How are the kids?
Socio-economic gradients in the cognitive development of ART children

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Abstract

The wellbeing of children born after Assisted Reproductive Technologies (ART) has been highly debated in the last years and is generally looked at with concern by policy makers and the public opinion. Although evidence exists that ART can be linked to higher risks of adverse health outcomes at birth, ART children seem to do fine later on in life and sometimes even show a better cognitive development compared to naturally conceived children. Such findings might seem counterintuitive, however, different factors are likely to play a role in how ART children develop, with different and possibly contrasting effects.

Using data from the first 5 waves of the UK Millennium Cohort Study, this paper compares the verbal cognitive development (as measured by the British Ability Scale) of children born through ART and "naturally conceived" children up to the age of 11. Women undertaking ART represent a specific part of the population, with ART mothers being on average older, better educated, more likely to be in employment and married compared to the rest of the population. Growth curve models show that ART children seem to perform better compared to the average, but the effect almost disappears when controls for parental background are added. Furthermore, differences in cognitive abilities between the two groups of children decrease with older age of the child, to almost disappear at the age of 11.

1. Introduction

Since the first *in vitro birth* in 1978, more than 5 million babies have been born with the help of Assisted Reproductive Technologies (ART) worldwide, and the number of couples seeking ART is constantly increasing (ESHRE, 2012). As some of those ART "children" are now approaching adulthood and in light of the heated debates on how to regulate ART use, there is an urgency to increase our knowledge about the actual outcomes of ART births. The wellbeing of children and families born with the help of ART have generally been looked at with concerns about possible negative effects on the child's health (Van Balen, 1998; Hart and Norman, 2009a), but also because of fears related to the consequences of growing up in what have been defined as "new family forms" (Golombok, 2015), especially in case of gamete donations, where the child might not be genetically related to one or both parents (Golombok et al., 1995).

Other than the strictly medical and health issues, assisted reproduction raises some broader questions in term of ethical and social norms (Van Balen, 1998; Mills et al., 20104; Kamphuis, 2014). This results in a lack of coherence in regulations across countries, reflecting social norms and ethical and religious beliefs (Mills et al., 2014) rather than the wellbeing of future parents and children and often leaving important choices to the single clinics and doctors. But how do ART children develop later in life? Do they or their families actually differ from those who were conceived "naturally"? In fact, different mechanisms might play a role and have potentially contrasting effects on the development of children born after ART, and evidence about the overall outcome of these children later in life remains scarce (Ilioi and Golombok, 2014; Hart and Norman, 2009a and b; Wagenaar, 2008). Several studies have shown that the use of ART is linked to higher risks of adverse health outcomes at birth, such as multiple births, low weight, preterm delivery and birth defects (Hansen et al., 2013; Hart and Norman, 2013a; Van Balen, 1998; Wilson et al., 2011; Mills et al., 2014), which might lead to poorer development later in life (Myrskyla et al., 2012, Black, 2005). However, women and couples undertaking ART represent a particular part of the population that is a highly selective group in terms of socio-demographic background and because of the strong desire to have a child (Van Balen, 1998; Golombok et al., 1995). Both aspects might be related to specific ways of experiencing parenthood and investing in the children's development with likely positive effects that might overcome the health impact of ART.

Indeed, the few existing studies on the development of children born after ART seem to conclude that they do not show significant differences when compared to naturally born ones (Ilioi and Golombock, 2014; Wagenaar et al., 2008a), and some even found a better cognitive development of ART children (Carson et al., 2011; Mains et al., 2011) and higher quality of parent-child relationships in ART families (Golombok et al., 1995, Colpin, 2002). Although some scholars proposed that this "good" performance might be related to parental background, very few studies have looked at it in a broader perspective or tried to investigate the different mechanisms that might play a role (Golombok, 2015).

Economic, sociological and demographic literature have underlined the importance of parental background and investment on the children's development (Myrskyla et al., 2104; Goisis, 2014; Liu et al., 2011). Parents have been shown to differ consistently in their approach to parenting depending on age, educational level and socio-economic status (Brooks-Gunn and Markman, 2005; Lareau, 2002) and this has important effect on children's health and cognitive and non-cognitive development.

The argument of this paper is that different and potentially contrasting effects of the use of ART might act on the child's cognitive development. On one side, the average older age of mothers undertaking ART and the technique itself might lead to higher risks of poorer health outcomes at birth, such as low birth weight and premature birth, which are often associated with lower cognitive outcomes. On the other, the older age and the specific parental background that often characterise ART parents might be linked to higher resources and a parenting style focussing on the investment in the child's development and might therefore lead to higher cognitive skills.

Using data from the UK Millennium Cohort study (MCS), this paper studies the cognitive development up to the age of 11 of children born after ART compared to naturally born children and what factors affect it. Advantages of the use of the MCS survey is the richness of information about parental background, style of parenting and the parent-child relationship, that allows to explore the different mechanisms that might be playing a role in the child's development. Other main advantage of the MCS is the standardised ability tests (British Ability Scale II) that MCS members perform at each wave, which provides a reliable measure of cognitive skills.

Using both cross sectional regression models and growth curve models and including different sets of confounders-mediating factors one by one, this paper tries to identify the different factors that might play a role in the cognitive development of ART children and if this is different from the development of children born from a "natural pregnancy".

The paper proceeds as follows: the next section provides an overview of the existing literature about the outcomes of children born after ART, and Section 4 of the literature about the impact on parental background on children's development. Section 5 explains the theoretical framework adopted in the paper and develops the main hypotheses. Section 6 describes the dataset used in the analysis and the main measures. Section 7 describes the statistical approach adopted. Section 8 presents the results and Section 9 concludes and proposes some discussion.

3. Previous research on the outcome of ART offspring

In the last decades, a consistent amount of literature has studied the medical outcomes of children born with the help of ART (see Hart and Norman, 2013a for a review). Concerns about the health conditions of these children are related both to the parent's health and age and to the treatment itself (Hansen et al., 2013). Others have stressed the possible effects related to the experience of infertility and the stressful treatment on parents' wellbeing and the development of their relationship with the child (Van Balen, 1998; Colpin, 2002), with negative influences on the psychological development of the child (Golombok, 1995; Colpin, 2002).

3.1 Health outcomes

There is consistent evidence that ART can be linked to adverse health outcomes at birth. Literature has shown that ART children have higher risk to be born prematurely, to have low birth weight and to present birth defects (Hansen et al., 2013; Van Balen, 1998; Wilson et al., 2011). This is partly due to the consistently high proportion of multiple births among ART births, which is considered as a main risk of ART (Fauser et al., 2011), but higher probabilities of adverse outcomes have also been observed among singleton babies (Hansen et al., 2013; Wilson et al. 2011). However, most existing studies showed no significant differences in physical growth and development after the perinatal period between children born after ART and spontaneously conceived ones (Wilson et al., 2011; Van Balen, 1998). Some found a slight increase in the risk of cerebral palsy in children born from IVF, however the effect disappeared after adjustment for low birth-weight and pre-term birth (Hart and Norman, 2009a).

3.2 Psychological development

The effects of fertility treatment might go beyond the immediate impact on the new-born child's health and are likely to affect children's outcomes later in life (Wilson et al., 2011; Hart and Norman, 2009b). ART treatments involve a number of processes that are very different from a spontaneous conception and this has the potential for the disturbance of early developmental processes (Wilson et al., 2011). Recent studies demonstrating changes in gene imprinting from in vitro culture to embryos raise concerns about the effects on the IVF on the children's development (). The full implications of imprinting defects are currently unknown, but there is evidence of a link between several imprinting genes and cognitive and neurological development which justify longer follow up studies (Mains et al., 2010). As several authors note, though, such studies are still very limited (Golombok et al., 1995; Mains et al., 2010).

However, despite the possible poorer health conditions at birth, ART children do not seem to differ significantly from naturally born ones in the way they develop later in life. Multiple investigations have shown that people born through ART function well in childhood concerning psychological well-being (Ilioi and Golombock, 2014; Wagenaar et al., 2008a), and no differences were found in the rate of children with developmental disorders (Wagenaar et al., 2008; Hart and Norman 2009a), nor in the behaviour and socio-emotional functioning compared to control groups (Hart and Norman, 2009b). Other studies have found that ART children have higher probabilities of experiencing behavioural problems (Carson et al. 2013).

3.3 Cognitive development

Studies about the development of cognitive abilities of ART children remain scarce. However, the existing ones show that, in general, children born after ART do not present particular problems in their cognitive development (Hart and Norman, 2013b). Some studies even found that children born after IVF or ICSI have a faster cognitive development compared to naturally born children (Mains et al, 2010; Carson et al., 2011). A study among the 20 first Australian IVF infants showed that they developed faster than the other children (Lancaster, 1987). However, the authors argue that the effect should not be attributed to the treatment itself, but rather to the specific characteristics of the first parents who were eligible for such techniques at the time (highly educated and well-motivated parents). Similarly, Mains and colleagues (2010) found that IVF offspring scored higher on standardised test than a group of matched peers in Iowa. They also showed that among other factors maternal age, parental education, child's BMI and parents' divorce affected the score. Of particular interest is a recent study by Carson and colleagues (2011) that examined the effect of pregnancy planning, fertility and assisted reproductive treatment on cognitive outcomes on children respectively at age 3 and 5, using data from the UK Millennium Cohort Study. Their findings show that children conceived through ART perform better in cognitive tests related to verbal skills with respect to "planned children" (children born as the result of what was defined an "intended" pregnancy by their parents), while they show lower scores in non-verbal tests and in spatial ability tests. The authors suggest that this might be due to the generally advantageous socio-economic position of couples undertaking assisted reproduction, which might have the greatest effect on language skills. This hypothesis is reinforced by the finding that "unplanned" children (born from an "unintended" pregnancy) tend to have significantly lower scores in the ability tests compared to planned ones, which would suggest the importance of a different investment in children. However, the authors do not further explore the impact of parental background and investment.

4. Parental Background and children development

The strong impact of the demographic and socio-economic characteristics of parents on their offspring development has been extensively studied in sociological, demographic and economic research. Although a complete review of such literature goes beyond the scope of this paper, it is important to underline the importance of considering such effects when looking at the development of children born after ART. The average older age and higher SES status that often characterise mothers and couples who undertake ART are likely to have an important influence on how their children development and need to be considered when studying the effects of ART on the child's development.

Maternal age and child development

The impact of parental age on children's outcomes has been widely explored in light of the continuous trend of fertility postponement that has occurred in the recent decades. Overall, the literature seems to agree on a negative impact of older parental age on the health outcome of the newborn children, but also on the positive effects of higher educational level and social status usually linked to it (Myrskyla et al., 2104; Goisis, 2014; Liu et al., 2011).

Both very young and advanced parental age were shown to have negative effects on health at birth: higher risk of miscarriages, stillbirth and infant mortality have been observed among teenage and older mothers (Myrskyla, 2014). The link between parental age and intelligence is less clear, but several studies showed that paternal age is often connected to better cognitive development and IQ scores (Liu et al., 2011). This is usually explained by the relationship with socioeconomic status, which has an influence on the child's environment (readiness for parenthood, energy, networks, preferences) and leads to a higher investment in children (Bradley and Corwyn, 2002). In the same direction, the findings of Goisis (2014) demonstrate that higher social status associated with fertility postponement compensates for increased risks of health complications that accompany later childbearing.

In what she defines the "diverging destinies" framework, MacLanahan (2004) argues that the trends associated with the second demographic transition have lead to greater disparities in children resources, with most educated parents gaining parental resources by delaying childbearing.

Parenting style

Parenting style is an important channel through which parental background impact the development of the child (among others, Gauthier et al., 2004; Brooks-Gunn and Markman, 2005). The term parenting encompasses the hundreds of activities that parents engage in either with or for their children, and scholars have adopted very diverse approaches and measures to study the way parents invest in their children. Parents differ in their social, economic and educational background, and scholars are unanimous in asserting that variations in parenting are associated with such characteristics (Brooks-Gunn and Markman, 2005). That parenting is influenced by social class in well known since the late fifties (Kohn, 1959). Literature has showed a link between parental talking (which is highly connected to education) and children's vocabulary (Brooks-Gunn and Markman, 2005) and a social gradient in the hours spent by parents with children in different activities (Kalil et al, 2012; Gauthier et al., 2004).

Lareau (2002) and then Cheadle and Amato (2010), introduced the idea of "concerted cultivation" meaning an approach that considers it crucial for the children to be involved in several organised activities expected to arm them with important life skills, a stress on the use of the language and the development of reasoning and talking as a preferred form of discipline. The approach is considered to be specific to middle- and upper class, in contrast to working- and lower class parents who are more inclined towards "natural growth" (Lareau, 2002).

An interesting theoretical model on the development of different parental style is provided by Belsky (1984), who maintains that parenting is affected by parent's work, social network, personality, marital relations, and the child's characteristics. This is in line with the general idea of parenting being influenced by socio-economic conditions and experience, and adds an interesting point for the purpose of this study, namely, the impact of the characteristics of the child on the development of parental style. All of these findings provided by the literature point to the direction of a likely important channel through which the experience of ART might be influential in the development of children.

5.Theory and Hypotheses

Several factors are likely to affect the development of children born after ART, possibly with very different effects, and make it hard to predict what the overall outcomes of ART births will be. This paper proposes a theoretical framework trying to take into account the different mechanisms that might play a role, first of all the impact of parental background. On one side, ART is linked to an increased risk of poorer health conditions (Hansen et al., 2013; Van Balen, 1998; Wilson et al., 2011), which might negatively affect the subsequent development of the child (Black, 2004; Myrskyla et al., 2012). There is evidence that preterm birth, low birth weight and other labour complications have negative effects on children's outcomes at later ages, from health conditions to educational attainment and even lower income (among others, Black at al., 2004). On the other side, the favourable parental characteristics of ART parents might act as a counterbalancing factor, leading to a positive development of ART children. A consistent literature has shown that parental age and socioeconomic characteristics have a strong impact on the child's development (among others, see Heckman, 2006; Cunha and Heckman, 2010) and generally agrees on an overall positive effect of older, highly educated parents on the child's health and wellbeing, that counterbalances the possible poorer health conditions linked to older ages at childbearing (McLahanan, 2004; Goisis, 2014; Myrskyla et al., 2012). We hypothesise that a similar mechanism might be acting in the development of ART children, who are likely to benefit from the specific characteristics of parents who undertake ART. In addition, due to the experience of infertility and fertility treatment, ART parents might develop a specific way of parenting and parent-child relationships (Golombok, 1995; Colpin, 2002) characterised by higher levels of warmth and a greater investment in the child's development (Golombok, 2015). In light of the existing literature, the following hypotheses are proposed about the cognitive development of ART children and the factors influencing it:

H1.1: ART births are more likely to be connected to negative health outcomes at birth such as low birth weight, preterm delivery, multiple births.

H1.2: Poorer health outcomes at birth connected to ART will be negatively associated with cognitive scores, leading to a negative impact on ART children's cognitive skills

H2.1: ART parents will differ from natural parents in the age at childbearing and socioeconomic conditions

H2.2: Parental background that characterises ART parents (older age at childbearing, higher educational level and income) is positively associated with cognitive ability in a way that counter-balance the negative effects linked health problems.

Therefore, our general hypothesis is that, overall, ART children will benefit from the positive effects of being born and raised by older, highly educated and high income parents and that this will be reflected in a good cognitive development of ART children compared to the one of naturally conceived peers.

H4: ART children will perform better in cognitive ability tests when compared to naturally born children

We don't directly consider in this study the potential effect of specific parenting styles that might be adopted by ART parents, although we do acknowledge that this is likely have a role in the development of children born after ART. By focussing on the parental back-ground, we implicitly consider that this might be related to specific way to approach parenting with potential positive effects on children's cognitive development.

6. Data

The Millennium Cohort Study is a nationally representative prospective cohort study of 18552 families across the UK. A random two-stage sample of all infants born in 2000-2001 and resident in the UK at 9 months was drawn from the Department of Social Security Child Benefit Registers. Ethnically diverse and disadvantaged areas were oversampled to ensure adequate representation. Baseline interviews captured sociodemographic and health information, including questions about pregnancy and fertility treatment. Following up surveys were conducted in 2003, 2005, 2007 and 2012. The surveys cover different topics such as health, development, behaviour, wellbeing, parenting in a detailed way, and information about their siblings and parents is collected as well.

This represents an advantage when compared to registered data, that do not include such kind of information about the environment where the child lives.

In this paper we only consider children born from either married or cohabiting parents, to avoid comparisons with lone mothers. We only include the ones who have available information for at least one of the waves after the first one, which leaves us with a final sample of 13,612 observations.

7. Measurements

The paper studies the cognitive development of children born through ART compared to children that were conceived naturally. The dependent variable is the child's verbal cognitive ability as measured in MCS waves 2-5, from the age of 3 to the age of 11. Main explanatory variable is whether the child was born with the help of one of the two main fertility treatment, IVF or ICSI. Different kinds of confounders/mediating factors are included in the analysis step by step, and will be explained in detail in the following sections.

Cognitive abilities

Children's cognitive development is assessed with three sub scales of the British Ability Scales, second edition (BAS II). The standardised tests undertaken by the cohort members to assess their cognitive skills and educational attainment is one particularly valuable element of the Millennium Cohort Study (Connelly, 2013). The BAS II is a battery of twelve core sub-tests of cognitive ability and educational achievement, suitable for children aged from two years and six months to seventeen years and eleven months. It has demonstrated sound validity and test-retest reliability (Elliott et al., 1997). The MCS cohort members have completed four of the BAS sub-tests. At age 3 MCS (wave 2) members completed the naming vocabulary component, which assesses verbal ability. This was repeated at age 5 (wave 3) together with the picture similarities and pattern construction components, which measure non-verbal and spatial abilities, respectively. The patterns construction component is repeated at age 7 (wave 4) together with a word reading test. At age 11 (wave 5), a Verbal similarity test is assessed.

To remedy the problem of comparability of test scores across different sets of items, in the MCS raw scores are converted into standardised scores. These are also adjusted to take into account the different ages of the MCS cohort members, a particularly important feature since MCS cohort members are born throughout the year and might then differ in their ability score for this reason (Connelly, 2013). Therefore, standardised scores indicate how a child's cognitive abilities have developed relative to his/her peers (Carson et al., 2001). In this work, standardised scores of the BAS II sub-tests measuring verbal ability undertaken by MCS cohort members are considered.

Explanatory variables

The main explanatory variable is wether the child was conceived with the help of ART. The two main kinds of fertility treatments are considered into the category, IVF and ICSI. In the MCS baseline interview, 186 mothers declared to have conceived after Assisted Reproductive Treatments (125 IVF and 61 ICSI) and 264 conceived with the help of Clomiphene Citrate, an ovarian inducing drug (OI). In the models, the effect of being born through ART is captured with a dummy variable (*ART*) taking value 1 if the child was conceived with the help of one of the two techniques, and 0 otherwise. The impact of being born with the help of OI is also considered with another dummy variable (*OI*).

Three main sets of confounders/mediating factors are included in the analysis: child's characteristics at birth, parental age and health characteristics and parental socioeconomic background. Basic demographic characteristics of the child include gender, age and whether the she/he was the result of a multiple birth (dummy variable *twin*). A first set of explanatory variables concerns the outcomes at birth: whether the child had low birth weight (*LBW* taking value 1 if the child's weight is lower than 2.5) or was born prematurely (*premature*) or through caesarian section (*caesarian*), and parity (*first born*). A general variable on whether the mother has experienced any problem during pregnancy is included. All information about the pregnancy outcomes are reported by the mother in the first wave. The second set includes the age of the mother at childbearing and a measure of self reported health, assessed on a 1 ("excellent health") to 4 ("poor health") self-reported scale. Parental socioeconomic characteristics include employment status of the mother (*employed, housewife*), partnership status (*married, cohabitant, single*), mother's education (*high education* if the mothers has high secondary or higher educational level), a measure of socio-economic status (*high SES,* based on the NS SEC classification), and a measure of deprivation (*OECD 60%* if the household income is lower than the OECD 60% median). All individual controls are time-invariant factors and the information is provided by parents' in the first wave.

8. Statistical Methods

First of all, descriptive statistics are provided to show the parental socio-demographic background and characteristics at birth of the MCS members and their performances in the BAS standardised sub-scores at the different waves. Two tailed t-tests are used to test whether the differences in parental characteristics and cognitive skills between ART and non-ART children are statistically significant.

To study the development in time of the MCS members' verbal cognitive skills and whether significant differences exist between ART-born and naturally-born children, first we show the average patterns of BAS tests results at the different waves on the sample divided by kind of birth. Growth curve models are then implemented to study the impact of time, ART birth and other factors both on the baseline and slope of the cognitive growth. Growth curve models are a special kind of random-coefficient models where it is the coefficient of time that vary randomly between subjects. This kinds of models, also sometimes referred to as *latent-trajectory models* or *latent growth-curve models*, have recently become very popular for the study of longitudinal data as they allow for the analysis of *inter-individual differences in intra-individual change* (Rabe, 2007). An advantage of such models is also that observations can be unbalanced, meaning that it is possible to include children for whom the observation at one wave is missing (Rabe, 2007).

The general expression of growth curve model is the following:

*Level 1: Yij= P0i + P1i*timej + eij*

Level 2: P0i= V00+S0i   P1i= V10+S1i

Where V00 and V01 represent the fixed part of the model, i.e. the predicted population mean intercept and mean slope, and S0i and S1i represent the random intercept and slope, i.e. the individual variability from the mean predicted average intercept and slope.

We first implement a set of empty models showing the effect of time (linear and quadratic) on the dependent variable to choose the optimal functional form of the trajectory over time-. A comparison of model fits between different specifications of the growth curve models (Akaike IC-AIC- and Bayesian IC -BIC- criteria[1], Table 4) suggests that a quadratic random effect model might be the best time metric for our model. Once the optimal baseline growth curve model has been established, we start including predictors. The different sets of regressor are included in the model one at a time, and the effect of these both on the initial cognitive level and on the growth rate (slope) are studied. Here the initial cognitive level refers to its first observation, when the children are 3 years old. Our main interest lies in the coefficients of ART, showing the effect of ART birth both on the baseline (cognitive ability at age 3) and on the growth slope.

A general specification of our model is then:

Model (1) : *COGij = B1 + B2*ART + B3*ART*t + B4*tj + B5*tj2 + B6* X + S1ij + S2ij*tj + ei*

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[1] AIC = -2LL + 2(n parameters)
BIC = -2LL + log(N)(n parameters)
Are measured of “deviance” statistics: smaller values are to be preferred.

where B2 will give us the effect of ART birth on the initial cognitive abilities (at age 3), B3 is the effect of ART birth on the growth rate of cognitive skills, B4 and B5 are the linear and quadratic fixed effects of time and S1 and S2 are the random intercept and slope. X is a vector including individual controls. Different sets of control variables are included one at a time in the models, including first basic demographic controls, then characteristics at birth and finally parental background characteristics. All predictors included in the models are time-invariant and the characteristics were measured at the first wave. The coefficients will then predict the random component of the growth trajectories to determine which variables are associated with individual showing higher or lower intercepts or steeper versus flatter slopes. All analyses were also performed only considering individuals for whom observations were available at all waves, with very similar results except for a loss in statistical significance.

9. Results

Table 1 shows descriptive statistics of the sample considered in the study, divided by whether the child was conceived through ART or not. The stars indicate whether the difference is statistically significant according to a two-tailed t-test. As expected, parents who conceived through ART seem to differ from "natural parents" in relation to several characteristics. They are on average older and more likely to be married, and ART mothers have on average a higher educational level and higher probability to be employed with respect to natural mothers, half of whom is not in work. ART parents are also more likely to belong to the highest UK income quantile and to belong to a higher socio-economic class. Self-reported health conditions of mothers are quite similar among the two groups, with a slightly higher proportion of ART mothers who declared to have excellent or good health conditions, which is not statistically different from non-ART mothers. As expected, ART children have higher probability of being born from a multiple pregnancy and of having low weight at birth (<2.5 Kg). Surprisingly, no ART children in the sample were born preterm of through a Caesarian section.

These descriptive results seem to confirm our hypothesis that ART parents belong to a selective part of the population (*HP 2.1.*), and they partly confirm the hypothesis about poorer health outcomes at birth of ART children (*HP 1.1.*). The very high proportion of married couples among the ART parents is particularly interesting in light of the highly discussed issue of ART and "new family forms" (Golombok, 2015). Indeed, despite the idea that families born with the help of IVF would intensify the existing trend of expansion of "non-standard" families, for the time being it seems that ART families tend to be of a very "traditional" type. These first results suggest that it is worth to study the development of ART children in light of the particular family conditions that they are likely to experience.

Table 2 shows the standardised ability scores of BAS tests measuring verbal ability at each wave (*naming vocabulary test* at age 3 and 5, *word reading test* at age 7, *verbal similarity test* at age 11), for ART and naturally-born children. ART born children on average perform better up to the third wave (age 7) and the difference is statistically significant (at 5% confidence), while there is no significant difference in the fourth wave (age 11). The finding about a difference in the cognitive scores up to the age of 7 is in line with what found in the literature (Carson et al., 2011), but is particularly interesting to notice that it disappears in the fifth wave, suggesting a convergence in the performances of ART and naturally-born children. These results would suggest, then, that it is worth studying the dynamic development of verbal cognitive skills in the two groups of children and the factors affecting it.

Figure 1 and 2 display the average cognitive development from age 3 to age 11 of ART and non-ART children (both genders together and separately by gender, respectively). A similar pattern to the one emerging from the previous descriptive table can be observed, with ART children (and especially females) starting with significant higher cognitive skills at early ages, but then converging to very similar level at the last observation. The drop in cognitive abilities which seems to occur at Wave 4 is hard to interpret, but might be linked to the different nature of the BAS test performed at this specific age and is reflected by the density distributions of BAS scores at each age (available in the Appendix). All the following analysis were also performed without considering the observation of cognitive skills at wave 4 and showed very similar results.

Tables 3 and 4 show to what extent the models with different time metrics account for variance in the outcome and the model fit comparisons. The first model is the most basic form of growth curve model, a random intercept-only model. Model (2) includes a linear random slope for the time and model (3) and (4) include respectively a fixed quadratic and a fixed random effect for time.

Table 5 displays the results of the growth curve models, that we use to study the effect of ART, parental characteristics and health outcomes at birth both on the "initial level" of cognitive development (age 3 in this case) and on the growth rate. These are all quadratic random intercept growth curve models where the different sets of predictors are included one at a time. The coefficients of the variables represent the impact of the regressors on the initial cognitive skill and the coefficients of the interactions between regressors and time represent their impact on the growth rate. The adjustment for age in the standardised scores is made within three months age and there may still be variation in the cognitive development of the cohort members within the same age group. For this reason, the age of the child (in months) is included in the models. Model (5) includes the basics characteristics of the child (gender, age) and the way of conception (if born through ART or not). Models (6) include parity, health outcomes at birth (low birth weight, multiple birth, preterm birth) and whether the child was conceived with the help of Ovarian Inducing drugs. Mother's age and self-reported health (dummy measure with value 1 for good or excellent health), whether the child was born after a planned pregnancy and whether he/she was ever breastfed and the different parental background characteristics are included in Model (7).

The results of the growth curve models seem to confirm what suggested by the descriptive results and give support to our hypotheses (*HP 2.2* and *HP 4*). They also add further insights on the impact of different factors on the children's verbal cognitive development in time. Being born though ART is significantly associated with a higher level of cognitive skills when these are first measured (age 3). This impact partly decreases when controls for the outcomes at birth are included in the model, but remains significant and the value of the coefficient is high (model 6). Both the magnitude and the significance of the effect decrease consistently in model (7) when controls for parental background are added, suggesting that most of the “ART effect” might be linked to parental characteristics. On the opposite, the effect of ART on the growth rate is slightly negative and significant in the first two models, in line with the convergence in ability already observed in the first part of our analysis.

A similar “convergent” pattern is followed by some of the parental background factors and characteristics at birth, which tend to have a consistent positive impact on the cognitive “baseline”, but a small negative impact on the rate of growth. For instance, being first born has a strong and positive impact on the initial level of cognitive skills, but the coefficient of the interaction with time is slightly negative, suggesting that the differences decrease with the age of the children. Interestingly, the coefficients of *female* are very similar. The same is true for having a highly educated and employed mother, or for parents belonging to a high socio-economic class. Such results are in line with previous literature showing a positive impact of older, highly educated and high income parents on the offspring cognitive development, but would suggest that such effects are mainly important in the children’s early year of life. A low birth weight seems to have the opposite effect, with a strong and negative coefficient on the initial ability level, but lightly positive on the growth rate. Low household income is also connected to significantly lower cognitive skills, but again with the effect decreasing over time.

Table 1. Descriptive statistics, naturally born and ART children

	Natural	ART
Parental characteristics		
Mother age	29.15	33.32 *
Father age	30.95	35.82
Married (%)	70.73	92.65 ***
Cohabitant (%)	29.26	7.34
Planned pregnancy (%)	62.3	100 ***
Mother's high education (%)	38.13	45.76 ***
Income (first quintile, %)	18.79	35.59 ***
Income (below OECD 60%)	27.08	11.86 ***
High SES (%)	30.27	42.93 ***
Mother employed (%)	47.50	59.32 ***
Mother housewife (%)	49.43 ***	34.44
Mother healthy (%)	83.74	84.4
Ever breastfed (%)	70.76	82.48 ***
English first language at home (%)	84.11	91.15 *
Birth outcomes		
First born (%)	40.11	73.42 ***
Twin (%)	2.31	32.76 ***
Triplet (%)	0.01	6.77 ***
Low Birth Weight (< 2.5 Kg, %)	5.19	20.9 ***
Premature birth (%)	0.019	0.0
Caesarian section (%)	0.06	0.0
Problems during pregnancy (%)	37.84	46.89 **

10. Conclusions and discussion

In this study descriptive results, cross sectional analysis and growth curve models all point out in the direction of a positive association between ART birth and children verbal cognitive abilities as measured by the BAS scale. The effect is strong when cognitive abilities are measured for the first time, at the age of three, but consistently decreases with time to almost disappear at the last observation, when the children are 11 years old. This “ART-effect” appears to be partly due to the significantly different characteristics of ART parents, on average older, better educated and with higher income, but it is still persistent (although significantly reduced) even after controls for parental background are included. Furthermore, ART is overall associated with higher cognitive skills despite the negative impact of negative outcomes at birth, also associated with ART.

These results are in line with the existing literature and seem to confirm our hypotheses of an overall positive impact of the specific characteristics of women and couples undertaking ART on offspring cognitive development, that overcome the negative effects related to negative outcomes at birth. Of particular interest and more difficult to interpret is the convergence in time of ART and non-ART children cognitive skills.

Table 2. BAS sub-tests standardised scores of naturally conceived and ART-children

	Natural	N	ART	N	Difference
BAS (S2) Naming Vocabulary	50.03	11640	53.05	141	-3.01***
BAS (S3) Naming Vocabulary	54.51	11955	57.90	152	-3.38***
BAS (S4) Word reading	49.75	9544	52.60	124	-2.85*
BAS (S5) Verbal similarity	59.14	10496	59.69	130	-0.55

Figure 1. Average cognitive development of ART and non-ART children

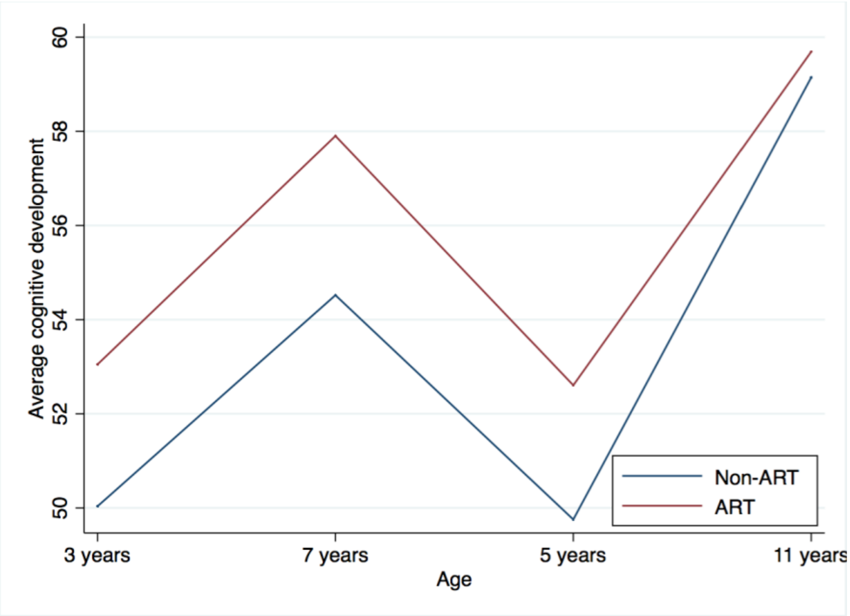

Figure 2. Average cognitive development of ART and non-ART children. Divided by gender

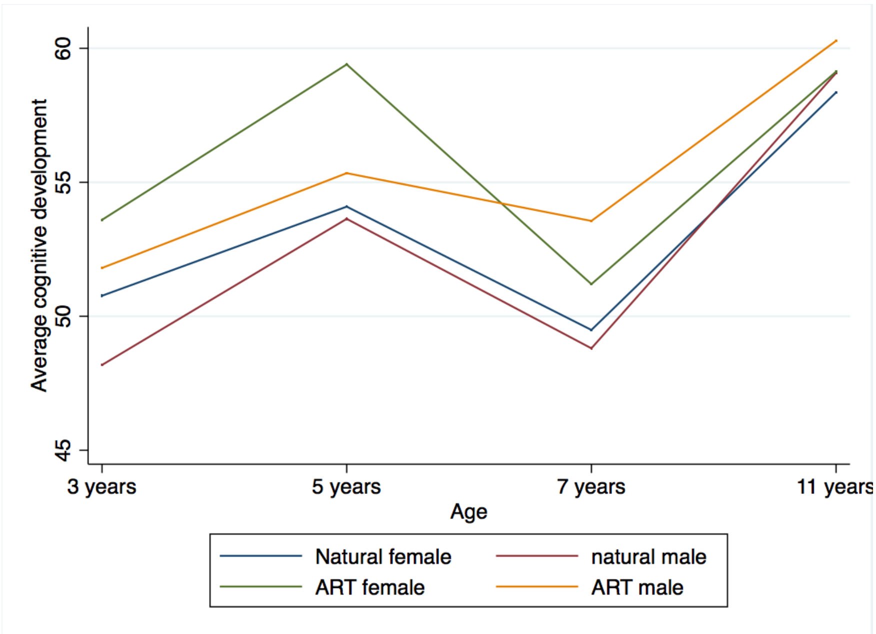

Table 3. Growth curve models on BAS verbal ability scores, wave 2-5

	Model (1)	*Model (2)*	*Model (3)*	*Model (4)*	*Model (5)*	*Model (6)*	*Model (7)*
var(cons)	38.5972	40.37487	41.0148	41.0148	40.86232	38.67529	27.03729
var(time)		2.57E-13	2.81E-13	1.07E-17	9.29E-17	7.88E-16	5.91E-12
var(time2)				1.64E-20	1.45E-19	9.83E-21	5.83E-14
var(residuals)	119.0699	110.8817	109.3013	109.3013	108.9374	109.1357	108.0581

Model (1): Empty model
Model (2): Linear random intercept model
Model (3): Quadratic fixed linear random intercept model
Model (4): Quadratic random intercept model
Model (5): ART and basic demographic predictors model
Model (6): ART, demographic and outcomes at birth predictors
Model (7): ART, demographic, outcomes at birth and parental background predictors

Table 4. Model fits comparison

Model	**Observations**	**LL**	**AIC**	**BIC**
(1) Empty model	44182	-173077.6	346161.2	346187.2
(2) Linear	44182	-171908.6	343827.2	343870.7
(3) Quadratic fixed, linear random time effects	44182	-171699.8	343411.7	343463.9
(5) Quadratic fixed, quadratic random time effects	44182	-171699.8	343405.7	343431.8

Table 5. Growth curve models on BAS verbal ability scores, wave 2-5

	Model (4)	Model (5)	Model (6)	Model (7)
Time	-5.001***	-4.535***	-4.294***	-4.383***
	(-14.06)	(-12.67)	(-11.36)	(-11.23)
Time2	1.034***	1.034***	1.007***	1.025***
	(20.51)	(20.56)	(18.99)	(19.36)
Age		0.0869	0.154	0.0625
		(0.61)	(1.04)	(0.44)
Female		3.963***	4.519***	4.466***
		(11.58)	(12.80)	(12.77)
Female*time		-0.932***	-1.026***	-1.023***
		(-10.34)	(-10.87)	(-10.87)
Twin		-2.542*	-1.354	-1.135
		(-2.36)	(-1.78)	(-1.38)
Twin*time		0.503	0.319	0.210
		(1.76)	(1.31)	(0.89)
ART		6.252***	5.221**	3.805*
		(3.90)	(2.37)	(1.87)
ART*time		-0.991*	-0.877*	-0.760
		(-2.36)	(-1.63)	(-1.50)
First born			4.898***	2.269***
			(12.75)	(9.18)
Firstborn*time			-0.600***	-0.229*
			(-5.86)	(-4.00)
LBW			-5.341***	-3.592***
			(-4.86)	(-4.08)
LBW*time			0.761***	0.576**
			(2.48)	(2.25)
Premature			-3.990	-3.832
			(-0.98)	(-0.95)

Table 5. Growth curve models on BAS verbal ability scores, wave 2-5

	Model (4)	Model (5)	Model (6)	Model (7)
Premature*time			0.633	0.470
			(0.58)	(0.43)
OI			2.147	1.115
			(1.62)	(0.86)
OI_time			0.0381	-0.0206
			(0.11)	(-0.06)
Planned pregnancy				0.989**
				(2.68)
Planned*time				-0.0940
				(-0.90)
Mothers age				0.226***
				(6.32)
Mum age*time				-0.177**
				(-1.85)
Mother's high education				2.611***
				(6.59)
Higheduc*time				0.135
				(1.27)
Employed mother				2.574***
				(9.22)
Employed*time				-0.684***
				(-7.00)
Married parents				-3.288***
				(-2.11)
Married*time				0.783***
				(7.38)

Table 5. Growth curve models on BAS verbal ability scores, wave 2-5

	Model (4)	Model (5)	Model (6)	Model (7)
OECD 60%				-7.990***
				(-17.65)
OECD 60*time				1.060***
				(8.73)
High SES				2.890***
				(6.98)
High SES*time				-0.203
				(-1.83)
_cons	56.849***	54.06***	52.59***	50.45***
	(98.17)	(37.42)	(34.91)	(33.71)
N	44182	44182	44158	44059

Table 6: Intraclass correlation coefficient

COG	ICC	[95% Conf. Interval]	
Individual	.2717323	.2595759	.2840454
Average	.5987941	.5837338	.6134438

Random effects: id Number of targets = 7475
Fixed effects: time Number of raters = 4

F test that ICC=0.00: F(7474.0, 22422.0) = 2.49 Prob > F = 0.000

Note: ICCs estimate correlations between individual measurements and between average measurements made on the same target.

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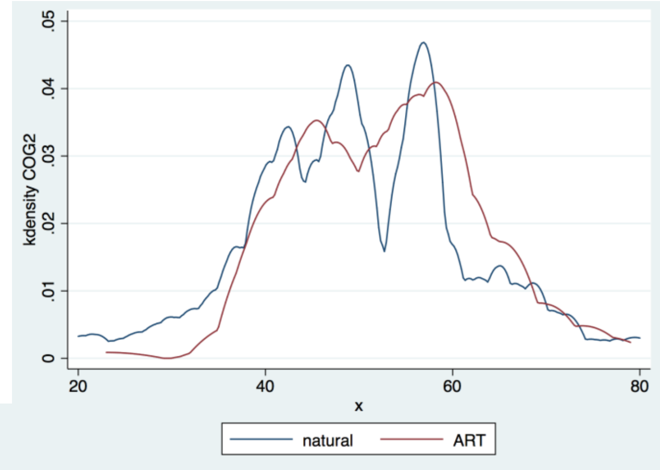
12. Appendix



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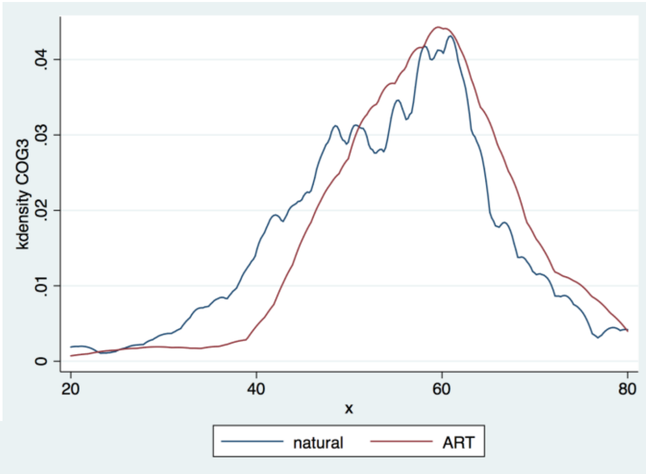

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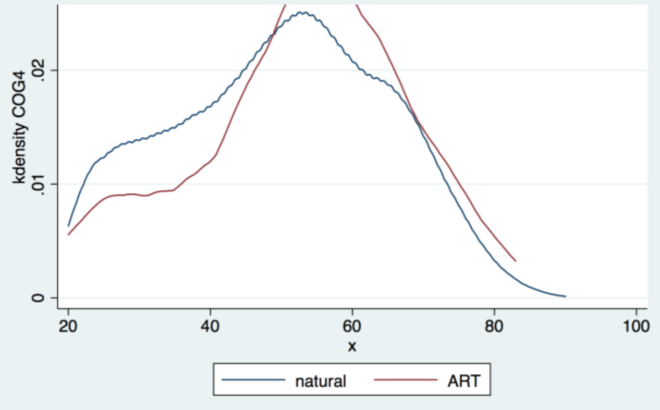

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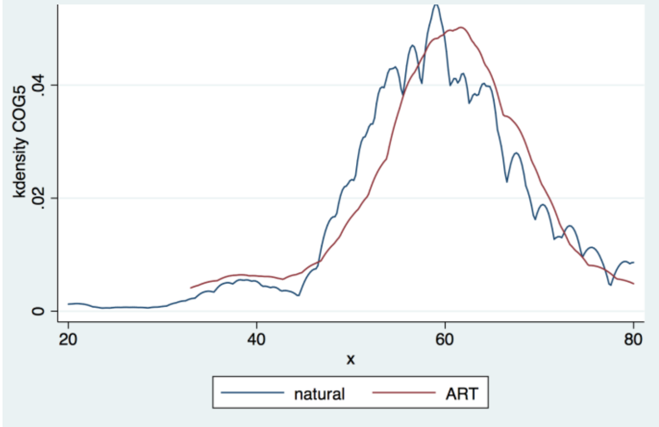

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