT; or • Amnio
Personal / family history that increases risk of fetus with chromosomal abnormality other than Down syndrome, trisomy 18, or trisomy 13	• CVS or Amnio without prior screening	• Amnio without prior screening	• Detailed ultrasound; and • Amnio
Twin gestation	• IPS; or • If NT not available, SIPS; or • If ≥ 35, Amnio without prior screening	• Quad; or • If ≥ 35, Amnio without prior screening	• Detailed ultrasound; and • If ≥ 35, Amnio
Pregnant following In vitro fertilization with intracytoplasmic sperm injection	• IPS; or • If NT not available, SIPS; or • CVS or Amnio without prior screening	• Quad; or • Amnio without prior screening	• Detailed ultrasound; and • Amnio

If the prenatal screen result is **screen positive for Down syndrome** (assuming gestational dating is confirmed) or **trisomy 18**, women should be counselled by their health care provider and offered NIPT or CVS / Amnio for diagnostic testing. See www.bcprenatalscreening.ca for details.

If the prenatal screen result is **screen positive for an open neural tube defect** (assuming gestational dating is confirmed), women should be referred to Maternal Fetal Medicine or Medical Genetics for a detailed ultrasound, counselling, and, if indicated, diagnostic testing.

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Table 3: Eligibility, Screen Cut-Offs, and Performance of Screening Tests [1]

		Serum Integrated Prenatal Screen (SIPS)	Integrated Prenatal Screen (IPS)	Quad Screen (QUAD)	Non-Invasive Prenatal Testing (NIPT)
WHO IS ELIGIBLE		All women who present for their first visit at ≤ 13^{+6} wks	Women who present for their first prenatal visit at ≤ 13^{+6} wks gestation and who: • Are 35 years or older at EDD ***OR*** • Are HIV positive ***OR*** • Are pregnant with twins ***OR*** • Are pregnant following IVF with ICSI	All women who present for their first prenatal visit between 14 and 20^{+6} wks gestation	• Women with a positive (IPS / SIPS / Quad) screen for Down syndrome or trisomy 18 ***OR*** • Women with a previous pregnancy with trisomy 21, 18, or 13 ***OR*** • Women with an increased risk (≥ 1/300) for Down syndrome based on ultrasound marker(s) and serum screen result
DOWN SYNDROME	**Screen cut-off**	**1:300**	**1:200**	**1:385**	
	Detection rate	< 35 yrs: 80% 35 – 39 yrs: 86% ≥ 40 yrs: 100%[2]	< 35 yrs: 100%[2] 35 – 39 yrs: 95% ≥ 40 yrs: 100%[2]	< 35 yrs: 86% 35 – 39 yrs: 85% ≥ 40 yrs: 100%[2]	> 99%
	False positive rate	< 35 yrs: 3% 35 – 39 yrs: 9% ≥ 40 yrs: 20%	< 35 yrs: 3% 35 – 39 yrs: 7% ≥ 40 yrs: 17%	< 35 yrs: 4% 35 – 39 yrs: 13% ≥ 40 yrs: 31%	< 0.1%
	Chance a screen negative result is a false negative result	< 0.1%	< 0.1%	< 0.1%	< 0.01%
TRISOMY 18	**Screen cut-off**	**1:300**	**1:300**	**1:300**	
	Detection rate	86%	92%	70%	~ 97%
	False positive rate[3]	0.3%	1%	0.4%	< 0.1%
	Chance a screen negative result is a false negative result	< 0.1%	< 0.1%	< 0.1%	< 0.01%

[1] Performance of screening tests applies to singleton pregnancies. SIPS / IPS / Quad data from Perinatal Services BC. British Columbia Perinatal Data Registry. Years provided: April 1, 2013 to March 31, 2017. Resource type: Tabulated data. NIPT data from published studies of the Harmony test, Ariosa Diagnostics, Inc.

[2] The detection rates listed are based on the small cohort of Down syndrome pregnancies in BC. SIPS, IPS and Quad are screening tests so may not have 100% detection rate.

[3] Higher false positive rate of IPS reflects that this test is done in women who are at a higher apriori risk.

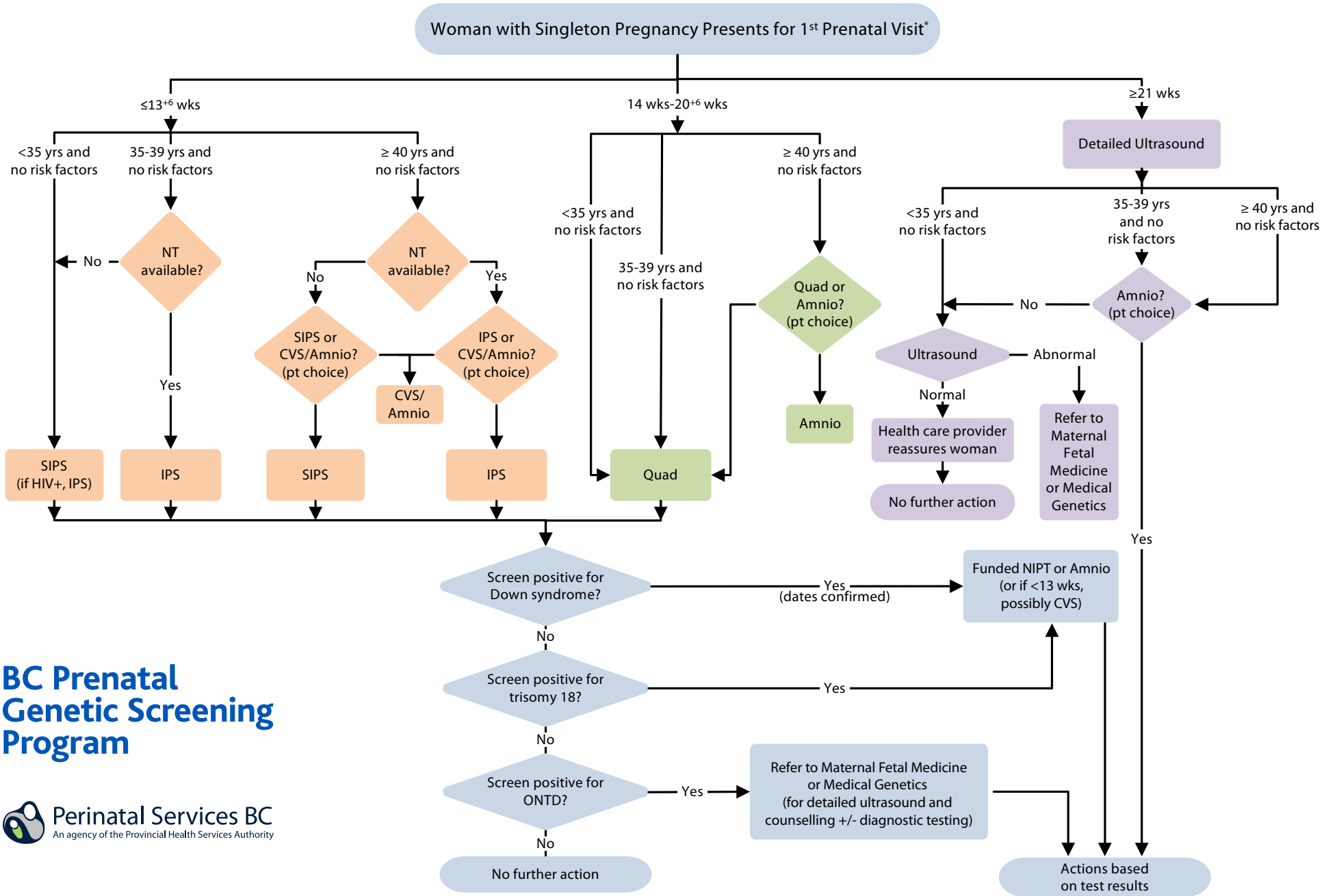
Table 4: Risk of Down Syndrome and Other Chromosome Abnormalities in Live Births by Maternal Age

Maternal Age (At Term)	Risk		Maternal Age (At Term)	Risk		Maternal Age (At Term)	Risk	
	Down Syndrome	Total Chromosome Abnormality		Down Syndrome	Total Chromosome Abnormality		Down Syndrome	Total Chromosome Abnormality
25	1 in 1,250	1 in 476	32	1 in 637	1 in 323	39	1 in 125	1 in 81
26	1 in 1,190	1 in 476	33	1 in 535	1 in 286	40	1 in 94	1 in 63
27	1 in 1,111	1 in 455	34	1 in 441	1 in 224	41	1 in 70	1 in 49
28	1 in 1,031	1 in 435	35	1 in 356	1 in 179	42	1 in 52	1 in 39
29	1 in 935	1 in 417	36	1 in 281	1 in 149	43	1 in 40	1 in 31
30	1 in 840	1 in 385	37	1 in 217	1 in 123	44	1 in 30	1 in 21
31	1 in 741	1 in 385	38	1 in 166	1 in 105	≥45	≥1 in 24	≥1 in 19

Source: Hecht CA and Hook EB. 1996

Algorithm 1

Prenatal Genetic Screening Recommendations for Women Who Present with *Singleton* Pregnancies



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* Excluding women with personal / family history that increases risk of fetus with Down syndrome, trisomy 18, or other chromosomal abnormality, who should be referred to Medical Genetics for counselling of their prenatal screening / diagnostic options.

See www.bcprenatalscreening.ca for more details on amniocentesis and NIPT options (both funded and self-pay).

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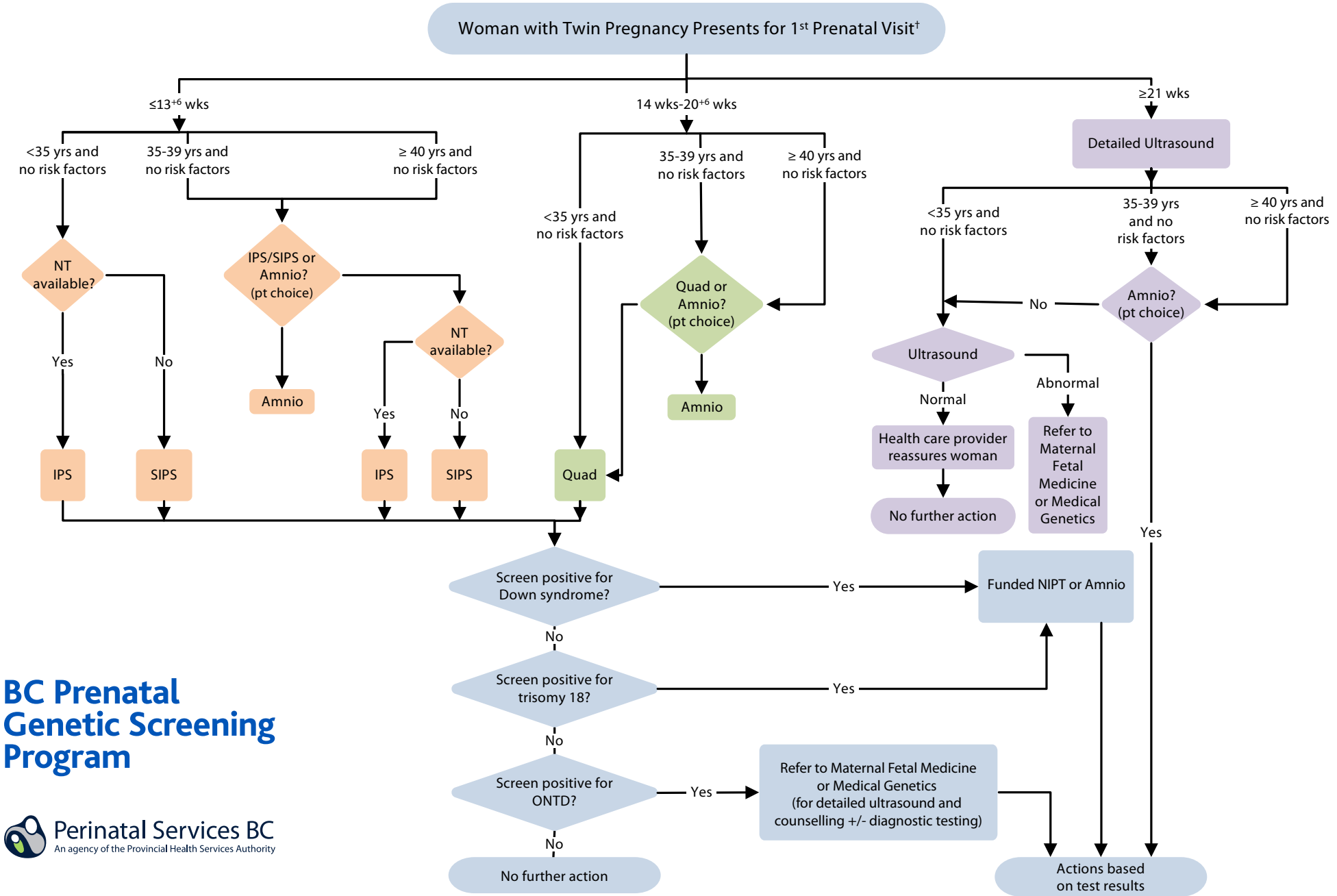
Algorithm 2

Prenatal Genetic Screening Recommendations for Women Who Present with *Twin* Pregnancies*



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* Screening in higher multiples will remain based on NT alone. If NT is not available and the woman is ≥35 years old, amniocentesis is an option.

† Excluding women with personal / family history that increases risk of fetus with Down syndrome, trisomy 18, or other chromosomal abnormality, who should be referred to Medical Genetics for counselling of their prenatal screening / diagnostic options.

See www.bcprenatalscreening.ca for more details on amniocentesis and NIPT options (both funded and self-pay).

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