# 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

<table>
<thead>
<tr>
<th>Test Name</th>
<th>Markers / Measurements</th>
<th>Possible Timeframe</th>
<th>Best Timeframe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Integrated Prenatal Screen (SIPS) blood test #1</td>
<td>PAPP-A, AFP, hCG, Inhibin-A</td>
<td>9–13+6 wks</td>
<td>10–11+6 wks</td>
</tr>
<tr>
<td>SIPS blood test #2</td>
<td>AFP, hCG, Inhibin-A</td>
<td>15–20+6 wks</td>
<td>15+2–16 wks</td>
</tr>
<tr>
<td>Integrated Prenatal Screen (IPS)</td>
<td>Same as SIPS (blood test #1 &amp; #2) with addition of NT ultrasound</td>
<td>See SIPS for blood tests</td>
<td>See SIPS for blood tests</td>
</tr>
<tr>
<td>Quad blood screen</td>
<td>Same as SIPS blood test #2</td>
<td>15–20+6 wks</td>
<td>15+2–16 wks</td>
</tr>
<tr>
<td>2nd trimester ultrasound</td>
<td>Detailed assessment of fetal anatomy and growth</td>
<td>18 weeks and onward</td>
<td>18–20 wks</td>
</tr>
</tbody>
</table>

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](http://www.bcprenatalscreening.ca)
- Perinatal Services BC; T 604-877-2121; [www.perinatalservicesbc.ca](http://www.perinatalservicesbc.ca)
- Canadian Down Syndrome Society; T (800) 883-5608; E 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.dsrfr.org](http://www.dsrfr.org)
- 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; [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)

## 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

# BC Prenatal Genetic Screening Program

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

<table>
<thead>
<tr>
<th>Characteristics of woman</th>
<th>Gestational Age at the First Prenatal Visit</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤13±6 weeks</td>
</tr>
<tr>
<td>&lt; 35 years</td>
<td>• SIPS (if patient is HIV+ &amp; NT is available, IPS)</td>
</tr>
<tr>
<td>35–39 years</td>
<td>• IPS; or if NT not available, SIPS</td>
</tr>
<tr>
<td>40+ years</td>
<td>• IPS; or if NT not available, SIPS; or CVS or Amnio without prior screening</td>
</tr>
<tr>
<td>Personal / family history that increases risk of fetus with Down syndrome or trisomy 18</td>
<td>• IPS; or if NT not available, SIPS; or CVS or Amnio without prior screening</td>
</tr>
<tr>
<td>Personal / family history that increases risk of fetus with chromosomal abnormality other than Down syndrome or trisomy 18</td>
<td>• CVS or Amnio without prior screening</td>
</tr>
<tr>
<td>Twin gestation</td>
<td>• IPS; or if NT not available, SIPS; or if ≥35, Amnio without prior screening</td>
</tr>
<tr>
<td>Pregnant following In vitro fertilization with intracytoplasmic sperm injection</td>
<td>• IPS; or if NT not available, SIPS; or CVS or Amnio without prior screening</td>
</tr>
</tbody>
</table>

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 further diagnostic testing. Self-pay **NIPT** is an option for any woman who qualifies for CVS/Amnio. See [www.bcprenatalscreening.ca](http://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.

January 2014
### Table 3: Eligibility, Screen Cut-Offs, and Performance of Screening Tests

<table>
<thead>
<tr>
<th></th>
<th>Serum Integrated Prenatal Screen (SIPS)</th>
<th>Integrated Prenatal Screen (IPS)</th>
<th>Quad Screen (QUAD)</th>
</tr>
</thead>
</table>
| 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  
  - Have a personal/family history that increases their risk of having a fetus with Down syndrome or trisomy 18  
  - Are HIV positive  
  - Are pregnant with twins  
  - Are pregnant following IVF with ICSI | All women who present for their first prenatal visit between 14 and 20+6 wks gestation |

#### Down Syndrome

<table>
<thead>
<tr>
<th>Screen cut-off</th>
<th>1:300</th>
<th>1:200</th>
<th>1:385</th>
</tr>
</thead>
</table>
| Detection rate | <35 yrs: 70%  
  35–39 yrs: 92%  
  ≥ 40 yrs: 97% | <35 yrs: 84%  
  35–39 yrs: 92%  
  ≥ 40 yrs: 96% | <35 yrs: 76%  
  35–39 yrs: 92%  
  ≥ 40 yrs: 97% |
| Chance result will be screen positive (includes true positives and false positives) | <35 yrs: 3.7%  
  35–39 yrs: 10.6%  
  ≥ 40 yrs: 25.3% | <35 yrs: 1.7%  
  35–39 yrs: 5.6%  
  ≥ 40 yrs: 14.3% | <35 yrs: 6.2%  
  35–39 yrs: 18.1%  
  ≥ 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%  
  ≥ 40 yrs: 94% | <35 yrs: 94%  
  35–39 yrs: 94%  
  ≥ 40 yrs: 97% |
| Chance a screen negative result is a false negative result | <0.1% | <0.1% | <0.1% |

#### Trisomy 18

<table>
<thead>
<tr>
<th>Screen cut-off</th>
<th>1:300</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detection rate</td>
<td>90%</td>
</tr>
<tr>
<td>Chance result will be screen positive (most of these will be false positives)</td>
<td>0.1%</td>
</tr>
<tr>
<td>Chance a screen negative result is a false negative result</td>
<td>&lt;0.1%</td>
</tr>
</tbody>
</table>

#### Open Neural Tube Defect (ONTD)

<table>
<thead>
<tr>
<th>Screen cut-off</th>
<th>AFP ≥2.5 MoM</th>
<th>AFP ≥2.5 MoM</th>
<th>AFP ≥2.5 MoM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detection rate</td>
<td>70%</td>
<td>70%</td>
<td>70%</td>
</tr>
<tr>
<td>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)</td>
<td>0.5%</td>
<td>0.5%</td>
<td>0.5%</td>
</tr>
<tr>
<td>Chance a screen negative result is a false negative result</td>
<td>&lt;0.1%</td>
<td>&lt;0.1%</td>
<td>&lt;0.1%</td>
</tr>
</tbody>
</table>

1. Performance of screening tests applies to singleton pregnancies.
2. Down syndrome detection rates for SIPS, IPS and Quad screens for women ≥ 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

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

Source: Hecht CA and Hook EB. 1996
Algorithm 1

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

Woman with Singleton Pregnancy Presents for 1st Prenatal Visit

- ≤13+ wks
  - <35 yrs and no risk factors
    - NT available?
      - Yes: SIPS (if HIV+, IPS)
      - No: IPS
  - 35-39 yrs and no risk factors
    - NT available?
      - Yes: SIPS or CVS/Amnio* (pt choice)
      - No: IPS
  - ≥40 yrs or any age with personal/family risk factors for Down syndrome or trisomy 18
    - NT available?
      - Yes: IPS or CVS/Amnio* (pt choice)
      - No: CVS/Amnio*

- 14 wks-20+ wks
  - ≥40 yrs or any age with personal/family risk factors for Down syndrome or trisomy 18
    - NT available?
      - Yes: Quad or Amnio* (pt choice)
      - No: −35 yrs and no risk factors
        - Yes: Amnio*
        - No: 35-39 yrs and no risk factors
          - No: Ultrasound
            - Normal: Health care provider reassures woman → No further action
            - Abnormal: Detailed Ultrasound
              - Amnio? * (pt choice)
                - Yes: Refer to Maternal Fetal Medicine or Medical Genetics → Normal: Health care provider reassures woman → No further action
                - No: Amnio* (or if <13 wks, Possibly CVS)

- ≥21 wks
  - 35-39 yrs and no risk factors
    - NT available?
      - Yes: Ultrasound
        - Normal: Health care provider reassures woman → No further action
        - Abnormal: Detailed Ultrasound
          - Amnio? * (pt choice)
            - Yes: Refer to Maternal Fetal Medicine or Medical Genetics → Normal: Health care provider reassures woman → No further action
            - No: Amnio* (or if <13 wks, Possibly CVS)

BC Prenatal Genetic Screening Program

Perinatal Services BC
An agency of the Provincial Health Services Authority

* women eligible for CVS or amniocentesis may be offered self-pay NIPT. See [www.bcprenatalscreening.ca](http://www.bcprenatalscreening.ca) for more details.

February 2014
Algorithm 2

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

- **Woman with Twin Pregnancy Presents for 1st Prenatal Visit**
  - ≤13+ wks
    - <35 yrs and no risk factors
      - NT available?
        - Yes: IPS
        - No: SIPS
    - 35-39 yrs and no risk factors
      - IPS/SIPS or Amnio?*
        - Yes: Amnio*
        - No: IPS/SIPS or Amnio?*
          - Yes: Amnio*
          - No: IPS/SIPS or Amnio?*
    - ≥40 yrs or any age with personal/family risk factors for Down syndrome or trisomy 18
      - NT available?
        - Yes: Quad or Amnio?*
        - No: Quad or Amnio?*
  - 14 wks-20+ wks
    - <35 yrs and no risk factors
      - NT available?
        - Yes: Quad or Amnio?*
        - No: Quad or Amnio?*
    - 35-39 yrs and no risk factors
      - NT available?
        - Yes: Quad or Amnio?*
        - No: Quad or Amnio?*
    - ≥40 yrs or any age with personal/family risk factors for Down syndrome or trisomy 18
      - NT available?
        - Yes: Quad or Amnio?*
        - No: Quad or Amnio?*
  - ≥21 wks
    - Detailed Ultrasound
      - Ultrasound
        - Normal
          - Yes: Amnio*
        - Abnormal
          - Refer to Maternal Fetal Medicine or Medical Genetics
    - <35 yrs and no risk factors
      - Amnio?*
        - Yes: Amnio*
        - No: No further action
    - 35-39 yrs and no risk factors
      - Amnio?*
        - Yes: Amnio*
        - No: No further action
    - ≥40 yrs or any age with personal/family risk factors for Down syndrome or trisomy 18
      - Amnio?*
        - Yes: Amnio*
        - No: No further action

Screen positive for Down syndrome?
  - Yes
    - Amnio*
  - No: Screen positive for trisomy 18?
    - Yes
      - Refer to Maternal Fetal Medicine or Medical Genetics (for detailed ultrasound and counselling +/- diagnostic testing)
    - No: No further action

* women eligible for amniocentesis may be offered self-pay NIPT. See www.bcprenatalscreening.ca for more details.
** 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.