Accelerating progress towards improved mental health and healthy behaviours in adolescents living in adversity: findings from a longitudinal study in South Africa

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ABSTRACT
Adolescents exposed to high levels of adversity are vulnerable to developing mental health challenges, with long-lasting adverse consequences. Promoting the psychological well-being of adolescents and protecting them from adverse experiences is crucial for their quality of life. There is a need for evidence on which combinations of protective factors can improve the wellbeing of adolescents to inform future programming efforts. We used data from a longitudinal study that took place in Khayelitsha, South Africa, a semi-urban impoverished community in Cape Town. Data were collected from adolescents when they were 12–14 years of age (n = 333) and again at follow-up when they were aged 16–19 years (n = 314). A path analysis was used to estimate associations between access to service, food security, safe environment, family support, and social support and five outcomes related to adolescent mental health and risky behaviours. The fitted model was used to calculate adjusted mean differences comparing different combinations of risk factors. Two protective factors (food security and safe environment) were positively associated with three outcomes relating to mental health and the absence of risky behaviours. Further investigation revealed that the presence of high food security and safer environments was associated with higher adjusted mean scores: +16.2% (p < .0001) in no substance use; +16.5% (p < .0001) in no internalising behaviour; +19.5% (p < .0001) in self-esteem; +12.2% (p < .0001) in positive peer relationships; and +11.4% (p < .0001) in no suicidal ideation. Interventions targeting adolescents, that aim to improve food security together with improving the safety of their environment, are likely to impact their well-being.

KEYWORDS
Accelerating; Adolescents; Mental Health; Healthy Behaviours

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Introduction

Adolescence is a rapid developmental phase, during which an individual undergoes major physical and psychological changes (World Health Organization, 2006b). Mental disorders during adolescence are common, and a strong predictor of mental health problems during adulthood (World Health Organization, 2020). Adolescents living in sub-Saharan Africa have high levels of exposure to poverty, inequality and violence, which may exacerbate each other (Cluver et al., 2019) and affect their mental health.

The United Nations General Assembly devised the Sustainable Development Goals (SDGs) in 2015 to guide international development policies to end poverty, protect the planet, and ensure that all people enjoy peace and prosperity by 2030 (Cluver et al., 2016; Cluver et al., 2019; Nations, 2016). SDG 3 focuses on good health and well-being across all ages, and comprises indicators relating to lowered mortality and morbidity, better mental health and lower substance use (United Nations Development Group, 2015).

The United Nations Development Group (UNDG) developed the Mainstream, Acceleration and Policy Support (MAPS) approach as an effective way of reaching the SDGs by 2030 (UNDP, 2017). Accelerators are a key concept in the MAPS. They are described as life circumstances or programmatic areas that directly influence multiple SDG outcomes (e.g., food security may not only reduce hunger, but also improve physical and mental health and schooling outcomes; UNDP, 2017).

The concept of accelerators was first used by Cluver et al. (2019) when they identified potential accelerators to improve progress towards the SDGs for adolescents living with HIV (Cluver et al., 2019). They found that three provisions (parenting support, government cash transfers, and safe schools) were associated with better outcomes across 11 SDG-aligned targets (Cluver et al., 2019). The accelerator approach has since been successfully applied in several studies (Cluver et al., 2020; Mebrahtu et al., 2021; Meinck et al., 2021). Of note, several of these studies have found positive effects of different accelerators on several indicators of mental health (Mebrahtu et al., 2021; Meinck et al., 2021). Building on such findings, the current study applies the accelerator approach to identify measures that may improve several, inter-related mental health outcomes simultaneously.

Multiple candidate accelerators are likely to affect mental-health related outcomes in the South African context. The gap between rich and poor in South Africa is among the widest in the world, with more than half of the country’s youth population living in poverty (De Lannoy et al., 2018; STATS SA, 2020). Poverty influences mental health through a variety of pathways and the relationship is complex and bidirectional (Dashiff et al., 2009). Adolescents who live in households and communities that are socially and economically disadvantaged are at an increased risk of exposure to household and community violence, food and income insecurity, which in turn are risk factors for poor mental health (Das-Munshi et al., 2016; Patel et al., 2007). Lastly, family, and social support are crucial to mental health and are robustly associated with mental health in adolescence (Kuhn & Laird, 2014).

While previous studies have established additive effects of multiple accelerators on previous outcomes, the concept requires further development to better inform policy decisions. The current study takes a unique approach, building on the established...
importance of high-quality programs (Castillo et al., 2019; World Health Organization, 2004), by investigating the differential effects of low, average, and high availability of accelerators.

**Methods**

The current analysis includes data from a longitudinal study that was conducted in South Africa between 1999 and 2017. Two time points of the study are included in the analysis: First, when the adolescents were between the ages of 12–14 years and second when the adolescents were between the ages of 16–19 years.

The aim of this analysis is to determine:

1. which of the five potential accelerator provisions (access to services, food security, safe environment, social support, and family support) are linked to outcomes relating to improved mental health and healthy behaviours in adolescents living in adversity; and
2. investigating these associations at different levels of accelerator exposure.

**Studies included in analysis**

*Thula Sana* was a randomised controlled trial (RCT) of a community-based intervention programme for mothers, which aimed to improve maternal sensitivity and responsiveness (Cooper et al., 2009). At 13 years of age, these children were re-enrolled into the Saving Brains study to evaluate the long-term impact of the *Thula Sana* intervention programme on child cognitive functioning. No significant long-term impact on child outcomes were observed (Tomlinson et al., 2020). *Zifune* was an RCT that aimed to evaluate the impact of a second-wave intervention for the *Thula Sana* cohort, intended to prevent interpersonal violence and abuse (Tomlinson et al., 2020). The current study utilises data from the Saving Brains 13-years assessment (T1) and the baseline measures of the Zifune study (T2) (see, Figure 1). Since the sample assessed at both time-points was not completely overlapping, our final sample size with full data at both time-points was N = 289.

**Sample and procedure**

Longitudinal data were collected from a sample of adolescents and their mothers living in Khayelitsha, a large township located in Cape Town, South Africa. Khayelitsha is characterised by high population density, widespread poverty rates, and high rates of HIV (Stinson et al., 2016). Data were collected in three phases: (1) *Thula Sana* (pregnancy to 18 months; five time-points of assessment); (2) *Saving Brains* (ages 12–14 years; one time-point of assessment); (3) *Zifune* (ages 16–19 years; three time-points of assessment).

All interviews and assessments were conducted by trained and supervised data collectors, experienced in working with vulnerable families, and in the participants vernacular language (isiXhosa). All three phases of the longitudinal study received ethical
approval. Thula Sana, was approved by the research ethics committee of the University of Reading (ref:99/20) and the University of Cape Town (ref:180/97). Ethical approval was granted by the Health Research Ethics Committee of Stellenbosch for Saving Brains (S12/04/113) and Zifune (N17/10/094).

Measures

Outcomes

We identified five measures that reflected SDG3-related mental health and risky behaviour constructs. Details on measures used and coding decisions are provided in Appendix 1. A variable for ‘no substance use’ (0–2) was created as a combined measure of no harmful drinking (score ≥8 on the AUDIT; Bohn et al., 1995, 1995/07/01) and no use of any illicit drugs. Internalizing behaviour was measured through the Youth Self Report (YSR; Achenbach, 1991) internalizing subscale (range: 0–62; reverse coded so that higher scores indicate lower levels of internalizing behaviour), which comprises the Anxious/Depressed, Withdrawn/Depressed, and the Somatic complaints subscales. Self-esteem was measured at T1 through the Self-Esteem Questionnaire (SEQ: range 42–168; split into quartiles; Wild et al., 2005) and at T2 through the Rosenberg Self-Esteem Scale (RSES: range: 0–30; split into quartiles; Rosenberg, 1965). Healthy peer relationships were measured through the Strengths and Difficulties Questionnaire (SDQ; Goodman, 1997) – Peer-Relationship Problems subscale (range: 0–10). Lastly, no suicidal ideation was measured through a single item present in the YSR. Since the aim of the analysis was to examine change over time, measures taken at follow-up were chosen as the primary outcome variable. However, we controlled for baseline scores to capture change processes potentially caused by the accelerator provision. An exception of this was the internalizing behaviour outcome, for which a measure was only available at T2.
**Hypothesised accelerator provisions**

We identified five hypothesised accelerators that may influence mental health and healthy behaviour outcomes. Since previous research found that continued access to protective factors are required in order for them to be effective (Cluver et al., 2019), we averaged scores across baseline and follow-up to capture the degree of exposure adolescents had to each factor over time. The hypothesized accelerators included in this study were as follows: 1) access to service, which consisted of a continuous score (0–4) capturing if the adolescent lived in a formal brick structure and had access to drinking water, a flush toilet, and electricity at their premises; 2) food security, which was measured through the Household Food Insecurity Access Scale (HFIAS: range:0–27; reverse coded so that higher scores indicates higher food security; Coates et al., 2007); 3) living in a safe environment, with adolescents not witnessing, or directly being exposed to community or household violence as measured through the Child Exposure to Community Violence (CECV) scale (range:0–69; reverse coded so that higher scores indicates higher levels of safety; Amaya-Jackson, 1998); 4) social support, which was assessed through the Inventory of Social Supportive Behaviour (ISSB; Barrera, 1981) that captures the extent of social support an individual receives from others (range:19–95; split into quartiles); 5) family support, which was measured through the Family Assessment Device – general functioning subscale that measures perceived family functioning. (FAD; range:12–48; split into quartiles; Epstein et al., 1983).

**Covariates**

We included two covariates in the analysis: (1) sex of the child; and (2) baseline score of the outcome measured.

**Analysis**

Analyses were conducted in Stata SE v.15. The following six steps were undertaken. *Step 1*: Comparison of those participants whose data was included versus not included in the analysis using t-tests and chi2 test as appropriate. Only participants who had data at both time-points were included in the analysis (see, Figure 1); *Step 2*: We conducted Pearson correlation analyses to ensure there were no multicollinearity between the five potential accelerator provisions. *Step 3*: We conducted separate regressions for each of the five SDG-3 related mental health outcomes, with each outcome being simultaneously regressed onto all hypothesized accelerators and control variables (T1 scores, sex). *Step 4*: We tested for evidence that associations between hypothesised accelerator and mental health outcomes may be moderated by sex using interaction terms. *Step 5*: We ran a path analysis with full information maximum likelihood to account for missing data. For this, we used path analysis including five single-outcome multivariable linear regression models, each regressing one of the five outcomes at follow-up on the five hypothesised protective factors, controlling for T1 scores and sex. Outcomes were set to be inter-correlated to account for potential clustering of different mental health outcomes. If a predictor was found to affect three or more outcomes, it was defined as a potential accelerator. *Step 6*: To reflect quality of provisions, we used our fitted SEM to calculate adjusted mean values for each outcome under exposure to low (−1 SD), average (mean score) and high (+1 SD) levels of each
accelerator and their combinations. We also calculated adjusted mean differences comparing different scenarios. This provides us with a better understanding of how the quality of the accelerators is associated with study outcomes.

Results

Descriptive information

Sociodemographic characteristics, potential accelerator provisions, and outcomes at baseline and follow-up are provided in Table 1. Participants not assessed during follow-up \((n = 43)\) had lower levels of access to running water and flush toilet on premises; both \(p < .001\) at baseline. No differences were found for any other potential accelerator provisions or outcomes \((p > .07)\). Of the retained sample, 51.38% were female, with an average age of 13.31 years at baseline and 17.20 years at follow-up.

Table 2 shows the results of the Pearson correlation analysis. We found a small negative association \((r = -.12)\) between social support and living in a safe environment, and small-to medium-sized positive associations between family support and access to services \((r = .14)\) and food security \((r = .32)\). With correlations being moderate at maximum, our findings suggest no multicollinearity between the hypothesized accelerators.

Multivariable associations between protective factors and outcomes

Table 3 shows the associations between potential accelerator provisions and SDG3-related mental health outcomes based on the results of the Structural Equation Model. Since we found no evidence that sex moderates the association between potential accelerators and study outcomes (see appendix 2), we only investigated main effects, retaining sex as a covariate.

The first potential accelerator provision, access to service, was not associated with any of the five outcomes \((p = 0.06–0.60)\). Food security was the first accelerator identified which was positively associated with no internalizing behaviour \((\beta = 0.34; p = 0.003)\), higher self-esteem \((\beta = 0.04; p = 0.005)\), and no suicidal ideation \((\beta = 0.01; p = 0.012)\). The second accelerator identified was safe environment, which was positively associated with no substance use \((\beta = 0.17; p = 0.02)\), no internalizing behaviour \((\beta = 2.74; p = 0.002)\), and healthy peer relationships \((\beta = 0.43; p = 0.032)\).

Social support was significantly associated with higher self-esteem \((\beta = 0.04; p = 0.052)\) but no other outcomes, therefore not qualifying as an accelerator. Lastly, family support was only positively associated with no internalizing behaviour \((\beta = 1.36; p = 0.024)\) and self-esteem \((\beta = 0.29; p = 0.000)\).

Being female positively predicted no substance use \((\beta = 0.42; p < 0.001)\), self-esteem \((\beta = 0.30; p = 0.012)\), and healthy peer relationships \((\beta = 0.95; p < 0.001)\) but was negatively related to no internalizing behaviour \((\beta = -3.95; p < 0.001)\). Being male positively predicted no internalizing behaviour, and no suicidal ideation \((\beta = -0.04; p = 0.186)\), but was negatively related to no substance use, self-esteem and peer relationships. The covariance between the outcomes is reported in Appendix 3.
Table 1. Sociodemographic characteristics, potential accelerator provisions, and outcomes at baseline and follow-up.

| Baseline (n = 333) | Retained (290) | Not-retained (43) | p-value | Follow-up (n = 290) |
|-------------------|---------------|-------------------|---------|---------------------|
| **Sociodemographic Characteristics** | | | | |
| Child Sex (female) | 149 (51.38%) | 18 (41.86%) | 0.24 | 149 (51.38%) |
| Child Age (M; SD) | 13.31 (1.84) | 13.30 (0.77) | 0.99 | 17.20 (0.64) |
| **Potential Accelerator Provisions** | | | | |
| Access to Services | | | | |
| Formal housing | 161 (55.51%) | 23 (53.49%) | 0.07 | 219 (75.52%) |
| Running water | 136 (46.89%) | 13 (30.23%) | 0.000*** | 191 (65.86%) |
| Flush Toilet | 217 (74.83%) | 19 (44.19%) | 0.001* | 213 (73.44%) |
| Electricity | 272 (93.79%) | 37 (86.05%) | 0.29 | 283 (97.59%) |
| Food Security (M; SD) | 9.93 (5.93) | 9.80 (5.35) | 0.90 | 7.11 (5.65) |
| (Range: 0–27) | | | | |
| Safe environment (M; SD) (Range: 0–69) | 0.46 (0.67) | 0.65 (0.84) | 0.08 | 0.87 (0.73) |
| Social Support (M; SD) (Range: 19–95) | - | - | - | 49.52 (15.17) |
| Family support (M; SD) | 25.47 (5.20) | 23.71 (5.59) | 0.61 | 26.61 (3.96) |
| (Range: 12–48) | | | | |
| **Outcomes** | | | | |
| No Substance use | | | | |
| No alcohol use | 278 (95.86%) | 40 (93.02%) | 0.40 | 230 (79.31%) |
| No drug use | 289 (99.66%) | 43 (100%) | 0.70 | 195 (67.24%) |
| No Internalizing behaviour (Range: 0–62) | - | - | - | 18.14 (8.69) |
| Self-esteem (IQR) | 121–141 | 120–138 | - | 27–30 |
| Healthy Peer-relationships (M; SD) (Range: 0–10) | 4.47 | 4.302 | 0.53 | 4.44 (1.84) |
| No Suicidal ideation | 284 (97.93%) | 42 (97.67%) | 0.91 | 201(95.26%)*** |

*Data missing for 79 participants; **Interquartile range are reported
Note. Participants retained and lost to follow-up were compared using Chi2 tests and T-tests as appropriate.

Table 2. Pearson correlations between accelerators.

|              | 1     | 2     | 3     | 4     | 5     |
|--------------|-------|-------|-------|-------|-------|
| 1. Access to services | 1     |       |       |       |       |
| 2. Food Security | 0.10  | 1     |       |       |       |
| 3. Safe Environment | -0.03 | 0.11  | 1     |       |       |
| 4. Social Support | 0.03  | 0.06  | -0.12*| 1     |       |
| 5. Family Support | 0.14* | 0.32**| 0.08  | 0.06  | 1     |

Quality of provisions/Adjusted mean values of mental health outcomes comparing different combinations of accelerator factors

Figure 2 shows the adjusted mean values for each outcome under exposure to low (−1 SD), average (mean score) and high (+1 SD) levels of each of the two identified accelerators (food security, safe environment) and their combinations. The first outcome, no substance use, had a possible score of 0–2. When fixing food security and environmental safety to their lowest scores, the adjusted mean score for no substance use was 1.36. Compared to this baseline scenario, fixing both protective factors to their average levels was associated with an 8.1% higher mean score. When fixing both protective factors to their highest values was associated with a 16.2% higher mean score on the no substance use scale.
Table 3. Path analysis results between the potential accelerator provisions and outcome variables.

|                  | 3.5 No substance use | 3.4 No Internalizing behaviour | 3.4 Self-esteem | 3.4 Healthy Peer relationships | 3.4 No Suicidal ideation |
|------------------|----------------------|-------------------------------|----------------|-------------------------------|--------------------------|
| Service support  | −0.21                | −0.45                         | 0.034          | −0.21                         | −0.01                    |
|                  | (−0.10; 0.06)        | (−1.43; 0.53)                 | (−0.09; 0.16)  | (−0.43; 0.01)                 | (−0.05; 0.02)            |
| Food security    | 0.01                 | 0.34                          | 0.04           | 0.01                          | 0.01                     |
|                  | (−0.01; 0.02)        | (0.12; 0.56)                  | (0.01; 0.07)   | (−0.05; 0.06)                 | (0.002; 0.02)            |
|                  | p = 0.596            | p = 0.365                     | p = 0.587      | p = 0.061                     | p = 0.497                |
| Safe environment | 0.17                 | 2.74                          | 0.12           | 0.43                          | 0.01                     |
|                  | (0.03; 0.32)         | (0.97; 4.52)                  | (−0.11; 0.36)  | (0.04; 0.83)                  | (−0.06; 0.08)            |
|                  | p = 0.020*           | p = 0.003**                   | p = 0.005**    | p = 0.838                     | p = 0.012*               |
| Social support   | 0.02                 | 0.38                          | 0.04           | 0.10                          | −0.004                   |
|                  | (−0.04; 0.09)        | (−0.44; 1.20)                 | (−0.07; 0.14)  | (−0.08; 0.28)                 | (−0.03; 0.02)            |
|                  | p = 0.478            | p = 0.361                     | p = 0.052*     | p = 0.207                     | p = 0.755                |
| Family support   | −0.04                | 1.36                          | 0.29           | 0.15                          | 0.12                     |
|                  | (−1.31; 0.06)        | (0.18; 2.53)                  | (0.14; 0.45)   | (−0.12; 0.41)                 | (−0.03; 0.06)            |
|                  | p = 0.471            | p = 0.024*                    | p = 0.000***   | p = 0.279                     | p = 0.588                |
| Sex              | 0.42                 | −3.95                         | 0.30           | 0.95                          | −0.04                    |
|                  | (0.27; 0.57)         | (−5.74; −2.15)                | (0.07; 0.54)   | (0.55; 1.35)                  | (−0.10; 0.02)            |
|                  | p = 0.000***         | p = 0.000***                  | p = 0.012*     | p = 0.000***                  | p = 0.186                |

Note: Each cell shows the regression coefficient $B$, 95% CI, and significance.

*p < 0.05; **p < 0.005; ***p < 0.001

No internalizing behaviour had a possible range of 0–62. When fixing food security and environmental safety to their lowest scores the adjusted mean internalizing behaviour score was 35.78. Compared to this baseline scenario, fixing both protective factors to their average levels was associated with an 8.3% higher predicted mean score. Fixing both protective factors to their highest values was associated with a 16.5% higher mean score on the no internalizing behaviour scale.

Good peer relationships had a possible score of 0–7. When fixing food security and environmental safety to their lowest scores the adjusted mean good peer relationship score was 4.19. Fixing both protective factors to their average levels was associated with a 6% higher predicted mean score. Fixing both protective factors to their highest values was associated with a 12.2% higher mean score.

Self-esteem had a possible score of between 1–4. When fixing food security and environmental safety to their lowest scores the adjusted mean self-esteem score was 2.56. Compared to the baseline scenario, fixing both protective factors to their average levels was associated with a 9.8% higher predicted mean score. Fixing both protective factors to their highest values was associated with a 19.5% higher mean score on the self-esteem scale.

Lastly, no suicidal ideation, had a possible score of between 0–1. Fixing both protective factors to their lowest score the adjusted mean score was 0.88. Fixing both protective factors to their average levels was associated with a 5.7% higher predicted mean score. Fixing both protective factors to their highest values was associated with a 11.4% higher mean score on no suicidal ideation. See appendix 4 for full results on quality of provisions.
In this analysis of data from a longitudinal study (Tomlinson et al., 2021) we identified two accelerators (food security and safe environment) that were associated with at least three domains of better mental health and healthier behaviours. This finding contributes to the emerging evidence on potential accelerators for supporting adolescent well-being.

Figure 2. Adjusted mean values for each outcome.

**Discussion**

In this analysis of data from a longitudinal study (Tomlinson et al., 2021) we identified two accelerators (food security and safe environment) that were associated with at least three domains of better mental health and healthier behaviours. This finding contributes to the emerging evidence on potential accelerators for supporting adolescent well-being.
across Africa (Cluver et al., 2019). Food security was positively associated with positive self-esteem, an absence of suicidal ideation, and no internalizing behaviour. Living in a safe environment was associated with healthy peer relationships, no internalizing behaviour and no substance use.

These findings are in line with previous accelerator studies that report being food secure and living in a safe environment having positive effects on mental health and healthy behaviours (Mebrahtu et al., 2021; Sherr et al., 2021). This highlights the importance of improving food security, as food security not only reduces hunger, but also improves physical and mental health. Living within a safe environment is also crucial for mental health and healthy behaviours.

We also investigated the effect of the accelerators at different quality levels and found that higher quality provision of accelerators, reflected in higher predicted scores on the utilized scales, generally predicted better outcomes, with exposure to average levels of both accelerators already leading to notable improvements. High quality on one and average quality on the other accelerator often led to substantial increases in outcome attainment, with high quality on both accelerators commonly leading to the largest effects. These findings suggest that resolving food security and safe environments may be more effective for improving a range of outcomes relating to mental health and healthy behaviours than resolving just one. The stepwise improvements also highlight the importance of the quality of these accelerators when aiming to improve mental health and health behaviour outcomes. Overall, these findings are in line with a recent study, that found that the presence of 2–3 accelerators could lead to substantial improvements across a range of SDG outcomes including indicators relating to mental health (Sherr et al., 2021).

This study supports other recent findings (Mebrahtu et al., 2021; Sherr et al., 2021) on the importance of food security and safe environments in the mental health and healthy behaviour of adolescents. It provides initial evidence on the potential benefits of combining these two accelerators, at a high-quality level, in mitigating adverse outcomes in adolescents in South Africa. Food security can be attained through various interventions such as providing nutritional support and enhancing access to food sources (De Groot et al., 2017; Sherr et al., 2021). An integrated approach should be taken to address the safety in communities, which includes addressing the underlying drivers of crime and violence (e.g., substance abuse and unemployment), and strengthening the criminal justice system and the police (Kruger et al., 2016). Safety has a direct impact on sustainable development and high levels of violence in South Africa has delayed economic growth and transformation. These findings are important for developing social policy initiatives for increasing food security and safe environment for enhancing the future achievements for adolescents in South Africa.

This study had a few limitations. First, the study utilised a small sample size, which could lower power and prevented us from doing sex-specific analyses. Second, only a small number of the sample reported suicidality, which may make predictions less reliable. Third, for some outcomes, different measures were used at baseline and follow-up. Lastly, although rigorous research methods ensure the highest possible internal validity, as an observational study we are unable to establish whether estimated associations are causal. Strengths were that the research was conducted using longitudinal data, that there were high retention rates, and we accounted for missing values using full
information maximum likelihood. Nevertheless, there is still a risk of residual confounding from unmeasured variables such as caregiver attitudes and knowledge, and future research should consider this.

**Conclusion**

It is concluded that promoting food security and safe environments are crucial to improve the mental health of adolescents while also promoting healthy behaviours. Resolving food security and safe environments may be more effective for improving a range of outcomes relating to mental health and healthy behaviours than just resolving one. It provides initial evidence on the potential benefits of combining these two accelerators, at a high-quality level, in mitigating adverse outcomes in adolescents in South Africa.

**Disclosure statement**

No potential conflict of interest was reported by the author(s).

**Data availability statement**

Data are formulated from a combination of the Saving Brains study and the Zifune study and ethically restricted from public sharing. Access enquiries should be addressed to the principal investigator (MT and SS) for both studies.

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