

## Abstract

# Breastfeeding Duration and Bone Mineral Density in Childhood: A Prospective Study within GUSTO Cohort <sup>†</sup>

Zoya Gridneva <sup>1,2,3,4,\*</sup> , Wei Wei Pang <sup>5,6</sup> , Philip Vlaskovsky <sup>7</sup> , Jacki L. McEachran <sup>1,3,4</sup> , Sharon L. Perrella <sup>1,2,3,4</sup> , Fabian Yap <sup>8</sup> , Mary E. Wlodek <sup>1,9,10,11,12</sup> , Yap-Seng Chong <sup>10,11,12</sup>, Johan G. Eriksson <sup>12,13,14,15</sup>, Donna T. Geddes <sup>1,2,3,4</sup> and Mya Thway Tint <sup>12,13</sup>

- <sup>1</sup> School of Molecular Sciences, The University of Western Australia, Crawley, WA 6009, Australia; jacki.mceachran@uwa.edu.au (J.L.M.); sharon.perrella@uwa.edu.au (S.L.P.); m.wlodek@unimelb.edu.au (M.E.W.); donna.geddes@uwa.edu.au (D.T.G.)
  - <sup>2</sup> International Society for Research in Human Milk and Lactation, Minneapolis, MN 55416, USA
  - <sup>3</sup> ABREAST Network, Perth, WA 6000, Australia
  - <sup>4</sup> UWA Centre for Human Lactation Research and Translation, Crawley, WA 6009, Australia
  - <sup>5</sup> Global Center for Asian Women's Health (GloW), Yong Loo Lin School of Medicine, National University of Singapore, Singapore 117597, Singapore; obgpww@nus.edu.sg
  - <sup>6</sup> Bia-Echo Asia Centre for Reproductive Longevity & Equality (ACRLE), Yong Loo Lin School of Medicine, National University of Singapore, Singapore 117597, Singapore
  - <sup>7</sup> Department of Mathematics and Statistics, School of Physics, Mathematics and Computing, The University of Western Australia, Crawley, WA 6009, Australia; philip.vlaskovsky@uwa.edu.au
  - <sup>8</sup> Department of Paediatrics, KK Women's and Children's Hospital, Singapore 229899, Singapore; fabian.yap.k.p@singhealth.com.sg
  - <sup>9</sup> Department of Obstetrics and Gynaecology, The University of Melbourne, Melbourne, VIC 3010, Australia
  - <sup>10</sup> Department of Obstetrics and Gynaecology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore 117597, Singapore; obgcys@nus.edu.sg
  - <sup>11</sup> National University Health System, Singapore 119228, Singapore
  - <sup>12</sup> Singapore Institute for Clinical Sciences (SICS), Agency for Science, Technology and Research (A\*STAR), Singapore 117609, Singapore; obgje@nus.edu.sg (J.G.E.); mya\_thway\_tint@sics.a-star.edu.sg (M.T.T.)
  - <sup>13</sup> Human Potential Translational Research Programme, Yong Loo Lin School of Medicine, National University of Singapore, Singapore 117597, Singapore
  - <sup>14</sup> Department of General Practice and Primary Health Care, University of Helsinki, 00014 Helsinki, Finland
  - <sup>15</sup> Folkhälsan Research Centre, 00250 Helsinki, Finland
- \* Correspondence: zoya.gridneva@uwa.edu.au; Tel.: +61-8-6488-4467
- <sup>†</sup> Presented at the Australian Breastfeeding + Lactation Research and Science Translation Conference (ABREAST Conference 2023), Perth, Australia, 10 November 2023.



**Citation:** Gridneva, Z.; Pang, W.W.; Vlaskovsky, P.; McEachran, J.L.; Perrella, S.L.; Yap, F.; Wlodek, M.E.; Chong, Y.-S.; Eriksson, J.G.; Geddes, D.T.; et al. Breastfeeding Duration and Bone Mineral Density in Childhood: A Prospective Study within GUSTO Cohort. *Proceedings* **2023**, *93*, 10. <https://doi.org/10.3390/proceedings2023093010>

Published: 22 December 2023



**Copyright:** © 2023 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

**Keywords:** lactation; breastfeeding duration; infants and children; bone mineral density; dual-energy X-ray absorptiometry; lumbar spine; solid food introduction; growth; GUSTO cohort; Asian

Nutrition contributes to bone mineral density (BMD) and plays a role in bone growth during infancy and childhood. However, the published relationships between breastfeeding exposure and BMD in infancy, childhood and adult life are not consistent. This cross-sectional study examined relationships of both breastfeeding duration and time of solid food introduction, with BMD in young Asian children from the Growing up in Singapore Towards healthy Outcomes (GUSTO) cohort.

Six-year-old children that were born healthy at term with available dual-energy X-ray absorptiometry (DXA) lumbar spine (LS) scans and data on the duration of any breastfeeding were included in the analysis ( $n = 207$ ; 103 boys, 104 girls; 110 Chinese, 34 Indian and 63 Malay). LS bone mineral apparent density (BMAD), i.e., volumetric BMD, was estimated according to the published equation based on bone mineral content (BMC) and bone area from L2 to L4 ( $BMC/A_p^{3/2}$ ) [1]. Outcomes in univariable and multivariable linear regression models included areal  $BMD_{LS}$  ( $aBMD_{LS}$ ) and  $BMAD_{LS}$  (to take account of bone size in growing children), and the standard deviation scores  $Z_{LS-BMAD}$  and  $Z_{LS-aBMD}$ .

Covariates adjusted for were maternal ethnicity, pre-pregnancy BMI, child's sex and both, child weight, and physical activity at 6 years of age.

Only 11 children were not breastfed, with the rest breastfed on average for  $7.6 \pm 11.5$  (0.0–54.8) months. At 6 years of age, no significant difference in  $BMD_{LS}$  was detected by maternal ethnicity. Boys had lower  $BMD_{LS}$  compared to girls ( $aBMD_{LS}$ :  $-0.025$  (95% CI:  $-0.040, -0.010$ ;  $p = 0.002$ )  $g/cm^2$ ;  $Z_{LS-aBMD}$ :  $-0.436$  (95% CI:  $-0.704, -0.168$ ;  $p = 0.002$ )  $g/cm^2$ ;  $BMAD_{LS}$ :  $-0.008$  (95% CI:  $-0.011, -0.005$ ;  $p < 0.0001$ )  $g/cm^3$ ;  $Z_{LS-BMAD}$ :  $-0.621$  (95% CI:  $-0.882, -0.360$ ;  $p < 0.0001$ )  $g/cm^3$ ). In the univariable model, children with longer breastfeeding duration had significantly lower  $aBMD_{LS}$ , but not  $BMAD_{LS}$  ( $aBMD_{LS}$ :  $-0.0007$  (95% CI:  $-0.001, -1.575$ ;  $p = 0.045$ )  $g/cm^2$ ;  $Z_{LS-aBMD}$ :  $-0.012$  (95% CI:  $-0.024, -0.0003$ ;  $p = 0.045$ )  $g/cm^2$ ). In the analysis stratified by sex, the association with breastfeeding duration was significant only for girls and only for  $aBMD_{LS}$  ( $aBMD_{LS}$ :  $-0.001$  (95% CI:  $-0.002, -0.0001$ ;  $p = 0.037$ )  $g/cm^2$ ;  $Z_{LS-aBMD}$ :  $-0.018$  (95% CI:  $-0.035, -0.001$ ;  $p = 0.037$ )  $g/cm^2$ ). Adjusting for covariates resulted in no significant relationships with breastfeeding duration.

The average time of solid food introduction was reported as  $5.5 \pm 1.2$  months (3.0–10.0;  $n = 188$ ; 93 boys, 95 girls). No significant relationship with time of solid food introduction was found in the entire group in both the univariable and adjusted models. However, in stratified analysis, boys with later solid food introduction had lower  $BMD_{LS}$  ( $aBMD_{LS}$ :  $-0.009$  (95% CI:  $-0.018, -0.0006$ ;  $p = 0.037$ )  $g/cm^2$ ;  $Z_{LS-aBMD}$ :  $-0.166$  (95% CI:  $-0.321, -0.010$ ;  $p = 0.037$ )  $g/cm^2$ ;  $BMAD_{LS}$ :  $-0.003$  (95% CI:  $-0.005, -0.0006$ ;  $p = 0.011$ )  $g/cm^3$ ;  $Z_{LS-BMAD}$ :  $-0.205$  (95% CI:  $-0.360, -0.050$ ;  $p = 0.010$ )  $g/cm^3$ ). These relationships persisted when adjusting for covariates.

Breastfeeding duration and time of solid food introduction may have a long-term impact on bone mineralization in young children. However, a more precise quantitative approach when measuring breastfeeding exposure, such as 24 h infant milk intake and intake of milk components, would be prudent. Understanding the factors influencing bone remodeling during these periods of rapid skeletal growth is important for determining effective interventions to enhance bone development in vulnerable infants and children.

**Author Contributions:** Conceptualization of GUSTO, Y.-S.C. and F.Y.; conceptualization of this study, M.T.T., Z.G. and D.T.G.; methodology, M.T.T., W.W.P., P.V. and Z.G.; data collection, M.T.T. and W.W.P.; formal analysis, Z.G.; investigation, M.T.T., Z.G. and W.W.P.; resources, M.T.T.; data curation, M.T.T., Z.G. and W.W.P.; writing—original draft preparation, Z.G.; writing—review and editing, W.W.P., P.V., J.L.M., S.L.P., F.Y., M.E.W., Y.-S.C., J.G.E., D.T.G. and M.T.T.; visualization, Z.G.; supervision, M.T.T. and D.T.G.; project administration, J.L.M.; funding acquisition, Y.-S.C., D.T.G. and J.L.M. All authors have read and agreed to the published version of the manuscript.

**Funding:** The GUSTO study is supported by the National Research Foundation (NRF) under the Open Fund-Large Collaborative Grant (OF-LCG; MOH-000504) administered by the Singapore Ministry of Health's National Medical Research Council (NMRC) and the Agency for Science, Technology and Research (A\*STAR). Z.G. was funded by an unrestricted research grant from Medela AG (Switzerland) and has been financially supported (in part) by the International Society for Research in Human Milk and Lactation - Family Larsson-Rosenquist Foundation Trainee Expansion Program. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

**Institutional Review Board Statement:** This study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of the National Healthcare Group Domain Specific Review Board and SingHealth Centralized Institutional Review Board, Singapore (DSRB:D/2009/00021, CIRB:2018/2767/D).

**Informed Consent Statement:** Written informed consent was obtained from all subjects involved in this study. The children filled out an assent form to document their understanding of and participation in the study, while their parents gave written informed consent.

**Data Availability Statement:** Restrictions apply to the availability of some, or all, data generated or analyzed during this study. The corresponding author will, upon request, detail the restrictions and any conditions under which access to some data may be provided.

**Acknowledgments:** We thank the contributions of study participants, clinical and home-visit staff, and the GUSTO Study Group.

**Conflicts of Interest:** D.T.G. declares participation in the Scientific Advisory Board of Medela AG. Z.G., J.L.M., S.L.P and D.T.G. are/were supported by an unrestricted research grant from Medela AG, administered by The University of Western Australia. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results. All other authors declare no conflicts of interest.

## Reference

1. Katzman, D.K.; Bachrach, L.K.; Carter, D.R.; Marcus, R. Clinical and anthropometric correlates of bone mineral acquisition in healthy adolescent girls. *J. Clin. Endocrinol. Metab.* **1991**, *73*, 1332–1339. [[CrossRef](#)] [[PubMed](#)]

**Disclaimer/Publisher's Note:** The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.