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Title: Prenatal diagnosis and socioeconomic status in the non-invasive prenatal testing era: a population-based study

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Conflicts of Interest

The authors have no conflicts to declare.

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Contribution to authorship

LH contributed to the intellectual planning and conception of the study, data analysis and interpretation, and wrote the manuscript. JB contributed to the intellectual planning of the study, performed the data analysis and critically reviewed the manuscript for intellectual content. AP and BH contributed to the data analysis and critically reviewed the manuscript for intellectual content. JH contributed to the intellectual planning and conception of the study, data analysis and interpretation, and critically reviewed the manuscript for intellectual content. All authors take responsibility for the integrity of this work and have given consent for publication of this final version.

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ABSTRACT

Background: Advances in technology can bring great benefits to human health, but their implementation may be influenced by socioeconomic factors, particularly in the field of prenatal screening for Down syndrome.

Aim: To analyze screening test indications for, and diagnostic yield of, prenatal diagnostic testing (PNDx) according to socioeconomic status.

Methods: Retrospective analysis of population-based data on PNDx and karyotype results for 2014-2015 in the Australian state of Victoria. Women having PNDx < 25

weeks due to combined first trimester screening (CFTS), second trimester serum screening (STSS), or noninvasive prenatal testing (NIPT) results were included. PNDx data were analysed by indication and maternal Index of Relative Socio-economic Advantage and Disadvantage (IRSAD), the latter determined by postcode.

Results: There were 145,206 births in 2014-15; 1906 women underwent PNDx for the indication of CFTS (70.1%), NIPT (17.8%) or STSS (12.0%). Covariates positively associated with NIPT-indicated PNDx, compared with CFTS-indicated testing, were residence in a region of socioeconomic advantage, metropolitan status, and maternal age. Women from the most advantaged regions had higher adjusted odds of NIPT-indicated testing compared with women from disadvantaged regions (aOR 5.72, 95% CI 2.95-11.09). The diagnostic yield of PNDx increased with socioeconomic region, from 14% in the lowest IRSAD quintile to 31.2% in the highest ($p < 0.0001$).

Conclusion: Population-based data reveal significant disparities in screening indications for PNDx and hence, in diagnostic yield, according to socioeconomic region. This finding may have ethical and policy implications for prenatal screening in Australia.

Introduction

Advances in technology can bring great benefits to human health, but their implementation may be influenced by socioeconomic factors, including in the field of prenatal screening for Down syndrome (trisomy 21).[1] Universal population-based screening for trisomy 21 has been an important part of maternity care for decades in Australia.[2] The two traditional prenatal screening tests, combined first trimester screening (CFTS) and second trimester serum screening (STSS), have false positive rates of up to 5.0% and 7.8% respectively.[3] These false positive results lead to a substantial number of women with normal fetuses being offered invasive prenatal diagnosis (PNDx) for confirmatory testing after a high risk result. Noninvasive prenatal testing (NIPT), a DNA sequencing-based method that analyses cell-free DNA in maternal plasma, became widely available in Australia in 2013. It is well recognized as the most effective screening tool for trisomy 21.[4,6] In contrast to CFTS and STSS, NIPT has a very low false positive rate (less than 0.1% for trisomy 21) and

its uptake has reduced the numbers of invasive prenatal diagnostic tests, without any apparent reduction in trisomy 21 detection.[6-8]

Screening practices and uptake of NIPT vary by country, according to medical resources, government or private health insurance support, and cultural attitudes to prenatal diagnosis.[9-11] A global survey of clinical implementation showed that the price of NIPT was limiting adoption and creating inequality of access in many countries.[12] Even in high income countries such as Australia, obstetric specialists have concerns about financial barriers to NIPT access.[13] Although a 2013 audit showed that Australian specialists offered NIPT to high risk women equally in private and public practice, over 90% of actual NIPT referrals actually took place in private practice in the first year of local availability (2013).[14]

International societies have emphasized that equity of access for all pregnant women is an essential component of the responsible introduction of NIPT into population-based screening programs.[15] In 2015, the Australian Atlas of Healthcare Variation was launched.[16] Using routinely available health data mapped by residence of patient, wide variations in rates of use of diagnostic tests and other health care interventions were observed. Clinical variation can identify problems with equity and appropriateness of care when these disparities are not due to underlying differences in patient needs or health preferences.[17] We aimed to apply this approach to analyse screening test indications for PNDx in the NIPT era. We hypothesized that women from socioeconomically advantaged and metropolitan areas would be more likely to have NIPT-indicated PNDx than socioeconomically disadvantaged or rural women.

Materials and Methods

This study analysed data on prenatal diagnosis in the Australian state of Victoria, which has approximately 73,000 births p.a. We obtained state-wide data on all women undergoing amniocentesis or chorionic villus sampling (CVS) prior to 25 weeks gestation from Jan 2014 to Dec 2015 from the Victorian Prenatal Diagnosis Database. This database has been described in detail elsewhere.[6] In brief, all four cytogenetic laboratories in the state contribute annual data on prenatal diagnostic testing, including maternal age and gestation at the time of testing, maternal postcode, type of diagnostic test, indication for test, karyotype result, and singleton or multiple

pregnancy. Amniocentesis and CVS samples were analysed either by G-banded karyotyping or chromosomal microarray, according to the clinical referral. Karyotype results were coded as a 'major abnormality' for all cases of aneuploidy, unbalanced rearrangements, polyploidy, level III mosaics, and pathogenic copy number variations (CNVs). 'Minor abnormalities' included confined placental mosaicism, uniparental disomy, balanced translocations, and variations of unknown or uncertain significance (VOUS). 'Diagnostic yield' was defined as the percentage of major abnormalities divided by the total number of tests.

Women were included in this analysis if their primary indication for PNDx was an increased risk result from CFTS, STSS or NIPT. At the time of the study, CFTS and STSS received a government insurance rebate and involved variable out-of-pocket costs for women, typically < AUD 200. NIPT was available from international or local providers, with an average cost of AUD 500-600.[12] There was no government or private health insurance rebate for NIPT. All components of PNDx are fully funded by the government for public patients if performed for approved indications, including the costs of analysis by chromosomal microarray. No major changes in funding structure occurred during the period of this study. Women undergoing PNDx for a primary indication of ultrasound abnormality, advanced maternal age, single gene testing or other primary indications were excluded. Selected data from 2014-15 have been previously reported within a larger study incorporating all indications from 2000-2015, and without analysis by socioeconomic status or geographical location as performed here.[18]

The postcode of residence for each woman was mapped to the corresponding local government area (LGA) and assigned the relevant Index of Relative Socio-economic Advantage and Disadvantage (IRSAD) allocated by the Australian Bureau of Statistics (ABS) from 2011 Census data. The IRSAD is a comprehensive metric of socioeconomic status, incorporating data on income, occupation, education, employment, and housing.[19] Women with a postcode outside the state of Victoria were excluded.

Data on livebirths from 20 weeks gestation by LGA over the study period were obtained from the ABS. These data underestimate the total births (including stillbirths

and terminations of pregnancy < 20 weeks) by < 1%,[20] and hence are considered an acceptable data source for births.

Statistical analysis was performed with STATA version 14 (StataCorp LLC, TX, USA). and PRISM 6 (Version 6.0h 2015, GraphPad Software Inc., CA, USA). We performed 2-tailed chi-squared tests for comparison of two proportions or trends, with a p value of < 0.05 being considered significant. Logistic regression was used to calculate adjusted odds ratios (aOR) of NIPT-indicated versus CFTS-indicated PNDx, taking into account IRSAD quintile, place of residence (metropolitan or rural), maternal age, and gestational age.

A data visualisation software program (Tableau 9.3, Tableau Software, Seattle, WA, USA) was used to create chloropleth LGA maps of IRSAD deciles and rates of prenatal testing by indication.

Ethics approvals were provided by the Royal Children's Hospital (Ref No. 3115A) and Monash Health HRECs (Ref. No. 12063B).

Results

Overall population characteristics

There were 145,206 births during the 24-month study period, 80.9% of which were born to women in metropolitan Victoria. The IRSAD scores for each LGA are shown in figure 1A. CFTS and STSS were accessed by 106,752 (73.5%) and 7440 (5.1%) of women respectively. The total number of women having NIPT was not available.

Of the 4003 women who underwent invasive PNDx prior to 25 weeks gestation in 2014-15 (2.8% of all births), 1906 (47.6 %) had a screening test result as the primary indication for testing and were included in the analysis. CFTS was the indication for testing in 1337 (70.1%), STSS in 229 (12.0%) and NIPT in 340 (17.8%). The overall PNDx rate was 1.3% and 3.1% for all women having FTS and STSS respectively. Of the 1906 women who were included, 88 (4.6%) had a secondary indication of ultrasound abnormality noted on their clinical referral, most commonly an enlarged nuchal translucency measurement. Twenty-four women (1.3%) were reported by the clinical referrer to have had both CFTS and high risk NIPT as their indication for

PNDx; these were analysed in the NIPT-indicated group. The exact proportion of women in our dataset using NIPT as a primary or second-tier screening test is unknown as we could not perform individual patient linkage. The geographical distribution of PNDx rates by screening test indication are shown in Figures 1B-D.

PNDx according to IRSAD quintile

The majority of women having PNDx were aged 35 years or more (60.2%). Compared with IRSAD quintile 1, IRSAD quintile 5 had significantly more women aged $\geq$ 35 years (67.2% vs 56.8%, $\chi^2 = 7.65$, $p = 0.006$). IRSAD 5 women also had a significantly higher percentage of PNDx for a screening test indication per 100 births, compared with IRSAD 1 (1.7% vs 1.2%, $\chi^2 = 23.17$, $p < 0.001$).

The percentage of PNDx tests performed for each screening test indication by IRSAD quintile is shown in Figure 2A. There was a significant increase in the percentage performed for NIPT with increasing socioeconomic advantage, from 5% in quintile 1 to 28% in quintile 5 (χ^2 trend = 60.61 $p < 0.0001$) and accordingly, a significant decrease in the percentage for FTS and STSS.

Univariate and multivariate analysis of NIPT-indicated versus CFTS-indicated testing

The results of the univariate and multivariate analysis of NIPT-indicated vs CFTS-indicated testing are shown in Table 1. In the unadjusted analysis, compared to women in the most disadvantaged regions (IRSAD quintile 1), women residing in quintile 5 regions were more than six times likely to have NIPT as their indication for invasive testing (odds ratio OR 6.77, 95% CI 3.59-12.78). There was also a positive relationship between NIPT-indicated testing and metropolitan residence, advanced maternal age and lower gestational age.

After adjusting for the above confounders (maternal age, gestational age and residential status), the association between IRSAD quintile and NIPT-indicated testing remained significant. The women in the most advantaged IRSAD quintile 5 regions were more than 5 times more likely to have NIPT-indicated testing than women from quintile 1 regions (aOR 5.72, 95% CI 2.95-11.09). Overall, an increasing likelihood for NIPT-indicated tests was evident with increasing IRSAD score. Another independent predictor of NIPT-indicated PNDx was gestation, with those at

gestational age 17-19 weeks being much less likely to be in the NIPT indication group than those at gestational age 10-13 weeks (aOR 0.48, 95%CI 0.29-0.79). The effect of maternal age and residential status on indication was attenuated following covariate adjustments.

Diagnostic yield

The percentage of tests that resulted in a confirmed diagnosis of a major chromosome abnormality for the total cohort was 25.2% (480/1906) (Table 2). The total diagnostic yields by screening test indication were 18.6% for CFTS, 3.9% for STS and 65.3% for NIPT. When analysed by IRSAD quintile, the diagnostic yields increased significantly with regions of socioeconomic-advantage, from 14.1% in the lowest IRSAD quintile to 31.2% in the highest quintile (χ^2 trend = 25.37, p = < 0.0001) (Figure 2b).

Discussion

Main findings

This study has revealed significant variation in screening indications for PNDx according to socioeconomic region, suggesting that utilization of NIPT is unevenly distributed in our population. While these findings are not unexpected, our state-wide dataset provides the first quantitative evidence that NIPT-indicated testing is skewed towards women living in the most socioeconomically advantaged areas, supporting concerns about the inequitable access to NIPT.[21]

The downstream effect of this variation is that women from disadvantaged regions are more likely to undergo invasive testing as a result of false positive screening results. Overall, 85.9% women residing in lowest IRSAD quintile regions had a normal result after PNDx, compared with 68.8% women from regions in the highest IRSAD quintile. As invasive testing carries a small risk of miscarriage,[22] this suggests that women from socioeconomically-disadvantaged areas may be exposed to this iatrogenic risk more frequently than advantaged women.

Not surprisingly, NIPT-indicated PNDx was associated with advanced maternal age on univariate analysis. There are several possible explanations for this. First, later

child-bearing is associated with higher maternal education and socioeconomic status. Second, maternal age is the most important risk factor for trisomy 21, and therefore older women may be more likely to use NIPT. However, even after controlling for maternal age in the analysis, the IRSAD score remained significantly associated with NIPT-indicated testing, showing that maternal age alone is not responsible for this finding.

The univariate and multivariate analysis also demonstrated a significant association of lower gestational age with NIPT-indicated testing. We believe this merely reflects the common clinical practice to offer NIPT at 10 weeks gestation[23], which is earlier than is possible for CFTS (11-13 weeks gestation).

Of note, while our geomapping showed an apparent predominance of NIPT-indicated testing in Melbourne metropolitan areas, this association was not significant after adjustment for IRSAD quintile. This suggests that the lower utilization of NIPT in rural areas is not due to physical location, but related to socioeconomic factors such as lower income or education in rural Victoria.

Strengths

The major strength of this study is our complete population-based ascertainment of PNDx, avoiding the selection bias introduced by hospital- or laboratory-based cohorts. We have a strong pre-existing paradigm of publicly-funded CFTS and STSS performed through a central state laboratory, which allowed observations on the impact of NIPT on PNDx to be drawn.

Our study is also timely, providing evidence for the significant association between socioeconomic advantage and NIPT-indicated testing on a population-wide basis within four years of its introduction to Australia. The vast majority of studies exploring socioeconomic influences on the uptake of prenatal testing for trisomy 21 were performed in the pre-NIPT era and do not capture the magnitude and speed of change created by NIPT.[24-25]

Limitations

Our study was limited to those women undergoing PNDx, and did not include data on women that underwent screening without proceeding to PNDx. While we obtained total numbers of CFTS and STSS tests from the single central laboratory, it was not possible to obtain statewide totals of NIPT due to multiple providers. We can only speculate that rate of NIPT-indicated PNDx reflects the overall uptake NIPT by IRSAD. We can estimate the total number of NIPT referrals based on an unselected cohort of over 5000 Australian women utilizing NIPT.[23] In this previous study, the screen positive rate was 2.2% and invasive testing rate in that high risk group was 73.4%. We calculated that 21,055 women would have been screened with NIPT (14.5% of births) to result in 340 NIPT-indicated diagnostic procedures in our cohort.

The utilization of NIPT as a second tier test may also have influenced our results by improving the apparent diagnostic yield of CFTS in the higher IRSAD quintiles (12.5% in IRSAD 1 vs 20.4% in IRSAD 5, table 2). If women from socioeconomically-advantaged regions were more likely to use NIPT as second tier test, then fewer would proceed to invasive testing after a false positive CFTS result, resulting in the higher diagnostic yield for CFTS in these women.

It is possible that the lower levels of NIPT-indicated testing observed in women from disadvantaged regions were a result of differences in patient preferences alone. Australian women rate safety and detection rates as their top priorities when selecting prenatal screening tests.[26] Given the superiority of NIPT in both these factors, we feel it is unlikely that disadvantaged women would select CFTS or STSS over NIPT if access barriers did not exist. It is therefore plausible that disadvantaged women had less NIPT-indicated PNDx in our cohort because they could not afford NIPT, or because their clinicians did not discuss this option with them. Maternity carers working in disadvantaged areas may be less likely to offer NIPT to patients, either due to lack of knowledge, or an assumption of low uptake.

The indications for diagnostic testing were obtained from the written clinical referral to the cytogenetic laboratory. It is possible that women with multiple indications for diagnostic testing had only one indication recorded, either by the clinician or the receiving laboratory. The finding that a substantial proportion of women who had invasive testing for an NIPT indication were between 17 and 24 weeks gestation suggests the use of NIPT as a secondary screen after serum screening, after an US-

detected abnormality at midtrimester morphology scan, and/or a general preference for amniocentesis rather than CVS for confirmatory testing. We were unable to perform individual linkage to serum screening datasets or to verify indications with the referring clinicians due to the conditions of the ethics approval. However, a further research protocol is now underway that will allow direct linkage between serum screening, NIPT referrals, prenatal diagnosis and postnatal cytogenetics datasets which should provide greater clarity on Victorian prenatal testing practices.

Another limitation of our study was that we were unable to link prenatal testing datasets to pregnancy outcomes, so procedure-related fetal losses and births of infants with Down syndrome were unable to be ascertained. Hence, the final impact of the lower diagnostic yield for PNDx in women from disadvantaged regions can only be surmised from the data provided in this study.

Data are now emerging from other countries that show clear benefits to incorporating government-funded NIPT into existing programs.[27,28] While CFTS alone performs well in our population and continues to be supported by professional societies[2], a recent study modelling the incorporation of NIPT within a CFTS-based model in Western Australia concluded that NIPT could be implemented in a manner that improves the detection rate of trisomy 21, reduces procedure-related fetal loss, at a lower cost per diagnosis than conventional screening.[29]

Conclusions

We have shown significant clinical variation in indications for prenatal diagnosis and diagnostic yield according to socioeconomic region in Victoria. This difference suggests an underlying disparity in the utilization of genomic advances in prenatal screening. Our results may assist health policy makers work towards the effective and equitable implementation of genomic advances to maternity care.

Details of ethics approval

Human Research Ethics Committee (HREC) approval for the prenatal diagnosis data collection and associated research was obtained from the Royal Children's Hospital HREC on 17 Jan 2012 (Ref. No. 31135A) and Monash Health HREC on 18 Apr 2012 (Ref. No. 12063B).

REFERENCES

1. Khoshnood, B, De Vigan C, Vodovar V, et al. Advances in Medical Technology and Creation of Disparities: The Case of Down Syndrome Am J Public Health 2006; 96: 2139-2144.
2. Royal Australian College of Obstetricians and Gynaecologists and Human Genetics Society of Australasia. Statement on prenatal screening and diagnosis of chromosomal and genetic conditions in the fetus 2015. https://www.ranzcog.edu.au/Statements-Guidelines. Accessed 15 March 2017.
3. Jacques AM, Collins VR, Muggli EE, et al. Uptake of prenatal diagnostic testing and the effectiveness of prenatal screening for Down syndrome. Prenat Diagn 2010; 30: 522-530.
4. Mackie FL, Hemming K, Allen S, Morris RK, et al. The accuracy of cell-free fetal DNA-based non-invasive prenatal testing in singleton pregnancies: a systematic review and bivariate meta-analysis. BJOG 2017; 124:32–46.
5. Gregg AR, Skotko BG, Benkendorf JL, et al. Noninvasive prenatal screening for fetal aneuploidy, 2016 update: A position statement of the American College of Medical Genetics and Genomics. Genet Med 2016; 18:1056-1065.
6. Hui L, Muggli E, Halliday JL. Population-based trends in prenatal screening and diagnosis for aneuploidy: a retrospective analysis of 38 years of state-wide data. BJOG 2016; 123: 90-97.
7. Robson S, Hui L. National decline in invasive diagnostic procedures in association with combined first trimester and cell-free DNA-based aneuploidy screening. Aust NZ J Obstet Gynaecol 2015; 55: 507-510.
8. Warsof SL, Larion S, Abuhamad AZ. Overview of the Impact of Noninvasive Prenatal Testing on Diagnostic Procedures. Prenat Diagn 2015; 35: 972-9.
9. Tu S, Rosenthal M, Wang D, et al. Performance of prenatal screening using maternal serum and ultrasound markers for Down syndrome in Chinese women: a systematic review and meta-analysis. BJOG 2016; 123 (S3): 12–22.
10. Li B, Sahota DS, Lao TT, et al. Applicability of first-trimester combined screening for fetal trisomy 21 in a resource-limited setting in mainland China. BJOG 2016; 123 (S3): 23–29.

11. Sago H, Sekizawa, Japan NIPT consortium. Nationwide demonstration project of next-generation sequencing of cell-free DNA in maternal plasma in Japan: 1-year experience. Prenat Diagn 2015; 35: 331-336.
12. Minear M, Lewis C, Pradhan S, Chandrasekharan S. Global perspectives on clinical adoption of NIPT. Prenat Diagn 2015; 25: 959-967.
13. Hui L, Teoh M, Piessens S, Walker SP. Early clinical experience of cell-free DNA-based aneuploidy screening: a survey of obstetric sonologists in Australia and New Zealand. Aust NZ J Obstet Gynaecol 2015; 55:138-143.
14. Hui L, Teoh M, da Silva Costa F, et al. Clinical implementation of cell-free DNA based aneuploidy screening: perspectives from a national audit. Ultrasound Obstet Gynecol 2015; 45: 10-15.
15. Dondorp w, de Wert G, Bombard Y, et al. Non-invasive prenatal testing for aneuploidy and beyond: challenges of responsible innovation in prenatal screening. Summary and recommendations. Eur Journal Hum Genet 2015; 1–3.
16. Duggan A, Koff E, Marshall V. Clinical variation: why it matters. Med J Aust 2016; 205: S3-4.
17. Buchan HA, Duggan A, Hargreaves J, et al. Health care variation: time to act. Med J Aust 2016; 205 (10 Suppl): S30-S33.
18. Hui L, Hutchinson B, Poulton A, Halliday JL. Population-based impact of noninvasive prenatal screening (NIPS) on screening and diagnostic testing for fetal aneuploidy. Genet Med 2017; doi: 10.1038/gim.2017.55. [Epub ahead of print]
19. Australian Bureau of Statistics. Census of Population and Housing: Socio-Economic Indexes for Areas (SEIFA), IRSAD. Available at <Australiahttp://www.abs.gov.au/ausstats/abs@.nsf/Lookup/2033.0.55.001main+features100042011> Accessed 1st July 2017.
20. State Government of Victoria Consultative Council on Obstetric and Paediatric Mortality and Morbidity. 2010 and 2011, Victoria's Mothers and Babies, Victoria's Maternal, Perinatal, Child and Adolescent Mortality 2014. Accessed 23 November 2014 at http://docs.health.vic.gov.au/docs/doc/Victorias-Mothers-and-Babies-Victorias-Maternal-Perinatal-Child-and-Adolescent-Mortality-2010-2011].

21. Allyse M, Minear MA, Berson E, et al. Noninvasive prenatal testing: a review of international implementation challenges. Int J Womens Health 2015; 7:113-126.
22. Akolekar R, Beta J, Picciarelli G, et al. Procedure-related risk of miscarriage following amniocentesis and chorionic villus sampling: a systematic review and meta-analysis. Ultrasound Obstet Gynecol 2015; 45: 16-26.
23. McLennan A, Palma-Dias R, da Silva Costa F, et al. Noninvasive prenatal testing in routine clinical practice - an audit of NIPT and combined first-trimester screening in an unselected Australian population. Aust N Z J Obstet Gynaecol 2016; 56(1):22-8.
24. Muggli EE, McCloskey, Halliday JL. Health behaviour modelling for prenatal diagnosis in Australia: a geodemographic framework for health service utilisation and policy development. BMC Health Serv Res 2006; 6:109.
25. Gitsels -van der Wal, Verhoeven PS, Mannien J, et al. Factors affecting the uptake of prenatal screening tests for congenital anomalies; a multicentre prospective cohort study. BMC Pregnancy Childbirth 2014; 14:264.
26. Lewis SM, Cullinane FM, Carlin JB, Halliday JL. Women's and health professionals' preferences for prenatal testing for Down syndrome in Australia. Aust NZ J Obstet Gynaecol 2006; 46: 205–211.
27. Chitty LS, Wright D, Hill M, et al. Uptake, outcomes, and costs of implementing non-invasive prenatal testing for Down's syndrome into NHS maternity care: prospective cohort study in eight diverse maternity units. BMJ 2016; 354: i3426.
28. Oepkes D, Page-Christiaens GC, Bax CJ, et al. Trial by Dutch laboratories for evaluation of non-invasive prenatal testing. Part I – clinical impact. Prenat Diagn 2016; 36: 1083-1090.
29. Maxwell S, O'Leary P, Dickinson JE and Suthers GK. Diagnostic performance and costs of contingent screening models for trisomy 21 incorporating non-invasive prenatal testing. Aust N Z J Obstet Gynaecol 2017; DOI:10.1111/ajo.12612. [ePub ahead of print]

Table legends

Table 1. Sociodemographic characteristics of women and associated odds of NIPT-indicated prenatal diagnosis

aOR, adjusted odds ratio; CFTs, combined first trimester screening; CI, confidence interval, IRSAD, Index of relative socioeconomic advantage and disadvantage; metro, metropolitan; NIPT, noninvasive prenatal testing; OR, odds ratio

Table 2. Results of prenatal diagnosis by screening test indication and index of relative socioeconomic advantage and disadvantage quintile

CFTS, combined first trimester screening; IRSAD, index of relative socioeconomic advantage and disadvantage; NIPT, noninvasive prenatal testing;

*Major chromosome abnormalities only, excluding confined placental mosaicism (n=5) and variations of unknown significance (n=99)

Figure legends

Figure 1. Index of relative socioeconomic advantage and disadvantage (IRSAD) and rates of prenatal diagnosis by screening indication and local government area

Figure 1A. IRSAD decile by local government area (Blue = relative advantage, orange = relative disadvantage)

Figure 1B. Rates of combined first trimester screening-indicated testing by local government area (tests per 10,000 births)

Figure 1C. Rates of combined NIPT-indicated testing by local government area (tests per 10,000 births)

Figure 1D. Rates of second trimester screening-indicated testing by local government area (tests per 10,000 births)

Figure 2. Screening indications and diagnostic yield by index of relative socioeconomic advantage and disadvantage (IRSAD) quintile

Figure 2A. Proportions of screening indications for prenatal diagnosis by IRSAD

* χ^2 trend = 13.32, p = 0.0003

** χ^2 trend = 60.61 P < 0.0001

*** χ^2 trend = 11.41, p =0.0007

Figure 2B. Diagnostic yield of prenatal diagnosis by IRSAD quintile

* χ^2 trend = 25.37 p = < 0.0001

NIPT, noninvasive prenatal testing; STSS second trimester serum screening; CFTS, combined first trimester screening; IRSAD, index of relative socioeconomic advantage and disadvantage

Variable	NIPT indicated tests (n = 340)	CFTS indicated tests (n=1337)	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)	P value aOR
IRSAD quintile					
IRSAD 1	11 (3.2%)	168 (12.5%)	ref	ref	-
IRSAD 2	21 (6.2%)	139 (10.4%)	2.31 (1.07-4.95)	2.34 (1.09-5.08)	0.029
IRSAD 3	47 (13.8%)	237 (17.7%)	3.03 (1.53-6.01)	2.91 (1.46-5.80))	0.002
IRSAD 4	85 (25.0%)	396 (29.6%)	3.28 (1.71-6.30)	2.99 (1.51-5.89)	0.002
IRSAD 5	176 (51.8%)	397 (29.7%)	6.77 (3.59-12.78)	5.72 (2.95-11.09)	< 0.001
Location					
Metro	301 (88.5%)	1068 (79.9%)	ref	-	-
Rural	39 (11.5%)	269 (21.1%)	0.51 (0.36-0.74)	0.84 (0.54-1.30)	0.43
Age group					
< 35 years	109 (32.1%)	530 (39.6%)	ref	ref	-
35-39 years	157 (46.2%)	524 (39.2%)	1.46 (1.11-1.91)	1.37 (1.04-1.81)	0.03
40+ years	74 (21.8%)	283 (21.2%)	1.27 (0.91-1.77)	1.25 (0.89-1.74)	0.20
Gestational age					
10-13 weeks	141 (41.5%)	399 (29.8%)	ref	ref	-

14-16	134 (39.4%)	609 (45.5%)	0.62 (0.48-0.81)	0.71 (0.54-0.94)	0.02
17-19	22 (6.5%)	152 (11.4%)	0.41 (0.25-0.67)	0.48 (0.29-0.79)	0.004
20-24	43 (12.6%)	177 (13.2%)	0.69 (0.47-1.01)	0.73 (0.49-1.08)	0.12

Table 1. Sociodemographic characteristics of women and associated odds of NIPT-indicated prenatal diagnosis

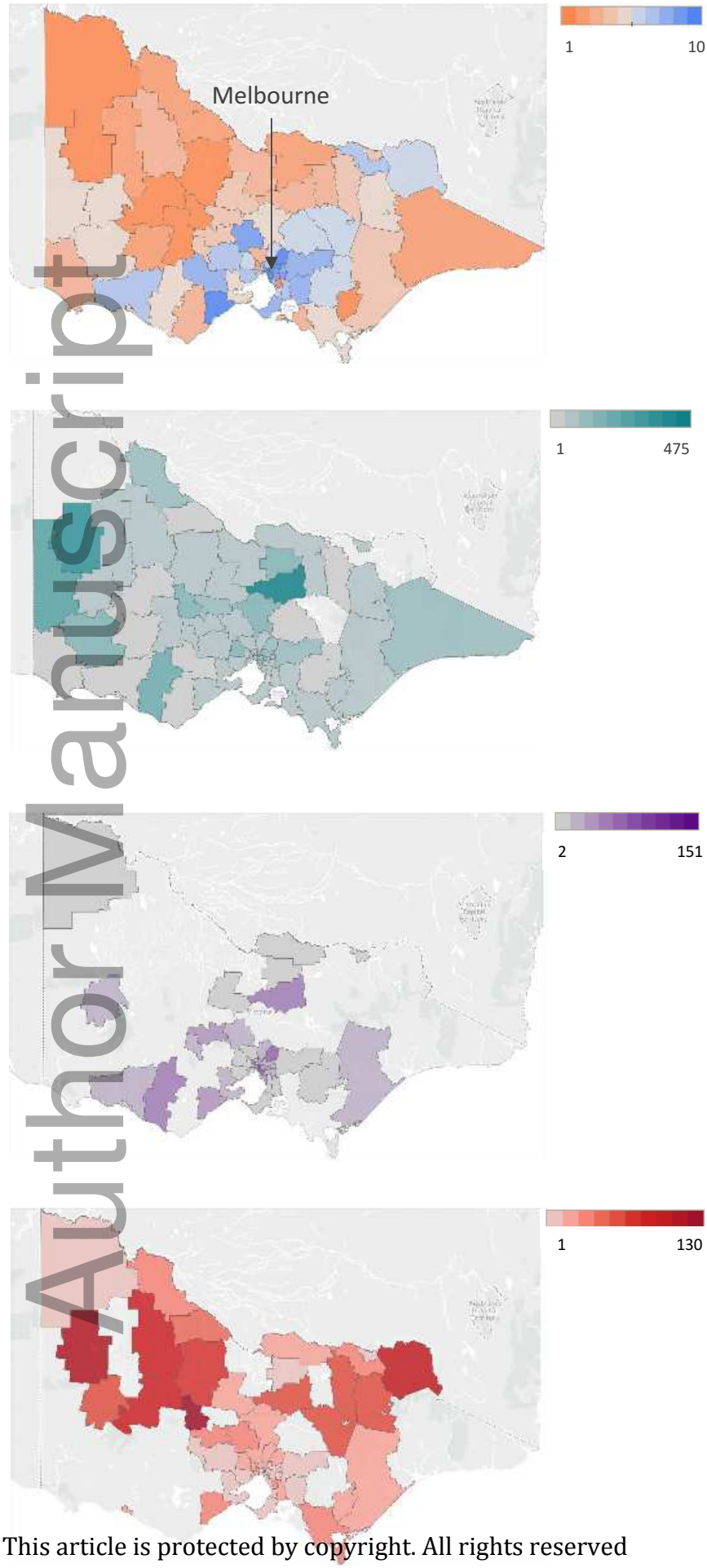
aOR, adjusted odds ratio; CFTs, combined first trimester screening; CI, confidence interval, IRSAD, Index of relative socioeconomic advantage and disadvantage; metro, metropolitan; NIPT, noninvasive prenatal testing; OR, odds ratio

Table 2. Results of prenatal diagnosis by screening test indication and IRSAD quintile

CFTS, combined first trimester screening; IRSAD, index of relative socioeconomic advantage and disadvantage; NIPT, noninvasive prenatal testing

IRSAD Quintile	Major abnormalities by indication for testing			Total major abnormalities/Total tests*
	CFTS	STSS	NIPT	
1	21/168 (12.5%)	2/41(4.9%)	8/11 (72.7%)	31/220 (14.1%)
2	22/139 (15.8%)	2/28 (7.1%)	13/21 (61.9%)	37/188 (19.7%)
3	57/237 (24.1%)	2/50 (4.0%)	29/47 (61.7%)	88/334 (26.3%)
4	68/396 (17.1%)	1/60 (1.7%)	61/85 (71.8%)	130/542 (24.0%)
5	81/397 (20.4%)	2/49 (4.1%)	111/176 (63.1%)	194/622 (31.2%)
Totals	249/1337 (18.6%)	9/229 (3.9%)	222/340 (65.3%)	480/1906 (25.2%)

*Major abnormalities only, excluding confined placental mosaicism (n=5) and variations of unknown significance (n=99)



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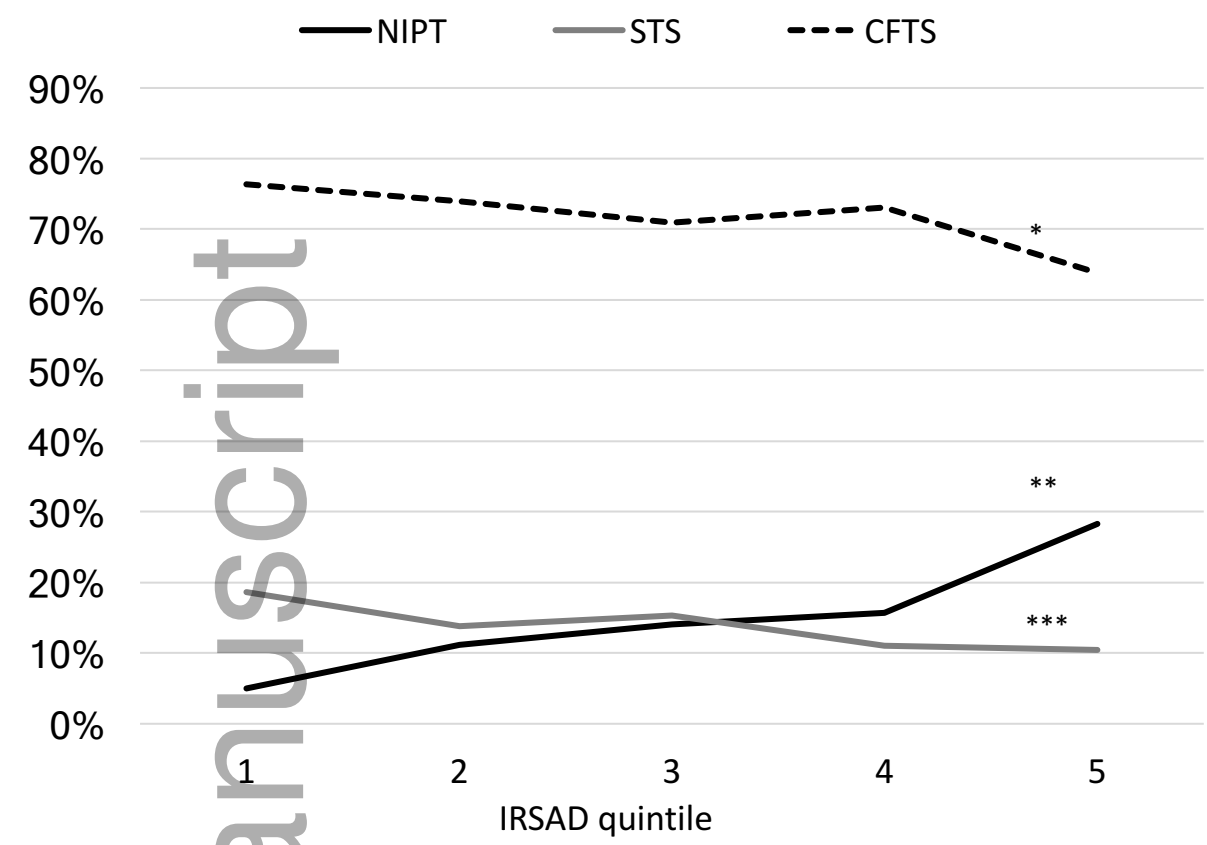

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