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**Preterm birth has impact on the long term  
health of two generations**

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**A thesis submitted in partial fulfilment of the  
requirements for the degree of Doctor of  
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## ABSTRACT

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Research over the last decade has provided clear evidence that children and young adults born very preterm have reduced insulin sensitivity. There is very little data on the metabolic changes, changes in body composition and blood pressure beyond young adulthood in preterm survivors, particularly those born moderately preterm, who constitute the vast majority of preterm survivors. To date the impact of parent's prematurity on the health of their children has not been assessed.

This thesis reports glucose metabolism, body composition and blood pressure profile of a cohort of 52 adults (31 preterm, 21 term at mean GA of 33.3 and 39.8 weeks respectively) aged between 34-38 years and their 61 healthy, pre-pubertal, term born offspring (37 of preterm parents, 24 of term parents) aged 5-10 years. The adult cohort, both preterm and term born, were a subgroup of a much larger cohort involved in two previous studies- the Auckland Steroid Trial and The Steroid Follow-up study.

Insulin secretion and insulin sensitivity were assessed using hyperglycaemic clamp in adults and frequently sampled intravenous glucose tolerance test in the offspring. Both the adults and their offspring had their body composition assessed using DXA scan and blood pressure measured using 24 hour ambulatory blood pressure monitor.

In the Adult study, compared to those born at term, those born preterm had ~50% reduction in insulin sensitivity, but had appropriate compensatory hyperinsulinaemia. The preterm subjects, especially men, also had increased total and abdominal adiposity. Although the mean blood pressure between the two groups was similar, preterm subjects had greater variability of blood pressure profile.

In the Offspring study, the offspring of preterm parents had similar insulin sensitivity and insulin secretion as the offspring of term parents but had increased total and abdominal adiposity. Although the mean blood pressure in both the

offspring groups was similar, comparison with an international reference data showed subtle changes in blood pressure in the offspring of preterm parents.

This study has confirmed and extended previous observations on preterm survivors. Reduction in insulin sensitivity occurs even in those with moderate prematurity (33 to 37 weeks) and this finding extends the potential group at risk of insulin resistance to up to 7% of the population. Our findings of increased adiposity and blood pressure changes suggest an increased risk of later adult diseases in those born preterm. This is the first study assessing the health of children born to preterm parents. We speculate that the increased adiposity observed in the offspring of preterm parents may reflect transmission of an epigenetically modified phenotype from their preterm parent. In conclusion, preterm birth has effects over at least 2 generations and the public health impact of prematurity may be larger than previously thought.

**“Can you fathom the mysteries of God?**

**Can you probe the limits of the Almighty?” Job 11:7.**

**Dedicated to John, Vineeth & Preethi**

**for their love and immense patience**

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---

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