First 1000 days: enough for mothers but not for children? Long term outcomes of an early intervention on maternal depressed mood and child cognitive development: Follow up of a randomised controlled trial

Mark Tomlinson [1,2*], Sarah Skeen[1], GJ Melendez-Torres[3], Xanthe Hunt[1], Chris Desmond[4], Barak Morgan[5], Lynne Murray[6], Peter J Cooper[6], Sujit D Rathod[7], Marguerite Marlow[1] & Pasco Fearon[8]

1. Institute for Life Course Health Research, Department of Global Health, Stellenbosch University, Stellenbosch, South Africa
2. School of Nursing and Midwifery, Queens University Belfast, Belfast, Northern Ireland, UK
3. Peninsula Technology Assessment Group, University of Exeter Medical School, Exeter, UK
4. Priceless, School of Public Health, Wits University.
5. Global Risk Governance Programme, Institute for Safety Governance and Criminology, Law Faculty, University of Cape Town, South Africa
6. School of Psychology and Clinical Language Sciences, University of Reading, Reading, UK
7. Department of Population Health, London School of Hygiene and Tropical Medicine, UK
8. Developmental Neuroscience Unit, University College London, UK

*Corresponding author

Abstract

Background: Child cognitive development is often compromised in contexts of poverty and adversity, and these deficits tend to endure and affect the child across the life-course. In the conditions of poverty and violence that characterise many low- and middle-income countries (LMIC), the capacity of parents to provide the kind of care that promotes good child development may be severely compromised, especially where caregivers suffer from depression. One avenue of early intervention focuses on the quality of the early mother-infant relationship. The aim of this study was to examine the long term impact of an early intervention to improve the mother-infant relationship quality on child cognitive outcomes at thirteen years of age. We also estimated current costs to replicate the intervention.

Method: We re-recruited 333 children from an early childhood maternal-infant attachment intervention, 'Thula Sana', when the children were 13-years old, to assess whether there were impacts of the intervention on child cognitive outcomes, and maternal mood. We used the Kaufman Assessment Battery to assess child cognitive development and the Patient Health Questionnaire (PHQ-9) and the Self-Reporting Questionnaire (SRQ-20).

Results: Effect estimates indicated a pattern of null findings for the impact of the intervention on child cognitive development. However, the intervention had an effect on caregiver psychological distress (PHQ-9, ES=-0.17 [CI: -1.95, 0.05] and SRQ-20, ES=-0.30 [CI: -2.41, -0.19)), but not anxiety. The annual cost per mother-child pair to replicate the Thula Sana intervention in 2019 was estimated at ZAR13,365 ($780).

Conclusion: In a socio-economically deprived peri-urban settlement in South Africa, a home visiting intervention, delivered by community workers to mothers in pregnancy and the first six postpartum months, had no overall effect on child cognitive development at 13 years of age. However, those caregivers who were part of the original intervention showed lasting

improvements in depressed mood. Despite the fact that there was no intervention effect on long-term child outcomes, the improvements in maternal mood are important.

Keywords: Infants; adolescence; cognitive development; home visiting intervention; parenting; low- and middle-income countries

Introduction

In the conditions of poverty and violence which characterise many low- and middle-income countries (LMIC), the capacity of parents to provide the kind of care that promotes optimal child development may be severely compromised, especially where caregivers suffer from mental health problems (Tomlinson, Cooper, & Murray, 2005). Delivering interventions during the perinatal period may contribute to the reduction of health inequities brought about by such harsh environments (Marmot et al., 2008), and may improve children's long-term developmental and health outcomes even into adulthood (Campbell et al., 2014). However, long-term outcome studies of such interventions are rare, and the evidence that they may have sustained effects remains inconclusive.

A large body of research in the last two decades is unequivocal that the first 1000 days of a child's life (conception to the end of the second year of life) are critical in terms of brain development (Shonkoff & Levitt, 2010; Shonkoff, Richter, van der Gaag, & Bhutta, 2012) and lay the foundations for healthy cognitive development (Richter et al., 2017). But in contexts characterised by poverty and adversity, child development is often compromised. Aspects of these difficulties include insecure child- caregiver attachment, delayed cognitive and language development, educational failure and, in the long term lowered earning capacity in adulthood (Gertler et al., 2014; S. Grantham-McGregor et al., 2007; Tomlinson et al., 2005). Key to many of these adverse effects on child development is the impact of adversity on parenting quality and parental mental health (Cooper et al., 1999).

There is a considerable literature from LMICs on interventions in the early years that target child cognitive development. Most notably, in Jamaica Grantham-McGregor and colleagues found that early child stimulation led to improvements in child and adult cognitive development across two decades, and that providing both a nutritional and

stimulation intervention yielded additional benefits (Gertler et al., 2014). In Pakistan, Yousafzai and colleagues found that children receiving caregiver-led responsive stimulation scored significantly higher on measures of language and cognitive development at 12 and 24 months of age (Yousafzai, Rasheed, Rizvi, Armstrong, & Bhutta, 2014).

The Jamaica and Pakistan interventions however explicitly targeted child cognitive development through a focus on early cognitive stimulation. However, the evidence for the impact on cognitive development of interventions targeting child socio-emotional development is more limited (Cooper et al., 2009). Less robust effects might be the result of 'domain specific' impacts of interventions (Rutter, 1995). Early intervention programmes targeting socio-emotional development for example, commonly focus on the early caregiver-infant relationship, both as an end in itself, but also to improve the security of child-caregiver attachment (Cooper et al., 2009). Child-caregiver attachment security in turn has been shown to have a significant impact on child socio-emotional development and can be adversely affected by socio-economic adversity and maternal stress and mental ill-health (Tomlinson et al., 2005). Previously, it was believed that the impact of attachment security was 'domain specific' and not associated, for example with cognitive development (Rutter, 1995). There is however increasing evidence that attachment security is associated with a wide range of developmental advantages across the life course (Bernier, Beauchamp, Carlson, & Lalonde, 2015). For instance, studies from a number of high income countries have found that early secure attachment is associated with later child and adolescent cognitive development (Drake, Belsky, & Fearon, 2014), improved language development, enhanced school performance (van Ijzendoorn, Dijkstra, & Bus, 1995; Young et al., 2002) as well as improved executive functions amongst children experiencing adversity (Menon, Katz, & Easterbrooks, 2020).

The majority of interventions targeting attachment do so by supporting caregivers to be more responsive and sensitive in their interactions with their young children which, from observational studies, is a well-established predictor of attachment security (De Wolff & Van Ijzendoorn, 1997). Such interventions, particularly when they are successful in promoting parental sensitivity, reliably improve attachment security (Bakermans-Kranenburg, Van Ijzendoorn, & Juffer, 2003; Kobak, Cassidy, Lyons-Ruth, & Ziv, 2006; Moss et al., 2011). Furthermore, there is extensive evidence that caregiving sensitivity and more responsive early interactions are robustly associated with broad benefits for child development, including cognitive and language development (NICHD(Bornstein et al., 2020; NICHD Early Child Care Research Network, 1999), and increases in child vocabulary up to age 15 years of age (Duncan, Schmitt, & Vandell, 2019).

A further mechanism by which improved mother infant interaction and secure attachment might impact on child cognitive development is by way of the 'secure base' behaviour so central to attachment theory. When securely attached young children explore their world, and engage in harmonious joint play activities with their caregiver, what they are doing is practicing the emotional and regulatory capacities that may then be generalized to tasks beyond the relationship with their caregiver (Landry & Smith, 2010; Perez & Gauvain, 2010). This evolving self-efficacy and self-regulation are key components of executive functions (Bernier et al., 2015). We have also previously argued (Tomlinson et al., 2015) that providing mothers with support creates a heightened awareness of infants needs and may provide them with the tools to act toward a powerfully motivated goal such as immunization, recognising illness, but most importantly that of optimal nutrition and thus helping their children to thrive. Increased awareness of child nutritional needs and

providing optimal nutrition is likely to be significantly associated with child cognitive development (Aurino, Schott, Behrman, & Penny, 2019).

It is plausible therefore, that improved maternal engagement and responsiveness in interaction may in turn be associated with improvements in child cognitive development. One of the objectives of this study is to establish whether in fact this is true in a LMIC context.

Despite the considerable evidence that maternal depression is linked to poor child outcomes (Murray, Halligan, & Cooper, 2019), treating maternal depression has rarely been shown to lead to developmental benefits for the child (Murray et al., 2019). Similarly, despite the evidence of the association between disrupted early interactions and maternal depression, there is a large body of evidence showing how targeting improvements in mother-infant interaction does not necessarily lead to improvements in caregiver depressed mood (Cooper et al., 2009; Parsons, Young, Rochat, Kringelbach, & Stein, 2012). There is however, promising evidence from the United States that combining home visiting and parenting interventions can improve both maternal mood and child development (Olds et al., 2019).

Long term benefit of early intervention

There is compelling evidence from a number of studies from the USA and Jamaica of the long-term benefits to child cognitive development of early interventions that target mothers and their young children (Eckenrode et al., 2010; Gertler et al., 2014). Other studies, however, have failed to find long-term benefits of interventions delivered in the early years (Maselko et al., 2015). Adverse environments characterised by extreme poverty and violence

may contribute towards overwhelming the effects of normally protective influences. This may provide one explanation for why many early intervention gains subsequently fade out over time in high-risk populations (Bailey, Duncan, Odgers, & Yu, 2017; Sameroff & Rosenblum, 2006).

The 'Thula Sana' ('hush baby') study was an individual Randomized Controlled Trial (RCT) conducted in a peri-urban settlement in Cape Town, South Africa, where community health workers (CHW) delivered a home-based intervention across the perinatal period. The content of the intervention was based closely on 'The Social Baby' (Murray & Andrews, 2002), but also incorporated principles of the World Health Organization's document 'Improving the Psychosocial Development of Children' (WHO, 1995). The aim was to sensitize caregivers to their infant's individual capacities and needs and in so doing improve infant-caregiver attachment security.

In the original study we assigned 449 women to the intervention (n=220) or control group (n=229). Primary outcome data were analysed for (n=156) for the intervention group and (n=162) for the control group. The intervention was associated with significant benefit to the mother-infant relationship, with mothers in the intervention group being assessed post-intervention and at 12 months more sensitive and less intrusive in their interactions with their infants (Cooper et al., 2009). The intervention was also associated with a higher rate of secure infant attachment at 18 months (Cooper et al., 2009). There was some indication of a benefit of the intervention in terms of maternal depressed mood at six months – but this did not reach significance (Cooper et al., 2009). There was no main effect of the intervention on child cognitive development at 18 months but there was an interaction between intervention and risk in relation to this outcome, with benefits observed for lower-risk dyads (Murray, Cooper, Arteche, Stein, & Tomlinson, 2016). In this cohort we have also shown that poor

language ability amongst children at age 13y ears was related to a range of concurrent adverse difficulties, such as attention deficits, self-esteem problems, and social withdrawal (St Clair, Skeen, Marlow, & Tomlinson, 2019). In the original study the intervention ended in early 2002 while the final follow up (when the children were aged 18 months) took place in early 2003.

In line with the 'Saving Brains' Initiative, the primary objective of the current study was to determine whether an early intervention is associated with effects on child cognitive development at age 13. In the light of our early findings of potential benefit for maternal mood, a secondary objective was to assess whether there was any further evidence of impact on maternal depressed mood 11 years later. Finally, we sought to estimate the costs of replicating the Thula Sana early childhood intervention.

Method

Thula Sana intervention

The original intervention was designed to be delivered by mothers in the local community who had received a three-week training program coupled with regular supervision (Cooper et al., 2009). The intervention comprised two home visits during pregnancy; weekly visits in the first two months postpartum; visits every two weeks for two months; and finaly monthly visits for two months (total of 16 visits).

Follow up

With funding from Grand Challenges Canada (Saving Brains # 0066-03), we followed up the cohort of mothers and children when the children were aged 13 years. The condition

of receiving funding from the Saving Brains grant was to assess the long term cognitive outcomes for children whose caregivers had received an intervention in the first 1000 days.

The Health Research Ethics Committee of Stellenbosch University (South Africa) gave ethical approval for the study (#: S12/04/113). All participants gave written informed consent to take part in the study. Trial registration number: ISRCTN25664149.

Participants and procedure

We employed a full-time recruiter for 18 months between 2012 and 2014 to track participants as we had not had contact with participants for over 10 years. Of the 449 participants originally randomised we were able to re-contact and enrol 333 participants (74%), 162 intervention and 172 control, no refusals) for this extended follow up. Many participants had remained in Cape Town (even if not in their original homes), but a substantial proportion had migrated to other parts of South Africa. We were able to track participants to 5 provinces and more than 25 towns. Participants who had moved were provided funding to travel to Cape Town for their assessment, and when this was not possible, we sent data collectors to the town in which they were living. Assessments in Cape Town were conducted in Khayelitsha at the research centre of the Institute for Life Course Health Research (Stellenbosch University) and involved a questionnaire for the primary caregiver and measurement of child cognitive development. All local participants were picked up from their homes by a driver, were given a meal at the start of the assessment and were all given an incentive voucher for their participation (R125/US$9). Data collectors had extensive training, all were experienced, and they were blind to group assignment.

Measures

Demographic: Demographic details were collected from the primary caregiver as part of the assessment using a structured questionnaire. These details included the caregiver's present education level, marital status, employment, and the number of children living in the family home.

Mental health measures

Patient Health Questionnaire. The Patient Health Questionnaire (PHQ-9) is a brief screening tool for depression. Caregivers were asked to rate how often, over the last two weeks they were bothered by a range of symptoms of depression. Items are scored on a scale of 0-3 , with each number representing the frequency of the symptom in question (3 = nearly every day; 2 = more than half the days; 1 = several days; and 0 = not at all) (Kroenke, Spitzer, Williams, & Lowe, 2010). The PHQ-9 has been extensively used and validated in a number of African countries (Adewuya, Ola, & Afolabi, 2006; Monahan et al., 2009) including South Africa (Bhana, Rathod, Selohilwe, Kathree, & Petersen, 2015; Cholera et al., 2014; Petersen, Hanass Hancock, Bhana, & Govender, 2014).

Self-Report Questionnaire: The Self-Report Questionnaire (SRQ-20) was developed by the World Health Organization for use in LMIC in order to screen for psychiatric disturbance. The SRQ-20 has 20 items (yes = 1; no = 0; maximum total score of 20), and measures depression, anxiety and somatic symptoms. The recall period is the last 30 days and a rating is made of the extent to which the respondent has been bothered by the symptoms. The SRQ-20 has been extensively used as a screening instrument for common mental disorders in Africa and

has been validated for South Africa using a cut-off point of 8 (Bhagwanjee, Parekh, Paruk, Petersen, & Subedar, 1998; Rumble, Swartz, Parry, & Zwarenstein, 1996).

The Generalized Anxiety Disorder Screen (GAD-7): The Generalized Anxiety Disorder Scale-7 (GAD-7) is a self-rated screening tool anxiety (Spitzer, Kroenke, Williams, & Lowe, 2006). It has 7 items that measure severity of symptoms with a maximum possible score of 21. It has been used in both clinical and research settings and has been used in a variety of cultural settings (Chibanda et al., 2016).

Child cognitive development

Kaufman Assessment Battery: The Kaufman Assessment Battery, Second Edition (KABC-II), measures cognitive processing. It has been shown to demonstrate little bias arising from school exposure (Greenop, Fry, & De Sousa, 2012). The KABC-II has gone through rigourous psychometric evaluation in the United States (Kaufman & Kaufman, 2004; Morgan, Rothlisberg, McIntosh, & Hunt, 2009; Reynolds, Keith, Fine, Fisher, & Low, 2007). In recent years, it has been used in many high-income countries (HICs) including Germany (Nguyen-Minh et al., 2013), France (Charkaluk et al., 2012) and Japan (Kurihara, 2010). The KABC-II has gained popularity in LMICs due to its inclusion of non-verbal tests and the assessment of a range of underlying cognitive processes (Kaufman, Lichtenberger, Fletcher-Janzen, & Kaufman, 2005), which gives children multiple opportunities to perform. Domains of cognitive development measures by the KABC-II include Sequential Processing, Simultaneous Processing, Learning Ability and Planning Ability. The battery has been used in Malawi (Boivin et al., 2011) and South Africa (Baumgartner et al., 2012; Ogunlade et al., 2011), and the battery has been shown to have good reliability and the originally validated structure of the

Kaufman Assessment Battery for Children, was maintained in in rural South Africa (Mitchell et al., 2018).

Costing

The cost analysis, derived from the initial Thula Sana budget, estimated the costs to a provider of replicating the intervention: it did not include costs to participants or the costs of conducting the research. We used a similar approach to Desmond and colleagues (Desmond et al., 2008) to isolate the costs of implementation from the research related costs. To estimate the costs of replication we included all line items that were exclusively for service delivery, implementation and staffing, and excluded all line items which related only to research (such as printing questionnaires). To assess intervention costs, we estimated the proportion related to programme implementation through discussions with individuals involved in the management of the original study. They were asked to select one of the following allocation weights (research versus implementation) for each shared line item: 80:20, 20:80 or 50:50, depending on whether the cost was considered mainly research, mainly intervention or equivalent. All costs were adjusted to ZAR2019 using the consumer price index (Dollar figures based on R15 to US$1). To estimate the cost of scaling up the intervention, in the first instance, we assumed no economies of scale, and multiplied the cost-per mother child pair by the desired scale. In the second instance, we adjusted staffing costs to better reflect government salary scales and assumed 10 rather than 16 sessions.

Data analysis

We began by describing the baseline sociodemographic, pregnancy, and depression characteristics of the participating mothers, stratified by their randomization allocation

group. Next, we estimated whether the allocation arms differed in mean scores on the primary outcomes (caregiver PHQ9, GAD7, & SRQ; child sequential processing, simultaneous processing, learning ability, planning ability, mental processing) after 13 years. Our estimation process proceeded in two stages. First, we used multiple imputation by chained equations to account for missing data on outcomes and key moderators. Our imputation model included salient baseline characteristics identified in Murray et al. (Murray, Cooper, Arteche, Stein, & Tomlinson, 2015) as well as key 12-month and 18-month follow-up outcomes. We undertook 25 imputations using predictive mean matching with 10 nearest neighbours for continuous outcomes and logistic regression for binary outcomes, estimating imputations separately by intervention and control groups and discarding 10 burn-in iterations per imputation. Second, we estimated intervention effects using pooled-sample bootstrapped linear regressions in which intervention group was the only predictor. We calculated percentile-based 95% confidence intervals using 1,000 bootstrap replications for each imputation to account for non-normality in the distribution of outcomes. Finally, we estimated effect sizes by dividing the mean difference by the control group standard deviation at follow-up.

Results

Participant characteristics

We were successful in contacting and recruiting 74.2% of the original sample. Mean age of the adolescents at follow up was 13.14 years (see Table 1). Over 50% of the sample were living in formal housing, while almost two-thirds of the caregivers were employed. There were no significant differences between intervention and control group participants at follow up.

Table 1: Sample characteristics at age 13years

	Intervention (n = 162)	**Control (n = 171)**	**Total (N = 333)**	**p-value; I vs C**
Child Characteristics				
Age (M; SD)	13.12 ± 0.537	13.16 ± 0.584	13.14 ± 0.561	0.516
Gender				
Female	81 (50)	86 (50.3)	167 (50.2)	0.957
Male	81 (50)	85 (49.7)	166 (49.8)	
	Intervention (N = 159)	**Control (N = 171)**	**Total (N = 330)**	**p-value; I vs C**
Caregiver Characteristic				
Biological Mother	117 (73.58)	109 (63.74)	226 (68.48)	0.054
Gender				
Female	151 (95)	156 (91.2)	307 (93)	0.182
Male	8 (5)	15 (8.8)	23 (7)	0.161
Employed [a]	106 (66.7)	98 (57.3)	204 (61.8)	0.080
Income [b]				
≤ 2000 Rand	63 (39.9)	69 (40.6)	132 (40.2)	0.895
≥ 2001 Rand	95 (60.1)	101 (59.4)	196 (58.8)	0.895
Education				
No formal schooling	3 (1.9)	4 (2.3)	7 (2.1)	0.776
Grade 1-7	57 (35.8)	76 (44.4)	133 (40.3)	0.112
Grade 8 or higher	99 (62.3)	91 (53.2)	190 (57.6)	0.097
Formal Housing	88 (55.35)	97 (56.73)	185 (56.06)	0.801
Water in Home	66 (41.5)	79 (46.2)	145 (43.9)	0.391
Toilet on premises	109 (68.6)	127 (74.3)	236 (71.5)	0,250
Electricity in home	148 (93.1)	162 (94.7)	310 (93.9)	0.529

[a] Includes full-time, part-time, casual work, and self-employed; [b] Income data missing for one intervention and one control participants

Between baseline and follow up 11 years later the socio-economic circumstances of the entire sample had improved markedly (with no group differences). At baseline almost 85% of women were living in a shack (informal dwelling usually self-constructed using wood and sheets of metal and commonly only one room) while the figure at 13 years was just under 50%. At baseline only 54% of women had water at home but this number had risen to 76% 11 years later. Finally, only just over 50% of households had electricity in the home at baseline but this had increased to almost 95% at follow up. The re-enrolled sample and those lost to follow up were similar across most characteristics. Lost-to-follow-up caregivers were, however, more likely to have been originally enrolled from the poorer of the two communities from which participants had been recruited in 1999-2000, were less likely to have been

married, and were slightly younger (see Table 2). (Also see Table 3 to compare the followed and not followed in each group, and not simply overall loss to follow up.)

Table 2: Characteristics of sample followed up and lost to follow up

	Intervention (n, %) (n=159)	**Control (n, %) (n=171)**	**Total followed up (n, %) (n=330)**	**Lost to follow up (n=119)**	**p-value: FU vs LTFU**
Area					
SST	85 (53.4)	85 (49.7)	170 (51.5)	75 (63.0)	0.031
Town II	74 (46.6)	86 (50.3)	160 (48.4)	44 (37.0)	
Major depressive disorder	25 (15.7)	24 (14.0)	49 (14.8)	23 (19.3)	0.254
Unplanned pregnancy	59 (37.1)	65 (38.0)	124 (37.6)	48 (40.3)	0,.95
Married/cohabiting	70 (44.0)	71 (41.5)	141 (42.7)	34 (28.8)	0.008
First child	63 (39.6)	60 (35.1)	123 (37.3)	43 (36.4)	0.872
Male child	79 (4.7)	86 (50.3)	165 (50.0)	42 (44.7)	0.363
Housing (shack)	132 (83.0)	144 (84.2)	276 (83.6)	108 (90.8)	0.058
Maternal age at baseline (mean, SD)	25.6 (5.3)	26.8 (6.1)	26.2 (5.7)	24.7 (4.9)	0.015

Note: FU – followed-up sample; LTFU – lost to follow-up

Table 3: Characteristics of sample followed up and lost to follow up in each group

	Intervention retained (n=159)	Intervention LTFU	*p*-value	Control retained (n=171)	Control LTFU	*p*-value
Area			0,161			0,103
SST	85 (53.4)	39 (63.9)		85 (49.7)	36 (62.1)	
Town II	74 (46.6)	22 (36.1)		86 (50.3)	22 (37.9)	
Major depressive disorder	25 (15.7)	11 (18.0)	0,679	24 (14.0)	12 (20.7)	0,230
Unplanned pregnancy	59 (37.1)	30 (49.2)	0,102	65 (38.0)	18 (31.0)	0,339
Married/cohabiting	70 (44.0)	16 (26.7)	0,019	71 (41.5)	18 (31.0)	0,157
First child	63 (39.6)	20 (33.3)	0,392	60 (35.1)	23 (39.7)	0,530
Male child	79 (49.7)	21 (50.0)	0,971	86 (50.3)	31 (59.6)	0,238
Housing (shack)	132 (83.0)	53 (86.9)	0,483	144 (84.2)	55 (94.8)	0,038
Maternal age (mean, SD)	25.6 (5.3)	25.2 (5.1)	0,644	26.8 (6.1)	24.3 (4.7)	0,004

LTFU – lost to follow-up

We were interested in two long term outcomes – child cognitive development and maternal depressed mood. Effect estimates indicated no evidence of differences on child cognitive development outcomes (Table 4). There was some signal of worse sequential processing in intervention group children as compared to control group participants (ES=-0.30), but group differences for all other domains, and for the overall mental processing index, were close to zero, with small effect sizes. In contrast, the intervention appeared to have had an effect on caregiver depression symptoms (PHQ-9 and SRQ-20), but not for anxiety. Effect sizes for both depression measures were small (-0.17 and -0.30, respectively).

Table 4: Child cognitive development and maternal mental health outcomes

Measure	Intervention	Control	Difference (95% CI)	Effect size
Child cognitive development				
Sequential processing	8.4 (1.2)	8.8 (1.2)	-0.35 (-0.11, -0.61)	-0.30
Simultaneous processing	8.1 (1.2)	8.1 (1.3)	-0.06 (-0.32, 0.19)	-0.05
Learning ability	9.0 (1.4)	9.0 (1.4)	-0.01 (-0.29, 0.27)	-0.01
Planning ability	7.4 (1.3)	7.4 (1.3)	-0.004 (-0.26, 0.26)	-0.003
Mental processing index	7.8 (1.0)	7.9 (1.0)	-0.14 (-0.34, 0.07)	-0.14
Maternal mental health				
PHQ-9	6.2 (4.3)	7.3 (5.7)	-0.95 (-1.95, 0.05)	-0.17
SRQ-20	5.4 (4.9)	6.9 (6.1)	-1.31 (-2.41, -0.19)	-0.30
GAD	4.7 (3.8)	4.9 (4.3)	-0.16 (-0.93, 0.60)	-0.03

Costing

The annual cost per mother-child pair to replicate the Thula Sana intervention in 2019 was estimated at R13 365 (US$891). This implies a cost of approximately R334 million to reach 25,000 mothers and infants. The vast majority (87%) of this cost is associated with personnel, with the balance associated with training and overhead costs. Nearly half of the personnel costs are associated with the cost of a high-level community health worker coordinator. It is important to note that the community health workers were costed at R4,025

per month. This is a reasonable estimate of the cost of staff of a similar level as those used in the original intervention. It is, however, higher than most community health workers are currently paid in the government sector. There is scope for cost savings if the intervention were replicated. The coordinator costs could be reduced to a more reasonable level (R20,000 per month) and the health workers paid at a similar rate as the state pays (R3,500 per month). Such reductions would reduce the cost per mother-child pair to R10,600. If the number of sessions could be reduced to 10, the cost would fall further to R6,950 per mother child pair. This entails a cost of R174 million for 25,000 mother-child pairs. There is evidence of benefits (across three years) from an early intervention, delivered in a similar area of Khayelitsha, where an average of 8 home visits produced benefits to breastfeeding, child growth, maternal mental health and child cognitive development (le Roux et al., 2013; Tomlinson et al., 2016). More research is needed to determine if sessions could be cut from this programme without substantially reducing effectiveness, allowing for the cost savings.

Discussion

In a socio-economically deprived peri-urban settlement in South Africa, a home visiting intervention, delivered by community workers to mothers in pregnancy and in the first six postpartum months, had no overall effect on child cognitive development at follow up when children were 13 years of age. The intervention did, however, have a long-term impact on maternal mood. These findings are significant for two reasons: they add to the growing literature tracking cognitive development interventions in early childhood; and the long-term benefit of interventions on maternal mood.

While the intervention had no overall effect on child cognitive development, it is important to remember that Thula Sana was primarily focused on providing the mother with

support in her attachment relationship with her infant (Murray et al., 2015) and not on direct cognitive stimulation of the infant. The parenting qualities most relevant to attachment (such as attunement to infant mood), may not be those directly linked with child cognitive outcomes (Murray et al., 2015). Indeed, the most robust findings linking later child cognitive development to early intervention are where the intervention explicitly provide some form of early stimulation such as booksharing [cognitive development assessed at 2 years of age] (Vally, Murray, Tomlinson, & Cooper, 2015) or responsive stimulation interventions [cognitive development assessed at 2 years of age] (Yousafzai et al., 2014). Interestingly, in both these studies effect sizes were moderate to large.

It is worth considering our findings in the light of other long-term follow-ups conducted in LMICs. Findings from a number of countries point to the difficulty of shifting cognitive outcomes in the long term. For instance, Charpak and colleagues in a twenty year follow up of a Kangaroo care intervention in Columbia found that despite the significant, long-lasting social and behavioral protective effects of Kangaroo care 20 years after the intervention, overall effects for IQ were not significant (Charpak et al., 2017). In Bangladesh, newborn supplementation with vitamin A was associated with improvement in scholastic achievement, such as reading, spelling, and math computation but this was in the absence of an impact on intelligence, memory, or motor function (Ali et al., 2017). A successful maternal mental health intervention in Pakistan showed no cognitive differences between children aged 7 years in the intervention or control groups of mothers had prenatal depression (Maselko et al., 2015), while Rochat and colleagues showed that large improvements in exclusive breastfeeding were unrelated to child cognitive development in children aged 7-11 years (Rochat et al., 2016). However, in a deviation from these general findings on cognition, an early multiple micronutrient supplementation intervention showed a significant impact on

child cognitive development in Indonesia (Prado et al., 2017). Clearly, further investigation is required to understand what types of complex interventions are required to deliver long-term gains in cognitive development. However, on the basis of the findings of Ali et al. (2017) and Prado et al. (2017), micronutrient supplementation appears to be a promising intervention component.

In this study, there were differences between those caregivers lost to follow up, and those retained. Lost-to-follow-up caregivers were more likely to have been originally enrolled from the poorer of the two original communities, were more likely to be unmarried, and were younger than retained caregivers. Poverty, single parenthood, and young age at parenthood often co-occur, and are related to poorer mental health outcomes, and challenges to child development (Kiernan & Huerta, 2008). It is possible that – for these caregivers and their children – the supportive impacts of the intervention may have been greater than for less vulnerable caregivers, as differential effects of parenting interventions on the basis of risk have been reported for children (and this may hold for adults) (Broning et al., 2017). By failing to retain these caregivers, intervention effects may have been obscured. It is also plausible that the converse is true, and that the impact on maternal mental health may have diminished if those mothers most vulnerable to mental health conditions were retained and assessed, as it is possible that if pervading socioeconomic challenges endure, then structural programming may be required to shift mental health outcomes (Fisher & Baum, 2010).

Aside from the general difficulty of shifting cognitive outcomes, another possible reason for the lack of impact was the young age of the infants at the time of the intervention. Most intervention studies in LMIC that have shown positive benefits for cognitive development are ones where support was provided to parents of older children (see, for instance, (Baker-Henningham, 2014; S. M. Grantham-McGregor, Fernald, Kagawa, & Walker,

2014; Wallander et al., 2014)). Indeed, unlike socio-emotional outcomes, there is evidence that interventions targeting cognitive outcomes can be successful then they begin during the pre-school years (Wachs, Georgieff, Cusick, & McEwen, 2014). Finally, in LMICs characterized by food insecurity, poor nutrition is another potential intermediate factor that may undermine initial gains – particularly in cognitive development (Black et al., 2017).

Assessing the extent to which the benefits of early interventions are maintained across the life course was the explicit aim of the 'Saving Brains Initiative'. The concept of 'fade out' has been used to describe what happens when early gains disappear over time (Bailey et al., 2017). Two prominent examples of the 'fade-out' of early intervention effects are the Perry Preschool (Schweinhart et al., 2005) and Head Start programs (Puma et al., 2012) where large and noteworthy end of treatment effects had disappeared over the course of the following years. Consistent with those observations, a meta-analysis of 67 high-quality early childhood education interventions showed a steady decline in program effects over time (Bailey et al., 2017). This 'fading' was observed regardless of the duration of the intervention, and regardless of when the intervention began. Protzko (Protzko, 2015), echoing the writing of Lee and Loeb (Lee & Loeb, 1995) on the same effect, posited that early gains (in IQ, particularly) fade within a year or so because after the intervention, the participants were systematically exposed to academic environments less stimulating than those they received in the study, resulting in an erosion of impact over time.

Bailey and colleagues (Bailey et al., 2017) sought to identify the key features of interventions, as well as the characteristics and environments of the children who participate in them, that sustain beneficial intervention effects from early childhood programs. They note that interventions likely to have a sustained impact are ones that target skill-building, that focus on cultivating sustaining environments, and that offer specific skills boosts (Bailey et al.,

2017). The sustaining environments perspective (Bailey et al., 2017) sees early investments as unproductive unless they are accompanied by subsequent sustained access to high-quality environments. Therefore, in LMICs, the focus might need to be on broad-based environmental investment, sustained interventions, and/or building contextual supports for the initial gains made by targeted interventions. In contexts of high risk and adversity the impact of early interventions will be more durable when there are follow up interventions (for example) during the early years of school (Wachs et al., 2014).

The finding of improvement in maternal should be interpreted with some caution. The differences we found on two of the three measures had small effect sizes. Having said that, the finding is important given that maternal mood was not a focus of the intervention. The long-term benefit to maternal mood is possibly explicable given that the intervention was centrally concerned with providing primary caregivers with psychological support – although it did not screen for or specifically treat maternal depression. A host of recent studies have shown improvements in maternal mood, with interventions that do not explicitly focus on mental health but rather provide other forms of support to caregivers. Group based interventions to reduce neonatal mortality in Nepal (Tripathy et al., 2010), home visiting in Cape Town focusing on HIV, maternal and child health (Rotheram-Borus, Tomlinson, Roux, & Stein, 2015), and studies targeting HIV testing of young children and improving early child development outcomes in Zimbabwe (Mebrahtu et al., 2019) have all shown benefits for maternal mental health. Further, where maternal mental health has been the subject of longitudinal follow up, some studies have shown long-term positive impacts at 3 years after a maternal depression-focused intervention (Goldfeld et al., 2021), and at 2 years post a non-maternal depression-focused intervention (Hiscock, Bayer, Hampton, Ukoumunne, & Wake, 2008). One of the hypotheses to explain improvements in mental health attributes them to

the mothers' improving social support networks, and problem-solving skills (Tripathy et al., 2010). Social support reduces the risk of depression perhaps particularly during pregnancy (Collins, Dunkel-Schetter, Lobel, & Scrimshaw, 1993; Milgrom et al., 2008; Rahman, Malik, Sikander, Roberts, & Creed, 2008). In the Thula Sana intervention, the relationship between the community health worker (mentor mother) and the caregiver provided a reliable form of social support for the latter. Likewise, problem solving skills, which might develop in the context of a group-based intervention may also protect against mental health difficulties (Bell & D'Zurilla, 2009).

Improvements in maternal mood are significant for a number of reasons. First and foremost, reducing parental depression reduces distress and suffering and improves quality of life. However, significant for researchers interested in improving child outcomes over time, is the fact that maternal mood is correlated with levels of child behavior problems (including internalizing and externalizing behaviours) (Brennan et al., 2000). Given the relationship between parental depression and cognitive outcomes, and the apparent sustained benefits for maternal mood associated with this intervention, it is possible that modest improvements in child cognitive outcomes were achieved, but we lacked the statistical power to detect them, and/or they may have been confined to subgroups differing in levels of background adversity, as was the case in infancy [30].

Cost implications for scaling

There is a relative dearth of costing data for early child development interventions. Our costing of the Thula Sana intervention provides important data on the cost implications of early interventions. The Thula Sana intervention was a high intensity intervention (16 home visits across 8-10 months including frequent high-level supervision and quality control.

The cost of R10,600 (US$706) per women is undoubtedly high and most likely not affordable at scale by most LMICs.

Strengths and limitations

To the best of our knowledge this is the longest follow up of an attachment intervention in a LMIC context. The rate of successful follow-up was remarkably high given its long-term nature and the long gap since the previous contact. Combined with carefully conducted multiple imputation analyses, we expect our analyses to have been unaffected by attrition. The sample retained at follow-up afforded reasonable statistical power, but we lacked statistical power for small intervention effects, which might reasonably be expected over such long periods. Moreover, there was higher sample attrition from the poorer community enrolled in the intervention. It is possible that this played a role in the failure to detect long-term effects, as past research suggests that those children most at risk of poor developmental outcomes, benefit most from supportive interventions (Broning et al., 2017; Tomlinson, Hunt, Watt, Naicker, & Richter, 2020). As such, attrition among the more disadvantaged children could have masked an intervention sub-group impact, diluting the overall long-term detectable effect. Finally, attachment interventions have been widely evidenced to support child socioemotional development, and so the aim of the present work was to explore the potential impacts of these types of interventions on cognitive development. Wile we may have found an impact on socioemotional development – and likely would have given existing literature -our primary interest in this study was to explore cross-domain effects of socioemotional interventions.

Conclusion

The initially promising Thula Sana intervention did not lead to detectable long-term improvements in cognitive functioning in early adolescence. Given the links between attachment, sensitive caregiving and maternal mood on the one hand, and cognitive development on the other, some improvement in later cognitive development might have been expected. The intervention, however, did lead to improvements over time in maternal mood. This is likely due to its provision of mothers with social support and problem-solving skills not previously at their disposal. Thus, the argument for early, attachment-based intervention remains. However, if intervention gains are to extend into the domain of child cognitive development, additional programmatic elements will be required.

What's known

- Poverty and adversity impacts on child cognitive development across the life-course
- There is evidence that early interventions targeting the caregiver-child relationship is associated with improved language and cognitive development

What's new

- Evidence on sustained benefits of early interventions across the life course is limited.
- An early intervention targeting the mother-infant relationship had a small impact on maternal mood 12 years later

What's relevant

- Early promising results did not lead to detectable long-term improvements in cognitive functioning
- If early gains are to be maintained and extend into other domains (such as child cognitive development), additional programmatic elements will be required

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*Corresponding author: Professor Mark Tomlinson, Institute for Life Course Health Research, Department of Global Health, Stellenbosch University, Stellenbosch, South Africa. Email: markt@sun.ac.za. Tel: +27-83-301-4868

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