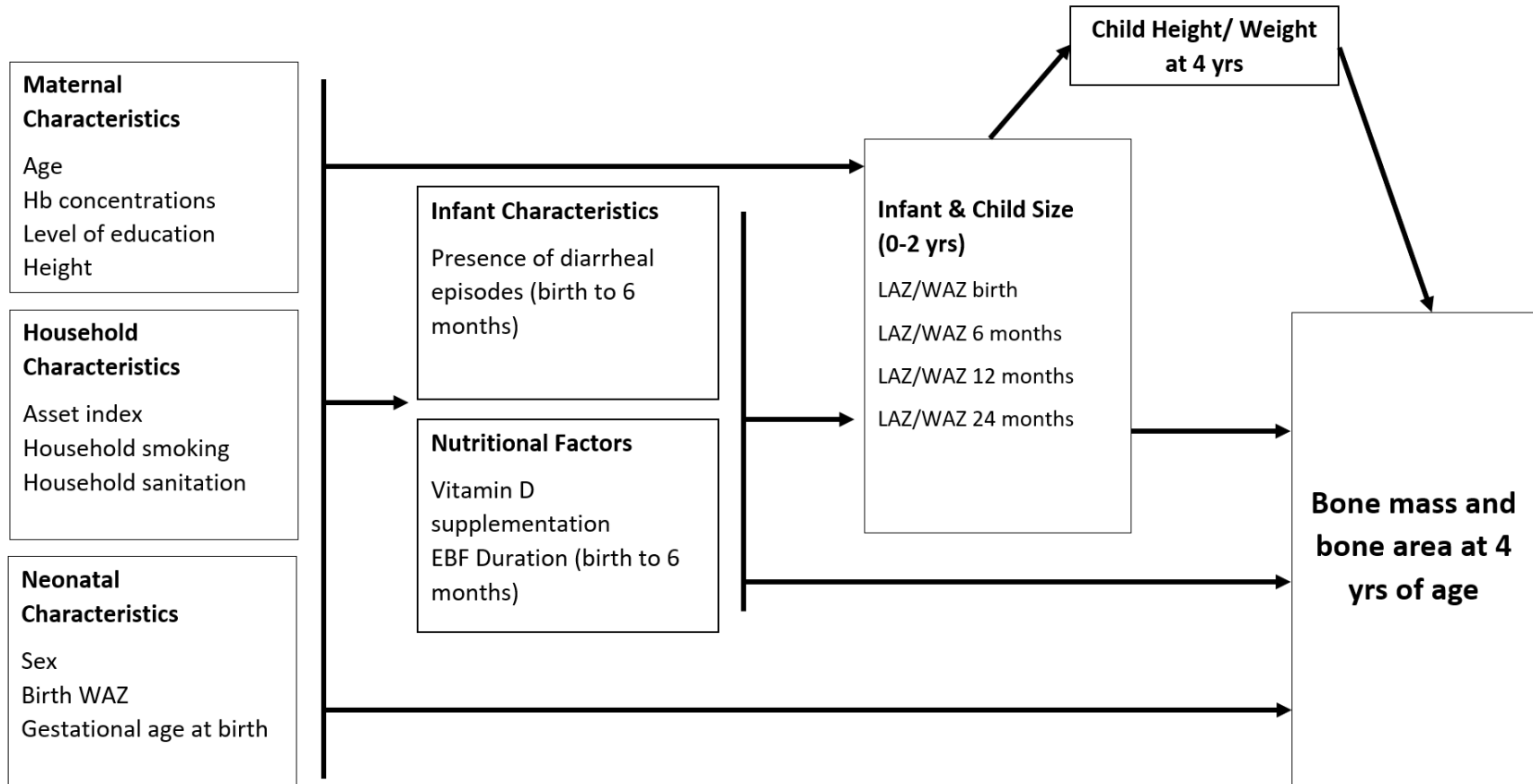


**Associations of linear growth and weight gain in the first 2 years with bone mass at 4 years
of age in children in Dhaka, Bangladesh**

Online Supplementary Material

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Supplemental Figure 1. Conceptual framework.

Figure shows hypothesized relationships between covariates included in analyses of the associations between linear growth, weight gain with bone mass and bone area at 4 years of age where maternal, household, neonatal, infant, and nutritional factors were hypothesized confounders of the association between early-life linear and ponderal growth on bone outcomes at 4 years of age; concurrent height and concurrent weight at 4 years of age were hypothesized as mediators of the relationship between early-life growth and bone mass at 4 years of age. EBF, exclusive breastfeeding; LAZ, length-for-age z-score; Hb, hemoglobin; WAZ, weight-for-age z-score.

Supplemental Table 1. Missing anthropometric and household characteristics data at each timepoint^a.

| Variable | N Missing | % Missing |
|--|------------------|------------------|
| Earliest LAZ (<45 days of age) | 17 | 2.8 |
| cLAZ at 6 months | 23 | 3.8 |
| cLAZ at 12 months | | 4.0 |
| cLAZ at 24 months | 2 | 0.3 |
| Earliest WAZ (<45 days of age) | 17 | 2.8 |
| cWAZ at 6 months | 23 | 3.8 |
| cWAZ at 12 months | | 4.5 |
| cWAZ at 24 months | 5 | 0.8 |
| Asset index | 2 | 0.3 |
| Presence of hand soap in handwashing station | 1 | 0.2 |
| Household smoking | 2 | 0.3 |

LAZ, length-for-age z-score; cLAZ, conditional LAZ; WAZ, weight-for-age z-score; cWAZ, conditional WAZ

^aMissing variables identified at each timepoint of interest within an overall cohort sample size of 599. In primary analysis examining the association of growth within the first 2 years of life and bone outcomes at 4 years, missing data were imputed using multivariate imputation by chained equations (MICE).

Supplemental Table 2. Associations between infant relative length gain from birth to 2 years of age and bone mineral content, density and area at 4 years of age, by child sex.

| | Unadjusted model | | Multivariable model ^a | | Adjusted for concurrent HAZ ^b | | Multivariable model including concurrent HAZ ^c | |
|--|--|----------|--|----------|--|----------|---|----------|
| | Difference in bone outcome (95% CI) ^d | <i>P</i> | Difference in bone outcome (95% CI) ^d | <i>P</i> | Difference in bone outcome (95% CI) ^d | <i>P</i> | Difference in bone outcome (95% CI) ^d | <i>P</i> |
| Boys (n=296) | | | | | | | | |
| TBLH BMC (g) | | | | | | | | |
| cLAZ (6 months) | 32.1 (26.6, 37.7) | <0.001 | 29.7 (24.5, 35.0) | <0.001 | 3.2 (-2.2, 8.6) | 0.24 | 0.8 (-5.7, 7.2) | 0.81 |
| cLAZ (12 months) | 35.9 (28.6, 43.3) | <0.001 | 33.9 (26.9, 40.9) | <0.001 | 7.3 (0.9, 13.8) | 0.03 | 4.0 (-3.6, 11.6) | 0.30 |
| cLAZ (24 months) | 48.2 (39.4, 57.0) | <0.001 | 47.5 (39.4, 55.7) | <0.001 | 13.9 (6.3, 21.6) | <0.001 | 9.0 (-0.2, 18.1) | 0.06 |
| HAZ at 4 years | – | – | – | – | 38.6 (33.8, 43.3) | <0.001 | 42.0 (35.0, 48.9) | <0.001 |
| TBLH aBMD (g/cm²) | | | | | | | | |
| cLAZ (6 months) | 0.019 (0.014, 0.024) | <0.001 | 0.017 (0.012, 0.023) | <0.001 | 0.004 (-0.003, 0.010) | 0.28 | 0.001 (-0.007, 0.008) | 0.82 |
| cLAZ (12 months) | 0.023 (0.017, 0.030) | <0.001 | 0.020 (0.013, 0.027) | <0.001 | 0.008 (0.001, 0.016) | 0.03 | 0.003 (-0.006, 0.012) | 0.49 |
| cLAZ (24 months) | 0.035 (0.027, 0.044) | <0.001 | 0.033 (0.025, 0.041) | <0.001 | 0.017 (0.008, 0.026) | <0.001 | 0.011 (0.0002, 0.022) | 0.05 |
| HAZ at 4 years | – | – | – | – | 0.021 (0.015, 0.026) | <0.001 | 0.024 (0.016, 0.032) | <0.001 |
| TBLH Bone Area (cm²) | | | | | | | | |
| cLAZ (6 months) | 44.8 (37.6, 52.1) | <0.001 | 42.0 (35.4, 48.7) | <0.001 | 1.9 (-4.2, 7.9) | 0.55 | 1.1 (-6.4, 8.6) | 0.77 |
| cLAZ (12 months) | 45.6 (35.9, 55.3) | <0.001 | 46.3 (37.4, 55.2) | <0.001 | 3.1 (-4.1, 10.3) | 0.40 | 4.1 (-4.8, 12.9) | 0.37 |
| cLAZ (24 months) | 56.9 (45.4, 68.5) | <0.001 | 59.2 (48.9, 69.5) | <0.001 | 5.9 (-2.7, 14.6) | 0.18 | 4.8 (-6.0, 15.6) | 0.39 |
| HAZ at 4 years | – | – | – | – | 57.4 (52.1, 62.8) | <0.001 | 59.3 (51.1, 67.4) | <0.001 |
| Girls (n=303) | | | | | | | | |
| TBLH BMC (g) | | | | | | | | |
| cLAZ (6 months) | 28.4 (22.7, 34.0) | <0.001 | 29.5 (24.1, 35.0) | <0.001 | 2.5 (-2.3, 7.4) | 0.31 | -1.5 (-8.1, 5.1) | 0.66 |
| cLAZ (12 months) | 39.8 (31.3, 48.4) | <0.001 | 39.1 (31.3, 46.9) | <0.001 | 10.3 (3.6, 16.9) | 0.003 | 5.7 (-2.4, 13.8) | 0.17 |
| cLAZ (24 months) | 43.3 (34.3, 52.2) | <0.001 | 36.9 (28.3, 45.4) | <0.001 | 3.8 (-3.6, 11.3) | 0.31 | -1.4 (-10.3, 7.6) | 0.76 |
| HAZ at 4 years | – | – | – | – | 40.6 (36.2, 45.0) | <0.001 | 45.6 (38.5, 52.7) | <0.001 |
| TBLH aBMD (g/cm²) | | | | | | | | |
| cLAZ (6 months) | 0.017 (0.012, 0.022) | <0.001 | 0.017 (0.011, 0.022) | <0.001 | 0.003 (-0.003, 0.009) | 0.38 | -0.004 (-0.012, 0.004) | 0.30 |
| cLAZ (12 months) | 0.027 (0.019, 0.035) | <0.001 | 0.026 (0.018, 0.034) | <0.001 | 0.011 (0.002, 0.019) | 0.01 | 0.003 (-0.006, 0.013) | 0.48 |
| cLAZ (24 months) | 0.028 (0.020, 0.036) | <0.001 | 0.025 (0.016, 0.034) | <0.001 | 0.006 (-0.003, 0.015) | 0.18 | -0.001 (-0.012, 0.010) | 0.85 |
| HAZ at 4 years | – | – | – | – | 0.022 (0.017, 0.028) | <0.001 | 0.031 (0.022, 0.039) | <0.001 |
| TBLH Bone Area (cm²) | | | | | | | | |
| cLAZ (6 months) | 40.8 (33.5, 48.1) | <0.001 | 43.3 (36.9, 49.6) | <0.001 | 3.6 (-1.6, 8.9) | 0.17 | 3.3 (-3.8, 10.4) | 0.36 |
| cLAZ (12 months) | 51.4 (40.5, 62.3) | <0.001 | 50.9 (41.9, 60.0) | <0.001 | 8.9 (1.7, 16.0) | 0.02 | 7.9 (-0.8, 16.6) | 0.07 |
| cLAZ (24 months) | 56.8 (45.2, 68.4) | <0.001 | 47.5 (37.4, 57.6) | <0.001 | 0.2 (-8.0, 8.4) | 0.97 | -1.7 (-11.5, 8.1) | 0.74 |
| HAZ at 4 years | – | – | – | – | 58.3 (53.5, 63.1) | <0.001 | 58.7 (51.0, 66.5) | <0.001 |

aBMD, areal bone mineral density; BMC, bone mineral content; cLAZ, conditional length-for-age z-score; HAZ, height-for-age z-score; TBLH, total body less head.

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^aAdjusted for asset index quintiles, presence of hand soap at handwashing station, household smoking, LAZ within 45 days of birth, WAZ within 45 days of birth, maternal age (years), maternal height (cm), mid-gestation maternal hemoglobin concentrations (g/L), gestational age at birth (weeks), maternal education category, vitamin D intervention group assigned at enrolment to the MDIG trial, treatment of drinking water, child sex, exclusive breastfeeding duration (weeks), and presence of diarrheal episodes in the first 6 months of life.

^bAdjusted for concurrent HAZ at 4 years of age.

^cAdjusted for covariates in multivariable model and concurrent HAZ at 4 years of age.

^dEffect estimate represents the difference in bone outcome per 1 unit increase in cLAZ or HAZ.

Supplemental Table 3. Associations between infant relative weight gain from birth to 2 years of age and bone mineral content, density and area at 4 years of age, by child sex.

| | Unadjusted model | | Multivariable model ^a | | Multivariable model including concurrent HAZ ^b | | Multivariable model including concurrent HAZ & WAZ ^c | |
|--|--|----------|--|----------|---|----------|---|----------|
| | Difference in bone outcome (95% CI) ^d | <i>P</i> | Difference in bone outcome (95% CI) ^d | <i>P</i> | Difference in bone outcome (95% CI) ^d | <i>P</i> | Difference in bone outcome (95% CI) ^d | <i>P</i> |
| Boys (n=296) | | | | | | | | |
| TBLH BMC (g) | | | | | | | | |
| cWAZ (6 months) | 12.0 (4.0, 20.1) | 0.004 | 14.4 (7.5, 21.3) | <0.001 | 7.2 (3.2, 11.1) | <0.001 | 0.3 (-3.9, 4.4) | 0.89 |
| cWAZ (12 months) | 4.0 (-7.8, 15.9) | 0.50 | 3.7 (-6.6, 14.0) | 0.48 | 3.7 (-2.0, 9.5) | 0.20 | -3.9 (-9.7, 2.0) | 0.19 |
| cWAZ (24 months) | 34.7 (22.9, 46.5) | <0.001 | 34.8 (24.9, 44.8) | <0.001 | 19.2 (13.5, 25.0) | <0.001 | 6.8 (0.5, 13.1) | 0.03 |
| HAZ at 4 years | – | – | – | – | 41.8 (38.4, 45.2) | <0.001 | 24.4 (18.7, 30.1) | <0.001 |
| WAZ at 4 years | – | – | – | – | – | – | 21.5 (15.6, 27.4) | <0.001 |
| TBLH aBMD (g/cm²) | | | | | | | | |
| cWAZ (6 months) | 0.012 (0.006, 0.018) | <0.001 | 0.013 (0.007, 0.018) | <0.001 | 0.008 (0.004, 0.013) | <0.001 | 0.003 (-0.002, 0.008) | 0.26 |
| cWAZ (12 months) | 0.005 (-0.004, 0.015) | 0.25 | 0.003 (-0.006, 0.012) | 0.51 | 0.003 (-0.004, 0.010) | 0.42 | -0.003 (-0.011, 0.005) | 0.44 |
| cWAZ (24 months) | 0.026 (0.017, 0.036) | <0.001 | 0.025 (0.017, 0.033) | <0.001 | 0.016 (0.009, 0.023) | <0.001 | 0.006 (-0.002, 0.014) | 0.13 |
| HAZ at 4 years | – | – | – | – | 0.024 (0.020, 0.029) | <0.001 | 0.011 (0.003, 0.018) | 0.004 |
| WAZ at 4 years | – | – | – | – | – | – | 0.017 (0.009, 0.024) | <0.001 |
| TBLH Bone Area (cm²) | | | | | | | | |
| cWAZ (6 months) | 10.3 (-0.6, 21.1) | 0.06 | 14.7 (5.4, 24.1) | 0.002 | 4.6 (-0.3, 9.4) | 0.06 | -2.3 (-7.5, 2.9) | 0.38 |
| cWAZ (12 months) | -1.2 (-17.3, 14.8) | 0.88 | 1.4 (-12.6, 15.5) | 0.84 | 1.5 (-5.5, 8.5) | 0.68 | -6.1 (-13.4, 1.1) | 0.10 |
| cWAZ (24 months) | 37.0 (21.1, 52.9) | <0.001 | 38.8 (25.3, 52.4) | <0.001 | 16.8 (9.7, 24.0) | <0.001 | 4.4 (-3.7, 12.5) | 0.29 |
| HAZ at 4 years | – | – | – | – | 59.0 (54.7, 63.2) | <0.001 | 41.5 (34.3, 48.8) | <0.001 |
| WAZ at 4 years | – | – | – | – | – | – | 21.5 (14.0, 29.1) | <0.001 |
| Girls (n=303) | | | | | | | | |
| TBLH BMC (g) | | | | | | | | |
| cWAZ (6 months) | 12.5 (4.2, 20.8) | 0.003 | 12.5 (4.9, 20.1) | 0.001 | 5.7 (1.5, 9.9) | 0.007 | -0.7 (-4.9, 3.6) | 0.76 |
| cWAZ (12 months) | 13.9 (2.4, 25.4) | 0.02 | 17.7 (6.9, 28.5) | 0.001 | 6.4 (0.6, 12.2) | 0.03 | -0.1 (-5.8, 5.6) | 0.98 |
| cWAZ (24 months) | 19.6 (6.8, 32.4) | 0.003 | 21.6 (9.7, 33.4) | <0.001 | 17.5 (11.1, 23.9) | <0.001 | 7.7 (1.2, 14.2) | 0.02 |
| HAZ at 4 years | – | – | – | – | 43.6 (40.3, 47.0) | <0.001 | 28.2 (22.9, 33.6) | <0.001 |
| WAZ at 4 years | – | – | – | – | – | – | 19.4 (13.9, 24.9) | <0.001 |
| TBLH aBMD (g/cm²) | | | | | | | | |
| cWAZ (6 months) | 0.009 (0.002, 0.016) | 0.008 | 0.008 (0.001, 0.014) | 0.02 | 0.004 (-0.002, 0.009) | 0.17 | -0.002 (-0.008, 0.003) | 0.45 |
| cWAZ (12 months) | 0.011 (0.002, 0.020) | 0.02 | 0.014 (0.005, 0.023) | 0.003 | 0.007 (-0.001, 0.014) | 0.07 | 0.001 (-0.007, 0.008) | 0.85 |
| cWAZ (24 months) | 0.020 (0.010, 0.030) | <0.001 | 0.021 (0.011, 0.031) | <0.001 | 0.018 (0.010, 0.026) | <0.001 | 0.009 (0.001, 0.018) | 0.03 |
| HAZ at 4 years | – | – | – | – | 0.027 (0.023, 0.031) | <0.001 | 0.013 (0.006, 0.020) | <0.001 |
| WAZ at 4 years | – | – | – | – | – | – | 0.018 (0.010, 0.025) | <0.001 |

| | Unadjusted model | | Multivariable model ^a | | Multivariable model including concurrent HAZ ^b | | Multivariable model including concurrent HAZ & WAZ ^c | |
|--|--|----------|--|----------|---|----------|---|----------|
| | Difference in bone outcome (95% CI) ^d | <i>P</i> | Difference in bone outcome (95% CI) ^d | <i>P</i> | Difference in bone outcome (95% CI) ^d | <i>P</i> | Difference in bone outcome (95% CI) ^d | <i>P</i> |
| TBLH Bone Area (cm²) | | | | | | | | |
| cWAZ (6 months) | 15.9 (4.7, 27.0) | 0.005 | 17.2 (7.2, 27.1) | 0.001 | 7.8 (3.1, 12.6) | 0.001 | 2.5 (-2.6, 7.6) | 0.33 |
| cWAZ (12 months) | 15.5 (-0.1, 31.0) | 0.05 | 20.2 (6.0, 34.3) | 0.005 | 4.7 (-2.1, 11.4) | 0.17 | -0.8 (-7.6, 6.0) | 0.82 |
| cWAZ (24 months) | 13.6 (-3.7, 30.8) | 0.12 | 16.7 (1.2, 32.2) | 0.04 | 11.1 (3.6, 18.5) | 0.004 | 2.9 (-5.0, 10.7) | 0.47 |
| HAZ at 4 years | – | – | – | – | 59.8 (55.9, 63.7) | <0.001 | 46.9 (40.5, 53.3) | <0.001 |
| WAZ at 4 years | – | – | – | – | – | – | 16.3 (9.7, 22.8) | <0.001 |

aBMD, areal bone mineral density; BMC, bone mineral content; cWAZ, conditional weight-for-age z-score; HAZ, height-for-age z-score; TBLH, total body less head.

^aAdjusted models for asset index quintiles, presence of hand soap at handwashing station, household smoking, LAZ within 45 days of birth, WAZ within 45 days of birth, maternal age (years), maternal height (cm), mid-gestation maternal hemoglobin concentrations (g/L), gestational age at birth (weeks), maternal education category, vitamin D intervention group assigned at enrolment to the MDIG trial, treatment of drinking water, child sex, exclusive breastfeeding duration (weeks), and presence of diarrheal episodes in the first 6 months of life; ^bAdjusted for covariates in multivariable model and concurrent HAZ at 4 years of age; ^cAdjusted for covariates in multivariable model and concurrent HAZ at 4 years of age and concurrent WAZ at 4 years of age; ^dEffect estimate represents the difference in bone outcome per 1 unit increase in cLAZ or HAZ.

Supplemental Table 4. Associations between infant relative length gain from birth to 2 years of age and bone mineral content, density and bone area at 4 years of age among term-born (≥ 37 weeks) infants compared to the full cohort.

| | Multivariable model (Full cohort, $n=599$) ^a | | Multivariable model (Term born, $n=549$) ^a | | Multivariable model including concurrent HAZ (Full cohort, $n=599$) ^b | | Multivariable model including concurrent HAZ (Term born, $n=549$) ^b | |
|--|---|----------|---|----------|---|----------|---|----------|
| | Difference in bone outcome (95% CI) | <i>P</i> | Difference in bone outcome (95% CI) | <i>P</i> | Difference in bone outcome (95% CI) | <i>P</i> | Difference in bone outcome (95% CI) | <i>P</i> |
| TBLH BMC (g) | | | | | | | | |
| cLAZ (6 months) | 29.4 (25.7, 33.1) | <0.001 | 29.3 (25.5, 33.2) | <0.001 | -0.4 (-4.9, 4.1) | 0.87 | -0.1 (-4.7, 4.4) | 0.95 |
| cLAZ (12 months) | 36.5 (31.4, 41.6) | <0.001 | 37.5 (32.1, 42.9) | <0.001 | 4.7 (-0.7, 10.1) | 0.09 | 5.4 (-0.3, 11.1) | 0.06 |
| cLAZ (24 months) | 43.0 (37.2, 48.8) | <0.001 | 43.3 (37.3, 49.3) | <0.001 | 3.8 (-2.5, 10.1) | 0.24 | 4.3 (-2.3, 10.8) | 0.20 |
| HAZ at 4 years | – | – | – | – | 44.1 (39.2, 49.0) | <0.001 | 43.7 (38.6, 48.8) | <0.001 |
| TBLH aBMD (g/cm²) | | | | | | | | |
| cLAZ (6 months) | 0.017 (0.013, 0.021) | <0.001 | 0.017 (0.013, 0.021) | <0.001 | -0.002 (-0.007, 0.004) | 0.51 | -0.002 (-0.007, 0.004) | 0.55 |
| cLAZ (12 months) | 0.023 (0.018, 0.029) | <0.001 | 0.024 (0.018, 0.029) | <0.001 | 0.003 (-0.003, 0.010) | 0.31 | 0.004 (-0.003, 0.010) | 0.32 |
| cLAZ (24 months) | 0.030 (0.024, 0.036) | <0.001 | 0.030 (0.024, 0.036) | <0.001 | 0.005 (-0.003, 0.013) | 0.19 | 0.005 (-0.003, 0.013) | 0.19 |
| HAZ at 4 years | – | – | – | – | 0.028 (0.022, 0.034) | <0.001 | 0.027 (0.021, 0.034) | <0.001 |
| TBLH Bone Area (cm²) | | | | | | | | |
| cLAZ (6 months) | 42.3 (37.9, 46.8) | <0.001 | 42.6 (37.9, 47.2) | <0.001 | 2.3 (-2.6, 7.3) | 0.36 | 2.9 (-2.2, 8.0) | 0.27 |
| cLAZ (12 months) | 48.1 (42.0, 54.2) | <0.001 | 49.7 (43.2, 56.3) | <0.001 | 5.3 (-0.6, 11.3) | 0.08 | 6.5 (0.3, 12.8) | 0.04 |
| cLAZ (24 months) | 53.9 (46.9, 61.0) | <0.001 | 54.4 (47.2, 61.7) | <0.001 | 1.2 (-5.9, 8.3) | 0.74 | 1.9 (-5.4, 9.2) | 0.61 |
| HAZ at 4 years | – | – | – | – | 59.3 (53.9, 64.7) | <0.001 | 58.9 (53.2, 64.5) | <0.001 |

aBMD, areal bone mineral density; BMC, bone mineral content; cLAZ, conditional length-for-age z-score; HAZ, height-for-age z-score; TBLH, total body less head.

^aAdjusted models for asset index quintiles, presence of hand soap at handwashing station, household smoking, LAZ within 45 days of birth, WAZ within 45 days of birth, maternal age (years), maternal height (cm), mid-gestation maternal hemoglobin concentrations (g/L), gestational age at birth, maternal education category, vitamin D intervention group assigned at enrolment to the MDIG trial, treatment of drinking water, sex, exclusive breastfeeding duration, and presence of diarrheal episodes in the first 6 months of life.

^bAdjusted models for covariates in multivariable model and concurrent HAZ at 4 years of age.

Supplemental Table 5. Associations between infant relative weight gain from birth to 2 years of age and bone mineral content, density and area at 4 years of age among term-born (≥ 37 weeks) infants compared to the full cohort.

| | Multivariable model (Full cohort, $n=599$) ^a | | Multivariable model (Term born, $n=549$) ^a | | Multivariable model including concurrent HAZ & WAZ (Full cohort, $n=599$) ^b | | Multivariable model including concurrent HAZ & WAZ (Term born, $n=549$) ^b | |
|--|---|----------|---|----------|---|----------|---|----------|
| | Difference in bone outcome (95% CI) | <i>P</i> | Difference in bone outcome (95% CI) | <i>P</i> | Difference in bone outcome (95% CI) | <i>P</i> | Difference in bone outcome (95% CI) | <i>P</i> |
| TBLH BMC (g) | | | | | | | | |
| cWAZ (6 months) | 13.2 (8.1, 18.3) | <0.001 | 12.9 (7.7, 18.1) | <0.001 | 0.4 (-2.5, 3.3) | 0.80 | 0.7 (-2.3, 3.7) | 0.64 |
| cWAZ (12 months) | 11.6 (4.2, 19.0) | 0.002 | 12.1 (4.4, 19.8) | 0.002 | -1.8 (-5.8, 2.2) | 0.38 | -0.9 (-5.2, 3.3) | 0.66 |
| cWAZ (24 months) | 29.3 (21.8, 36.9) | <0.001 | 30.0 (22.0, 38.0) | <0.001 | 7.6 (3.2, 12.0) | 0.001 | 7.9 (3.2, 12.6) | 0.001 |
| HAZ at 4 years | – | – | – | – | 27.2 (23.3, 31.0) | <0.001 | 27.8 (23.7, 31.8) | <0.001 |
| WAZ at 4 years | – | – | – | – | 19.8 (15.8, 23.8) | <0.001 | 18.9 (14.8, 23.0) | <0.001 |
| TBLH aBMD (g/cm²) | | | | | | | | |
| cWAZ (6 months) | 0.010 (0.006, 0.015) | <0.001 | 0.010 (0.006, 0.015) | <0.001 | 0.001 (-0.002, 0.005) | 0.46 | 0.002 (-0.002, 0.006) | 0.36 |
| cWAZ (12 months) | 0.009 (0.002, 0.015) | 0.006 | 0.009 (0.002, 0.015) | 0.009 | -0.001 (-0.006, 0.004) | 0.76 | -0.001 (-0.006, 0.005) | 0.82 |
| cWAZ (24 months) | 0.024 (0.017, 0.030) | <0.001 | 0.025 (0.018, 0.032) | <0.001 | 0.008 (0.003, 0.014) | 0.004 | 0.009 (0.003, 0.016) | 0.003 |
| HAZ at 4 years | – | – | – | – | 0.013 (0.008, 0.018) | <0.001 | 0.013 (0.008, 0.019) | <0.001 |
| WAZ at 4 years | – | – | – | – | 0.016 (0.011, 0.021) | <0.001 | 0.016 (0.010, 0.021) | <0.001 |
| TBLH Bone Area (cm²) | | | | | | | | |
| cWAZ (6 months) | 15.0 (8.3, 21.6) | <0.001 | 14.2 (7.3, 21.2) | <0.001 | -0.2 (-3.7, 3.2) | 0.89 | -0.3 (-3.8, 3.2) | 0.86 |
| cWAZ (12 months) | 12.3 (2.4, 22.2) | 0.02 | 13.3 (3.0, 23.6) | 0.01 | -3.5 (-8.2, 1.3) | 0.15 | -2.2 (-7.2, 2.9) | 0.40 |
| cWAZ (24 months) | 29.1 (19.1, 39.1) | <0.001 | 29.2 (18.5, 39.8) | <0.001 | 3.2 (-2.2, 8.6) | 0.24 | 2.7 (-2.9, 8.4) | 0.34 |
| HAZ at 4 years | – | – | – | – | 44.1 (39.4, 48.8) | <0.001 | 45.4 (40.6, 50.2) | <0.001 |
| WAZ at 4 years | – | – | – | – | 19.4 (14.6, 24.2) | <0.001 | 18.2 (13.3, 23.2) | <0.001 |

aBMD, areal bone mineral density; BMC, bone mineral content; cWAZ, conditional weight-for-age z-score; HAZ, height-for-age z-score; TBLH, total body less head.

^aAdjusted models for asset index quintiles, presence of hand soap at handwashing station, household smoking, LAZ within 45 days of birth, WAZ within 45 days of birth, maternal age (years), maternal height (cm), mid-gestation maternal hemoglobin concentrations (g/L), gestational age at birth, maternal education category, vitamin D intervention group assigned at enrolment to the MDIG trial, treatment of drinking water, sex, exclusive breastfeeding duration, and presence of diarrheal episodes in the first 6 months of life.

^bAdjusted models for covariates in multivariable model, concurrent HAZ at 4 years of age, and concurrent WAZ at 4 years of age.

Supplemental Table 6. Associations between infant relative length gain from birth to 2 years of age and bone mineral content, density and area at 4 years of age, comparing MICE and complete case models.

| | Multivariable model (MICE model, <i>n</i> =599) ^a | | Multivariable model (Complete case, <i>n</i> =554) ^a | | Multivariable model including concurrent HAZ (MICE model, <i>n</i> =599) ^b | | Multivariable model including concurrent HAZ (Complete case, <i>n</i> =554) ^b | |
|--|---|----------|--|----------|---|----------|--|----------|
| | Difference in bone outcome (95% CI) | <i>P</i> | Difference in bone outcome (95% CI) | <i>P</i> | Difference in bone outcome (95% CI) | <i>P</i> | Difference in bone outcome (95% CI) | <i>P</i> |
| TBLH BMC (g) | | | | | | | | |
| cLAZ (6 months) | 29.4 (25.7, 33.1) | <0.001 | 28.7 (25.0, 32.5) | <0.001 | -0.4 (-4.9, 4.1) | 0.87 | -2.4 (-7.0, 2.1) | 0.30 |
| cLAZ (12 months) | 36.5 (31.4, 41.6) | <0.001 | 37.1 (31.9, 42.2) | <0.001 | 4.7 (-0.7, 10.1) | 0.09 | 3.2 (-2.4, 8.7) | 0.27 |
| cLAZ (24 months) | 43.0 (37.2, 48.8) | <0.001 | 42.4 (36.5, 48.3) | <0.001 | 3.8 (-2.5, 10.1) | 0.24 | 1.5 (-5.0, 8.1) | 0.65 |
| HAZ at 4 years | – | – | – | – | 44.1 (39.2, 49.0) | <0.001 | 46.5 (41.3, 51.6) | <0.001 |
| TBLH aBMD (g/cm²) | | | | | | | | |
| cLAZ (6 months) | 0.017 (0.013, 0.021) | <0.001 | 0.017 (0.013, 0.021) | <0.001 | -0.002 (-0.007, 0.004) | 0.51 | -0.004 (-0.009, 0.002) | 0.18 |
| cLAZ (12 months) | 0.023 (0.018, 0.029) | <0.001 | 0.024 (0.019, 0.029) | <0.001 | 0.003 (-0.003, 0.010) | 0.31 | 0.002 (-0.005, 0.008) | 0.62 |
| cLAZ (24 months) | 0.030 (0.024, 0.036) | <0.001 | 0.030 (0.024, 0.036) | <0.001 | 0.005 (-0.003, 0.013) | 0.19 | 0.003 (-0.005, 0.011) | 0.49 |
| HAZ at 4 years | – | – | – | – | 0.028 (0.022, 0.034) | <0.001 | 0.031 (0.024, 0.037) | <0.001 |
| TBLH Bone Area (cm²) | | | | | | | | |
| cLAZ (6 months) | 42.3 (37.9, 46.8) | <0.001 | 41.5 (36.9, 46.0) | <0.001 | 2.3 (-2.6, 7.3) | 0.36 | 0.4 (-4.8, 5.6) | 0.88 |
| cLAZ (12 months) | 48.1 (42.0, 54.2) | <0.001 | 49.0 (42.7, 55.2) | <0.001 | 5.3 (-0.6, 11.3) | 0.08 | 4.3 (-2.1, 10.7) | 0.18 |
| cLAZ (24 months) | 53.9 (46.9, 61.0) | <0.001 | 52.4 (45.2, 59.6) | <0.001 | 1.2 (-5.9, 8.3) | 0.74 | -1.4 (-8.9, 6.0) | 0.71 |
| HAZ at 4 years | – | – | – | – | 59.3 (53.9, 64.7) | <0.001 | 61.2 (55.3, 67.1) | <0.001 |

aBMD, areal bone mineral density; BMC, bone mineral content; cLAZ, conditional length-for-age z-score; HAZ, height-for-age z-score; MICE, multiple imputation by chained equations; TBLH, total body less head.

^aAdjusted models for asset index quintiles, presence of hand soap at handwashing station, household smoking, LAZ within 45 days of birth, WAZ within 45 days of birth, maternal age (years), maternal height (cm), mid-gestation maternal hemoglobin concentrations (g/L), gestational age at birth, maternal education category, vitamin D intervention group assigned at enrolment to the MDIG trial, treatment of drinking water, sex, exclusive breastfeeding duration, and presence of diarrheal episodes in the first 6 months of life.

^bAdjusted models for covariates in multivariable model and concurrent HAZ at 4 years of age.

Supplemental Table 7. Associations between infant relative weight gain from birth to 2 years of age and bone mineral content, density and area at 4 years of age, comparing MICE and complete case models.

| | Multivariable model (MICE model, <i>n</i> =599) ^a | | Multivariable model (Complete case, <i>n</i> =551) ^a | | Multivariable model including concurrent HAZ & WAZ (MICE model, <i>n</i> =599) ^b | | Multivariable model including concurrent HAZ & WAZ (Complete case, <i>n</i> =551) ^b | |
|--|---|----------|--|----------|--|----------|--|----------|
| | Difference in bone outcome (95% CI) | <i>P</i> | Difference in bone outcome (95% CI) | <i>P</i> | Difference in bone outcome (95% CI) | <i>P</i> | Difference in bone outcome (95% CI) | <i>P</i> |
| TBLH BMC (g) | | | | | | | | |
| cWAZ (6 months) | 13.2 (8.1, 18.3) | <0.001 | 13.3 (8.3, 18.4) | <0.001 | 0.4 (-2.5, 3.3) | 0.80 | -0.1 (-3.0, 2.8) | 0.92 |
| cWAZ (12 months) | 11.6 (4.2, 19.0) | 0.002 | 12.3 (5.0, 19.6) | 0.001 | -1.8 (-5.8, 2.2) | 0.38 | -2.1 (-6.0, 1.9) | 0.31 |
| cWAZ (24 months) | 29.3 (21.8, 36.9) | <0.001 | 28.7 (20.9, 36.4) | <0.001 | 7.6 (3.2, 12.0) | 0.001 | 6.8 (2.4, 11.3) | 0.003 |
| HAZ at 4 years | – | – | – | – | 27.2 (23.3, 31.0) | <0.001 | 26.7 (22.7, 30.7) | <0.001 |
| WAZ at 4 years | – | – | – | – | 19.8 (15.8, 23.8) | <0.001 | 20.7 (16.6, 24.7) | <0.001 |
| TBLH aBMD (g/cm²) | | | | | | | | |
| cWAZ (6 months) | 0.010 (0.006, 0.015) | <0.001 | 0.011 (0.006, 0.015) | <0.001 | 0.001 (-0.002, 0.005) | 0.46 | 0.001 (-0.003, 0.005) | 0.64 |
| cWAZ (12 months) | 0.009 (0.002, 0.015) | 0.006 | 0.009 (0.003, 0.016) | 0.004 | -0.001 (-0.006, 0.004) | 0.76 | -0.001 (-0.006, 0.004) | 0.68 |
| cWAZ (24 months) | 0.024 (0.017, 0.030) | <0.001 | 0.023 (0.017, 0.030) | <0.001 | 0.008 (0.003, 0.014) | 0.004 | 0.007 (0.001, 0.013) | 0.02 |
| HAZ at 4 years | – | – | – | – | 0.013 (0.008, 0.018) | <0.001 | 0.013 (0.008, 0.018) | <0.001 |
| WAZ at 4 years | – | – | – | – | 0.016 (0.011, 0.021) | <0.001 | 0.017 (0.012, 0.023) | <0.001 |
| TBLH Bone Area (cm²) | | | | | | | | |
| cWAZ (6 months) | 15.0 (8.3, 21.6) | <0.001 | 15.1 (8.4, 21.8) | <0.001 | -0.2 (-3.7, 3.2) | 0.89 | -0.5 (-4.1, 3.1) | 0.79 |
| cWAZ (12 months) | 12.3 (2.4, 22.2) | 0.02 | 13.2 (3.5, 22.9) | 0.008 | -3.5 (-8.2, 1.3) | 0.15 | -3.5 (-8.5, 1.4) | 0.16 |
| cWAZ (24 months) | 29.1 (19.1, 39.1) | <0.001 | 28.3 (18.0, 38.5) | <0.001 | 3.2 (-2.2, 8.6) | 0.24 | 2.8 (-2.8, 8.4) | 0.32 |
| HAZ at 4 years | – | – | – | – | 44.1 (39.4, 48.8) | <0.001 | 44.1 (39.2, 49.0) | <0.001 |
| WAZ at 4 years | – | – | – | – | 19.4 (14.6, 24.2) | <0.001 | 19.6 (14.6, 24.6) | <0.001 |

aBMD, areal bone mineral density; BMC, bone mineral content; cWAZ, conditional weight-for-age z-score; HAZ, height-for-age z-score; MICE, multiple imputation by chained equations; TBLH, total body less head.

^aAdjusted models for asset index quintiles, presence of hand soap at handwashing station, household smoking, LAZ within 45 days of birth, WAZ within 45 days of birth, maternal age (years), maternal height (cm), mid-gestation maternal hemoglobin concentrations (g/L), gestational age at birth, maternal education category, vitamin D intervention group assigned at enrolment to the MDIG trial, treatment of drinking water, sex, exclusive breastfeeding duration, and presence of diarrheal episodes in the first 6 months of life.

Online Supplementary Material

^bAdjusted models for covariates in multivariable model, concurrent HAZ at 4 years of age and concurrent WAZ at 4 years of age.