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LIFE COURSE EPIDEMIOLOGY

Low birthweight and subsequent emotional and behavioural outcomes in 12-year-old children in Soweto, South Africa: findings from Birth to Twenty

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Background The fetal origins hypothesis suggests that an adverse prenatal environment, indexed by low birthweight (LBW), may increase the risk of developing later disease. Recently the hypothesis has been extended to psychological outcomes, especially depression. The aim of this analysis was to test, for the first time in a developing country setting, the association between LBW and psychological symptoms, in Soweto, South Africa.

Methods A sample of 1029 children was drawn from Birth to Twenty, a longitudinal cohort followed from pregnancy to young adulthood. This sample completed the Youth Self Report at age 12 years, a validated psychological measure of behavioural and emotional adjustment. Scores were compared between LBW (<2500 g) and normal birthweight children using multivariate analysis with adjustment for potential birth and life events confounding factors.

Results No associations were found between LBW and total [adjusted odds ratio (OR) 1.09, 95% confidence interval (CI) 0.69–1.74], internalizing (adjusted OR 0.81, 95% CI 0.52–1.28) or externalizing profiles (adjusted OR 0.81, 95% CI 0.49–1.36). The only difference detected was for the internalizing sub-profile of Somatic Complaints (adjusted OR 2.02, 95% CI 1.21–3.38), which on subgroup analysis was greatest among females.

Conclusions We found no convincing evidence of an association between LBW and emotional and behavioural outcomes in 12-year olds in this sample in urban South Africa. To our knowledge, this is the first published assessment of this association in a developing world context.

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Introduction

Low birthweight (LBW) is an enormous public health problem in the developing world with an estimated prevalence of 15% in sub-Saharan Africa.[1] It is associated with a number of adverse outcomes, including increased morbidity and risk of mortality in the first year of life.[2] Birthweight is thus regarded as an important public health indicator.[1]

LBW is a useful marker for strained fetal development and intrauterine stress. The fetal origins hypothesis associates LBW with an increased risk of a range of ill-health in adult life, particularly cardiovascular disease and diabetes.[3] An intergenerational risk cycle is initiated because LBW mothers are themselves more likely to have LBW infants, with each generation carrying the physiological burden of the previous one.[4] The long-term effect of such adaptations on the infant are believed to occur through programming. This refers to 'a critical period when a system is plastic and sensitive to the environment, followed by loss of plasticity and a fixed functional capacity(p S2)'.[3]

There has been speculation that the fetal environment may also influence subsequent risk of psychological problems. LBW has been associated with increased behavioural and psychiatric problems in pre-school and, school-age children and early adolescents, including both externalizing (hyperactivity, inattention) and internalizing symptoms (anxiety, withdrawal, depression).[5–8] However, further studies are needed to elucidate the sex differences[8] and the role of social disadvantage in increasing vulnerability.[7] It is suggested that when adverse events come at a critical time, such as in utero, they can permanently alter the stress response.[9] It is unclear, however, whether this theory also applies to anxiety or depression, with an inconsistent outcome between LBW and depression in studies. There are studies showing an association in both males and females,[10–15] some only in females,[16,17] others stronger in males[18,19] and some that show no association.[7,20–24] However, as far as we are aware, all research to date has been undertaken in the resource-rich countries of the North, despite the fact that the majority of LBW children are born in poor countries in the South. In addition, psychological morbidity amongst adolescents in low-income countries is high, with diagnosable psychopathology affecting an estimated 10–20% of youth worldwide.[25] Despite this, there are very little data available examining the mental health and adjustment of children and adolescents in poor countries.

The aim of this study is to examine the association between LBW and assessed psychological adjustment in an urban group of young adolescents living in Soweto, South Africa, with a particular focus on internalizing symptoms. The LBW prevalence in Soweto at the time of enrolment of the cohort was ~11%.[26] We hypothesized that LBW would be associated with later problems of emotional and psychological adjustment, in particular internalizing symptoms, and that the association would be stronger in pubertal females. To our knowledge this is the first study examining a possible association between LBW and psychological outcomes in a developing world setting.

Methods

Design and setting

The sample for this study was drawn from the Birth to Twenty (BT20) cohort study in Soweto, South Africa. The BT20 cohort was defined by the timing of a singleton birth within a defined period (from 23 April to 8 June, 1990), with continued residence for at least 6 months post-birth within the Soweto–Johannesburg area. The BT20 study provides a unique setting in which to examine the association between LBW and later psychological adjustment. First, BT20 is a prospective study and thus suited to examining associations between early life and later outcomes; it is in a developing world context, where the environment poses different mental health risks, as well as a higher likelihood of under-nutrition pre-disposing to LBW infants. Finally, the children were born during a period of profound socio-political change as South Africa made the transition from *Apartheid* to democracy, placing unique environmental stresses on the cohort.

The original design and recruitment of BT20 is explained in detail elsewhere.[26,27] Ethical clearance for the study was granted by the Committee for Research on Human Subjects at the University of the Witwatersrand, South Africa.

Study population

The original cohort consisted of 3273 children and their families. The total cohort is roughly representative of the Soweto–Johannesburg population, except for an under-representation of White children, as recruitment did not occur in private health facilities (utilized by many White families) and there was higher attrition in White families as the study progressed.[26] Greater attrition in higher socio-economic classes is a general feature in developing world cohorts.[28] At the year 11–12 data collection wave there were 884 attrition cases primarily due to heavy circular migration, unreliable postal addresses and

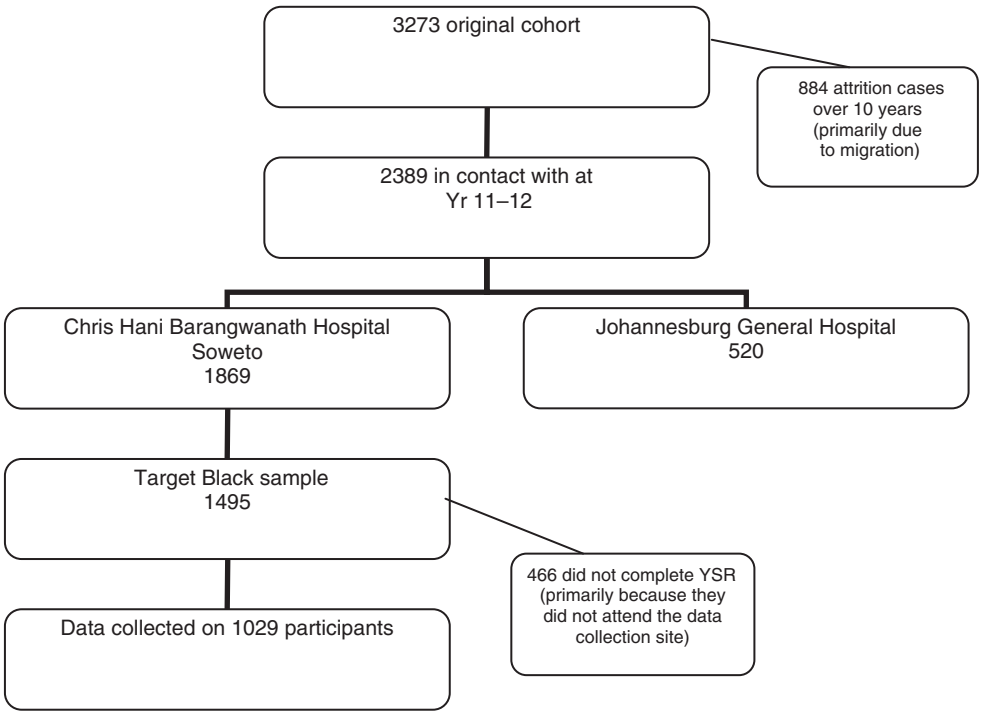

Figure 1 Flow chart outlining sample selection

staff shortages. The cohort was assessed at two data collection sites, one based at Chris Hani Baragwanath Hospital in Soweto and the other at the University of the Witwatersrand Medical School in Johannesburg (Figure 1). Due to the resources required to administer the 112-item Youth Self Report (YSR), a measure of emotional and behavioural outcome, it was decided to administer it only to Black children attending Chris Hani Baragwanath hospital ($n = 1495$). Of this target sample, $n = 1029$ (69%) completed the YSR and 466 did not, primarily as they did not present to the data collection site. Of this sample, 91.7% were Black and 8.3% were from a mixed ancestral background. The responders were compared with all Black non-responders from the original BT20 cohort on key demographic variables (Table 1) to assess for selection biases.

Measures

Anthropometric measures

Birthweight was measured at birth using hospital scales. The accuracy of birth data recorded on health and administrative records was analysed early in the study.[29] LBW was defined as a weight at birth of <2500 g, as set internationally by the World Health Organization (WHO).[1]

Gestational age

Gestational age was based on the mother's report of her last menstrual period and infant birth date.

Emotional and behavioural outcomes

The YSR is a questionnaire designed for adolescents aged 11–18 years. The 112-item checklist was developed by the Achenbach System of Empirically Based Assessment (ASEBA).[30,31]

The YSR syndrome scales consist of eight subscales, three of which make up the internalizing scale (anxious/depressed, withdrawn/depressed, somatic complaints), two which make up the externalizing (rule-breaking behaviour, aggressive behaviour) and three remaining subscales (social problems, thought problems and attention problems). Particular focus was placed on the internalizing subscales as these map most closely onto the depressive symptoms assessed in other research. The total score is an addition of all eight subscales and an additional 10-item list of 'other problems'. Scoring above the 97th percentile (T-score above 69) is classed as clinical, and scoring between the 92nd (T-score above 64) and 97th percentile is classed as subclinical, based on normalized and widely used values per gender as given by ASEBA.[30,31]

Extensive psychometric data from diverse cultural samples have been published for the ASEBA scales. The internalizing and externalizing scales of the YSR on US samples have an internal consistency of 0.90, test–retest reliability of 0.85, long-term stability of 0.56. Findings from other societies have generally approximated those from the USA.[32] Demographic variables such as race and socio-economic status (SES) account for a relatively small proportion of score variance.[33] A seven-country study of adolescents found the

YSR to be a methodologically sound source of information on adolescent psychology across different countries, despite differences in culture and language.[34] The YSR has not been validated in South Africa, but the South African Child Assessment Schedule (SACAS) closely based on the Child Behaviour Checklist (from which the YSR is derived) has.[35] In the present study, minor language edits were made to render some items colloquially understandable,[36] and items were completed with a trained fieldworker in the respondent's language of choice (English, isiZulu, seSotho) to overcome potential reading and language understanding problems.

Pubertal status

Pubertal development was determined through self-assessment of pubic hair and genital/breast development in boys and girls using the Tanner scaling technique. This technique has been validated in this population.[37]

Material and social environment

SES was based on a score derived from a listing of household assets (television, washing machine, refrigerator, telephone, motor vehicle) and categorized into an SES asset score by adding the number of assets in the household at the child's birth.[38]

Life events

A numerical score was derived from positive responses to a list of 17 life events that may have occurred in the child's life in the previous 6 months at age 12 assessment. These events included known social risk factors for adolescent depression such as death of a family member, marital discord and divorce.[39]

Statistical analyses

Birthweight and YSR were both dichotomized in order to enhance clinical relevance. Birthweight was classed as LBW (<2500 g) and normal birthweight (NBW) (≥2500 g). Clinical rates for YSR profiles were low in this population, thus the YSR was reclassified into two categories: a normal and a joint subclinical/clinical category. Our primary results were with regard to the main YSR scales, total, externalizing and internalizing profiles, with secondary results analysing their subscales.

The statistical analysis was conducted in stages. First, the association between LBW and all YSR categories was examined using Pearson's Chi-square test. Secondly, logistic regression models were run controlling for potential confounding variables. The models were adjusted for mother's age, marital status, maternal education and SES year 12 assets score as they are likely confounders for psychological outcomes in adolescents. There are strong biological reasons for adjusting for gestational age. The fetal origins hypothesis is traditionally associated with term LBW infants due to intrauterine growth retardation, with pre-term infants associated with higher mortality. We have included all infants in our analysis but adjusted for gestational age to control for pre-maturity.

Secondly, we hypothesized that the effect of LBW would vary between boys and girls, as has been found in other studies.[16] This was confirmed in our study by evidence of interaction for the crude analysis of total ($P=0.053$) and internalizing ($P=0.059$) scores, but not for externalizing scores ($P=0.785$). Therefore, we also ran models separately for males and females.

Thirdly, we also looked for increased vulnerability to mental-health risk factors in LBW adolescents as seen in the Costello *et al*. study.[16] Percentages of subclinical/clinical scorers on the main YSR scales in LBW and NBW groups were compared across increasing life events in both sexes.

We then performed some sensitivity analyses. First, linear regression models were run with continuous YSR outcomes and logistic regression models using continuous birthweight, to capture more subtle relationships. Secondly, we looked specifically at psychological risk in two groups: those within the highest and lowest 5% categories for birthweight across the sample. This was done to account for a possible contextually inappropriate marker of LBW (set at 2500 g)[1] and also to ensure that a possible increased psychological risk in high birthweight infants[10,40,41] did not potentially dilute the results for LBW infants.

Finally, as previous studies have postulated that puberty might trigger the physiological vulnerability to depression caused by LBW in females,[16] we were interested to assess this interaction in females. Our crude analysis did not confirm a significant interaction for total ($P=0.689$), internalizing ($P=0.877$) or externalizing ($P=0.100$) scores. We thus did not run separate analyses for females stratified by pubertal stage.

All analyses were conducted using SPSS Version 15.0 (Chicago, SPSS).

Results

Sample characteristics

The total analytical sample size was 1029 (467 males and 562 females). Detailed sample and non-responder characteristics are shown in Table 1. Only 14.4% of the population had five basic socio-economic assets at home. The mean birthweight was 3059.9 g [501.5 standard deviation(SD)], with $n=123$ (12.0%) with a birthweight <2500 g. Amongst males 9.4% ($n=44$) were LBW and amongst females 14.1% ($n=79$) were LBW.

At assessment, 20% of the sample was pre-pubertal and 44% were in mid-puberty, according to Tanner's staging with females more advanced in their pubertal

Table 1 Sample characteristics for categorical variables

Variable	Categories	*n* (%) in sample *n* = 1029	*n* (%) non-responders in cohort *n* = 1624
Gender	Male	467 (45.4)	817 (50.3)
	Female	562 (54.6)	807 (49.7)
Birthweight	LBW	123 (12.0)	165 (10.2)
	NBW	906 (88.0)	1459 (89.8)
Gestational age at birth	<36 weeks	49 (4.8)	77 (4.8)
	⩾36 weeks	980 (95.2)	1513 (95.2)
	Missing		34
Place of birth	Soweto/Deapmeadow	933 (90.7)	1473 (90.7)
	Former Indian/Coloured	71 (6.9)	16 (1.0)
	Suburban Johannesburg	18 (1.7)	111 (6.8)
	Inner city	7 (0.7)	24 (1.5)
Parity	1	385 (37.4)	571 (35.2)
	2	281 (27.3)	509 (31.3)
	3	182 (17.7)	294 (18.1)
	4	95 (9.2)	131 (8.1)
	⩾5	86 (8.4)	119 (7.3)
Hospital type at birth	Public	948 (92.1)	1543 (95.0)
	Private	81 (7.9)	81 (5.0)
Mother's age at birth (years)	⩽20	233 (22.6)	349 (21.5)
	21–25	299 (29.1)	492 (30.3)
	26–30	244 (23.7)	435 (26.8)
	31–35	160 (15.5)	232 (14.3)
	36–40	79 (7.7)	103 (6.3)
	>41	14 (1.4)	13 (0.5)
Marital status at birth	Married	342 (33.5)	443 (27.4)
	Living together	44 (4.3)	143 (8.8)
	Separated/divorced/widowed	19 (1.9)	12 (0.7)
	Single	616 (60.3)	1020 (63.0)
	Missing	8	6
Maternal education at birth	No Formal	6 (0.6)	40 (2.7)
	⩽Grade 7	112 (12.0)	270 (18.0)
	Grades 8–10	419 (44.9)	637 (42.5)
	Grades 11–12	329 (35.3)	432 (28.8)
	Post-school	67 (7.2)	120 (8.0)
	Missing	96	125
House type at birth	Flat, house	719 (78.1)	957 (69.6)
	Other (shack, hostel, shared, room, garage, cottage)	202 (21.9)	418 (30.4)
	Missing	108	249
House ownership at birth	Own house	216 (23.6)	288 (21.1)
	Not own house	698 (76.4)	1077 (78.9)
	Missing	115	259
Early life SES assets score	0–no assets	93 (11.4)	239 (20.0)
(combination of TV + car + fridge	1 asset	136 (16.7)	215 (18.0)
+ washing machine + phone)	2 assets	164 (20.2)	248 (20.8)

Continued

Table 1 Continued

Variable	Categories	*n* (%) in sample *n* = 1029	*n* (%) non-responders in cohort *n* = 1624
	3 assets	218 (26.8)	287 (24.1)
	4 assets	154 (18.9)	152 (12.7)
	5–all assets	48 (5.9)	52 (4.4)
	Missing cases	21	431
Year 12 SES assets score (combination of TV + car + fridge + washing machine + phone)	0–no assets	35 (3.4)	
	1 asset	80 (7.8)	
	2 assets	273 (26.7)	
	3 assets	268 (26.2)	
	4 assets	218 (21.3)	
	5–all assets	148 (14.4)	
	Missing cases	7	
Year 12 puberty	Pre-pubertal	181 (19.5)	
	Early pubertal	337 (36.4)	
	Mid-puberty	408 (44.1)	
	Missing	103	
Life events	Family moved	53 (5.2)	
	Birth of a sibling	55 (5.4)	
	Death of a parent	22 (2.2)	
	Hospitalization of sibling	82 (8.1)	
	Marriage of parent	18 (1.8)	
	Divorce of parent	20 (2.0)	
	Change of school	203 (19.9)	
	Hospitalization	29 (2.8)	
	Separation of parents	25 (2.5)	
	Increased parental arguments	134 (13.2)	
	Hospitalization of parents	93 (9.1)	
	Death of close friend	44 (4.3)	
	Separation from family for >2 weeks	155 (15.2)	
	Death of sibling	19 (1.9)	
	Death of grandparent	83 (8.2)	
	Sibling leaves home	66 (6.5)	
	Loss of job in parent	93 (9.1)	
	Missing	11	

development. A gestational age <36 weeks was recorded for 4.8% of the sample.

Life events ranged from 1.8% (death of a sibling) to 19.7% (change of school) and 61.1% of the sample had experienced at least one life event.

Youth self-report scores

It was found that 183 (39.2%) males and 158 (28.1%) females scored in the subclinical/clinical category on YSR total scores. The mean score for males was 48.0 (12.0 SD) and females 50.0 (14.0 SD). The subclinical/clinical rates were scored in 276 (26.8%) adolescents in the externalizing category and 424 (41.2%) in the internalizing category. Within the subscales, the combined subclinical/clinical rates were 239 (23.2%) anxious/depressed, 14 (1.4%) withdrawn/depressed, 131 (12.7%) somatic complaints, 254 (24.7%) social problems, 136 (13.2%) thought problems, 63 (6.1%) attention problems, 124 (12.1%) rule-breaking behaviour, 42 (4.1%) aggressive behaviour. The low number of subclinical/clinical cases for the withdrawn/depressed group resulted in insufficient data for analysis of this subscale.

Table 2 Associations between LBW and subsequent emotional and behavioural problems at age 12 years

	BT20 sample				
YSR profile score	LBW $n=123$ (subclinical/clinical profile)	NBW $n=906$ (subclinical/clinical profile)	Crude OR (95% CI) $n=1029$	Crude OR (95% CI) $n=926$	Adjusted OR[a] (95% CI) $n=926$
Total	43 (35.0%)	298 (32.9%)	1.10 (0.74–1.63)	1.01 (0.66–1.53)	1.09 (0.69–1.74)
Internalizing	49 (39.8%)	375 (41.4%)	0.94 (0.64–1.38)	0.88 (0.59–1.32)	0.81 (0.52–1.28)
Externalizing	32 (26.0%)	244 (26.9%)	0.95 (0.62–1.47)	0.84 (0.53–1.33)	0.81 (0.49–1.36)
Anxious/depressed	26 (21.1%)	213 (23.5%)	0.87 (0.55–1.38)	0.87 (0.54–1.41)	0.79 (0.46–1.35)
Somatic complaints	24 (19.5%)	107 (11.8%)	1.81 (1.11–2.95)	1.79 (1.06–3.01)	1.55 (0.80–2.64)
Social problems	34 (27.6%)	220 (24.3%)	1.91 (0.78–1.82)	1.12 (0.72–1.76)	1.03 (0.62–1.71)
Thought problems	16 (13.0%)	120 (13.2%)	0.98 (0.56–1.82)	0.78 (0.41–1.46)	0.73 (0.36–1.47)
Attention problems	8 (6.5%)	55 (6.1%)	1.08 (0.50–2.32)	1.00 (0.44–2.26)	0.83 (0.33–2.10)
Rule-breaking behaviour	14 (11.4%)	110 (12.1%)	0.93 (0.52–1.68)	0.82 (0.42–1.58)	0.71 (0.36–1.49)
Aggressive behaviour	4 (3.3%)	38 (4.2%)	0.77 (0.27–2.19)	0.71 (0.21–2.35)	0.63 (0.16–2.42)

[a]Adjusted for gestational age, mother's age, marital status, maternal education, SES year 12 assets score.

Table 3 Associations between LBW and subsequent emotional and behavioural problems at age 12 by gender

	Males		**Females**	
YSR profile score	Crude OR (95% CI) *n=415*	Adjusted OR[a] (95% CI) *n=415*	Crude OR (95% CI) *n=511*	Adjusted OR[a] (95% CI) *n=511*
Total	0.69 (0.34–1.39)	0.68 (0.31–1.49)	1.41 (0.84–2.39)	1.63 (0.90–3.00)
Internalizing	0.63 (0.32–1.22)	0.56 (0.26–1.20)	1.38 (0.82–2.32)	1.36 (0.75–2.46)
Externalizing	0.74 (0.31–1.73)	0.57 (0.22–1.49)	0.84 (0.48–1.46)	0.84 (0.50–1.59)
Anxious/depressed	0.89 (0.44–1.79)	0.81 (0.37–1.77)	1.19 (0.59–2.39)	1.14 (0.50–2.59)
Somatic complaints	0.86 (0.29–2.54)	0.60 (0.16–2.22)	2.46 (1.31–4.51)	2.14 (1.02–4.51)
Social problems	0.71 (0.30–1.65)	0.46 (0.17–1.27)	1.36 (0.80–2.33)	1.56 (0.84–3.00)
Thought problems	1.13 (0.48–2.68)	1.14 (0.41–3.11)	0.61 (0.23–1.58)	0.54 (0.18–1.65)
Attention problems	1.17 (0.38–4.10)	0.91 (0.28–3.70)	0.93 (3.13–2.74)	0.62 (0.16–2.40)
Rule-breaking behaviour	0.34 (0.05–2.57)	0.39 (0.05–3.11)	0.85 (0.42–1.73)	0.65 (0.28–1.53)
Aggressive behaviour	0.87 (0.20–3.85)	0.74 (0.14–3.84)	0.72 (0.09–5.87)	0.56 (0.04–8.63)

[a]Adjusted for gestational age, maternal education, SES assets year 12, maternal age and marital status.

Associations between LBW and emotional and behavioural problems at 12 years

There was no evidence in this study to support an association between LBW and the main YSR profiles on unadjusted analyses (Table 2). The adjustment for potential confounders resulted only in a relatively modest change in the relationship between LBW and most YSR profiles. On further analysis of subscales, an association was found between LBW and the somatic complaints subscale score [crude odds ratio (OR) 1.81, 95% confidence interval (CI) 1.11–2.95] which was weaker on adjusted analysis (adjusted OR 1.55, 95% CI 0.80–2.64). No other associations were found.

The analyses were then conducted separately for males and females (Table 3). No associations were found between LBW and YSR scores amongst males. In females the only positive finding was evidence suggesting an association between LBW and the Somatic Complaints Profile (adjusted OR 2.14, 95% CI 1.02–4.51).

LBW adolescents were not at an appreciably increased vulnerability to life events in total (Figure 2) externalizing and internalizing scales in both males and females.

The results of linear regression models using continuous YSR outcomes were consistent with prior analyses. There was little evidence for an association between LBW and YSR; total scores [regression coefficient −0.14 (95% CI −2.69 to 2.41), males 2.55 (−1.42 to 6.51), females −1.376 (95% CI −4.74 to 1.98); internalizing [regression coefficient −0.015 (95% CI −1.17 to 0.87), males 1.21 (95% CI −0.43 to 2.85), females −0.75 (95% CI −2.05 to 0.56);

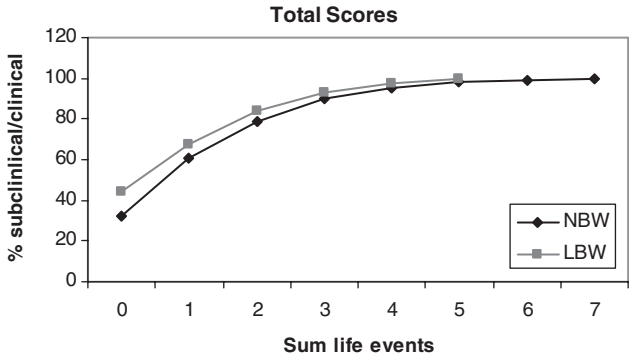

Figure 2 Risk of subclinical/clinical profile on total scores of NBW and LBW adolescents by number of adverse life events

externalizing [regression coefficient 0.24 (95% CI −0.57 to 1.05), males 0.83 (95% CI −0.51, 2.16), females −0.05 (95% CI −1.08 to 0.98)]. An association was found, however, in the sub-category of somatic complaints in females, with a regression coefficient of −0.065 (95% CI −1.21 to −0.08), as in binary models. When we conducted analyses using birthweight as a continuous variable the same association between LBW and somatic symptoms in females was found. In addition, we found some evidence of increased total problems as birthweight increased in males (Wald 4.701, $P = 0.030$). However, this was not found in any of the preceding analyses. Our analyses at 5% cut offs for low and high birthweights did not yield differences in overall effects.

Discussion

In this large prospective population cohort in a developing country setting, we found no evidence for a relationship between LBW and later psychological symptoms at age 12 years. We also did not find an increased vulnerability to adversity in LBW adolescents, and no increased risk in pubertal girls. There was one consistent subgroup finding of note; that is, LBW girls were found to have higher somatic complaints scores than those with NBW.

Despite several studies supporting a link between LBW and later poor psychological outcome,[5–8,10–19] this relationship particularly with regard to depression is mixed in the literature. Our results add to the uncertainty, by suggesting there may be no relationship, or that it is weaker in a developing country setting.

It is possible that the fetal origins hypothesis does not apply to later risk of depression in a context of adversity, with multiple contributing factors to poor adjustment. Despite a sizeable amount of evidence that supports the fetal origins theory for cardiovascular diseases and diabetes,[42] the literature does indicate that the interpretation of potential underlying biological mechanisms which can explain such an association remains unclear.[43–45] The studies looking at programming effects on depression are fairly recent and are particularly prone to methodological limitations, such as the lack of standardized tools for measuring depression[46] and confounding and random error,[47] which can both generate spurious associations.[48] Costello and colleagues[16] have questioned whether the inconsistent findings are due to differences in associations between birthweight and depression in different age–sex groups. However, there has been inconsistent evidence found for gender differences in the fetal origins hypothesis.[49,50] The inconsistency in findings with regards to birthweight and depression, in addition to methodological limitations discussed above, may also be due to birthweight providing a crude proxy for neurodevelopmental assessment.[24]

The association between LBW and somatic complaints, particularly in females, was inconsistent with the main findings of this study. It is possible that this finding may reflect a higher rate of physical health problems associated with LBW rather than psychological symptoms or reflect the proposed suggestion from earlier studies that somatic manifestations of depression are more dominant in an African setting.[51] However, as somatic symptoms are a subscale of the overall internalizing scale, care needs to be taken not to over interpret this result, which may be a spurious finding.

The contradictory finding of increased total problems with increasing birthweight in males is inconsistent with the fetal origins hypothesis. It was not confirmed on subset analysis of those in the top 5% birthweight category, and may be a spurious finding, although recent studies have noted increased psychological symptoms in high birthweight infants.[10,40,41]

These findings need to be considered in light of the strengths and limitations of the study. The developing world context of BT20 is a primary strength of this study and we are aware of no other studies in this field undertaken in developing nations; a notable limitation given the important potential health implications of LBW for these countries. The prevalence of LBW in this study (11%) is higher than similar studies in high-income settings.[16,17] A recent review of birthweight as a risk factor for ischaemic heart disease, an area that has provided much evidence for the hypothesis, noted that data were 'almost entirely derived from high-income study populations' (p. 1248).[45] There are several other strengths to the study. These include the longitudinal design, enabling the prospective collection of data, and so eliminating recall bias, and the use of a population cohort, reducing the risk of ascertainment bias in the sample. This is particularly relevant for gestational age and birthweight variables. The use of the YSR is another strength, as it has been widely used and validated in diverse cultures.[34] It is also completed by the

young person themselves, rather than by other reporters, who may not be able to accurately report emotional symptoms in the youth. Finally, we were able to assess gestational age, which has not been possible in a number of other studies.

There are also a number of limitations to consider. First, like many longitudinal studies there has been attrition.[27] In particular in Soweto, South Africa, the BT20 study had to deal with a population of frequent circular migration between rural and urban populations, and also other difficulties in tracing families.[26] However, currently the BT20 team is in contact with >70% of the cohort,[26] which is a lower rate of attrition in comparison with other developing country cohorts.[27,28] Moreover, the purposeful administration of the 112-item YSR to Black participants at the Chris Hani Baragwanath site may have given an analytical data sample ($n = 1029$) not entirely representative of the whole population. However, comparisons between variables in the sample and non-responders (Table 1) display key similarities such as percentage of LBW (12 and 10.2%) and gestational age (<36 weeks, 4.8% in both groups). However, selection bias cannot be excluded particularly with the relative lower SES in non-responders. The more socially disadvantaged children may be less likely to present for assessment and may be at higher risk for development of psychological symptoms. The potential for selection bias within this study for 12-year olds with better psychological health may explain the lack of association between birthweight and later psychological problems.

Secondly, although the YSR is a validated measure of emotional and behavioural functioning, it is not a diagnostic assessment of psychiatric disorder. Moreover, the YSR was conducted as an interviewer-assessed questionnaire in the respondent's preferred language. This may have increased overall understanding of the questions, but also introduced social desirability bias. Thirdly, the use of 2500 g as a marker for increased perinatal morbidity and fetal distress, which is based on studies from the developed world, may not be appropriate in all settings,[1] despite being used internationally. Our continuous analyses adjusted for gestational age, and sample subset analysis of those in the lowest 5% category for birthweight, however, intend to overcome the issue of using a possibly contextually inappropriate cut off for LBW.

Thirdly, although power calculations (provided upon request) displayed sufficient power to detect moderate changes we may not have had sufficient power to detect smaller effects. Lastly, as the prevalence of depression is low at age 12 years, further follow up is required to provide a test of the depression hypothesis at an age when it is more prevalent. Nonetheless, emotional and behavioural problems (including those that comprise high levels of anxiety and depressive symptomatology) are common at age 12 years and the use of a continuous scale has enabled assessment of these domains, which are also known to be likely to develop to depression.

In summary, the findings of this study do not support an association between LBW and higher subsequent rates of psychological symptoms including depression, which may suggest that the fetal origins hypothesis in relation to psychological outcomes is not upheld within this developing world cohort. It displays the need to further assess the fetal origins hypothesis in lower- and middle-income countries. This is particularly important given the high number of LBW infants in such countries and the ramifications of psychological disturbance on the fulfilment of their potential.

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KEY MESSAGES

- There is no convincing evidence for an association between LBW and later emotional and behavioural outcomes at age 12 years in this sample in Soweto, South Africa.
- The fetal origins hypothesis requires further investigation in developing world settings.

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