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## Disparities in uptake of Prenatal Screening in Canada: A population-based cohort study

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**Running Title:** Unequal uptake of PNS in Ontario, Canada

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## ABSTRACT

**Background:** It is recommended that all pregnant women be offered prenatal screening (PNS) for Down syndrome and open neural tube defects. However, emerging private-pay prenatal tests may compromise access. Screening rates and associated maternal, health care provider and regional characteristics warrant consideration in order to optimize the offer of this component of prenatal care.

**Methods:** A population-based retrospective cohort study was conducted in Ontario, Canada with pregnant women  $\geq 16$  weeks gestation in 2007-2009. We ascertained PNS rates using linked health administrative and PNS datasets, and examined maternal, provider, and regional characteristics associated with screening uptake. Relative rates were estimated.

**Results:** Of 264,737 pregnant women, 62% received screening. A greater proportion of women initiated screening in the first rather than second trimester (50.0% vs. 12.2%). Screening rates were lower among rural compared to urban women; adjusted relative rate (aRR) =0.64 (95% confidence intervals [CI] 0.63-0.66). Compared with women receiving first trimester care from obstetricians, those receiving family physician or midwifery care were less likely to screen (aRR=0.91; 95% CI 0.90-0.92; aRR=0.40; 95% CI 0.38-0.43, respectively). Women in lower income neighbourhoods were slightly less likely to screen (aRR=0.95; 95% CI 0.94-0.96, lowest versus highest quintile), but immigrants were more likely to screen than non-immigrants (aRR=1.15; 95% CI 1.15-1.16).

**Interpretation:** There are significant regional, provider and maternal differences in PNS use.

Access discrepancies will intensify with private-pay non-invasive prenatal testing; policy efforts to reduce barriers to PNS and optimize its offer are warranted.

**Key words:** Prenatal Screening, access to health services, population-based

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## INTRODUCTION

The Society of Obstetrics and Gynecology of Canada recommends that all pregnant women be offered a range of prenatal screening (PNS) tests to identify pregnancies at risk for specific chromosome abnormalities and open neural tube defects [1]. Most women will gain reassurance in the first or early second trimester that their fetus is unlikely to be affected by a specific disorder; those identified to be at high risk will offered diagnostic testing to guide further counselling and decision-making about pregnancy course and necessary care at delivery.

Professional guidelines do not specify one particular screening protocol because local infrastructure, timing of prenatal care, and value-based preferences vary, but they do specify that a high performing test must be universally available to women, regardless of ability to pay [1-4].

Screening practices and performance parameters differ across jurisdiction [5-8] (Table 1) and are shifting quickly. Most prominently, non-invasive prenatal testing (NIPT) for chromosome abnormalities (i.e. using maternal serum as a source of fetal DNA) is becoming commonplace, reducing the demand for risk-bearing invasive prenatal diagnosis [9-11]. Particularly in jurisdictions where this remains available only through private pay [12-14], attention to access barriers is important. Literature to date suggests that despite international policies recommending universal offer of PNS, uptake varies by maternal preferences [15-20], provider practice patterns [21-25], and maternal socio-demographic characteristics [26-32].

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3 In light of the shifting and increasingly market-driven landscape of PNS in Canada [33], our  
4 objectives were to describe screening rates for publically insured screening tests across  
5 healthcare regions in Ontario (population 13 million) and to determine whether there are  
6 regional, provider, or maternal characteristics associated with screening uptake that warrant  
7 consideration as policy efforts mobilize to optimize the availability of emerging technology.  
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## 17 **MATERIALS AND METHODS**

### 18 **Study design**

19  
20 We conducted a population-based retrospective cohort study on pregnancies > 16 weeks  
21 gestation and an estimated conception date between December 1 2007 and November 30 2009.  
22  
23 We chose 16 weeks gestation since most women should be offered PNS by this point in their  
24 pregnancy. The study used multiple linked health and demographic datasets from Ontario,  
25 Canada. Ontario provides universal health care insurance that includes access to all routine  
26 pregnancy care services for all legal residents.  
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### 40 **Databases**

41 Regional PNS laboratories routinely upload screening results into a centralized database, now the  
42 Better Outcomes Registry and Network (BORN Ontario). Using encoded health card numbers,  
43 we linked the PNS data to health administrative datasets housed at the Institute for Clinical  
44 Evaluative Sciences (ICES; linkage rate = 94%). Databases included the Discharge Abstract  
45 Database (DAD), the Same-Day Surgery (SDS) database, and the National Ambulatory Care  
46 Reporting System (NACRS) administered by the Canadian Institute for Health Information  
47 (CIHI). These contain demographic and clinical information from all Ontario-based acute-care  
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3 facilities, day surgery clinics, and emergency departments, respectively [34]. Other databases  
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5 included the Ontario Health Insurance Plan (OHIP) fee-for-service claims file, which provides  
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7 diagnostic and service provision information for approximately 94% of Ontario physicians; the  
8  
9 Ontario Registered Persons Database (RPDB), which includes demographic information for all  
10  
11 residents eligible to receive health care in Ontario; the ICES physician database (IPDB), which  
12  
13 records physician demographics and specialties; and the Citizenship and Immigration Canada  
14  
15 (CIC) file for immigrants landed in Ontario since 1985. Research Ethics Boards at Sunnybrook  
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17 Hospital in Toronto and the Children's Hospital of Eastern Ontario in Ottawa, Canada approved  
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19 this study.  
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### 27 **Study cohort**

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29 Live and stillbirths were identified using hospitalization discharges; gestational age at delivery  
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31 was used to estimate conception date [35]. Deliveries with an indeterminate gestational age were  
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33 excluded. Spontaneous and therapeutic abortions were determined using the DAD, SDS,  
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35 NACRS, and OHIP. Gestational age at abortion was used to estimate conception date and to  
36  
37 exclude aborted pregnancies with a gestation  $\leq 16$  weeks. We included aborted pregnancies  
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39 where gestational age was not recorded if the woman had an OHIP service code denoting care or  
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41 diagnostic imaging  $> 16$  weeks gestation. Aborted pregnancies with no gestational age recorded  
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43 and no OHIP records denoting care  $> 16$  weeks gestation were excluded. We considered one  
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45 pregnancy per woman during the study period, prioritizing those that reached delivery and then  
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47 those that occurred earliest within the study period.  
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### 52 **Outcome measure: uptake of PNS**

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Five regional laboratories support PNS in Ontario. For all pregnancies in our cohort, we used the PNS dataset to determine receipt and modality of PNS (Table 1). Women receiving PNS that did not conform to routine modalities were classified as ‘Other.’

### **Predictors of screening**

We categorized maternal age at delivery/abortion ( $\leq 20$  years; 21-34 years;  $\geq 35$  years) as this is a predictor of screening [28]. We linked all women to previous birth hospitalizations to determine maternal age at the time of first childbirth ( $\leq 20$  years; 21-34 years;  $\geq 35$  years), a strong indicator of social risk [36]. We enumerated parity by all previous deliveries (0, 1, 2,  $\geq 3$ ) and identified those that were stillbirths. We identified women with a spontaneous or therapeutic abortion in the past 5 years using DAD, SDS, NACRS, and OHIP records [37]. A unique maternal-newborn matching number on the mother’s delivery record and on the infant’s hospital birth record enabled linkage [35, 38] to identify those with a prior delivery of a child with a congenital malformation diagnosed in hospital within one year of birth.

Postal code of residence at conception was used to link to 2006 Census data to describe neighborhood income quintiles, a proxy for socioeconomic status [39, 40]. Each woman was assigned a Rurality Index of Ontario (RIO) score specific to the year 2008, categorized as major urban (score of 0-9), non-major urban (score of 10-39) and rural (score  $\geq 40$ ) [41]. The CIC dataset determined immigration status; categorized as Canadian resident, Immigrant landed  $\geq 5$  years ago, Immigrant landed  $< 5$  years ago, and refugee status.

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3 We used all OHIP records 14 weeks following estimated conception date to identify the first  
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5 trimester care provider for each woman in a hierarchical fashion. Women for whom there were  
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7 prenatal care visit billings were assigned to the physician providing the majority of those services  
8  
9 (family physician – FP or obstetrician - OB). The remaining women were assigned to the FP  
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11 providing the majority of other primary care services during the first trimester. Women with  
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13 outpatient billings to other physicians were assigned as “other”, and women with no billings  
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15 were assigned to midwifery care (if there were midwifery-specific OHIP records during the  
16  
17 pregnancy) or to no care.  
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### 22 23 24 **Statistical analysis**

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26 Since the outcome – being screened - was common (>60%) in our cohort, we used log-binomial  
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28 regression to examine the associations between factors of interest and receipt of screening [42].  
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30 We tested correlations among variables prior to selecting variables to enter into the multivariate  
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32 model. Statistical analyses were conducted using SAS 9.2 (SAS Institute INC., Cary, North  
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34 Carolina). All tests were two-tailed;  $p < 0.05$  was used as the level of statistical significance.  
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### 41 **RESULTS**

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43 We identified 264,737 pregnancies >16 weeks gestation during the study period. Overall, 62% of  
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45 women in the cohort received PNS during their pregnancy, but uptake varied considerably by  
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47 region (80% had screening in central Toronto, <40% had screening in southwest and northern  
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49 regions). Overall, approximately 50% of pregnant women initiated screening in the first trimester  
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51 (i.e. integrated PNS or first trimester combined screening) and 12% initiated screening in the  
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53 second trimester (serum integrated screening or the 4 marker QUAD test; [Figure 1](#)). While  
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3 screening initiated in the first trimester was more common across all regions, reaching 58-66% in  
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5 central, urban regions (regions 5-8), the difference in the proportion of women who initiated  
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7 screening in the first compared to second trimester was marginal in four - of the more remote -  
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9 regions (regions 1, 10, 13, 14; [Figure 1](#)).  
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15 First or second trimester screening varied by maternal socio-demographic, regional, and provider  
16 characteristics. More specifically, 80-84% of women over 21 years at delivery versus only 63%  
17 of women  $\leq 20$  were screened in the first trimester ( $p < 0.001$ ). Almost 83% of recent refugee  
18 immigrants versus 65% of less recent refugee immigrants pursued screening in the first trimester  
19 ( $p < 0.001$ ). As income quintile increased, so did the proportion of women pursuing first trimester  
20 screening (72% and 87% from lowest to highest income quintile;  $p < 0.001$ ), with a greater  
21 proportion of first trimester screening in urban versus rural women (82% vs 64%, respectively;  
22  $p < 0.001$ ). Rates of screening were lower in women who received FP or midwifery care versus  
23 OB care (57-69% vs 83%;  $p < 0.001$ ; Table 2). Median overall screening rates – at the provider  
24 practice level - were higher for OBs (median 75%; IQR 52%-90%) compared with FPs (median  
25 59%; IQR 33%-81%).  
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43 After adjustment for all predictors, rurality was a major predictor of overall screening rates;  
44 women from rural (Relative Rate [aRR] 0.67; 95% Confidence Interval [95% CI] 0.66-0.68) and  
45 non-major urban areas (aRR 0.76; 95% CI 0.75-0.76) were less likely to be screened than women  
46 from major urban areas. Prenatal care provider type was also associated with receipt of  
47 screening. Compared with women receiving first trimester care from an OB, those receiving FP  
48 care were slightly less likely to receive screening (aRR 0.91; 95% CI 0.90-0.92) and those  
49 receiving care that was not billed as specifically prenatal (by FPs or other physicians) or those  
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3 receiving care from a midwife were even less likely to receive screening [(aRR 0.72; 95% CI  
4 0.71-0.73); (aRR 0.65; 95% CI 0.64-0.67); (aRR 0.40; 95% CI 0.38-0.43), respectively] (Table  
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12 Other factors associated with lower screening rates were younger maternal age at  
13 delivery/abortion (aRR 0.85; 95% CI 0.84-0.86) for mothers  $\leq 20$  years versus mothers  $\geq 35$   
14 years) and multi-parity (aRR 0.76; 95% CI 0.75-0.78 for mothers with parity  $\geq 3$  versus  
15 nulliparous mothers). Immigrants, regardless of landing date or refugee status, were more likely  
16 to receive screening than non-immigrants (aRR 1.15; 95% CI 1.15-1.16). Women living in areas  
17 with lower income were less likely to receive screening (aRR 0.95; 95% CI 0.94-0.96 for lowest  
18 versus highest quintile), although this association was modest (Table 3).  
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## 32 INTERPRETATION

33  
34 This large, population-based study indicates that while uptake of first trimester screening is  
35 higher than second trimester screening, there are significant differences in use of PNS among  
36 pregnant women in Ontario. Uptake varies by region and relatedly, by urban/rural location.  
37  
38 Receipt of PNS is higher in those cared for by obstetricians and higher – although to a lesser  
39 extent - in women with fewer social risks. These differences exist in the context of high first  
40 trimester prenatal visit rates and a universal health insurance system.  
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50 The association between uptake and living in remote areas is consistent with population-based  
51 studies in other jurisdictions [28, 31, 32], and with surveys that report reduced screening offer  
52 among rural providers [21-23, 25]. In a study of prenatal care provider practices, reasons  
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3 associated with low rates of screening offer include maternal age <35, lack of relevant family  
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5 history, or lack of patient request [21-23]. Low antenatal care volume (i.e. <50 pregnant  
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7 women/year) was also associated with low screening uptake [21]. A similar study found that  
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9 52.2% of FPs in Newfoundland routinely offered PNS to all pregnant women and identified the  
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11 same reasons for non-offer [25]. These studies also identified providers' generalized concerns  
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13 about false positive results, limited availability of abortion/supportive services for affected  
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15 pregnancies, and the value-laden nature of screening for disabilities as barriers to screening [21-  
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17 23, 25]. Our *population-level* finding that PNS varies by prenatal care provider type is novel.  
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19 The aforementioned studies did not identify provider group differences in attitudes related to  
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21 PNS offer. Since 47% of pregnant women in Ontario receive at least some prenatal care from  
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23 FPs [34], further attention to the practices of different provider types is warranted.  
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32 The association of maternal socio-demographic characteristics, age and income related barriers  
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34 with lower screening has been reported in other jurisdictions, but with stronger effects than those  
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36 identified herein [28-30, 32]. While predictors may differ across jurisdictions, age and income  
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38 may have revealed stronger effects elsewhere because provider and regional effects were  
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40 untested. While multi-parity is often associated with older age and greater risk for aneuploidy,  
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42 we found reduced screening uptake among multiparous women. This could reflect lower  
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44 perceived risk or greater comfort with the notion of an affected child [15], or could reflect a  
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46 provider assumption that those who declined screening once, may decline it in subsequent  
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48 pregnancies. Reassuringly, immigrant status was not identified as a barrier to screening, unlike  
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50 studies of other screening tests (e.g. PAP smears) [43]. Finally, the first-trimester initiated  
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52 screening tests were more common across all regions. As efforts shift towards non-invasive  
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3 testing strategies and first trimester pregnancy health assessments [44], high rates of first  
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5 trimester-initiated tests suggest that Ontario is well positioned to move towards a first trimester  
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7 based screening paradigm [33].  
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### 10 11 12 **Strengths and Limitations**

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15 This study represents the first Canadian population-level analysis of PNS uptake and comes at a  
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17 time when specific attention to access challenges is of utmost importance. It is limited in its  
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19 ascertainment of screening uptake in that it does not reflect screening *offer*; it is the offer of  
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21 screening that is universally recommended but current data infrastructure precludes this analysis.  
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23 Other limitations include (i) potential over-estimate of first trimester screening rates since some  
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25 results coded as first trimester screening may reflect intended but incomplete integrated PNS, (ii)  
26  
27 our inability to capture uptake of NIPT given its recent entry into the screening environment in  
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29 Ontario, (iii) our exclusion of provider care not captured in OHIP billing data (e.g. salaried  
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31 physicians at community health centres), and (iv) our incomplete capture of midwifery care. In  
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33 addition, a small proportion of women appeared to receive screening but no prenatal care,  
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35 perhaps underestimating prenatal care provided. Finally, by only linking 94% of the screening  
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37 records to ICES data, we may have slightly underestimated screening rates, but there is no  
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39 evidence to suggest that linkage rate would vary by any of the characteristics evaluated.  
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### 48 **Conclusion and implications for practice, policy, and future research**

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50 These findings highlight existing vulnerabilities in the PNS system in Ontario, Canada and have  
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52 important implications for the delivery and evaluation of evolving PNS services. As PNS  
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54 technologies advance and services extend beyond the detection of aneuploidies and open neural  
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3 tube defects to more common adverse pregnancy and/or developmental outcomes [42], attending  
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5 to access in an increasingly strained fiscal environment is challenging but important. As a  
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7 complex intervention, ensuring access requires optimizing education and preference-sensitive  
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9 decision-making among pregnant women and prenatal care providers as well as measuring *offer*.  
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11 A whole systems approach to screening - one that engages all components of a screening system  
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13 in a comprehensive and evaluative process [45] may be well-suited to optimizing access and  
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15 maximizing the overall quality of this service. Specific attention through outreach and education  
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17 is owed to women residing in remote areas and women who receive early prenatal care from  
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19 non-obstetricians. While these findings are specific to the Ontario context, national research and  
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21 policy attention to PNS infrastructure is needed as this recommended service is inconsistently  
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23 funded/available across jurisdictions [46]. The expanding presence of market-driven pressures  
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25 from US-based vendors offering non-invasive prenatal testing for private pay can only fuel  
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27 further access challenges, warranting a unified and forward-thinking response from the prenatal  
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29 care community.  
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39 ***Contribution to authorship:***

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41 All authors meet authorship criteria. All authors contributed substantially to conception and  
42  
43 design, acquisition of data, analysis and interpretation of data. RH, MC, and AG drafted the  
44  
45 article and revised it critically for important intellectual content. XM, TH and MW revised it  
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47 critically for important intellectual content and all authors gave final approval of the version to  
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49 be published.  
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54 ***Details of ethics approval:***  
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Ethics approval for this study was obtained from Research Ethics Boards at Sunnybrook Hospital Sciences Centre in Toronto, Canada, approved Nov 11, 2011, reference 2012 0900 283 000 and the Children's Hospital of Eastern Ontario in Ottawa, Canada, approved June 17, 2013, reference 11/175X.

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**Table 1: Publically funded PNS tests in Ontario\***

Screening Modality	Timing	Markers analyzed	Detection Rate/ False Positive Rate <sup>6</sup>
<b>First Trimester combined Screening (FTS)</b>	Week 11-13	NT, PAPP-A, <i>fbhCG</i>	83.9%/4.0%
<b>Integrated PNS (IPS)</b>	1 <sup>st</sup> phase Week 11-13	NT, PAPP-A	88.4%/3.3%
	2 <sup>nd</sup> phase <sup>^</sup> Week 15-20	AFP, hCG, uE3	
<b>Serum Integrated PNS (SIPS)</b>	1 <sup>st</sup> phase Week 11-13	PAPP-A	FPR=3.3%**
	2 <sup>nd</sup> phase <sup>^</sup> Week 15-20	AFP, hCG, uE3, DIA	
<b>Four-marker second trimester serum screening (QUAD)</b>	Week 15-20	AFP, hCG, uE3, DIA	82.5%/5.6%***

AFP = Alpha-Fetoprotein; DIA = Dimeric Inhibin-A; *fbhCG* = free-beta subunit of human Chorionic Gonadotropin; hCG = human Chorionic Gonadotropin; NT = Nuchal Translucency; PAPP-A = Pregnancy-Associated Plasma Protein A; uE3 = unconjugated Estriol

<sup>^</sup>Result issued upon the completion of 2<sup>nd</sup> phase of the screening; if 2<sup>nd</sup> phase incomplete, reported as FTS.

\*Other available tests are AFP only for ONTD, NT only for multiple pregnancies, and PAPP-A plus second trimester QUAD test when NT is not available at the first trimester. Non-invasive prenatal testing is insured for high-risk women and available through private pay for women who do not meet high-risk criteria.

\*\* Insufficient data to generate detection rate. This is an estimate for the FPR given the small volume of uptake on this particular screen test in Ontario.<sup>i</sup>

\*\*\*Unpublished data

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**Table 2 – Characteristics of study cohort by trimester screened**

<b>Characteristic</b>	<b>Total pregnancies (N)</b>	<b>Total screened pregnancies N (%)</b>	<b>Proportion screened in 1<sup>st</sup> trimester</b>	<b>Proportion screened in 2<sup>nd</sup> trimester</b>	<b>P value</b>
<b>TOTAL</b>	264,737	164,783(62.2%)	132,355	32,428	
<b>Maternal age at delivery/abortion</b>					
≤ 20 years	19,622	7894 (40.2%)	4,986 (63.2%)	2,908 (36.8%)	<0.001
21 to 34 years	197,976	122489 (61.9%)	98,308 (80.3%)	24,181 (19.7%)	
≥ 35 years	47,139	34400 (73.0%)	29,061 (84.5%)	5,339 (15.5%)	
<b>Maternal age at first delivery</b>					
≤ 20 years	38,411	16096 (41.9%)	10,786 (67.0%)	5,310 (33.0%)	<0.001
21 to 34 years	126,701	71172 (64.0%)	102,750 (81.1%)	23,951 (18.9%)	
≥ 35 years	28,453	21986 (77.3%)	18,819 (85.6%)	3,167 (14.4%)	
<b>Parity (previous deliveries)</b>					
0	134,061	86098 (64.2%)	69,353 (80.6%)	16,745 (19.4%)	<0.001
1	87,628	56134 (64.1%)	45,820 (81.6%)	10,314 (18.4%)	
2	30,525	17215 (56.4%)	13,396 (77.8%)	3,819 (22.2%)	
3 or more	12,523	5336 (42.6%)	3,786 (71.0%)	1,550 (29.0%)	
<b>Previous delivery of a stillborn child</b>	2,163	1436 (66.4%)	1,160 (80.8%)	276 (19.2%)	0.66
<b>Previous abortion in the past 5 years</b>	39,047	24504 (62.8%)	19,726 (80.5%)	4,778 (19.5%)	0.44
<b>Previous delivery of a child with a congenital anomaly</b>	9,229	5284 (57.3%)	4,124 (78.0%)	1,160 (22.0%)	<0.001
<b>Immigration status</b>					
Canadian resident	193,187	111734 (57.8%)	18,691 (77.9%)	5,303 (22.1%)	<0.001
Non-refugee immigrant – landed ≥ 5 years ago	31,308	23991 (76.6%)	17,082 (74.3%)	5,895 (25.7%)	
Non-refugee immigrant – landed < 5 years ago	31,274	22977 (73.5%)	2,758 (75.0%)	921 (25.0%)	
Refugee immigrant – landed ≥ 5 years ago	5,423	3679 (67.8%)	1,580 (65.9%)	819 (34.1%)	
Refugee immigrant – landed < 5 years ago	3,545	2399 (67.7%)	92,244 (82.6%)	19,490 (17.4%)	
<b>Neighbourhood income quintile</b>					
1 (lowest)	60,660	35653 (58.8%)	25,629 (71.9%)	10,024 (28.1%)	<0.001
2	53,750	32980 (61.4%)	25,485 (77.3%)	7,495 (22.7%)	
3	53,273	33367 (62.6%)	27,270 (81.7%)	6,097 (18.3%)	
4	53,604	34722 (64.8%)	29,687 (85.5%)	5,035 (14.5%)	
5 (highest)	41,928	27474 (65.5%)	23,912 (87.0%)	3,562 (13.0%)	
Missing	1,522	587 (38.6%)	372 (63.4%)	215 (36.6%)	
<b>Rurality index</b>					
Major urban (RIO score 0-9)	199,919	136297 (68.2%)	111,869 (82.1%)	24,428 (17.9%)	<0.001
Non-major urban (RIO score 10-39)	45,320	21222 (46.8%)	15,921 (75.0%)	5,301 (25.0%)	
Rural (RIO score 40+)	16,697	6457 (38.7%)	4,158 (64.4%)	2,299 (35.6%)	
Missing	2,801	807 (28.8%)	407 (50.4%)	400 (49.6%)	
<b>First trimester care provider</b>					
Prenatal OB physician care	84,553	64726 (76.6%)	63,251 (82.8%)	13,134 (17.2%)	<0.001
Prenatal GP/FP physician care	118,520	76385 (64.5%)	55,790 (86.2%)	8,936 (13.8%)	
Primary GP/FP physician care	36,684	18415 (50.2%)	10,460 (56.8%)	7,955 (43.2%)	
Other physician care	7,707	2997 (38.9%)	572 (83.6%)	112 (16.4%)	
Midwife only care	2,562	684 (26.7%)	2,063 (68.8%)	934 (31.2%)	
No care	14,711	1576 (10.7%)	219 (13.9%)	1,357 (86.1%)	

\*Row percentages are presented in this table\*\* Distribution of missing data across health regions not reported due to small cell sizes for some types of testing

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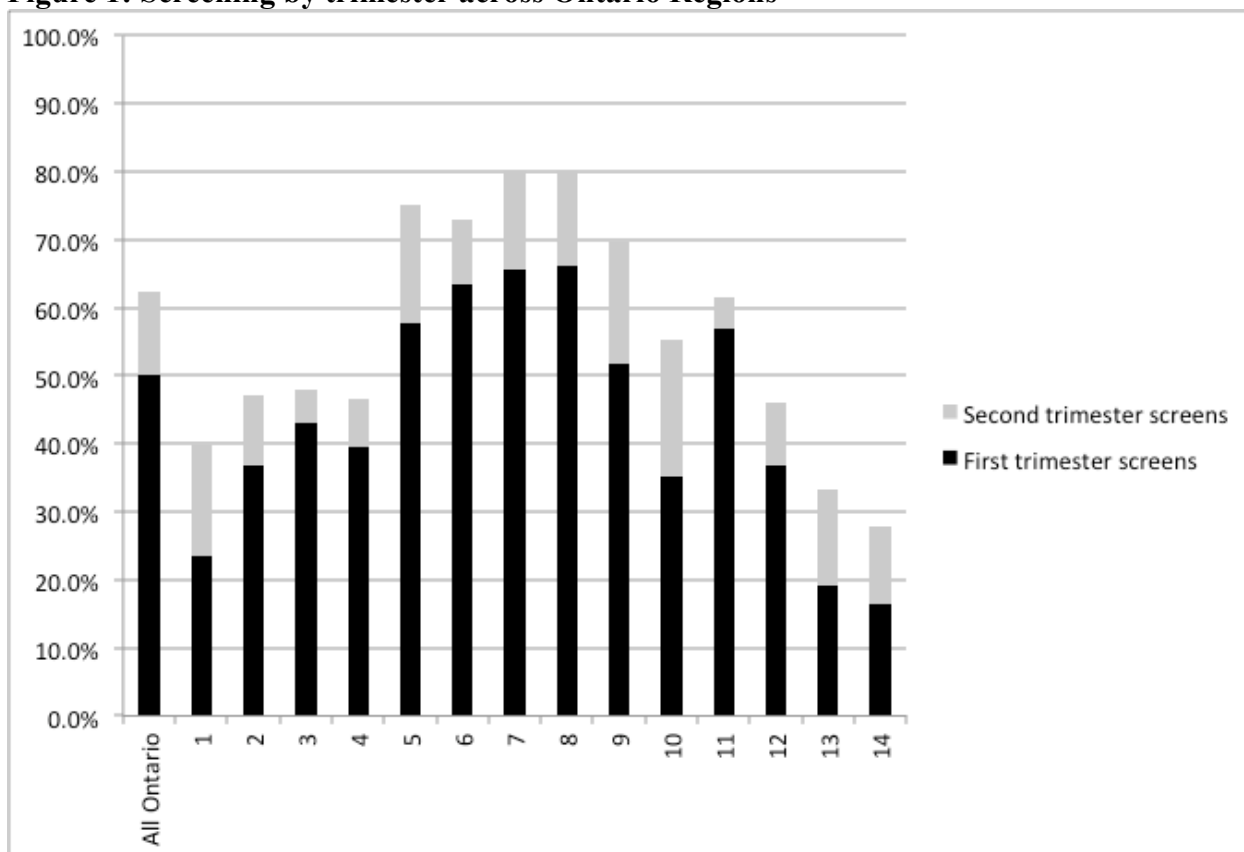
**Table 3 – PNS coverage and rate ratios by study characteristics**

<b>Characteristic</b>	<b>Total pregnancies (N)</b>	<b>Unadjusted RR (95% CI)</b>	<b>Adjusted RR (95% CI)</b>
<b>TOTAL</b>	<b>264,737</b>		
<b>Maternal age at delivery/abortion</b>			
≤ 20 years	19,622	0.55 (0.54-0.56)	0.81 (0.80-0.83)
21 to 34 years	197,976	0.85 (0.84-0.86)	0.94 (0.93-0.95)
≥ 35 years	47,139	1.00 (ref)	1.00 (ref)
<b>Maternal age at first delivery</b>			
≤ 20 years	38,411	0.54 (0.53-0.55)	0.85 (0.84-0.86)
21 to 34 years	126,701	0.83 (0.82-0.84)	1.00 (0.99-1.01)
≥ 35 years	28,453	1.00 (ref)	1.00 (ref)
<b>Parity (previous deliveries)</b>			
0	134,061	1.00 (ref)	1.00 (ref)
1	87,628	1.00 (0.99-1.01)	0.97 (0.96-0.97)
2	30,525	0.88 (0.87-0.89)	0.89 (0.89-0.90)
3 or more	12,523	0.66 (0.65-0.68)	0.76 (0.75-0.78)
<b>Previous delivery of a stillborn child</b>	2,163	1.07 (1.04-1.10)	1.04 (1.03-1.06)
<b>Previous abortion in the past 5 years</b>	39,047	1.01 (1.00-1.02)	1.00 (0.99-1.01)
<b>Previous delivery of a child with a congenital anomaly</b>	9,229	0.92 (0.90-0.93)	1.00 (0.99-1.02)
<b>Immigration status</b>			
Canadian resident	193,187	1.00 (ref)	1.00 (ref)
Non-refugee immigrant – landed ≥ 5 years ago	31,308	1.33 (1.32-1.34)	1.15 (1.15-1.16)
Non-refugee immigrant – landed < 5 years ago	31,274	1.27 (1.26-1.28)	1.15 (1.14-1.16)
Refugee immigrant – landed ≥ 5 years ago	5,423	1.17 (1.15-1.20)	1.08 (1.06-1.10)
Refugee immigrant – landed < 5 years ago	3,545	1.17 (1.14-1.20)	1.10 (1.08-1.12)
<b>Neighbourhood income quintile</b>			
1 (lowest)	60,660	0.90 (0.89-0.91)	0.95 (0.94-0.96)
2	53,750	0.94 (0.93-0.95)	0.97 (0.96-0.98)
3	53,273	0.96 (0.95-0.97)	0.97 (0.96-0.98)
4	53,604	0.99 (0.98-1.00)	0.98 (0.98-0.99)
5 (highest)	41,928	1.00 (ref)	1.00 (ref)
Missing	1,522	0.59 (0.55-0.63)	0.97 (0.93-1.01)
<b>Rurality index</b>			
Major urban (RIO score 0-9)	199,919	1.00 (ref)	1.00 (ref)
Non-major urban (RIO score 10-39)	45,320	0.69 (0.68-0.70)	0.76 (0.75-0.76)
Rural (RIO score 40+)	16,697	0.57 (0.56-0.58)	0.67 (0.66-0.68)
Missing	2,801	0.42 (0.40-0.45)	0.63 (0.60-0.67)
<b>First trimester health care provider</b>			
Prenatal OB physician care	84,553	1.00 (ref)	1.00 (ref)
Prenatal GP/FP physician care	118,520	0.84 (0.83-0.85)	0.91 (0.90-0.92)
Primary GP/FP physician care	36,684	0.66 (0.65-0.66)	0.72 (0.71-0.73)
Other physician care	7,707	0.51 (0.49-0.52)	0.65 (0.64-0.67)
Midwife only care	2,562	0.35 (0.33-0.37)	0.40 (0.38-0.43)
No care	14,711	0.14 (0.13-0.15)	0.15 (0.14-0.16)

CI = Confidence Interval; RIO = Rurality Index of Ontario; RR = Rate Ratio;  
 a - Row percentages are presented in this table for each characteristic



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**Figure 1: Screening by trimester across Ontario Regions**

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## References

1. Chitayat D, Langlois S, Wilson RD, et al. PNS for fetal aneuploidy in singleton pregnancies: CCMG-SOGC Clinical Practice Guideline. *J Obstet Gynaecol Can* July 2011;736-50.
2. Benn P, Borell A, Chiu R, Cuckle H, Dugoff L, Faas B, et al. Position statement from the aneuploidy screening committee on behalf of the board of the international society for prenatal diagnosis. *Prenatal Diagnosis* epub May 21 2013;622-629.
3. Wilson JM, Jungner YG. Principles and practice of mass screening for disease. *Boletín de la Oficina Sanitaria Panamericana* 1968;65:281–393.
4. Raffle A, Gray M. *Screening: Evidence and practice*. New York: Oxford University Press; 2009.
5. Tapon D. Prenatal testing for Down syndrome: comparison of screening practices in the UK and USA. *Journal of Genetic Counseling* 2010;19:112–30.
6. Boyd PA, Devigan C, Khoshnood B, Loane M, Garne E, Dolk H, et al. Survey of PNS policies in Europe for structural malformations and chromosome anomalies, and their impact on detection and termination rates for neural tube defects and Down's syndrome. *BJOG: International Journal of Obstetrics and Gynaecology* 2008;115:689–96.
7. Okun N, Summers AM, Hoffman B, Huang T, Winsor E, Chitayat D, et al. Prospective experience with integrated PNS and first trimester combined screening for trisomy 21 in a large Canadian urban center. *Prenatal Diagnosis* 2008;28:987-92.
8. Summers AM, Farrell SA, Huang T, Meier C, Wyatt PR. Maternal serum screening in Ontario using the triple marker test. *Journal of Medical Screening* 2003;10:107-11.
9. Lalanía S, Laua W. Non-invasive prenatal diagnosis – a new era. *University of British Columbia Medical Journal (UBCMJ)* 2013; 4:29-31.
10. Rose NC, Lagrave D, Hafen B, Jackson M. The impact of utilization of early aneuploidy screening on amniocenteses available for training in obstetrics and fetal medicine. *Prenatal Diagnosis* 2013 ;33:242-44.
11. Morgan S, Delbarre A, Ward P. Impact of introducing a national policy for prenatal Down syndrome screening on the diagnostic invasive procedure rate in England. *Ultrasound in Obstetrics and Gynecology* 2013;41:526-29.
12. Antenatal Results and Choices. Non-invasive prenatal testing for Down's syndrome (NIPT) [Internet]. London: Antenatal Results and Choices; 2014 [cited 2013 Sept 30].

- 1  
2  
3 Available from: <http://www.arc-uk.org/tests-explained/down-s-syndrome-screening/non-invasive-prenatal-testing-for-down-s-syndrome>.  
4  
5  
6
- 7 13. Morris S, Karlsen S, Chung N, Hill M, Chitty LS. Model-based analysis of costs and  
8 outcomes of non-invasive prenatal testing for Down's syndrome using cell free fetal  
9 DNA in the UK National Health Service. *PLoS One* 2014;9:e935-59.  
10
  - 11 14. Agarwal A, Sayres LC, Cho MK, Cook-Deegan R, Chandrasekharan S. Commercial  
12 landscape of non-invasive prenatal testing in the United States. *Prenatal Diagnosis*  
13 2013;33:521-31.  
14
  - 15 15. Carroll JC, Brown JB, Reid AJ, Pugh P. Women's experience of maternal serum  
16 screening. *Canadian Family Physician*. 2000;46:614-20.  
17
  - 18 16. Gidiri M, McFarlane J, Holding S, Lindow SW. Maternal serum screening for Down  
19 syndrome: Are women's perceptions changing? *BJOG: International Journal of*  
20 *Obstetrics and Gynaecology* 2007;114:458-61.  
21
  - 22 17. Dormandy E, Michie S, Hooper R, Marteau TM. Low uptake of PNS for Down syndrome  
23 in minority ethnic groups and socially deprived groups: a reflection of women's  
24 attitudes or a failure to facilitate informed choices? *International Journal of*  
25 *Epidemiology* 2005; 34:346-52.  
26
  - 27 18. Williams C, Sandhall J, Lewando-Hundt, Heyman B, Spencer K, Grellier R. Women as  
28 moral pioneers? Experiences of first trimester antenatal screening. *Social Science and*  
29 *Medicine* 2005;61:1983.  
30
  - 31 19. van den Berg M, Timmermans DRM, Kleinveld DH, van Eijk JT, Knol DL, van der Wal  
32 G, et al. Are counselors' attitudes influencing pregnant women's attitudes and  
33 decisions on PNS? *Prenatal Diagnosis* 2007;27:518-24.  
34
  - 35 20. Spencer K, Aitken D. Factors affecting women's preference for type of PNS test for  
36 chromosomal anomalies. *Ultrasound in Obstetrics and Gynecology* 2004;24:735-739.  
37
  - 38 21. Permaul-Woods JA, Carroll JC, Reid AJ, Woodward CA, Ryan G, Domb S, et al. Going  
39 the distance: the influence of practice location on the Ontario Maternal Serum  
40 Screening Program. *Canadian Medical Association Journal* 1999; 161:381-85.  
41
  - 42 22. Carroll JC, Reid AJ, Woodward CA, Permaul-Woods JA, Domb S, Ryan G, et al. Ontario  
43 Maternal Serum Screening Program: practices, knowledge and opinions of health care  
44 providers. *Canadian Medical Association Journal* 1997; 156: 775-84.  
45
  - 46 23. Dormandy E, Marteau TM. Uptake of a PNS test: the role of health care professionals'  
47 attitudes towards the test. *Prenatal Diagnosis* 2004;24:864-68.  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3 24. Cavanagh J, Matthews M. Maternal serum screening in Newfoundland and Labrador: Do  
4 attitude and knowledge affect physicians' practice? *Canadian Family Physician*  
5 2006; 52:1268-69.  
6
- 7  
8 25. Crane CS, Hutchens D, Bennett K, O'Grady T, Duff A, Macgregor D. Maternal serum  
9 screening: practice patterns of physicians in Newfoundland. *Journal of Obstetrics and*  
10 *Gynaecology Canada* 2003; 25:825-29.  
11
- 12  
13 26. Khoshnood B, Blondel B, De VC, Breart G. Socioeconomic barriers to informed decision  
14 making regarding maternal serum screening for down syndrome: results of the French  
15 National Perinatal Survey of 1998. *American Journal of Public Health* 2004; 94:484-  
16 91.  
17
- 18  
19 27. Khoshnood B, De Vigan C, Blondel B, Vodovar V, Casio E, Goffinet F. Long term trends  
20 for socio-economic differences in prenatal diagnosis of Down syndrome: diffusion of  
21 services or persistence of disparities? *BJOG: International Journal of Obstetrics and*  
22 *Gynaecology* 2008;115:1087-95.  
23
- 24  
25 28. Maxwell SJ, Brameld K, Bower C, Dickinson JE, Goldblatt L, Hadlow N, et al. Socio -  
26 demographic disparities in the uptake of PNS and diagnosis in western Australia.  
27 *Australian and New Zealand Journal of Obstetrics and Gynaecology* 2011; 51: 9-16  
28
- 29  
30 29. Rowe R, Garcia J, Davidson LL. Social and ethnic inequalities in the offer and uptake of  
31 PNS and diagnosis in the UK: a systematic review. *Public Health* 2004; 118:177-84.  
32
- 33  
34 30. Rowe R, Puddicombe D, Hockley C, Redshaw M. Offer and uptake of PNS for Down  
35 syndrome in women from different social and ethnic backgrounds. *Prenatal*  
36 *Diagnosis* 2008; 28:1245-50.  
37
- 38  
39 31. Muggli EE, Collins VR, Halliday JL. Mapping uptake of prenatal diagnosis for Down  
40 syndrome and other chromosome abnormalities across Victoria, Australia. *Australian*  
41 *and New Zealand Journal of Obstetrics and Gynaecology* 2006; 46:492-500.  
42
- 43  
44 32. O'Leary P, Breheny N, Reid G, Charles T, Emery J. Regional variations in PNS across  
45 Australia: Stepping towards a national policy framework. . *Australian and New*  
46 *Zealand Journal of Obstetrics and Gynaecology* 2006; 46:427-32.  
47
- 48  
49 33. Ontario PNS Advisory Subcommittee. PNS in Ontario: The Road Forward. Policy  
50 Report submitted to the Ontario Maternal Child Screening Committee, June 2013.  
51
- 52  
53 34. Chan B. Supply of physicians services in Ontario. *Hospital Quarterly* 1999-2000  
54 Winter;3:17.  
55
- 56  
57 35. Iron K, Zagorski BM, Sykora K, Manuel DG. Living and dying in Ontario: An  
58 opportunity for improved health information. ICES Investigative Report. Toronto:  
59 Institute for Clinical Evaluative Sciences; 2008.  
60

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2  
3  
4  
5  
6  
7  
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47  
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50  
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52  
53  
54  
55  
56  
57  
58  
59  
60
36. Jutte DP, Roos NP, Brownell MD, Briggs G, MacWilliam L, Roos LL. The ripples of adolescent motherhood: social, educational and medical outcomes for children of teen and prior teen mothers. *Academic Pediatrics* 2010;10:293-301.
37. Dunn S, Wise MR, Johnson LM, Anderson G, Ferris LE, Yeritsyan N, Croxford R, Fu L, Degani N, Bierman AS. Reproductive and Gynaecological Health. In: Bierman AS, editor. Project for an Ontario Women's Health Evidence-Based Report: Volume 2: Toronto; 2011.
38. Campitelli MA, Inoue M, Calzavara AJ, Kwong JC, Guttman A. Low rates of influenza immunization in young children under Ontario's universal influenza immunization program. *Pediatrics* 2012;129:e1421-30.
39. Wilkins R, Khan S. PCCF+ Version 5H User's Guide. Automated geographic coding based on the Statistics Canada Postal Code Conversion files, including postal codes through October 2010 (Statistics Canada, Catalogue 82F0086-XDB); 2010.
40. Finkelstein MM. Ecologic proxies for household income: how well do they work for the analysis of health and health care utilization? *Canadian Journal of Public Health* 2004; 95:90-4.
41. Kralj B. Measuring "rurality" for purposes of health care planning: An empirical measure for Ontario. Toronto: Ontario Medical Association; 2005.
42. McNutt LA, Wu C, Xue X, Hafner JP. Estimating the relative risk in cohort studies and clinical trials of common outcomes. *American Journal of Epidemiology* 2003;157: 940-43.
43. Lofters AK, Moineddin R, Hwana SW, Glazier RH. Low rates of cervical cancer screening among urban immigrants: a population-based study in Ontario, Canada. *Medical Care* 2010;48:611-18.
44. Society of Obstetricians and Gynaecologists of Canada Genetics Committee. Technical update: Obstetrical complications associated with abnormal maternal serum marker analytes. *Journal of Obstetrics and Gynecology* 2008; 918-32.
45. Hayeems RZ and Chakraborty P. A practical definition and key concepts of population-based screening. *BORN Bulletin* 2012; 3.
46. Morain S, Greene MF, Mello MM. A new era in non-invasive prenatal testing. *New England Journal of Medicine* 2013;1-4.
-