Assessment of developmental outcome in very low birth weight infants in Southern Africa using the Bayley Scales of Infant Development (III)

Daynia Elizabeth Ballot, Tanusha Ramdin, David Rakotsoane, Faustine Agaba, Tobias Chirwa, Victor Alan Davies, Peter Alan Cooper

ABSTRACT

Objective The study aimed to compare the developmental outcome of very low birth weight infants with a group of normal-term controls in a tertiary hospital in sub-Saharan Africa.

Design A group of 105 very low birth weight infants were assessed at a mean age of 17.6 months (95% CI 16.7 to 18.6) using the Bayley Scales of Infant Development, Third Edition, and compared with a group of normal-term controls at the same mean age.

Results Seven of the study infants (7%) had developmental delay (a score below 70), compared with none in the control group (p<0.04). Three of the seven study infants were delayed on all three subscales, one of whom had cerebral palsy. A further 34% of the study infants were ‘at risk’ of developmental delay (a score below 85). There was no difference in the mean composite score between the study group and controls for the cognitive (p=0.56), motor (p=0.57) or language (p=0.66) subscales. There was no difference in mean composite scores on all subscales between infants who were appropriate for gestational age and those who were small for gestational age. Cognitive and motor scores remained stable in paired assessments of study infants before and after 1 year of age; language scores decreased significantly (p<0.001). Mechanical ventilation was the only risk factor significantly associated with a cognitive score below 85 in study infants.

Conclusion Very low birth weight infants in sub-Saharan Africa are at risk of developmental delay and require long-term neurodevelopmental follow-up.

BACKGROUND

Survival of very low birth weight infants (VLWBI) in low-income and middle-income countries (LMICs) continues to increase with improvements in neonatal care. However, VLWBI remain vulnerable to brain damage during the first few weeks of life, with potential lifelong consequences. The monitoring of developmental outcome is, therefore, an essential part of neonatal care.

What is already known on this topic?

- Very low birth weight infants (VLWBI) are at risk of neurodevelopmental handicap.
- There is limited information on the outcome of VLWBI in sub-Saharan Africa.
- The Bayley Scales of Infant Development, Third Edition (BSID (III)) was developed in a Western English-language population.

What this study hopes to add?

- This study showed that 7% of VLWBI in South Africa had developmental delay.
- In paired BSID (III) assessments in VLWBI in South Africa, language scores decreased significantly after the age of 1 year.
- Mechanical ventilation was the only risk factor associated with poor developmental outcome in study infants.

There is very little recent information on the developmental outcome of VLWBI in sub-Saharan Africa. It is important to have current local data in order to establish proper interventions to improve outcome in these infants. The survival of VLWBI in high-income countries is likely to be very different as the postneonatal problems encountered and the resources available are not the same. Reports from LMCIs suggest that VLWBI have a high risk of neurodevelopmental handicap. A study conducted by Thompson et al in Cape Town in 1993 showed that 22% of infants with a birth weight below 1250 g suffered from major handicap. Cooper and Sandler reported on the developmental outcome of VLWBI in Soweto in 1997 and found that 17% of survivors had evidence of significant handicap. A previous study conducted in the same neonatal unit as the
current study in central Johannesburg in 2006–2009, using the Bayley Scales of Infant Development, Third Edition (BSID (III)), showed that the developmental outcome of VLBWIs was within the normal range, but almost one-third of the infants were considered to be at risk of poor developmental outcome with a score below 85 on cognitive, motor and language subscales. Of note, there was no control group in the previous study. A study from Malawi reported that preterm infants had increased rates of handicap compared with a group of term controls.

There has been a marked change in neonatal care in South Africa since the publication of these studies, with a significant increase in the use of surfactant and nasal continuous airways pressure (NCPAP) rather than assisted mechanical ventilation. In the study unit, extremely low birth weight infants (ELBWI) who were previously not offered ventilatory support could now be provided with surfactant and NCPAP in a high care area, which resulted in a twofold improvement in survival of these infants. In the study by Cooper and Sandler, adverse developmental outcome was strongly associated with mechanical ventilation. It is important to document whether the change in neonatal care is associated with a difference in neonatal outcome, in particular whether there is an increase in handicap among survivors. A recent study from India reported ELBW survivors to be at high risk of adverse neurodevelopmental and behavioural outcome.

Developmental assessment is a complex issue and is closely linked to social, language and cultural norms. The BSID (III) is a tool developed and validated in a group of children in the English language in a Western culture. The Malawi Developmental Assessment Tool is an example of an assessment tool developed for use in the African context, but may be equally problematic for children growing up in an inner city such as Johannesburg. Despite possible cultural differences, the BSID (III) has been used for developmental assessment by several researchers in Southern Africa. Use of a control group from the same social and cultural background provides a benchmark for comparison of developmental outcome of high-risk children when using a tool such as the BSID (III).

Long-term follow-up is difficult to conduct in sub-Saharan Africa. Many mothers reside in neighbouring provinces or countries, experience financial constraints, are dependent on their own income as their sole means of support and may not understand the need for follow-up of an apparently well baby. Infants approaching 1 year of age are frequently sent to live with their grandparents in the surrounding areas, while mothers return to work. The rate of compliance in subsequent follow-up assessment is therefore reduced after 1 year. It is important to know if developmental assessment conducted in the first year of life remains unchanged as the child grows older.

The aim of this study was to assess the developmental outcome of a group of VLBWIs in comparison to normal controls using the BSID (III) as the assessment tool. Secondary objectives were to determine the number of VLBWIs who had developmental delay, to establish variability between BSID (III) assessments done before and after 1 year of age, to compare the development of ELBWIs with children >1000 g at birth, and to compare development between VLBWIs who were appropriate for gestational age (AGA) and small for gestational age (SGA) at birth.

METHODS

Mothers with VLBWIs born between 1 July 2013 and 31 December 2013 who were discharged from the neonatal unit were invited to attend the study clinic. Children who attended at least one follow-up study clinic visit were included in the study group. Children with obvious abnormalities (eg, trisomy 21) likely to affect neurodevelopment were excluded. A group of well term babies (‘normal infants’) who had gone home with their mothers after birth during the same period were enrolled and followed up at the same clinic. The developmental outcome of the ‘normal infants’ has been reported elsewhere.

Gestational age was assessed by maternal menstrual history and clinical assessment using the Ballard score. Infants were classified as AGA or SGA using the Fenton Growth calculator for preterm infants (www.peditools.org/fenton2013/index.php).

Children were seen every three months. The study clinic did not function as a general clinic—parents would attend the local municipal clinic if the infants were suffering from any intercurrent illnesses. Owing to an anticipated high study fallout rate after 1 year of age, BSID (III) assessments were done at 9–12 months of age and again at 15–18 months of corrected age. The BSID (III) assessments for both VLBWI and control infants were done by the same appropriately trained physiotherapist or paediatrician, who was blinded to the child’s neonatal information. The age corrected for the degree of prematurity was calculated by a clinic nurse and used for determining the BSID (III) scores; the person conducting the BSID (III) assessment was not aware of the degree of prematurity of the subject. A Cronbach’s alpha intraclass correlation of 0.89 was determined between different observers.

Measures taken to ensure a reasonable rate of follow-up included sending a text message reminder of the appointment, refund of transport costs, tracing and rebooking of defaulters. If a child had defaulted from follow-up, the BSID (III) assessment was done at the next follow-up visit that the child attended. Children with developmental problems were referred to the appropriate paediatric or allied medical unit for therapy.

The child’s weight, height and skull circumference were measured at each visit and plotted on WHO (www.who.int) growth charts; the growth parameters were expressed as Z scores derived from these charts. Maternal education was classified as none, primary school only,
high school graduate or college/university education. Receipt of the South African government’s social grant for child support was used as a measure of poor socio-economic status.

Sample size calculation
A previous study in the same setting showed that the mean composite score in VLBWI was 89 with an SD of 15. The normative population of the BSID (III) has a mean of 100 with an SD of 15. A sample of 30, with α=0.05 and β=0.80, would be required to detect a statistical difference between these two means. If the control mean was set at 97, a sample size of 44 would be required with α=0.05 and β=0.80 to detect a significant difference between the means. Thus there should be at least 50 subjects in each group, assuming a loss to follow-up rate of 12%.

Statistical analysis
Data were entered into a neonatal database using Research Electronic Data Capture (REDCap) software. Data were exported into IBM SPSS V.23 for statistical analysis. The composite cognitive, language and motor scores were used as outcomes for the purpose of statistical analysis. All continuous variables had normal distribution, so data were described using mean and 95% CI. For the purpose of analysis, the latest BSID (III) assessment was reported in the whole group. The BSID (III) assessments done in the same children were compared by paired t-test. The development of ELBWI was then compared with those infants >1000 g at birth using unpaired t-test. The development of AGA and SGA infants was compared using unpaired t-test. Statistical significance was considered at a level of 0.05.

Developmental delay was classified ‘at risk’ if a composite BSID (III) score was below 85 on any of the language, cognitive or motor scales, and as ‘delayed’ if a composite BSID (III) score was below 70 on any of the subscales. χ² or Fisher’s exact test was used to investigate statistical associations between classified developmental delay and study group.

Univariate analysis using binary logistic regression was used to establish determinants of a score below 85 on each of the BSID (III) subscales. Maternal variables included demographic and obstetric information, education and child support grant, while VLBWI variables included demographics, birth weight, gestational age, neonatal complications and growth parameters. Variables with a significant association at p<0.1 were entered into a multi-variable logistic regression model to determine adjusted ORs for significant determinants of a BSID (III) score below 85 on each subscale.

## RESULTS
A total of 134 mothers of VLBWIs attended at least one neonatal follow-up visit, one child died, one was untestable, three families relocated and twenty-four VLBWIs were lost to follow-up before a BSID (III) assessment could be done. There were thus 105 VLBWIs in the final study sample (see figure 1), giving a follow-up rate of 78% (105/134). The mean birth weight was 1143.5 g (95% CI 1099.6 to 1187.4) and the mean gestational age was 29.6 weeks (95% CI 29.1 to 30.1). The majority of the VLBWIs were female (61; 58%). There were 72 (69%) VLBWIs with a birth weight above 1000 g and 33 (31%) with a birth weight below 1000 g. Twenty-four per cent (25/105) of the VLBWIs were SGA infants. Other

### Table 1

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Received antenatal care</td>
<td>88</td>
</tr>
<tr>
<td>Received antenatal steroids</td>
<td>45</td>
</tr>
<tr>
<td>Black ethnicity</td>
<td>99</td>
</tr>
<tr>
<td>Primiparous mother</td>
<td>31</td>
</tr>
<tr>
<td>Maternal hypertension</td>
<td>30</td>
</tr>
<tr>
<td>Maternal HIV</td>
<td>26</td>
</tr>
<tr>
<td>Delivered by caesarean</td>
<td>76</td>
</tr>
<tr>
<td>Resuscitated at birth with bag and mask</td>
<td>30</td>
</tr>
<tr>
<td>Early-onset sepsis</td>
<td>5</td>
</tr>
<tr>
<td>Respiratory distress syndrome</td>
<td>89</td>
</tr>
<tr>
<td>Surfactant replacement therapy</td>
<td>80</td>
</tr>
<tr>
<td>Nasal continuous airways pressure</td>
<td>70</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>17</td>
</tr>
<tr>
<td>Retinopathy of prematurity (grade 2 or more)</td>
<td>5</td>
</tr>
<tr>
<td>Patent ductus arteriosus</td>
<td>11</td>
</tr>
<tr>
<td>Intraventricular haemorrhage grade 3 or 4</td>
<td>0</td>
</tr>
<tr>
<td>Cystic periventricular leucomalacia</td>
<td>0</td>
</tr>
<tr>
<td>Necrotising enterocolitis (stage 2 or more)</td>
<td>4</td>
</tr>
<tr>
<td>Exchange transfusion</td>
<td>1</td>
</tr>
<tr>
<td>Sepsis after day 3</td>
<td>21</td>
</tr>
<tr>
<td>Received oxygen on day 28</td>
<td>32</td>
</tr>
<tr>
<td>Steroids for chronic lung disease</td>
<td>17</td>
</tr>
<tr>
<td>Birth defect</td>
<td>3</td>
</tr>
</tbody>
</table>
demographic and clinical information of the VLBWI is shown in table 1. There were 74 control infants who were born at term with a mean birth weight of 2.7 kg (95% CI 2.6 to 2.8) and half were female. Most (78%) were delivered vaginally. Thirty per cent were HIV-exposed, but none were infected with HIV. Further information on the control group is published elsewhere.16

**BSID (III) assessment in the whole group of VLBWI compared with controls**

There were 105 BSID assessments done at a mean age of 17.6 months (95% CI 16.7 to 18.6). A score above 85 is considered normal. The mean cognitive score was 93.1 (95% CI 90.1 to 96.1), the mean language score was 93.6 (95% CI 91.0 to 96.1) and the mean motor score was 97.2 (95% CI 91.0 to 96.1). The comparison between the VLBWIs and controls is shown in table 2. The control group was assessed at a significantly older age, so the control group was reported as the total group and a subgroup who were assessed at the same mean age as the VLBWIs. There were no statistically significant differences in any of the scores between the VLBWIs and controls.

There was no statistical difference between any of the other variables.

**Paired BSID (III) assessments**

There were 56 VLBWIs who had two BSID (III) assessments—the first at a mean age of 10.4 months (95% CI 10.0 to 10.8) and again at a mean age of 19.0 months (95% CI 18.6 to 19.4). The differences in the mean scores for each subscale are shown in table 3. There was a statistically significant difference in language scores between the two assessments but no difference in cognitive and motor scores.

**ELBW compared with bigger infants**

There were 34/105 (32%) infants with a birth weight below 1000 g. BSID (III) assessments are compared between ELBW and bigger infants in table 4. There were no statistically significant differences on any of the developmental scores between the two groups.

**Comparing AGA with SGA infants**

The mean scores for AGA and SGA VLBWI are compared in table 5. There were no statistically significant differences in any of the scores between the two groups.

**Developmental delay**

Seven of the study infants (7%) had developmental delay (a score below 70), compared with none in the control group (p=0.04) (table 6). Three of the seven study infants were delayed on all three subscales, one of whom had cerebral palsy. A further 34% of the study infants were ‘at risk’ of developmental delay (a score below 85).

**Cut-off of 85**

There were 43 VLBWIs (41%) with a BSID (III) below 85 on any subscale. Six VLBWIs had scores below 85 on all three subscales and five VLBWIs had two subscales below 85.

**Cut-off of 70**

There were 12 BSID (III) scores below 70 on any subscale in seven (6.6%) of the VLBWI group—none of the control group was classified as delayed on any subscale (p=0.04) (See table 6). There were three VLBWIs who had developmental delay (score <70) on all three

### Table 2 Comparison for mean BSID (III) scores between VLBWI and control infants

<table>
<thead>
<tr>
<th></th>
<th>VLBWI, n=105</th>
<th>Control, n=74</th>
<th>Subgroup of controls, n=50</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (95% CI)</td>
<td>Mean (95% CI)</td>
<td>Mean (95% CI)</td>
</tr>
<tr>
<td>Adjusted age</td>
<td>17.6 (16.7 to 18.6)</td>
<td>19.4 (18.4 to 20.4)*</td>
<td>17.6 (16.6 to 18.6)</td>
</tr>
<tr>
<td>Cognitive</td>
<td>93.1 (90.1 to 96.1)</td>
<td>92.2 (89.4 to 95.0)</td>
<td>91.6 (87.7 to 94.5)</td>
</tr>
<tr>
<td>Language</td>
<td>93.6 (91.0 to 96.1)</td>
<td>94.8 (92.5 to 97.1)</td>
<td>94.8 (91.9 to 97.7)</td>
</tr>
<tr>
<td>Motor</td>
<td>97.2 (91.0 to 96.1)</td>
<td>98.8 (96.8 to 101.0)</td>
<td>98.2 (95.5 to 100.8)</td>
</tr>
</tbody>
</table>

*Mean age significantly different from that of VLBWI.

BSID (III), Bayley Scales of Infant Development, Third Edition; VLBWI, very low birth weight infant.

### Table 3 Comparison between paired Bayley Scales of Infant Development, Third Edition assessments in the same infants

<table>
<thead>
<tr>
<th></th>
<th>First assessment, n=56</th>
<th>Second assessment, n=56</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (95% CI)</td>
<td>Mean (95% CI)</td>
<td></td>
</tr>
<tr>
<td>Corrected age (months)</td>
<td>10.4 (10.0 to 10.8)</td>
<td>19.0 (18.6 to 19.4)</td>
<td></td>
</tr>
<tr>
<td>Cognitive</td>
<td>95.9 (92.6 to 99.1)</td>
<td>91.8 (87.4 to 96.3)</td>
<td>0.11</td>
</tr>
<tr>
<td>Motor</td>
<td>94.7 (90.8 to 98.7)</td>
<td>97.5 (93.7 to 101.2)</td>
<td>0.33</td>
</tr>
<tr>
<td>Language</td>
<td>104.3 (101.5 to 107.0)</td>
<td>91.7 (88.3 to 95.0)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
subdomains, one of whom was diagnosed with cerebral palsy. Three VLBWIs had isolated cognitive delay and one had isolated language delay. None of the ELBWIs in the group had a composite score below 70 on any of the subscales. No VLBWI was blind or had major hearing loss requiring the use of hearing augmentation.

Determinants of BSID (III) score below 85 on each subscale in VLBWI

Logistic regression model results show that conventional mechanical ventilation was significantly associated with a language subscale below 85. There were no other significant associations with any maternal, neonatal, sociodemographic, growth parameters and a score below 85. These findings confirm the need for long-term neurodevelopmental follow-up of VLBWIs in order to identify and support those with handicap at an early stage.

The rate of developmental delay reported in the present study is considerably less than that reported in East Africa, where 11% of VLBWI survivors had cerebral palsy. It must be noted, however, that the current study showed that, although most of the VLBWIs had normal developmental function, this remains a vulnerable group of infants. Developmental delay was present in 6.6% of VLBWIs, one of whom had cerebral palsy. In contrast, there was no developmental delay in the normal control infants. A further 34% of the VLBWIs were classified to have cerebral palsy. Three VLBWI survivors had isolated cognitive delay and one had isolated language delay. None of the ELBWIs in the group had a composite score below 70 on any of the subscales. No VLBWI in sub-Saharan Africa was blind or had major hearing loss requiring the use of hearing augmentation.

DISCUSSION

The present study from Johannesburg, South Africa, showed that, although most of the VLBWIs had normal developmental function, this remains a vulnerable group of infants. Developmental delay was present in 6.6% of VLBWIs, one of whom had cerebral palsy. In contrast, there was no developmental delay in the normal control infants. A further 34% of the VLBWIs were classified to have cerebral palsy. These findings confirm the need for long-term neurodevelopmental follow-up of VLBWIs in order to identify and support those with handicap at an early stage.

The rate of developmental delay reported in the present study is considerably less than that reported in East Africa, where 11% of VLBWI survivors had cerebral palsy. However, it must be noted, however, that the current study was conducted in a large tertiary academic hospital. The majority of VLBWI in sub-Saharan Africa are born and treated outside academic services. It is very likely that the rate of developmental delay in these infants is much greater than that reported in the current study. Further research should be conducted to determine the rate of handicap in VLBWIs born outside an academic setting in sub-Saharan Africa, so that appropriate follow-up and interventions can be developed.

The developmental outcome of VLBWIs in the current study is slightly better than previously reported in the same study setting. The composite scores for each BSID (III) subscale are marginally higher than previously reported and fewer VLBWI survivors had scores below 70 than in the previous study.

The developmental outcome of a small group of ELBWIs in the present study was the same as infants with a birth weight above 1000 g. In addition, none of the ELBWIs had developmental delay. There was no significant difference in the developmental scores for VLBWIs who were AGA compared with those who were SGA at birth. This is in agreement with a report of developmental outcome of VLBWI survivors in India. These results are preliminary. Further research needs to be conducted to determine the developmental outcomes of ELBWI and SGA infants in sub-Saharan Africa.

There was no significant change in the cognitive or motor assessments in paired assessments in the VLBWI; however, the language score was significantly reduced in the later assessment. This is similar to the control group in the study setting, where language scores were significantly decreased in the BSID (III) assessment done at

| Table 4 | Developmental outcome for infants above and below 1000 g at birth |
| Subscale | <1000 g birth weight, n=34 | >1000 g birth weight, n=71 | p Value |
| Corrected age | 18.5 (16.7 to 20.2) | 17.3 (16.2 to 18.4) | 0.23 |
| Cognitive | 95.4 (89.7 to 101.1) | 92.7 (88.7 to 96.7) | 0.74 |
| Motor | 98.9 (95.2 to 102.5) | 96.4 (92.7 to 100.2) | 0.42 |
| Language | 94.2 (90.8 to 97.6) | 94.2 (90.8 to 97.6) | 0.46 |

| Table 5 | Developmental outcome for appropriate for gestational age (AGA) infants compared with small for gestational age (SGA) infants |
| Subscale | SGA, n=25 | AGA n=80 | p Value |
| Cognitive | 95.4 (89.7 to 101.1) | 92.4 (88.8 to 96.0) | 0.40 |
| Motor | 94.1 (90.6 to 97.6) | 93.4 (90.2 to 99.8) | 0.82 |
| Language | 99.8 (95.2 to 104.3) | 96.4 (93.0 to 99.8) | 0.77 |

| Table 6 | Comparison of developmental delay between very low birth weight infant (VLBWI) and control groups |
| Composite score | VLBWI (105) n (%) (95% CI) | Control (74) n (%) (95% CI) | p Value |
| Cognitive <70 | 5 (6.7) (2.6 to 11.9) | 0 | 0.04 |
| Cognitive <85 | 25 (24.0) (16.7 to 32.8) | 19 (25.6) (17.1 to 36.6) | 0.78 |
| Language <70 | 4 (3.8) (1.5 to 9.3) | 0 | 0.14 |
| Language <85 | 19 (18.1) (11.9 to 26.5) | 12 (16.2) (9.5 to 26.2) | 0.84 |
| Motor <70 | 3 (2.9) (1.0 to 8.1) | 0 | 0.27 |
| Motor <85 | 16 (15.2) (9.6 to 23.3) | 4 (5.2) (2.1 to 13.1) | 0.05 |
an older age in the same children. This change may be related to the fact that many of the children in the study setting do not speak English as a mother tongue; hence, language assessment is performed through an interpreter or based on the parent’s report. Unlike the control group, the motor score in VLBWIs remained unchanged, whereas in control infants it increased significantly in the later assessment.

**Study limitations**

Loss to follow-up remains a problem in long-term outcome studies in South Africa. Although the follow-up rate of 78% in the current study was reasonable, there were still 22% of children who were lost. Reasons for defaulting could not be determined. Attendance at follow-up clinic is onerous, especially when mothers return to work. Mothers may be reluctant to take significant amounts of time off work to attend clinic for fear of losing employment. It is also possible that mothers do not see the need for follow-up if they perceive their children to be well. Lack of finance is another possible reason; although transport costs were refunded, mothers still had to get to the clinic and needed money in order to do this. Almost one-third of the patients in the current study were foreign nationals and these mothers may have returned home.

Accurate assessment of gestational age is also a problem in the study setting. Mothers generally present at antenatal clinic in the second trimester or do not attend antenatal care at all. Accurate assessment of gestational age by means of first trimester sonar was therefore not available in most patients.

Developmental assessment of young children is difficult in the best circumstances. The BSID (III) tool was developed using a Western English-language population. There are cultural and language differences in the study population. Many of these issues should be counteracted by the control group, but it appears that language may not be properly assessed in the local setting using the BSID (III). It is difficult to have a single language tool for use in South Africa as there are 12 official languages.

Accurate assessment of sociodemographic status is difficult in the study context. The social grant is only provided to South African citizens and almost one-third of the mothers in the current study were foreign nationals. In addition, many mothers have undisclosed sources of income.

Two of the three HIV-infected babies were lost to follow-up, so the outcome of these high-risk infants was unknown.

**CONCLUSION**

The present study showed that VLBWIs are at risk of developmental delay, emphasising the need for long-term neurodevelopmental follow-up in these infants. Paired BSID (III) assessments done at different ages in the same children showed that cognitive and motor scores remained stable, but language scores decreased significantly with age. The only risk factor for delayed development in the present study was mechanical ventilation. Further research needs to be done on the neurodevelopmental outcome of ELBWIs and VLBWIs born outside an academic setting in sub-Saharan Africa.

**Acknowledgements**

The study was funded by a Self-Initiated Research Grant from the South African Medical Research Council.

**Competing interests**

None declared.

**Patient consent**

Parental/guardian consent obtained.

**Ethics approval**

The study was approved by the Human Research Ethics Committee of the University of the Witwatersrand.

**Provenance and peer review**

Not commissioned; externally peer reviewed.

**Data sharing statement**

Data can be made available upon reasonable request to the corresponding author.

**Open Access**

This is an Open Access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

© Article author(s) (or their employer(s) unless otherwise stated in the text of the article) 2017. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

**REFERENCES**


6. Cooper PA, Sandler DL. Outcome of very low birth weight infants at 12 to 18 months of age in Soweto, South Africa. *Pediatrics* 1997;99:537–44.


