Prenatal diagnosis for monogenic conditions: a population-based study from 2010-2020

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Introduction

- Prenatal diagnosis is available for monogenic conditions (PNDx-M) identified through paediatric exome sequencing and reproductive carrier screening.
- The aim of this study was to analyse the number and range of PNDx-M performed in the Australian state of Victoria between 2010 to 2020.

Methods

- We analysed population-based data on all PNDx-M procedures performed at <25weeks' gestation.
- Statistical significance testing was performed using X^2 test for trend.
- Annual births were obtained from the Australian Bureau of Statistics

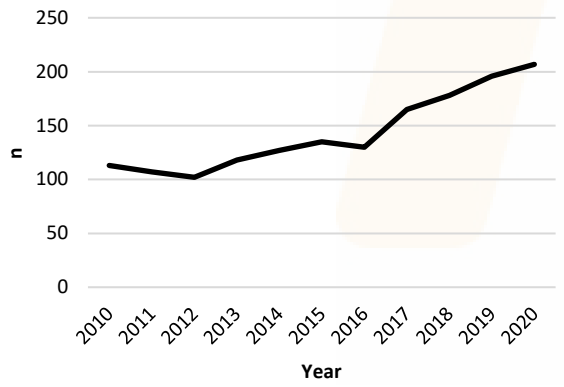
Conclusion

- Our population-based study demonstrated an significant increase in the frequency and range of PNDx-M performed in Victoria over the past decade.
- PNDx-M is now the third most common indication for invasive prenatal testing
- This is likely due to increasing use of genomics in paediatrics, enabling the identification of genetic variants responsible for rare diseases, as well as increased availability of reproductive carrier screening
- The importance of genomics in pregnancy care is expected to increase as technology and accessibility improve

Results

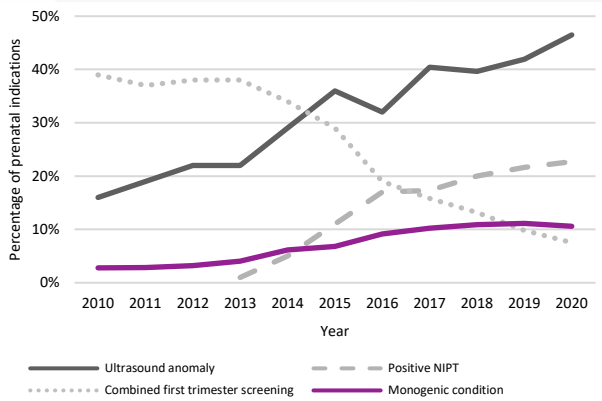
- There were a total of 1578 PNDx-M procedures during the 10 year study period.
- The annual frequency increased from 114 in 2010 to 207 in 2020 ($p<0.0001$) (**Figure 1**).
- The rate of PNDx-M as a proportion of registered births changed from 1.6/1000 to 2.3/1000 PNDx-M per Victorian births over the same time period.

Figure 1. Annual number of PNDx-M



- PNDx-M has replaced combined first trimester screening (CFTS) as the third most common indication for prenatal diagnosis in Victoria.
- The most common indications for prenatal diagnosis in 2020 were ultrasound anomaly 46.5%, non-invasive prenatal testing (NIPT) 22.7%, monogenic condition 10.6% and combined first trimester screening 7.5%, (**Figure 2**).

Figure 2. Top four indications for prenatal diagnosis



- The number of unique conditions for which PNDx-M were performed has more than doubled, from 43 in 2010 to 103 in 2020 (**Figure 3**).
- The four most common monogenic conditions account for 3.9% of total PNDx-M in 2020, compared with 9.3% in 2010 (**Table 1**).

Figure 3. the Annual number of unique conditions analysed through PNDx-M

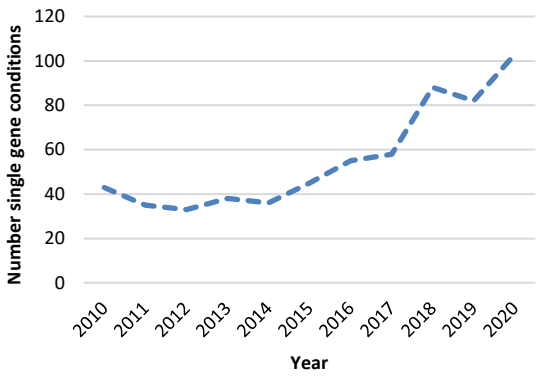


Table 1. Ten most common monogenic conditions examined through PNDx-M between 2010-2020

Monogenic condition	Frequency	%Total PNDx-M (n=1578)
Thalassaemia	301	19.1
Fragile X syndrome	232	14.7
Cystic fibrosis	194	12.3
Duchenne muscular dystrophy	52	3.3
Spinal muscular atrophy	51	3.2
Huntington disease	27	1.7
Myotonic dystrophy	26	1.6
Haemophilia	22	1.4
Congenital adrenal hyperplasia	17	1.1
Polycystic kidney disease 4 (PKD4)	16	1.0

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