Maternal and infant factors had a significant impact on birthweight and longitudinal growth in a South African birth cohort

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ABSTRACT

Aim: This birth cohort study investigated longitudinal infant growth and associated factors in a multiethnic population living in a low-resource district surrounding the town of Paarl in South Africa.

Methods: Between March 2012 and October 2014, all mothers attending their second trimester antenatal visit at Paarl Hospital were approached for enrolment. Mother–infant pairs were followed from birth until 12 months of age. Comprehensive socio-demographic, nutritional and psychosocial data were collected at birth, two, six and 12 months. Infant anthropometry was analysed as z-scores for weight and height. Linear regression was used to investigate predictors of birthweight, and linear mixed-effects models were used to investigate predictors of infant growth.

Results: Longitudinal anthropometric data from 792 infants were included: 53% were Black African, 47% were mixed race, and 15% were born preterm. Stunting occurred in 13% of infants at 12 months. Maternal height, antenatal alcohol and tobacco use, ethnicity and socioeconomic status were significant predictors of birthweight. In the adjusted mixed-effects model, birthweight was a significant predictor of growth during the first year of life.

Conclusion: Birthweight was an important predictor of growth trajectory during infancy. Birthweight and growth were influenced by several important modifiable factors.

INTRODUCTION

Childhood malnutrition, which encompasses both undernutrition and overweight or obesity, is highly prevalent in low- and middle-income countries (LMIC) (1). Although global rates of stunting in children under five years of age have decreased over the past decade, the prevalence of stunting in sub-Saharan Africa has continued to rise (1). Obesity rates in children and adults in LMIC have also been rising, and these are referred to as the double burden of malnutrition (1,2).

South Africa comprises multiethnic populations, with varying socioeconomic circumstances, psychosocial factors, disease exposures and cultural practices. Differences in child growth patterns may occur in such population groups, and these reflect genetic or environmental factors or a combination of these (3,4). The prevalence of psychosocial factors, such as maternal depression, intimate partner violence (IPV) and substance abuse – including alcohol and tobacco consumption – in LMIC is high and has been associated with poor infant outcomes, including low birthweight and poor infant growth (5).

Key notes
- This large cohort study investigated the factors associated with birthweight and longitudinal infant growth in a resource-poor setting.
- Birthweight was a major predictor of growth trajectory during infancy, after adjusting for socioeconomic status, ethnicity, prematurity and intra-uterine growth restriction.
- Alcohol or tobacco consumption during pregnancy was high in this population and was associated with both poor birth outcomes and poor postnatal growth during infancy.

Abbreviations
AGA, Appropriate for gestational age; BMI, Body mass index; BMIZ, Body mass index for age z-score; HFAZ, Height-for-age z-score; IPV, Intimate partner violence; IQR, Interquartile range; LBW, Low birthweight; LMIC, Low and middle-income countries; SES, Socioeconomic score; SGA, Small for gestational age; WFAZ, Weight-for-age z-score; WFHZ, Weight-for-height z-score; WHO, World Health Organization.
Few cohort studies from LMIC have investigated child growth longitudinally, and no longitudinal studies of growth patterns in South African infants from different ethnic backgrounds have been carried out. The aim of this study was to describe patterns of growth and factors that had an impact on growth in South African infants enrolled in the Drakenstein Child Health Study.

PATIENTS AND METHODS
The primary aim of the Drakenstein Child Health Study birth cohort was to investigate the epidemiology, risk factors, aetiology and long-term impact of respiratory illness on child health, including investigations into growth and nutrition in early childhood (6).

Study population
Pregnant women living in a resource-poor area surrounding an agricultural town were enrolled during their second trimester of pregnancy at two primary healthcare facilities serving different ethnic communities: TC Newman serving a mixed race community and Mbekweni serving a Black African community. This means that the two clinics were synonymous with ethnicity. Women who were less than 18 years of age, those who were unable to provide informed consent or those who intended to leave the area within a year were excluded. All the infants that were born to mothers enrolled into the study were included in the analysis. All pregnant women who were enrolled into the study received standard antenatal care at a single district level hospital.

Measures
Socio-demographic and health information were obtained from questionnaires administered to the mothers during antenatal and postnatal study visits. Four socio-demographic variables were used to generate a relative socio-economic score (SES): education, employment, household income and assets. Participants were stratified into quartiles based on their SES score. These quartiles were labelled as low, low-to-moderate, moderate-to-high or high SES, to enable comparisons within the study population (7).

All births occurred at a single public hospital, Paarl hospital, which provides general hospital and emergency care for a population of more than 600 000 people living in a vast geographical area of approximately 22 500 square kilometres. It is based in a predominantly semirural region 60 kilometres from Cape Town in the Southern tip of South Africa.

Birthweight and length were measured at the hospital. Gestational age at birth was estimated based on an antenatal ultrasound carried out in the second trimester (68%), and if this was unavailable, then fundal height (28%) or maternal recall of the last menstrual period (4%) was used. Trained study staff collected serial anthropometric measurements on the infants at two, six and 12 months. The infant’s length was measured in centimetres to the nearest completed 0.5 cm, and their weight was measured in kilograms to the nearest completed 10 g, according to standard operating procedures. Maternal height was measured to the nearest 0.1 cm at enrolment, using a wall-mounted stadiometer. The birth anthropometrical measurements were conducted by trained labour ward staff, and the birthweights and lengths were obtained from the patients’ folders. When we compared the labour ward staff measurements of infant anthropometry with study staff measurements in a subgroup of patients, we found no significant differences.

Weight was measured, in the light or no clothing, using the TAN1584 digital platform scale (Tanita, IL, USA) and recumbent length using the seca210 length-measuring mat (seca, Hamburg, Germany). The latter was performed on a firm surface by two staff members. The equipment was calibrated weekly. All anthropometric measurements were carried out twice for each child, with a third measurement if the difference between the first and second measurement differed by more than 0.5 cm for length or more than 0.5 kg for weight. Study staff underwent regular anthropometric training and assessment every three months, and this was conducted by the lead anthropometrist.

Four time points were used for the purposes of this analysis: birth, two, six and 12 months of age. A valid anthropometric measurement was within four weeks before or after that time point.

With regard to nutritional information, the infant feeding practice was categorised based on the World Health Organization’s (WHO) Infant and Young Child feeding indicators, namely exclusive breastfeeding or bottle feeding, which included infant cows’ milk-based formula with or without breast milk or semisolids (8).

Validated questionnaires were administered to mothers antenatally and six weeks postpartum to assess psychosocial factors (5). The Edinburgh Postnatal Depression Rating Scale was used to assess maternal depression and a score of at least 13 was classified as probable depression (5). An IPV questionnaire was used to assess recent exposure to physical, emotional and sexual IPV (5). Exposure was categorised as above the threshold if a participant reported more than one incident of IPV during the previous year. The Alcohol, Smoking and Substance Involvement Screening test was used to assess maternal alcohol consumption based on a scoring system that was previously described (5). Tobacco smoking was measured using maternal urinary cotinine levels antenatally and postnatally using the IMMULITE 1000 Nicotine Metabolite Kit (Siemens Medical Solutions Diagnostics, Caernarfon, UK). A urinary cotinine level of ≥500 ng/mL was used as the threshold to dichotomise mothers into active smokers and nonsmokers based on the manufacturer’s recommendations.

Statistical analysis
Birthweight and length were converted to z-scores for gender and gestational age using the INTERGROWTH-21st standards (9). Infants were classified into low birthweight (LBW) if they weighed less than 2500 g at birth, preterm if they born at less than 37 weeks of gestational age and small...
for gestational age (SGA) if they weighted less than the 10th percentile for gestational age, based on gender and gestational age. Corrected gestational age was used to calculate the WHO z-score of preterm infants.

The weight and length measurements following birth were converted to z-scores based on age and gender, using Anthro software (WHO, Geneva, Switzerland) (10). Weight-for-age z-scores (WFAZ), height-for-age z-scores (HFAZ), weight-for-height z-scores (WFHZ) and body mass index (BMI) for age z scores (BMIZ) were calculated. BMI was calculated using the formula

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\text{BMI} = \frac{\text{weight in kilograms}}{\text{length in centimetres}^2}.
\]

Growth patterns in the study population were analysed at each time point by calculating the median WFAZ and HFAZ as well as between the time points by calculating the difference in WFAZ and HFAZ. At each time point, indicators of malnutrition were calculated so that infants with an HFAZ < -2 were classified as stunted, those with a WFAZ < -2 as underweight for age, those with a WFHZ < -2 as wasted and those with a BMI for age > 2 as overweight and > 3 as obese. Growth patterns and indicators of malnutrition

| Table 1 Maternal demographic and psychosocial characteristics and infant birth outcomes |
|-----------------------------------------------|-----------------|-----------------|-----------------|--------------------|
| Variable                                      | Mbekweni (Black African) – n (%) | TC Newman (Mixed race) – n (%) | Total – n (%) | p-value |
| Maternal demographic and psychosocial characteristics | | | | |
| Number of mothers                             | 418 (53) | 371 (47) | 789 | <0.001 |
| Median [IQR] gestation at enrolment           | 23 [20-26] | 21 [19-25] | 22 [20-25] | <0.001 |
| Ethnicity                                      | | | | |
| Black/African                                  | 414 (99) | 5 (1) | 419 (53) | | |
| Mixed race                                     | 4 (1) | 363 (98) | 367 (47) | | |
| Other                                          | 0 (0) | 3 (0.8) | 3 (0.4) | | |
| Median [IQR] age at enrolment (yrs)            | 26.7 [22.2-31.8] | 24.8 [21.3-29.1] | 25.7 [21.8-30.7] | <0.001 |
| Median [IQR] height (cm)                       | 160 [156-164] | 158 [153-162] | 159 [155-163] | <0.001 |
| Educational achievement                        | | | | |
| Primary education only                         | 42 (10) | 29 (8) | 71 (9) | |
| Some secondary education                       | 225 (54) | 182 (49) | 407 (52) | 0.021 |
| Completed secondary education                  | 122 (29) | 144 (39) | 266 (34) | | |
| Tertiary education                             | 29 (7) | 16 (4) | 45 (6) | | |
| Antenatal urine cotinine – active smoker       | 58 (14) | 190 (51) | 248 (31) | <0.001 |
| Antenatal self-reported alcohol use            | 34 (8) | 105 (28) | 139 (18) | <0.001 |
| Antenatal depression – above threshold (EPDS)  | 114 (27) | 90 (24) | 204 (26) | 0.335 |
| Recent intimate partner violence (antenatal) – above threshold | 110 (26) | 146 (39) | 256 (32) | <0.001 |
| Primigravida                                   | 134 (32) | 146 (39) | 280 (35) | 0.033 |
| HIV-infected                                   | 158 (38) | 10 (3) | 168 (21) | <0.001 |
| Unemployed                                     | 327 (78) | 260 (70) | 587 (74) | 0.009 |
| Average household income                       | | | | |
| <R1000/month                                   | 203 (49) | 127 (34) | 330 (42) | | |
| R1000-R5000/month                             | 167 (40) | 174 (47) | 341 (43) | <0.001 |
| >R5000/month                                   | 48 (11) | 70 (19) | 118 (15) | | |
| SES quartile                                   | | | | |
| Lowest SES                                     | 144 (34) | 69 (19) | 213 (27) | <0.001 |
| Low-moderate SES                               | 109 (26) | 88 (24) | 197 (25) | | |
| Moderate-high SES                              | 99 (24) | 94 (25) | 193 (24) | | |
| Highest SES                                    | 66 (16) | 120 (32) | 186 (24) | | |
| Early postpartum maternal psychosocial         | | | | |
| characteristics (n = 366)                      | | | | |
| Self-reported tobacco use                       | 6 (3) | 91 (54) | 97 (27) | <0.001 |
| Self-reported alcohol use                       | 10 (5) | 44 (26) | 54 (15) | <0.001 |
| Depression – above threshold (EPDS)            | 47 (24) | 29 (17) | 76 (21) | 0.115 |
| Recent intimate partner violence – above threshold | 42 (21) | 47 (28) | 89 (24) | 0.149 |
| Infant birth outcomes                          | | | | |
| Number of infants                              | 421 (53) | 371 (47) | 792 | | |
| Infant sex                                     | | | | |
| Female                                         | 210 (50) | 164 (44) | 374 (47) | | |
| Median [IQR] gestation at delivery (weeks)     | 39 [38-40] | 39 [37-40] | 39 [38-40] | 0.360 |
| Preterm birth (<37 weeks)                      | 64 (15) | 55 (15) | 119 (15) | 0.882 |
| Low birthweight (<2500 g)                      | 45 (11) | 71 (19) | 116 (15) | 0.001 |
| Small for gestational age                      | 96 (23) | 107 (29) | 203 (26) | 0.052 |
were stratified by study site, in other words ethnicity. Significant differences in WFAZ and HFAZ, indicators of malnutrition, and changes in WFAZ and HFAZ between time points were identified using chi-square or Fisher’s exact tests for categorical variables and t-tests or Wilcoxon rank-sum tests (Mann–Whitney tests) for continuous variables.

Variables significantly associated with infant WFAZ at birth were explored. Two linear regression models were built to investigate maternal height and antenatal smoking, based on urinary cotinine levels, as independent predictors of interest. For all models, regression coefficients with 95% confidence intervals (95% CIs) were calculated to determine the strength of these associations.

Based on the literature, known variables associated with infant growth during the first year of life were explored using linear mixed-effects models. Ethnicity and SES were included as fixed effects and WFAZ at birth and age at time of study visit were included as random effects. Three models were built. The first adjusted model (model one) included all variables that were significant in the unadjusted model. The final model (model two) only included the variables that remained significant in model one.

The statistical analysis was conducted using Stata 12 (StataCorp Inc, College Station, TX, USA).

Ethical approval was obtained from the University of Cape Town, Faculty of Health Sciences Human Research Ethics Committee and the Provincial Child Health Research committee. Written informed consent was obtained from all the participants.

## RESULTS
From March 2012 to October 2014, we enrolled 789 mothers with a median age of 25.7 (21.8–30.7) years who had given birth to 792 infants, including three pairs of twins (Table 1) and all of these infants completed their birth study visit. At the time of analysis, 681 infants (93%) completed their two-month study visit, 517 (71%) completed their six-month study visit and 342 (47%) completed their 12-month study visit (Fig. S1). We excluded 62 infants from the growth analysis due to incomplete data: 35 infants at two months and 27 infants at six months. In addition, 97 mother–infants pairs were lost to follow-up during the course of the study. The mothers who were lost to follow-up were significantly younger than those who remained in the

| Table 2 Infant anthropometry and feeding |
|-----------------------------------------|
| Variable                               | Mbekweni (Black African) | TC Newman (Mixed race) | Total | p-value |
| Birth, (n)                              | 421 [-1.2 to 0.3]        | -0.7 [-1.4 to -0.1] | -0.5 [-1.3 to 0.1] | <0.001 |
| Median WFAZ [IQR]                      | 0.1 [-0.8 to 1.1]        | 0.003 [0.8 to 0.9] | 0.1 [-0.8 to 1.0] | 0.019 |
| 2 months, (n)                           | 344                      | 337                  | 681    |         |
| Median WFAZ [IQR]                      | -0.1 [-0.9 to 0.6]       | -0.5 [-1.4 to -0.2] | -0.3 [-1.1 to 0.4] | <0.001 |
| Median HFAZ [IQR]                      | -0.5 [-1.3 to 0.5]       | -0.9 [-1.9 to 0.0] | -0.7 [-1.6 to 0.2] | <0.001 |
| Median change in WFAZ between birth and 2 months [IQR] (n = 681) | 0.3 [-0.5 to 1.0]       | 0.1 [-0.5 to 0.7] | 0.2 [-0.5 to 0.9] | 0.017 |
| Median change in HFAZ between birth and 2 months [IQR] (n = 681) | -0.7 [-1.6 to 0.3]       | -1.0 [-1.8 to -0.1] | -0.9 [-1.7 to 0.2] | 0.040 |
| 6 months, (n)                           | 243                      | 274                  | 517    |         |
| Median WFAZ [IQR]                      | 0.5 [-0.4 to 1.2]        | -0.05 [-1.0 to 0.8] | 0.2 [-0.7 to 1.0] | <0.001 |
| Median HFAZ [IQR]                      | -0.2 [-1.3 to 0.7]       | -0.7 [-1.6 to 0.2] | -0.4 [-1.5 to 0.5] | 0.002 |
| Median change in WFAZ between 2 and 6 months [IQR] (n = 500) | 0.5 [-0.1 to 1.2]       | 0.4 [-0.1 to 1.0] | 0.4 [-0.1 to 1.1] | 0.455 |
| Median change in HFAZ between 2 and 6 months [IQR] (n = 500) | 0.3 [-0.8 to 1.3]       | 0.2 [-0.5 to 0.9] | 0.2 [-0.6 to 1.1] | 0.732 |
| 12 months, (n)                          | 155                      | 187                  | 342    |         |
| Median WFAZ [IQR]                      | 0.3 [-0.5 to 1.0]        | -0.1 [-1.1 to 0.6] | 0.1 [-0.8 to 0.8] | <0.001 |
| Median HFAZ [IQR]                      | -0.3 [-1.2 to 0.6]       | -0.6 [-1.6 to 0.2] | -0.5 [-1.4 to 0.4] | 0.014 |
| Median change in WFAZ between 6 and 12 months [IQR] (n = 305) | 0.1 [-0.5 to 0.6]       | -0.03 [-0.5 to 0.3] | 0.02 [-0.5 to 0.4] | 0.262 |
| Median change in HFAZ between 6 and 12 months [IQR] (n = 305) | -0.01 [-0.9 to 0.8]     | 0.2 [-0.7 to 0.8] | 0.1 [-0.8 to 0.8] | 0.417 |

Infant feeding categories

| Variable                               | Mbekweni (Black African) | TC Newman (Mixed race) | Total | p-value |
|-----------------------------------------| 143 (42)                | 163 (48)               | 306 (45) | <0.001 |
| Exclusive breastfeeding                  | 81 (24)                 | 11 (3)                 | 92 (14) |         |
| Mixed feeding                           | 120 (35)                | 163 (48)               | 283 (42) |         |
| 6 months, (n)                           | 243                     | 274                    | 517    |         |
| Exclusive breastfeeding                  | 22 (9)                  | 23 (8)                 | 45 (9) |         |
| Mixed feeding                           | 190 (78)                | 248 (91)               | 438 (85) | <0.001 |
| 12 months, (n)                          | 155                     | 187                    | 342    |         |
| Exclusive breastfeeding                  | 57 (37)                 | 117 (63)               | 177 (51) |         |
| Mixed formula feeding                   | 91 (59)                 | 53 (28)                | 149 (43) | <0.001 |
| Solids only                             | 7 (5)                   | 17 (9)                 | 24 (7) |         |

WFAZ, weight-for-age z-score; HFAZ, height-for-age z-score.
study (median age 23.3 years versus 26.0 years; \( p = 0.003 \)), had higher levels of education \( (p = 0.030) \) and were more likely to be primigravid \( (p = 0.048) \). There were no significant differences in birth characteristics between the infants who were lost to follow-up and those who remained.

The study population had a predominantly low income, with 43% of households earning below the minimum wage of 5000 South African Rands per month (11). Only half of the participants in the highest SES quartile reported a household income that was higher than that level. Just over a third (34%) of the Black African households fell into the lowest SES quartile and they were relatively poorer than mixed race households (Table 1). The reported levels of antenatal substance use were significantly higher in mothers of mixed race infants than Black African infants. More than half of the mixed race mothers were active smokers (51%) based on their antenatal urinary cotinine levels and more than a quarter (28%) reported consuming alcohol antenatally and postnatally. More than a quarter of mothers (26%) were classified as experiencing probable postnatal depression. Recent IPV was significantly higher among mixed race mothers than Black African mothers.

The median gestational age at birth was 39 weeks, but 15% of babies were born preterm (Table 1). More than a quarter of infants (26%) were born SGA while 15% were LBW (Table 1). The median WFAZ at birth was below the WHO reference population, and this was more marked in mixed race babies (Table 2). Of the 119 infants born preterm, 87 were late preterm (34–37 weeks), 20 were moderately preterm (32–34 weeks), and 12 were very preterm (<32 weeks). The median (IQR) gestation of the preterm infants was 35 (33–36) weeks. The median (IQR) birthweight of the preterm infants was 2.5 (2.05–2.88) kg. In total, 106 of the preterm infants were appropriate for gestational age (AGA), and 13 were SGA. The median WFAZ improved from birth to two months, with a median change of 0.2 between birth and two months. Between two and six months, infants exhibited higher weight gain than height gain. At six months, Black African infants were, on average, heavier and taller than mixed race infants. The period of highest weight gain during infancy was between birth and six months, with a difference in WFAZ of 0.7 (Table 2). At 12 months, the median WFAZ of the sample was almost identical to the WHO median, with a slowing up of weight gain between six and 12 months. Median HFAZ remained negative at all time points, indicating that the infants had slower linear growth and remained shorter than infants from the reference WHO population (Table 2). On average, children born to Black African mothers weighed more and were taller at birth and remained heavier and taller at each time point than those born to mixed race mothers (Table 2).

Malnutrition, either under or over nutrition, occurred consistently throughout infancy (Table 3). Stunting was the most prevalent indicator of undernutrition at all time points, ranging from 17% of infants at two months to 13% by 12 months. At 12 months of age, 2% of the children were obese and 6% were overweight and the rates were higher among black African than mixed race infants (Table 3).

In the unadjusted models of infant WFAZ at birth, ethnicity, household income, gravidity, maternal alcohol and tobacco use, recent IPV and maternal height were significantly associated with lower WFAZ at birth (Table 4). Only variables that were significant in the unadjusted models were included into the multivariate model. Psychosocial and nutritional models were built separately. In the psychosocial multivariate model, the associations between both maternal alcohol and tobacco use and lower WFAZ at birth remained significant, independent of ethnicity and SES (Table 4). In the nutritional model, increased maternal height, which was used as a proxy for maternal nutritional status, remained significantly associated with higher infant WFAZ at birth, when adjusted for ethnicity and SES (Table 4).

In the univariate analysis, birthweight, ethnicity, SES, antenatal and postnatal IPV and antenatal and postnatal maternal substance use – specifically alcohol or tobacco – were significantly associated with infant growth, as measured by repeated WFAZ measurements over the first year of life (Table 5). However, only birthweight and antenatal and postnatal maternal substance use remained significantly associated with infant growth after controlling for ethnicity and SES. In the final multivariate model, birthweight, ethnicity; SES and antenatal maternal substance use remained significantly associated with growth during infancy, adjusted for infant age at the time of measurement. Infant WFAZ at birth was an important predictor of WFAZ

| Table 3 Prevalence of infant malnutrition |
|------------------------------------------|
| Variable | Mbekweni (Black African) – n (%) | TC Newman (Mixed race) – n (%) | Total – n (%) | p-value |
|-------------|----------------|----------------|-------------|---------|
| 2 months, (n) | 344 | 337 | 681 |  
| Wasting | 22 (6) | 9 (3) | 31 (5) | 0.020 |
| Stunting | 42 (12) | 73 (22) | 115 (17) | 0.001 |
| Underweight | 20 (6) | 39 (12) | 59 (9) | 0.008 |
| Overweight for age | 18 (5) | 10 (3) | 28 (4) | 0.137 |
| Obese | 4 (1) | 1 (0.3) | 5 (0.7) | 0.186 |
| 6 months, (n) | 243 | 274 | 517 |  
| Wasting | 13 (5) | 8 (3) | 21 (4) | 0.162 |
| Stunting | 25 (10) | 45 (16) | 70 (14) | 0.042 |
| Underweight for age | 7 (3) | 21 (8) | 28 (5) | 0.016 |
| Overweight | 31 (13) | 16 (6) | 47 (9) | 0.006 |
| Obese | 17 (7) | 8 (3) | 25 (5) | 0.031 |
| 12 months, (n) | 155 | 187 | 342 |  
| Wasting | 3 (2) | 9 (5) | 12 (4) | 0.237 |
| Stunting | 12 (8) | 31 (17) | 43 (13) | 0.014 |
| Underweight for age | 3 (2) | 16 (9) | 19 (6) | 0.008 |
| Overweight | 14 (9) | 8 (4) | 22 (6) | 0.074 |
| Obese | 6 (4) | 1 (0.5) | 7 (2) | 0.030 |
throughout the first year, independent of ethnicity, SES and antenatal maternal substance use.

**DISCUSSION**

In this South African birth cohort, we found a high prevalence of LBW and SGA infants and a mean WFAZ at birth below the WHO reference population. Despite some catch-up growth, a substantial prevalence of childhood stunting was observed in this sample. Black African children had better nutritional status from birth that persisted throughout infancy compared to mixed race infants. We also demonstrated an emerging group of overweight and obese infants, with a higher prevalence among black African infants. Antenatal maternal smoking and alcohol consumption and maternal height were important independent predictors of infant birthweight. Birthweight, SES, ethnicity and maternal antenatal alcohol and tobacco consumption were important determinants of the infant’s longitudinal growth during the first year of life.

Our results were consistent with studies that showed that birthweight was a strong determinant of longitudinal infant growth in the first year (1). In our sample, factors such as maternal smoking and alcohol consumption during pregnancy, gravidity and poor maternal nutrition were strong predictors of a lower weight at birth (Table 5) and were consistent with findings from other studies (1,12–14). LBW is a significant risk factor for poor growth during infancy and may be due to prematurity, being born SGA or a combination of these factors (1). The prevalence of LBW infants in this study was higher than the figures reported by other African and South African studies (15,16). Our findings that birthweight was a predictor of growth during infancy may be due to the high prevalence of LBW and SGA infants in this population. However infant birthweight was still a significant independent predictor of infant growth during the first year in the subgroup analysis, when infants with LBW or SGA were excluded (p < 0.001) (Table S1). As demonstrated in other studies, infants born term SGA and preterm SGA had significantly slower growth than those born preterm and term AGA (Table S2, Fig. S2) (1,17,18). Only 10% of the preterm infants were early preterm, which is a very small proportion.

We demonstrated the independent negative effects that smoking and alcohol consumption during pregnancy had on both birthweight and postnatal infant growth, which

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**Table 4** Association between maternal factors and infant weight-for-age z-score (WFAZ) at birth

| Variable                        | Median WFAZ [IQR] | Unadjusted regression coefficient [95% CI] | p-value | (A) Psychosocial-behavioural model: Adjusted regression coefficient [95% CI] | p-value | (B) Nutritional model: Adjusted regression coefficient [95% CI] | p-value |
|---------------------------------|------------------|-------------------------------------------|---------|-----------------------------------------------------------------------------|---------|----------------------------------------------------------------|---------|
| Recruitment site                |                  |                                           |         |                                                                             |         |                                                               |         |
| TC Newman (Mixed race)          | −0.7 [−1.4 to −0.1] | Reference                             |         | Reference                                                                  |         | Reference                                                      |         |
| Mbeloventi (Black African)      | −0.4 [−1.2 to 0.3] | 0.3 [0.2 to 0.5]                       | <0.001  | 0.2 [0.01 to 0.3]                                                         | 0.040   | 0.3 [0.1 to 0.4]                                                | <0.001  |
| Highest SES                     | −0.4 [−1.0 to 0.3] | Reference                             |         | Reference                                                                  |         | Reference                                                      |         |
| Moderate-high SES               | −0.7 [−1.4 to 0.01] | −0.2 [−0.4 to −0.01]                    | 0.028   | −0.2 [−0.4 to −0.03]                                                      | 0.027   | −0.3 [−0.5 to −0.1]                                             | 0.011   |
| Low-moderate SES                | −0.5 [−1.4 to 0.04] | −0.2 [−0.4 to −0.01]                    | 0.044   | −0.2 [−0.4 to 0.001]                                                      | 0.051   | −0.2 [−0.5 to −0.04]                                           | 0.019   |
| Lowest SES                      | −0.7 [−1.4 to 0.04] | −0.2 [−0.4 to 0.01]                    | 0.068   | −0.2 [−0.4 to −0.003]                                                     | 0.046   | −0.3 [−0.5 to −0.05]                                            | 0.016   |
| Gravida                         | −0.4 [−1.2 to 0.2] | Reference                             |         | Reference                                                                  |         | Reference                                                      |         |
| Primigravida                    | −0.8 [−1.5 to −0.1] | −0.4 [−0.5 to −0.2]                    | <0.001  |                                                                             |         |                                                               |         |
| Antenatal utine cotinine        | −0.4 [−1.1 to 0.3] | Reference                             |         | Reference                                                                  |         | Reference                                                      |         |
| Nonsmoker                       | −0.8 [−1.5 to −0.2] | −0.4 [−0.6 to −0.3]                    | <0.001  | −0.3 [−0.5 to −0.1]                                                        | 0.001   |                                                               |         |
| Active smoker                   | −0.5 [−1.2 to 0.2] | Reference                             |         | Reference                                                                  |         | Reference                                                      |         |
| Any self-reported alcohol use   | −0.9 [−1.6 to −0.3] | −0.4 [−0.6 to −0.2]                    | <0.001  | −0.3 [−0.5 to −0.1]                                                        | 0.010   |                                                               |         |
| Antenatal depression (EPDS)     | −0.5 [−1.3 to 0.1] | Reference                             |         | Reference                                                                  |         | Reference                                                      |         |
| Recent intimate partner violence| −0.6 [−1.3 to −0.01] | −0.1 [−0.2 to 0.1]                    | 0.554   |                                                                             |         |                                                               |         |
| Maternal height                 | 0.03 [0.02 to 0.04] | <0.001                                 |         | 0.02 [0.01 to 0.03]                                                       | <0.001  |                                                               |         |
persisted after controlling for SES and ethnicity. This may have been partially mediated through the effects of alcohol and tobacco on foetal growth (14,19). However, further investigations into the mechanistic effects on postnatal growth are required, for example the effects of these substances on infant micronutrient status, foetal programming, the intestinal microbiome and epigenetic alterations (20). Similar effects of antenatal tobacco or alcohol exposure on infant micronutrient status, foetal programming, the intestinal microbiome and epigenetic alterations (20). Similar effects of antenatal tobacco or alcohol exposure on foetal growth (14,19). However, further investigations into the mechanistic effects on postnatal growth are required, for example the effects of these substances on infant micronutrient status, foetal programming, the intestinal microbiome and epigenetic alterations (20).

Socioeconomic score (SES) was an important determinant of infant growth. Consistent with other studies in LMIC, higher SES promoted infant growth (22). This may have been due to better maternal health, better nutritional knowledge, being more able to afford formula or complementary feeding and better health seeking behaviour (23). Ethnic disparities in infant health have been described in several multiethnic countries globally and have mainly resulted from differences in maternal health, access to healthcare services and SES (4). Unexpectedly, black African infants had higher birthweights and better longitudinal growth than mixed race infants, despite coming from lower SES households, and these effects persisted after controlling for birthweight and SES. Additional genetic or environmental interactions may be important in determining growth during infancy and these require further investigation (1).

We found a high prevalence of stunting in this sample, particularly at two months of age, with a marginal decline by 12 months of age. These results were consistent with cross-sectional South African studies that have reported a similar high prevalence of stunting in children (24). The high prevalence of stunting is surprising given the study setting, with access to healthcare facilities, free maternal antenatal care, nutritional programmes and a strong primary healthcare programme. SES, maternal, nutritional, genetic, or infant factors, such as environmental enteric dysfunction may have been contributory factors and further studies of these are underway.

In contrast, we also found a concerning prevalence of overweight or obese infants. To the best of our knowledge, no previous studies have documented the prevalence of overweight and obese infants in South Africa. These findings may reflect changes in lifestyle, diet or poor feeding practices (25) and a detailed analysis of such factors is
CONCLUSION
Our findings of the predictive nature of birthweight on growth trajectory during infancy emphasise the importance of maternal health and antenatal care on infant growth. Simple, cost-effective interventions that focus on maternal health, such as programmes to reduce alcohol consumption and smoking and improve nutrition, may improve birthweights and subsequent postnatal growth, thereby promoting child health. Further studies are required to investigate environmental and genetic determinants of infant growth in LMIC.

ACKNOWLEDGEMENTS
We thank the hospital, clinic and study staff at Paarl Hospital, Mbekweni and TC Newman for supporting this study, together with the families and children who took part.

FINANCIAL SUPPORT
The Drakenstein Child Health Study is funded by the Bill and Melinda Gates Foundation (OPP 1017641), The Discovery Foundation, South Africa, The South African Medical Research Council, GlaxoSmithKline (GSK)/South African Thoracic Society, The Harry Crossley Foundation and The Hamilton-Naki Foundation.

CONFLICT OF INTEREST
There are no conflicts of interest to declare.

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**SUPPORTING INFORMATION**

Additional Supporting Information may be found in the online version of this article:

**Figure S1** Flow chart of infants included at each study visit between March 2012 and October 2014.

**Figure S2** Longitudinal infant WFA z scores stratified by prematurity and weight.

**Table S1** Mixed effects model of variables associated with infant weight-for-age z-scores (WFAZ; repeated measurements) at 2 months, 6 months, and 12 months; infants born preterm and/or SGA excluded.

**Table S2** Mixed effects model of variables associated with infant weight-for-age z-scores (WFAZ; repeated measurements) at 2 months, 6 months, and 12 months; restricted to infants born preterm and/or SGA.