

# BMJ Open The Australian Temperament Project Generation 3 study: a population-based multigenerational prospective cohort study of socioemotional health and development

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## ABSTRACT

**Purpose** The Australian Temperament Project Generation 3 Study (ATPG3) was established to examine the extent to which offspring social and emotional development is shaped in the decades prior to conception, in parent and grandparent histories of psychosocial adjustment (eg, emotional regulation, relationship quality and prosociality) and maladjustment (eg, depressive symptoms, substance use and antisociality).

**Participants** The Australian Temperament Project (ATP) commenced in 1983 as a population representative survey of the social and emotional health of 2443 young Australians (Generation 2: 4–8 months old) and their parents (Generation 1). Since then, families have been followed from infancy to young adulthood (16 waves). Between 2012 and 2018, the cohort was screened biannually for pregnancies (Generation 3), with assessments conducted in the third trimester of pregnancy, and at 8 weeks and 1 year postpartum.

**Findings to date** A total of 1167 offspring (607 female) born to 703 Generation 2 parents (400 mothers) were recruited into the ATPG3 Study. Findings to date highlight: (1) strong continuities in depressive symptoms and substance use from adolescence through to becoming a parent; (2) a role for persistent preconception mental health problems in risk for parent–child bonding difficulties, as well as infant emotional reactivity and behaviour problems; (3) the importance of secure attachments in adolescence in reducing long-term risk for postpartum mental health problems; and (4) the protective nature of perceived social support, both preconception and postpartum, in strengthening relationship quality and social support during the COVID-19 pandemic.

**Future plans** Assessments of ATPG3 families in preschool and middle childhood are currently funded and underway. We intend to maintain the offspring cohort through childhood, adolescence, young adulthood and into parenthood. Data will be used to map preconception determinants of emotional health, and enhance approaches to population monitoring and

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ The Australian Temperament Project Generation 3 Study is rare example of a prospective, population representative, intergenerational cohort study which now spans close to four decades.
- ⇒ The study has repeated assessments of physical health, relational health, emotional health and positive development from early childhood to young adulthood and into parenthood.
- ⇒ The study has repeated assessments of the social context of development, including family, school, peer and community life across the same period.
- ⇒ The study has been subject to selection, measurement and confounder biases over time; these have been actively minimised through quality retention methods, psychometrically validated measures and rich assessment of socioeconomic context.

targeted intervention over the life course and across generations.

## INTRODUCTION

Social and emotional development in early childhood plays a seminal role in shaping patterns of mental health and disorder across the life course, with investments in this period remaining a central priority in national and international social, educational and health policy development.<sup>1 2</sup> To date, approaches to prevention of psychosocial, educational and early health risks in childhood have mostly focused on intervening post-conception, particularly during the antenatal and perinatal periods, but also in the years of early childhood. However, a growing body of research is pointing to



aetiological pathways that extend much further back in time. This has created widespread interest in the intergenerational origins of health and disease, and in particular, to relationships between exposures accrued by parents (through all stages of development from birth to reproduction) and outcomes in their offspring.<sup>3,4</sup>

Across many countries, the preconception period has lengthened dramatically in recent history too. Prior to the industrial revolution, first births typically happened in the mid to late teens. Now, the median age of first time mothers in many developed economies is in the 20s.<sup>5,6</sup> In Australia, for example, this has extended to the late 20s (28.9 years for first births; 30.7 years for all births).<sup>7</sup> This extended period coincides with major changes in child, adolescent and young adult lifestyles that may influence future parenting capacities.<sup>8</sup> These include higher rates of depression, anxiety and drug use, and increasing rates of obesity and related metabolic disorders.<sup>9</sup> They also include new expectations that parents will meet the financial, educational and emotional support needs of their children well into early adulthood.

Such rapid changes in reproductive behaviour have led organisations such as the US Centers for Disease Control<sup>3</sup> and the WHO<sup>4</sup> to change the definition of preconception care from ‘preparation for pregnancy’ to ‘a continuum of care designed to meet the needs of a woman through the various stages of her reproductive life’ (ie, all the stages of psychosocial and sexual development from childhood to parenthood). To date, the focus of preconception work has been on mothers, which leaves a substantial knowledge gap around the role of fathers (and other caregivers) in child health and development.<sup>10</sup>

The focus has also been on prevention of physical health problems, in particular preventable causes of child deaths (malnutrition and infectious diseases),<sup>4</sup> and intergenerational transmission of stunting and related metabolic conditions.<sup>11</sup> Much less attention has been given to psychosocial problems such as maternal and paternal mental disorders, intra-familial relationships, child behaviour problems and educational difficulties. In all cases, optimal points for intervention in intergenerational risk pathways remain unclear, and almost nothing is known about potential contextual (environmental) risk modifiers which severely limits options for intervening in intergenerational cycles of risk.<sup>12</sup>

Understanding preconception pathways that promote optimal offspring social and emotional development is equally important for informing innovation in practice and policy. These pathways define a separate class of processes that promote infant potentials either directly or indirectly through negating risk pathways. Examples include intergenerational transmission of constructive, warm and sensitive parenting<sup>13</sup> which is an important prerequisite for offspring attachment

security and adjustment. Sensitive parenting is also likely to play a role in buffering the effects of other preconception risks factors.

By far, the most significant barrier to progressing intergenerational research is lack of quality prospective data in human populations. Most existing intergenerational studies cover only two generations and are based on small ‘at risk’ samples, with variable study designs (public record studies, single report studies, cross-sectional, retrospective). Very few have followed parents from birth and almost all rely on retrospective assessments of parents-of-parents (grandparents),<sup>14</sup> despite parental life histories being so intimately bound to those of their own parents, socially and biologically. Importantly, most studies lack follow-up of offspring across pregnancy which precludes investigation of transmission pathways.

As a result, intergenerational theory is in its infancy.<sup>15</sup> The most relevant theoretical framework is the Developmental Origins of Health and Disease,<sup>16</sup> which traditionally focusses on post-conception exposures (first 1000 days) and has only recently extended into the preconception period. Within this framework, transmission pathways have been loosely grouped into three broad classes:

1. *Direct transmission through epigenetic modifications* to parental gametes that are maintained across conception or are established in response to the postpartum environment.<sup>17</sup> Such mechanisms may have been conserved in evolution to allow for fine-tuning of biological systems to meet the unique demands of a particular generation.
2. *Indirect transmission through factors that persist into pregnancy*, with a wealth of data showing long-term adverse associations between infant birth size and adult blood pressure, diabetes, ischaemic heart disease and stress sensitivity.<sup>18</sup>
3. *Indirect transmission through factors that persist into early childhood*, among the most notable being factors that undermine responsive parental caregiving (eg, parental sensitivity), which have been consistently associated with adverse child outcomes in both observational<sup>1</sup> and experimental designs.<sup>19</sup>

### ATPG3 objectives

The Australian Temperament Project Generation 3 Study (ATPG3) was established to advance understanding of the role of preconception exposures on early childhood social and emotional development. It was designed to allow not only broad assessment of lifestyle exposures that cross generations, but also a deeper understanding of possible genetic, epigenetic and neurodevelopmental lines of transmission that link lifestyle exposures from previous generations to the health and development of the next. Key objectives of this project are to identify parent and grandparent preconception predictors of parental perinatal mental health and well-being, parent–child bonding, offspring socioemotional adjustment, offspring

attachment, fetal neurodevelopment and offspring social epigenome programming.

## COHORT DESCRIPTION

### Cohort selection

ATPG3 follows third generation offspring born to parents participating in the original Australian Temperament Project (ATP) cohort, which commenced as a community survey administered to a Victorian representative sample of 2443 infant offspring (aged 4–8 months) and their parents, in 1983. Families were recruited through Maternal and Child Health (MCH) centres in 20 urban and 47 rural local government areas in the state of Victoria, Australia. The local government areas were randomly selected, on the advice of the Australian Bureau of Statistics, to provide a representative sample of Victoria.<sup>20</sup> The parent or caregiver of every 4–8 month old child who attended an MCH centre in a selected local government area in a specified 2-week period was given a survey to complete by the MCH nurse, who also completed one about the health and development of the infant. MCH centres achieved contact with 94% of live births at the time. Approximately 3000 questionnaires were distributed, with 2443 usable questionnaires returned (81%). Comparison to Victorian statistics for the same period showed that the sample obtained was representative.<sup>20</sup>

Three years later (1986), a representative subsample of 2023 families participating in the original survey consented to follow-up and have now completed a maximum of 16 waves of assessment from early childhood to young adulthood. Generation 1 and, from 11 to 12 years of age, Generation 2 were invited to participate via mail surveys approximately every 2 years until 19–20 years and every 4 years thereafter. Participants completed age-appropriate questionnaires and rating scales providing detailed assessments of temperament, social and emotional development, health and family and social context. With parent consent, teachers also provided information at age-appropriate levels. Further information regarding the sample characteristics and procedures of the ATP are available elsewhere.<sup>21</sup>

Due to initial concerns about the impact of repeated administration of questionnaires, a randomly selected two-thirds of the sample was surveyed in wave 2 (1984), and remaining third plus half of the wave 2 sample (again, randomly selected) were surveyed in wave 3 (1985). As a result, there was a 2-year gap in contact for one-third of the participants, before they had fully engaged with the study. Efforts were made to recontact all participants from the original sample in wave 4 (1986), but the largest loss to follow-up occurred at this stage, with 420 participants (17%) not re-engaging in the study (see online supplemental figure S1). With improved resources for tracing families over time, there has only been gradual sample loss to follow-up since wave 4.

Recruitment of offspring into ATPG3 occurred between 2012 and 2018, when ATP participants were aged 29–35

years, representing the peak period of first births in Australia.<sup>7</sup> Every 6 months, identification of pregnancies and infants occurred via emails or phone calls to participants. Participants reporting a pregnancy or newborn were posted participant information and a consent form and subsequently contacted via phone to discuss the study. Offspring missed during pregnancy were eligible for inclusion at the 8 weeks and 1 year postpartum waves of assessment.

### Recruitment and response rates

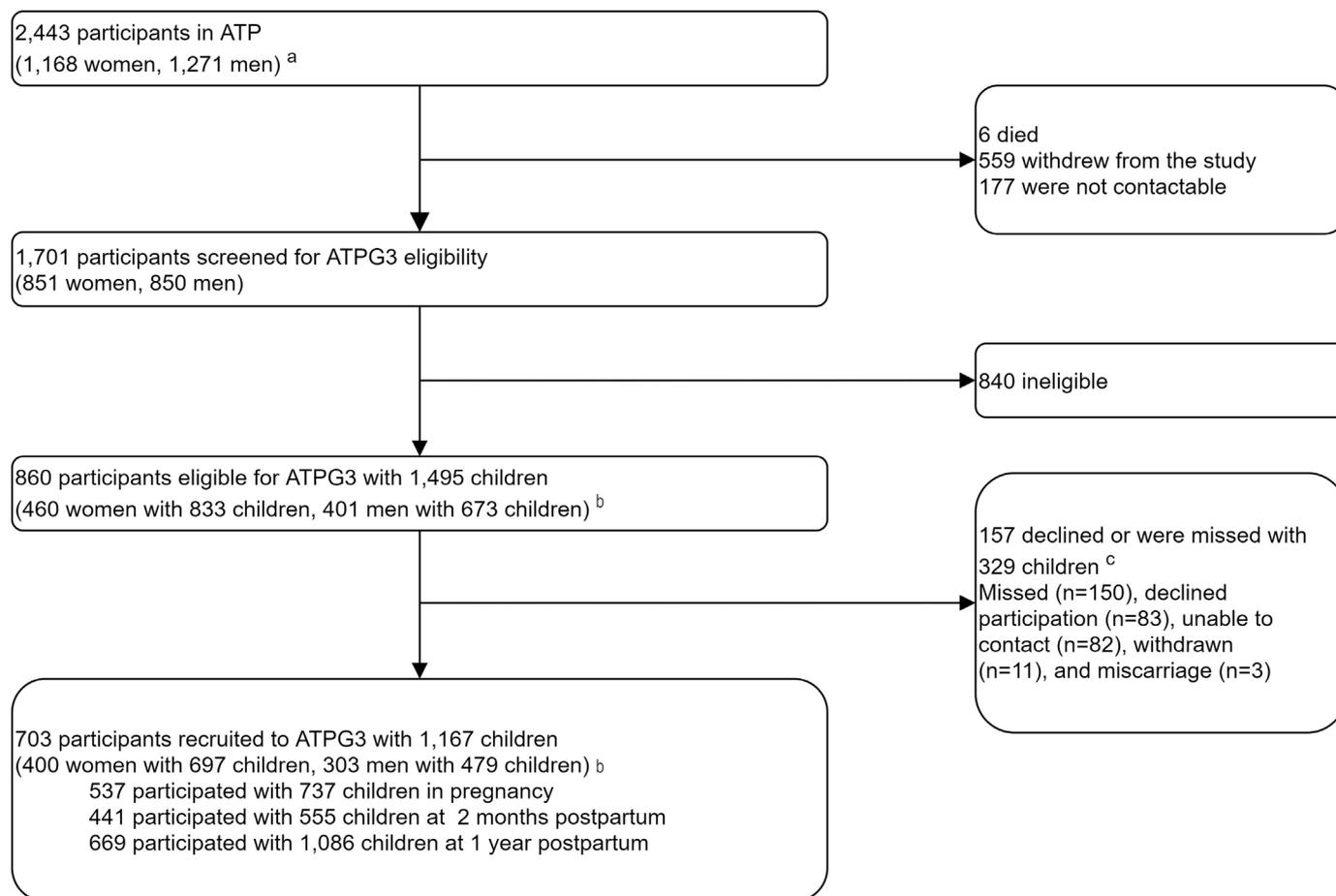
The flow of participants from ATP to ATPG3 is shown in figure 1. Generation 2 participants (n=1701) were screened for ATPG3 Study eligibility. A total of 1167 children born to 703 Generation 2 participants participated in ATPG3. Many parents participated with more than one child: 45% with one child, 43% with two children, 11% with three children and 1% with four children.

Among eligible children, the main reasons for non-participation were missing the assessment at the eligible age, declining participation or unable to be contacted, with very few withdrawing or experiencing miscarriage. Participation rates were highest at 1 year postpartum, with 1086 infants born to 669 Generation 2 parents. The lower rate of participation in pregnancy (737 pregnancies; 537 participants), compared with 1 year postpartum, reflected difficulties detecting pregnancies and completing surveys prior to birth. Response rates were lowest at 8 weeks postpartum (555 children; 441 parents) because, due to funding restrictions, this wave commenced in 2014, approximately 2 years after recruitment for the other perinatal waves had begun. Sample retention has been enhanced with a variety of participant engagement strategies, including regular participant newsletters, a study website and a Facebook page. Of the 1167 children recruited to the ATPG3 Study, 6 (from five families) have been lost to follow-up (withdrawn or deceased).

### Sample characteristics

Baseline family and infant characteristics of ATP participants who were screened, identified as eligible and participated in ATPG3 are shown in table 1. Compared with the original ATP community survey sample (n=2443, ascertained in 1983), in the screened sample (n=1701), we found marginally higher rates of drop out in Generation 1 parents who were non-Australian born and had lower education levels. Those who participated in the ATPG3 study (n=703) were broadly representative of those eligible to participate (n=860) on baseline characteristics.

Table 2 presents the characteristics of the recruited ATPG3 offspring sample. Just over half the sample were female and just under half were first-born. Few were part of a multiple birth. Parent reports of low birth weight and preterm births in the ATPG3 sample were similar to reported rates for the general Victorian population.<sup>22</sup>



**Figure 1** Flowchart of The Australian Temperament Generation 3 Study (ATPG3) participants from recruitment to 1 year postpartum data collection. Note: study entry could occur during any perinatal wave. ATPG3 eligibility defined as all children younger than 18 months identified during screening (December 2011 to September 2018); until mid-2013 recruitment included children up to 3 years of age. <sup>a</sup>Four ATP participants missing sex data. <sup>b</sup>The number of children by women and men does not sum to total number of children because, 9 of 1167 children recruited came from five ATP couples. <sup>c</sup>One child participated in ATPG3 with the other ATP parent.

### Study design and instrumentation

ATPG3 is unique in its three-generation prospective design with 15 waves of preconception data from infancy to adulthood (27–28 years) and comprehensive assessments of next generation offspring from pregnancy to early childhood. The majority of ATPG3 families (85%) had preconception data available for 10 or more waves. Only a small minority (6%) had fewer than five waves of preconception data. Participants with fewer waves of preconception data had been lost to follow-up at some point and were recruited back into the cohort in 2010 (wave 15) after an intensive round of tracing using new internet resources and other techniques.

#### Generation 1 and 2 assessments (preconception exposures)

Measurement domains of the ATP (Generations 1 and 2) are summarised in table 3 and represent three major preconception windows: childhood, adolescence and young adulthood. Waves 1–9 were concerned with key aspects of child development, including temperament and behaviour, the parent–child bond and school transitions. Waves 10–12 were concerned with positive

development as well as the emergence of emotional and behavioural problems in adolescence. In this phase, DNA was collected as were data on puberty, physical health, sexual and reproductive health, substance use and positive development (including civic action, social capital, life satisfaction, attachment security). Waves 13–15 were concerned with young adulthood, in particular the social and educational transitions made in this period of the life course, one of the more significant being the transition to parenthood. The original ATP cohort also has prospective data on Generation 1 participants, including parenting, socioeconomic context, temperament, personality and behaviour.

#### Generation 3 offspring assessments

The ATPG3 design has three waves of perinatal assessment in pregnancy, at 8 weeks and at 1 year postpartum. At each wave, ATPG3 families were invited to complete a computer-assisted telephone interview or web survey. Instrumentation of the ATPG3 has focused on quality assessments of parent and offspring social-emotional well-being across the perinatal periods, with particular

**Table 1** Baseline characteristics of all Australian Temperament Project (ATP) participants, those screened for ATP Generation 3 (ATPG3) eligibility, those eligible for ATPG3 and those participating in ATPG3

Baseline characteristics (1983)	All ATP participants			Screened for ATPG3			Eligible for ATPG3			ATPG3 participants		
	N=2443			N=1701			N=860			N=703		
	N	n	%	N	n	%	N	n	%	N	n	%
<i>G1 Family background</i>												
<i>G1 Education</i>												
Mother low education	2384	1718	72	1689	1165	69	853	592	69	700	474	68
Father low education	2331	1207	52	1668	820	49	850	394	46	698	318	46
<i>G1 Country of birth</i>												
Mother non-Australian born	2407	479	20	1696	284	17	857	130	15	702	107	15
Father non-Australian born	2378	634	27	1686	399	24	856	193	23	702	159	23
<i>G2 Infant characteristics</i>												
G2 Sex (male)	2439	1271	52	1701	850	50	860	400	47	703	303	43
Difficult temperament	2409	463	19	1696	312	18	857	161	19	702	128	18
Behaviour problems	2404	565	24	1694	389	23	856	198	23	701	157	22

Note: Baseline characteristics assessed at recruitment in 1983. G1=Generation 1; G2=Generation 2.

Low education=completed high school or less. Difficult temperament=mean score >3 on combined subscales of Approach-Withdrawal, Cooperation and Irritability of Revised Infant Temperament Questionnaire rated on a 6-point Likert-type scale, from 1 (almost never) to 6 (almost always). Behaviour problems=mean score of >2, including items ('Colic', 'Sleep problems' and 'Excessive crying') rated on a 4-point Likert-type scale, from 1 (none) to 4 (severe).

focus on parent mental health, relationships and social context, and infant emotional regulation, behaviour and attachment security. Where possible, we used the same measures used with Generation 2 in our Generation 3 assessments. Perinatal assessments are described in further detail below and in [table 3](#).

*Life@Trimester 3* occurred at 28–32 weeks gestation and allowed comprehensive assessment of preconception influences on gestation. We assessed a broad range of influences on fetal development with a particular focus

on the general health and psychosocial well-being of the mother, including pregnancy health, perceived social support, mental health and substance use, bonding with the fetus and stressful life events. Consent for birth record linkage was obtained (see the Data linkage section).

*Life@8 weeks postpartum* was the first contact with ATP families after birth to assess the early postnatal social experience. Measures were administered by CATI and included four major domains: infant health, maternal postnatal depression, family social support and stressful life events.

*Life@1 year postpartum* assessments were conducted with the Primary Caregiver (typically the Generation 2 mother) and captured information on a range of indicators relevant to the social and emotional development of the infant. This included infant temperament and behaviour, the quality of the parent-infant bond as well as parent physical and mental health, substance use, socio-economic security and social and emotional support. A shorter survey of the Secondary Caregiver (typically the father) captured their work, education and living arrangements, emotional health, substance use, life events and experiences of being a parent.

*Father participation:* While mothers were the focus of participation in the pregnancy and 8 week assessments, regardless of whether they were the ATP Generation 2 cohort participant or partner of the cohort participant, at *Life@1* (and for subsequent assessments) we have actively sought to include the participation of fathers, including in cases of family dissolution. Generation 2 parents not

**Table 2** Characteristics of 1167 recruited offspring born to 703 ATP cohort participants

	N	n	%
<i>Sex</i>			
Male	1167	560	48
<i>Parity</i>			
1	1167	553	47
2	1167	415	36
≥ 3	1167	199	17
<i>Multiple birth status</i>			
Multiple birth	1119	40	4
<i>Birth outcomes</i>			
Born preterm (<37 weeks)	1116	86	8
Low birth weight (<2.5 kg)	1104	70	6

ATP, Australian Temperament Project.

**Table 3** Summary of major developmental indicators within the preconception waves of the Australian Temperament Project (ATP) and the ATP Generation 3 Study (ATPG3)

Developmental stage and age	ATP Generations 1 & 2 1983–2010			ATP Generation 3 2012–		
	G2 Childhood 4–8 months to 11–12 years	G2 Adolescence 13–14 to 17–18 years	G2 Adulthood 19–20 to 27–28 years	In utero	8 weeks postpartum	1 year postpartum
Wave	1–9	9–12	13–15	1	2	3
<i>Measurement domains</i>						
Socioemotional assessments						
Temperament/personality	✓ <sup>39</sup>	✓ <sup>40</sup>	✓ <sup>41 42</sup>			✓ <sup>39</sup>
Depression/anxiety	✓ <sup>43</sup>	✓ <sup>44–46</sup>	✓ <sup>47</sup>	✓ <sup>47</sup>	✓ <sup>48</sup>	✓ <sup>47 49</sup>
Substance use and misuse		✓	✓	✓	✓	✓
Aggression/hyperactivity	✓ <sup>43</sup>	✓ <sup>50</sup>	✓ <sup>51</sup>			✓
Eating patterns/behaviours	✓	✓ <sup>52</sup>				✓
Prosocial behaviour/competencies		✓ <sup>53</sup>	✓ <sup>21</sup>			✓ <sup>49</sup>
Social skills	✓ <sup>54</sup>	✓ <sup>54</sup>	✓ <sup>55</sup>			✓
Physical assessments						
Birth outcomes	✓			✓	✓ <sup>56</sup>	
Exercise, nutrition and sleep	✓	✓	✓	✓	✓	✓
General health	✓ <sup>57</sup>	✓	✓	✓	✓	✓
Peri-pubertal profiling		✓				
Medical/prescription history			✓	✓	✓	✓
Neurodevelopment (sonography)*				✓		
Relational assessments						
Partner relationship quality			✓ <sup>58</sup>	✓ <sup>59</sup>		
Parenting behaviours		✓				✓ <sup>60</sup>
Parent–child relationship/bond	✓	✓	✓ <sup>61</sup>	✓ <sup>62</sup>		✓ <sup>63</sup>
Peer relationships	✓ <sup>64</sup>	✓ <sup>65</sup>	✓ <sup>61</sup>			
Attachment (incl. SSP)*						✓
Contextual assessments						
Parent living arrangements	✓	✓	✓	✓	✓	✓
Stressful life events	✓	✓	✓	✓	✓	✓
Parent social support			✓ <sup>61</sup>	✓ <sup>66</sup>	✓ <sup>66</sup>	✓ <sup>66</sup>
Employment	✓	✓	✓	✓	✓	✓
Education	✓	✓	✓	✓	✓	✓
School achievement	✓ <sup>54</sup>	✓ <sup>54</sup>				
School bonding		✓ <sup>67</sup>				
Income/financial security	✓	✓	✓	✓	✓	✓
Family social disadvantage	✓	✓	✓	✓	✓	✓
Neighbourhood disadvantage	✓	✓	✓	✓	✓	✓

Note: The initial population representative, community sample, comprising 2443 4–8 month old Generation 2 (G2) infants and their parents (Generation 1; G1; mean age 27.9 years-mothers, 30.5 years-fathers), was recruited through Maternal and Child Health centres in the state of Victoria, Australia, in 1983. Numbers refer to references which indicate key measurement instruments used to assess each construct.  
\*Nested assessments.

living with their Generation 3 child have been invited to participate and given the option to skip questions pertaining to the child if they do not feel they can answer them.

The ATPG3 Study also included three nested studies which are now complete:

1. *Nested Neurodevelopmental Study*: A subset of Generation 2 mothers (n=51 with 57 children) participated in a nested study of fetal neurodevelopment between November 2015 and January 2018. G2 mothers reporting pregnancies were invited to have a trans-abdominal ultrasound to assess fetal neurodevelopment and give a hair sample to provide a cortisol biomarker of stress across the pregnancy. The aim of this nested assessment was to identify preconception and gestational predictors of fetal neurodevelopment.
2. *Nested Genetic Study*: The purpose of DNA collections was twofold: (1) to develop polygenic risk scores that can be studied directly or used to adjust for genetic confounding in social epidemiological studies; and (2) to examine epigenetic processes by which social exposures may be translated into longer term biological risks, including direct effects on gene programming as well as broader impacts on biological ageing (ie, 'how the environment gets under the skin'). At 8 weeks and 1 year postpartum, parents were invited to provide a DNA saliva sample from their infant (8 weeks: n=281 parents of 350 children; 1 year: n=223 parents of 276 children).
3. *Nested Observational Studies*: A subset of ATPG3 families attended a 60 min observational session assessing infant attachment security with Generation 2 parents at 1 year postpartum (n=249 parents of 312 children). The assessment involved administration of the Strange Situation Procedure (SSP),<sup>12</sup> the gold-standard assessment of infant attachment patterns. The ~20 min SSP comprises two separation and reunion episodes, the first separation occurring in the presence of a stranger, the second without the stranger to create a more demanding separation experience. Videotaped SSP data were analysed by certified coders using the coding scales for the Organised<sup>23</sup> and Disorganised categories.<sup>24</sup> Coding of parental caregiving behaviour was completed using a 25-item version of the Maternal Behaviour Q-sort<sup>25 26</sup> adapted for use with the SSP. Parental behaviour was scored by certified coders who are blind to the SSP attachment classifications. Parents also provided the infant's Victorian MCH Records, which contain prospectively collected information on a range of indicators of early child development including height and weight, cognitive and motor development, language skills, vision and vaccinations given since birth.

### Early and middle childhood assessments

Follow-ups during early and middle childhood are underway. *Life@4* assesses the health and well-being of parents and children, when children turn 4 years of age,.

Epidemiological assessments are based on a survey, either administered by CATI or web-survey, assessing the child's social and emotional development (including temperament, behaviour, physical health), parent physical and mental health and substance use, parent-child relationship quality, partner relationship quality and socioeconomic security. A nested observational assessment at age 4 (suspended in March 2020 due to the COVID-19 pandemic) included assessment of child attachment security, psychometric testing and several parent-child tasks. Height and weight data and DNA were also collected.

*Life@6* commenced in 2019 as a web survey which due to the demands of extended COVID-19 lockdowns has been redesigned as a data linkage wave to minimise respondent burden (see the Data linkage section). *Life@9* commenced in 2021 with a CATI or web-survey to be completed by G2 parents assessing the child's social and emotional development, including temperament, behaviour, physical health, and the family and socioeconomic context. To assess impacts of the pandemic on the health and well-being of ATPG3 families, brief web surveys were sent to Generation 2 parents in May-September 2020 and in October-December 2021. All Generation 2 cohort parents are invited to participate regardless of their carer status and where they are living.

### Data linkage

Linkage to existing administrative and educational datasets provides key information from other sources while minimising respondent burden. A birth assessment will be made by record linkage to the Victorian Perinatal Data Collection (VPDC), a State Government database that collects routine information on the mother and infant at the time of delivery. VPDC data are recorded by the consulting obstetrician or midwife and contain detailed information on the delivery, APGAR scores, and complications of pregnancy and some demographics. VPDC record linkage minimises respondent burden at the time of birth and maximises access to physician-recorded data.

Linkage to the Victorian School Entrant Health Questionnaire (SEHQ) is sought to assess parent-reported child and family psychosocial and physical health and educational factors on the transition to school. The SEHQ is administered through schools and includes the Parental Evaluation of Developmental Status,<sup>27</sup> Strengths and Difficulties Questionnaire<sup>28</sup> and family factors such as the experience of stressful life events, providing an assessment of socioemotional health and well-being at school entry.

Linkage to the National Assessment Program (Literacy and Numeracy; NAPLAN), a national assessment of academic development administered to students in years 3, 5, 7 and 9, will also be sought. This dataset provides national benchmarking data on language and numeracy development, administered by teachers in classrooms. NAPLAN linkage will provide key information on education outcomes under test conditions in primary and secondary school.

Linkage to the Australian Medicare Benefits Schedule and Pharmaceutical Benefits Schedule will also be sought. These administrative datasets provide detailed information on healthcare (medical services and prescription medicines) and will augment parent-reported health and medical survey data while minimising reporting and recall bias.

### Patient and public involvement

We did not include public involvement in the development or design of the ATP or ATPG3 studies.

### FINDINGS TO DATE

We have so far published on strong continuities of mental health and substance use. Specifically, data showed that the majority of Generation 2 mothers (81%) and fathers (83%) with perinatal depressive symptoms had a history of preconception mental health problems (prospectively assessed depression/anxiety).<sup>29</sup> We have also shown that for most mothers, perinatal alcohol (65%), tobacco (90%) and cannabis (59%) use is commonly preceded by preconception use, which was also prospectively assessed in adolescence and young adulthood.<sup>30</sup>

We have further shown important associations between prospectively assessed preconception parental mental health histories and relational and child outcomes. A history of persistent symptoms of depression or anxiety predicted poorer emotional bonding with infants at 1 year post-birth in both mothers and fathers ( $\beta_{\text{range}} = -0.42$  to  $-0.55$ ).<sup>31</sup> Higher levels of infant reactivity and behaviour problems were also observed in infants of mothers with a history of mental health problems in both adolescence and young adulthood compared with those without problems during these periods ( $\beta_{\text{range}} = 0.38$ – $0.52$ ).<sup>32 33</sup>

We have also examined pre-conception relational factors, finding that prospectively assessed attachment security in adolescence reduced risk for postpartum mental health difficulties ( $\text{OR}_{\text{range}} = 0.62$ – $0.55$ ),<sup>34</sup> and perceived social support assessed prospectively during both the preconception and postpartum periods enhanced relationship quality and social support during the COVID-19 pandemic ( $\beta_{\text{range}} = 0.11$ – $0.22$ ).<sup>35</sup>

### STRENGTHS AND LIMITATIONS

ATPG3 is unique in its three-generation prospective design with 15 waves of preconception data in females and males from infancy to adulthood (27–28 years) and comprehensive assessments of next generation offspring from pregnancy to early childhood. The ATPG3 Study is providing new opportunities to understand the role of parental life histories (from birth to adulthood) in structuring the environments within which their children (the next generation) will live and grow. It will also provide an opportunity to understand the role of grandparents in social and emotional development.

A striking feature of the original ATP cohort is the richness of preconception data available on G2 positive development, including repeated measures of constructs such as social competence, life satisfaction, volunteering, civic action and prosociality. This provides a rare opportunity to extend the scope of current research from prevention of disease and disorder to more extensive investigation of protective factors and positive pathways important to promoting a secure start to life. The project will also advance a new area of science investigating biological embedding of social exposures (epigenetics). Through a combination of cross-generation, cross discipline and cross method approaches, this study has the potential to transform the focus of policy and prevention directed towards promoting a healthy start to emotional life.

Important sources of bias common to all mature cohort studies should be considered. These can be broadly grouped under selection, measurement and confounding biases.<sup>36</sup>

### Selection biases

The cohort commenced as a representative sample of 2443 Victorian infants (aged 4–8 months) and their parents in 1983. Over 70% of ATP participants were still active in the study at commencement of ATPG3. Those participating in ATPG3 are broadly similar to those screened on baseline characteristics. However, compared with the original sample, families retained in the study are less ethnically diverse and have higher education levels and more skilled occupations. These trends are typical for longitudinal studies.<sup>37</sup> As noted above, loss to follow-up in ATPG3 has been exceedingly low with only five families withdrawing since commencement in 2012. However, participation in the pregnancy and 8 week surveys was lower than at 1 year due to difficulties recruiting prior to and soon after birth. Additionally, we only included infants born to participants aged 29–35 years, the peak reproductive years; it is possible that the profiles of older and younger parents are different. There is potential for selection bias due to non-random participation or missing data in ATPG3. To minimise bias due to missing data in the achieved sample, we used multiple imputation.

### Measurement biases

To reduce potential bias due to differential reporting (shared method variance), the study included multiple informants in the preconception period (parent, nurse, teacher and self-reports) and in the perinatal period (mother and father reports; observed data in our nested studies). A limitation common to intergenerational cohort studies is that prospective preconception information is available on only one parent within each family.

### Confounder bias

ATPG3 has access to a large set of potential confounders assessed over multiple decades. Specifically, the study has detailed, and repeated, assessments of socioeconomic disadvantage, family structure, country of origin and

significant life events. Additionally, when examining associations between antenatal factors and later outcomes within ATPG3, we can further adjust for relevant periconceptional and early antenatal confounds. However, there remains potential for bias due to unknown or unmeasured confounding and also confounding due to confounder measurement error.

## COLLABORATION

ATPG3 has yielded a large prospective three-generation cohort that will allow life course researchers to make significant contributions based on robust knowledge of social and biological pathways that link generations. Data will be stored indefinitely. While study protocols do not permit potentially re-identifiable participant data to be made publicly available, we welcome collaboration with the ATPG3 research team subject to appropriate permissions and ethical approval. Enquiries about collaboration are possible through our institutional data access protocol: <https://lifecourse.melbournechildrens.com/data-access/>. We have also established, and had funded, a new *Intergenerational Cohort Consortium*<sup>38</sup> that brings the ATPG3 together with two additional prospective intergenerational cohorts in Australia and New Zealand. This enables further capability for cross cohort data pooling, replication and thematic analysis. Overall, emerging findings from this programme of research point to the seminal (but often neglected) importance of the preconception period, and the need to invest in every age and stage of the early life course, from childhood to parenthood, to secure the foundations of the next generation.

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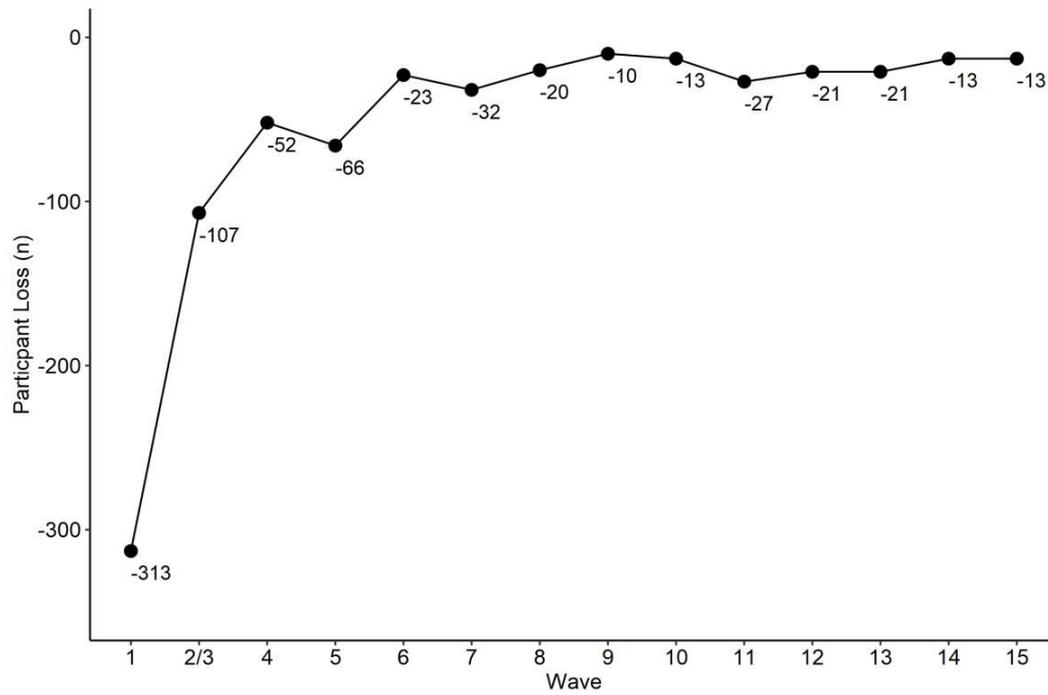
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Supplementary File Figure S1. Australian Temperament Project participant progressive loss to follow-up after each wave.

Note: waves 2 and 3 combined to account for the sampling procedures. Values represent the number of participants who were not engaged in the study after a particular wave (e.g., 313 after wave 1, 420 (313+107) after wave 3, and so on).