

# 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 (e.g. amniocentesis).

The screening tests offered will vary according to the gestational age at the time of presentation and maternal age at the time of delivery.

**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	10 – 13 <sup>+6</sup> wks	10 <sup>+2</sup> – 11 <sup>+6</sup> wks
SIPS blood test #2	AFP uE3 hCG Inhibin-A	15 – 20 <sup>+6</sup> wks	15 <sup>+2</sup> – 17 wks
Integrated Prenatal Screen (IPS)	Same as SIPS (blood tests #1 & #2) with addition of NTultrasound <sup>1</sup>	See SIPS for blood tests 11 – 13 <sup>+6</sup> wks	See SIPS for blood tests 12 – 13 <sup>+3</sup> wks
Quad blood test	Same as SIPS blood test #2	15 – 20 <sup>+6</sup> wks	15 <sup>+2</sup> – 17 wks
MS-AFP	AFP	15 – 20 <sup>+6</sup> wks	15 <sup>+2</sup> – 17 wks
2nd trimester ultrasound	Detailed assessment of fetal anatomy and growth	18 weeks and onward	18 – 20 wks

<sup>1</sup> If an NT ultrasound is performed, a separate first trimester dating ultrasound is not necessary.

## Resources

- BC Prenatal Genetic Screening Program; guideline and related patient teaching resources; [www.bcprenatalscreening.ca](http://www.bcprenatalscreening.ca)
- Canadian Down Syndrome Society; T (800) 883-5608; E [info@cdss.ca](mailto:info@cdss.ca); [www.cdss.ca](http://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](http://www.dsrf.org)
- Genetics Home Reference (US National Library of Medicine); [www.ghr.nlm.nih.gov](http://www.ghr.nlm.nih.gov)
- Lower Mainland Down Syndrome Society (Canada); T (604) 591-2722; [www.lmdss.com](http://www.lmdss.com)
- Society of Obstetricians and Gynaecologists, Clinical Practice Guidelines (Canada); [www.sogc.org/guidelines](http://www.sogc.org/guidelines)
- Spina Bifida and Hydrocephalus Association of BC; T (604) 878-7000; E [info@sbhabc.org](mailto:info@sbhabc.org); [www.sbhabc.org](http://www.sbhabc.org)
- Support Organization For Trisomy 18, 13, and Related Disorders (SOFT; US); [www.trisomy.org](http://www.trisomy.org)

## Questions about prenatal screening in BC

Prenatal Biochemistry Laboratory: T (604) 875-2331 • (0800-1600 hrs, M-F)

## 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

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

CHARACTERISTICS OF WOMAN	GESTATIONAL AGE AT THE FIRST PRENATAL VISIT		
	≤ 13 <sup>+6</sup> WEEKS	14 – 20 <sup>+6</sup> 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 or trisomy 18	• 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 chromosomal abnormality other than Down syndrome or trisomy 18	• 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 <i>In vitro</i> fertilization & 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 date is confirmed) or **trisomy 18**, women should be counselled by their health care provider and offered further diagnostic testing (e.g. amniocentesis).

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

**Table 3: Indications, Screen Cut-Offs, and Performance of Screening Tests<sup>1</sup>**

		SERUM INTEGRATED PRENATAL SCREEN (SIPS)	INTEGRATED PRENATAL SCREEN (IPS)	QUAD SCREEN (QUAD)
<b>WHO IS ELIGIBLE?</b>		All women who present for their first prenatal visit at $\leq 13^{+6}$ wks	Women who present for their first prenatal visit at $\leq 13^{+6}$ wks gestation and who: <ul style="list-style-type: none"> <li>• Are <math>\geq 35</math> years or older at EDD;</li> <li>• Have a personal/family history that increases their risk of having a fetus with Down syndrome or trisomy 18;</li> <li>• Are HIV positive;</li> <li>• Are pregnant with twins; and</li> <li>• Are pregnant following IVF and ICSI</li> </ul>	All women who present for their first prenatal visit between 14 and $20^{+6}$ wks gestation
DOWN SYNDROME	Screen cut-off	1:300	1:200	1:385
	Detection rate <sup>2</sup>	<35 yrs: 79% 35 – 39 yrs: 92% $\geq 40$ yrs: 97%	<35 yrs: 84% 35 – 39 yrs: 92% $\geq 40$ yrs: 96%	<35 yrs: 76% 35 – 39 yrs: 92% $\geq 40$ yrs: 97%
	Chance result will be screen positive (includes true positives and false positives)	<35 yrs: 3.7% 35 – 39 yrs: 10.6% $\geq 40$ yrs: 25.3%	<35 yrs: 1.7% 35 – 39 yrs: 5.6% $\geq 40$ yrs: 14.3%	<35 yrs: 6.2% 35 – 39 yrs: 18.1% $\geq 40$ yrs: 39.4%
	% of total screen positives that are false positives (screens are positive, but babies are unaffected)	<35 yrs: 97% 35 – 39 yrs: 95% $\geq 40$ yrs: 94%	<35 yrs: 94% 35 – 39 yrs: 94% $\geq 40$ yrs: 89%	<35 yrs: 98% 35 – 39 yrs: 97.5% $\geq 40$ yrs: 96%
TRISOMY 18	Screen cut-off	1:300	1:300	1:300
	Detection rate	90%	90%	60% – 70%
	Chance result will be screen positive (most of these will be false positives)	0.1%	0.1%	0.2%
	Chance a screen negative result is a false negative result	<0.1%	<0.1%	<0.1%
OPEN NEURAL TUBE DEFECT (ONTD)	Screen cut-off	AFP $\geq 2.5$ MoM	AFP $\geq 2.5$ MoM	AFP $\geq 2.5$ MoM
	Detection rate	70%	70%	70%
	Chance result will be screen positive (most of these will not have ONTD but are at increased risk for pre-eclampsia or other pregnancy related complications)	1–2%	1–2%	1–2%
	Chance a screen negative result is a false negative result	<0.1%	<0.1%	<0.1%

<sup>1</sup> Performance of screening tests applies to singleton pregnancies.

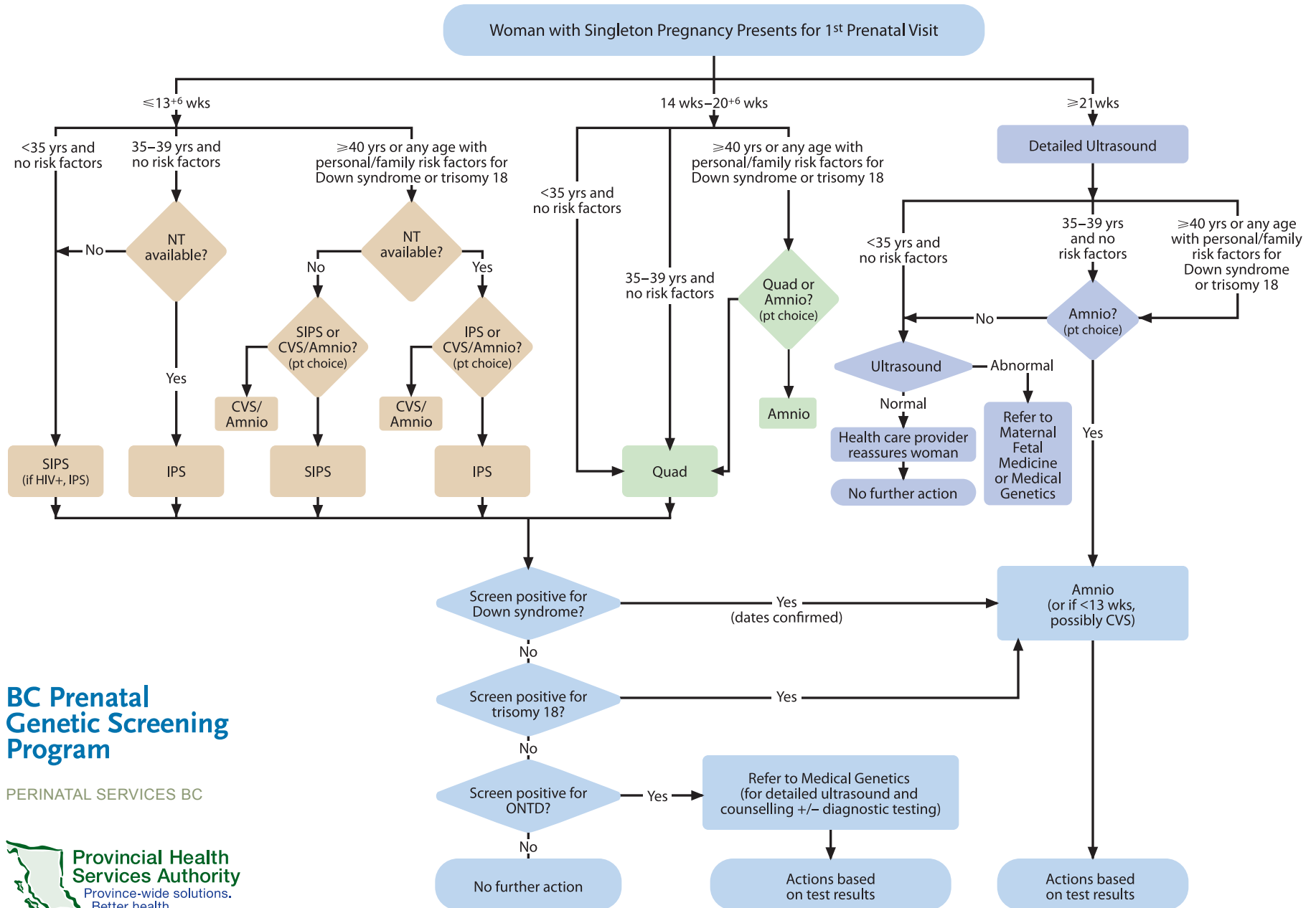
<sup>2</sup> Down syndrome detection rates for SIPS, IPS and Quad screens for women  $\geq 35$  years old assume ultrasound was used as dating method.

**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	$\geq 45$	$\geq 1$ in 24	$\geq 1$ in 19

# Algorithm 1

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



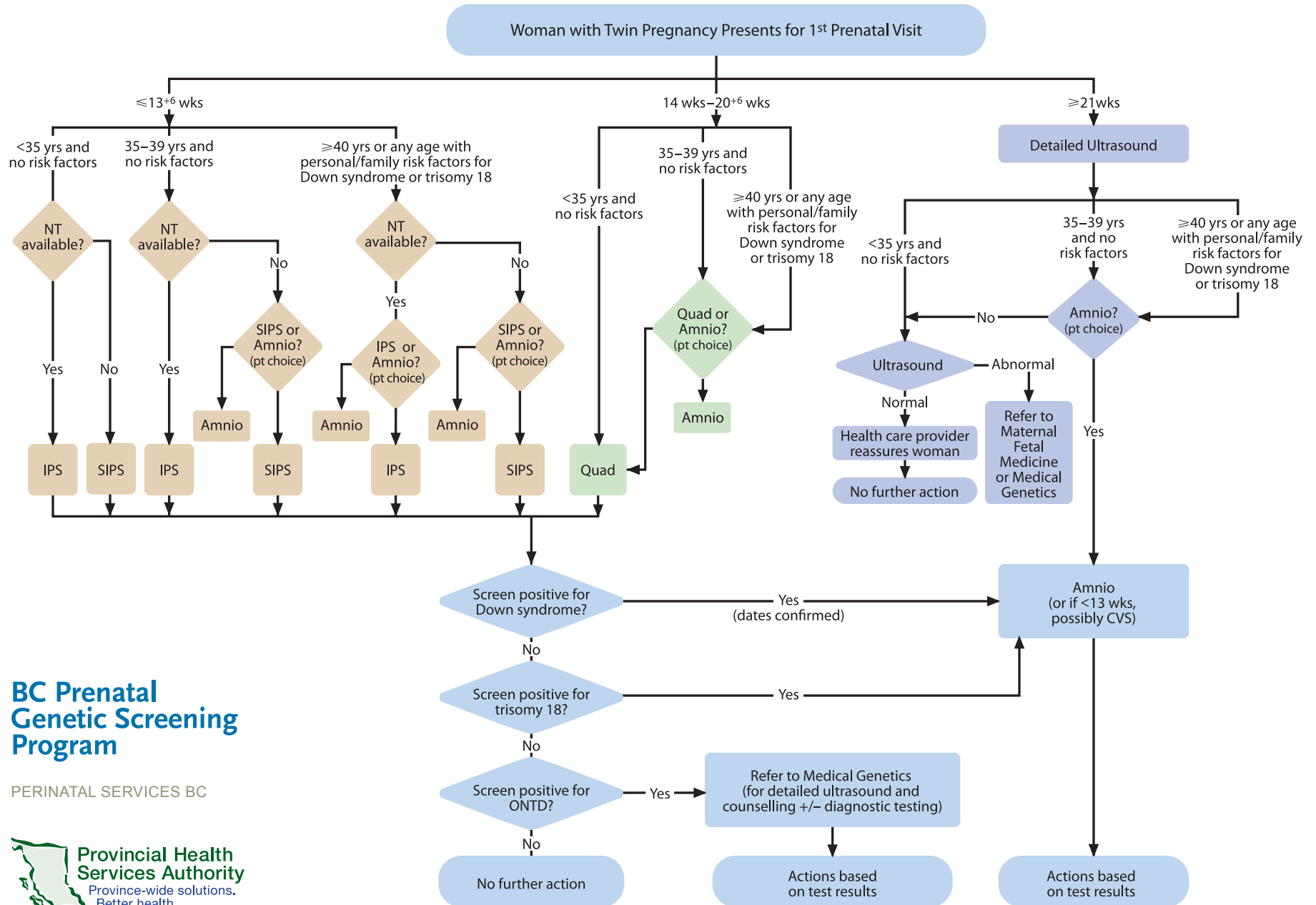
**BC Prenatal Genetic Screening Program**

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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  $\geq 35$  years old, amniocentesis is an option.