American Journal of
Preventive Medicine

RESEARCH BRIEF

Natural Transitions of Non–High-Density Lipoprotein Cholesterol Levels in Children Aged 9–11 Years

Yaxing Meng, PhD,[1,2,3,4] Tetsuhiro Kidokoro, PhD,[5,6,7] Natsuko Imai, PhD,[8] Russell J. Thomson, PhD,[1,9] Grant R. Tomkinson, PhD,[6] Costan G. Magnussen, PhD[1,2,3,4,6]

Introduction: U.S. guidelines recommend universal lipid screening in children aged between 9 and 11 years, with follow-up screening at ages 17–21 years. Non–high-density lipoprotein cholesterol is the preferred marker. However, the stability of non–high-density lipoprotein cholesterol within the screening window remains unclear. This study aimed to estimate the probabilities of non–high-density lipoprotein cholesterol transitioning between its classifications (acceptable, borderline high, and high) during the 9–11-year age period and the average duration that it remains stable within each classification.

Methods: This study included 496 Japanese children with non–high-density lipoprotein cholesterol measured between ages 9 and 11 years. Data were collected from 2015 to 2019, and analyses were conducted in 2024. A time-homogeneous continuous-time Markov model was used to estimate the probabilities of transitioning among non–high-density lipoprotein cholesterol classifications—acceptable (<120 mg/dL), borderline high (120-144 mg/dL), and high (≥145 mg/dL)—and the average duration children remained in a given non–high-density lipoprotein cholesterol classification before transitioning.

Results: At the population level, all non–high-density lipoprotein cholesterol classifications identified at age 9 years were estimated to remain stable for more than 2 years. Children with acceptable non–high-density lipoprotein cholesterol had a mean duration of 10.6 years (95% CI=7.8, 14.5) before transitioning to another classification, with an estimated 0.90 probability of maintaining in the acceptable classification during the 9–11-year window.

Conclusions: Non–high-density lipoprotein cholesterol classifications identified at age 9 years remained stable for over 2 years, supporting the appropriateness of screening at any point within the 9–11-year window. These findings offer insights into optimal lipid-screening practices, thereby enhancing early cardiovascular disease prevention.

INTRODUCTION

Early cardiovascular prevention involves risk-factor screening to identify at-risk children, with non–high-density lipoprotein cholesterol (non–HDL-C) serving as a key factor. The National Heart, Lung, and Blood Institute (NHLBI) guideline recommends universal screening of non-HDL-C in children aged 9–11 years.[1] This age window was chosen

From the [1]Baker Heart and Diabetes Institute, Melbourne, Australia; [2]Baker Department of Cardiometabolic Health, Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne, Melbourne, Australia; [3]Research Centre of Applied and Preventive Cardiovascular Medicine, University of Turku, Turku, Finland; [4]Centre for Population Health Research, University of Turku and Turku University Hospital, Turku, Finland; [5]Faculty of Sport Science, Nippon Sport Science University, Setagaya, Japan; [6]Alliance for Research in Exercise, Nutrition and Activity (ARENA), University of South Australia, Adelaide, Australia; [7]Graduate School of Health and Sports Science, Juntendo University, Chiba, Japan; [8]Faculty of child education and care, Tokyo Kasei University, Tokyo, Japan; and [9]Analytical Edge, Hobart, Australia

Address for correspondence: Costan G. Magnussen, PhD, Baker Heart and Diabetes Institute, 75 Commercial Road, Melbourne, Australia 3004. E-mail: Costan.Magnussen@baker.edu.au.

0749-3797/$36.00
https://doi.org/10.1016/j.amepre.2025.108243

because it precedes the peripubescent period when lipid levels change considerably and nonuniformly, varying by sex, race, and stage of sexual maturation.[2,3] However, the natural transition between non−HDL-C classifications in this age window has not been examined. This is relevant because children could be measured at any point in this 2-year period, commencing lipid screening and clinical decisions.[1] Although this screening window also avoids the peripubescent changes in lipid levels, it is not known how stable non−HDL-C remains over this period. Understanding the transition probabilities between these classifications could be used to refine clinical guidelines by ensuring that screenings are appropriately timed and potentially adjusted according to the initial non−HDL-C levels observed in the 9−11-year age window. This study aimed to estimate natural transition among non−HDL-C classifications from ages 9 to 11 years.

METHODS

A total of 548 4th-grade students (aged 9−10 years) from 3 of 14 primary schools in Saku, Japan, were recruited for and participated in a cross-sectional study. Two years later, when participants were in Grade 6 (aged 11−12 years), 505 (92%) attended a follow-up survey. This study comprised 496 children with non−HDL-C measurements in both Grades 4 and 6. Parents/guardians provided informed consent. The study adhered to the Declaration of Helsinki and received approval from the institutional ethical advisory committee of Nippon Sport Science University (Project Identification Code 021-H005). Detailed statistical methods and lipids measurements are provided in the Appendix (available online), Appendix Table 1 (available online), and Appendix Figure 1 (available online) and summarized below.

Nurses collected nonfasting venous blood samples. Non−HDL-C was determined as total cholesterol minus high-density lipoprotein cholesterol and classified as acceptable (<120 mg/dL [<3.10 mmol/L]), borderline high (120−144 mg/dL [3.10−3.73 mmol/L]), and high (≥145 mg/dL [≥3.75 mmol/L]).[1]

The time-homogenous multistate Markov model[4−7] was used to estimate mean transition probabilities of non−HDL-C classifications and mean sojourn times,[4] indicating the average time spent in a specific non−HDL-C classification before transitioning to another classification. The model can estimate the sojourn times beyond the observed follow-up period. The multistate Markov model was fitted using the msm package of R 3.5.3, providing a framework for modeling processes that involve transitions between discrete states over time.[4]

RESULTS

Appendix Table 2 (available online) shows participant characteristics. Total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL-C), non−HDL-C, and BMI increased with the severity of non−HDL-C classifications (Appendix Table 3, available online). Estimated mean sojourn time of acceptable non−HDL-C was 10.6 (95% CI=7.8, 14.5) years, which was longer than the time for those with borderline-high (2.2 years) or high (2.5 years) levels (Table 1). Participants with acceptable non−HDL-C consistently had a high probability of maintaining their classification, with transition probabilities of 0.92 (95% CI=0.90, 0.94) annually and 0.87 (95% CI=0.84, 0.91) over 2 years (Table 2). For those with borderline-high non−HDL-C, the probability of reverting to acceptable non−HDL-C was consistently higher than that of progressing to high non−HDL-C (transition probability for all participants=0.25 [95% CI=0.18, 0.31] vs 0.10 [95% CI=0.06, 0.15] for 1 year and 0.39 [95% CI=0.31, 0.47] vs 0.13 [95% CI=0.08, 0.19] for 2 years). This difference was more pronounced in females, where the reversion probability was approximately 4-fold higher in females vs 2-fold higher in males. For example, 2-year transition probability was 0.43 (95% CI=0.30,

Table 1. Mean Sojourn Time in Non−High-Density Lipoprotein Cholesterol Classifications in Japanese School Children

Non−high-density lipoprotein cholesterol classifications	All[a]		Males		Females	
	n[b]	Mean sojourn time (95% CI), years	*n*[b]	Mean sojourn time (95% CI), years	*n*[b]	Mean sojourn time (95% CI), years
Acceptable (< 120 mg/dL)	362	10.6 (7.8, 14.5)	177	12.1 (7.5, 19.5)	185	9.5 (6.3,14.1)
Borderline high (≥120 and <145 mg/dL)	111	2.2 (1.6, 2.9)	53	1.6 (1.1, 2.4)	58	2.8 (1.9, 4.2)
High (≥145 mg/dL)	23	2.5 (1.4, 4.8)	10	2.7 (1.0, 7.2)	13	2.4 (1.1, 5.4)

[a]Model adjusted for sex.
[b]The number of participants in the non−high-density lipoprotein cholesterol classification at Grade 4.

Table 2. One- and 2-Year Transition Probabilities of Non—High-Density Lipoprotein Cholesterol Classifications From Grade 4 (Aged 9—10 Years) to Grade 6 (Aged 11—12 Years) in Japanese School Children

	All [a]			To Males			Females		
From	Acceptable	Borderline high	High	Acceptable	Borderline high	High	Acceptable	Borderline high	High
One-year									
Acceptable[b]	0.92 (0.90, 0.94)	0.07 (0.05, 0.09)	0.005 (0.003, 0.01)	0.93 (0.92, 0.96)	0.06 (0.03, 0.07)	0.01 (0.003, 0.01)	0.91 (0.90, 0.94)	0.09 (0.06, 0.10)	0.004 (0.001,0.005)
Borderline high[b]	0.25 (0.18, 0.31)	0.66 (0.58, 0.72)	0.10 (0.06, 0.15)	0.28 (0.20, 0.38)	0.57 (0.43, 0.66)	0.15 (0.09, 0.22)	0.21 (0.19, 0.23)	0.73 (0.70,0.77)	0.06 (0.03,0.08)
High[b]	0.05 (0.02, 0.08)	0.26 (0.14, 0.39)	0.69 (0.54, 0.84)	0.05 (0.01, 0.11)	0.23 (0.07, 0.36)	0.72 (0.56, 0.91)	0.04 (0.03,0.04)	0.29 (0.23,0.32)	0.67 (0.63, 0.74)
Two-year									
Acceptable[b]	0.87 (0.84, 0.91)	0.12 (0.08, 0.14)	0.01 (0.009, 0.02)	0.89 (0.85, 0.93)	0.09 (0.05, 0.13)	0.02 (0.01, 0.03)	0.85 (0.83, 0.87)	0.14 (0.12, 0.16)	0.01 (0.07, 0.02)
Borderline high[b]	0.39 (0.31, 0.47)	0.48 (0.39, 0.56)	0.13 (0.08, 0.19)	0.43 (0.30, 0.56)	0.37 (0.30, 0.50)	0.19 (0.09, 0.29)	0.35 (0.36, 0.45)	0.56 (0.49, 0.51)	0.09 (0.05, 0.12)
High[b]	0.14 (0.06, 0.22)	0.36 (0.19,0.48)	0.51 (0.29, 0.73)	0.15 (0.03, 0.35)	0.30 (0.09, 0.42)	0.55 (0.27, 0.87)	0.13 (0.11, 0.20)	0.41 (0.29, 0.44)	0.47 (0.35, 0.59)

Note: Values indicate transition probabilities and their 95 % CIs. These estimates were derived from multistate Markov Models.
[a]All models adjusted for sex.
[b]Non—high-density lipoprotein cholesterol classifications are acceptable (<120 mg/dL), borderline high (≥120 and <145 mg/dL), and high (≥145 mg/dL). To convert values from mg/dL to mmol/L, multiply by 0.02586.

0.56) vs 0.19 (95% CI=0.09, 0.29) in males but 0.35 (95% CI=0.36, 0.45) vs 0.09 (95% CI=0.05, 0.12) in females.

DISCUSSION

This study evaluated the natural transition of non−HDL-C classifications during the NHLBI-recommended screening window of ages 9−11 years.[1] The average duration of stability within a non−HDL-C classification exceeded 2 years across all classifications. Children with acceptable non−HDL-C had a high (∼0.9) estimated probability of maintaining their initial classification within the 2-year period. These findings support current guideline recommendations for the initial universal lipid screening age.[1,8,9]

Guidelines[1,8,9] recommend conducting universal pediatric lipid screening between ages 9 and 11 years. Because screening can occur at any point within the 9−11-year window, concerns exist regarding whether the timing of screening might influence non−HDL-C classification assignment. Previous research has shown a strong correlation between non−HDL-C levels measured in Finnish youth at ages 9 and 11 years (stability coefficients: 0.71−0.86).[10] The average sojourn time is >2 years, supporting the appropriateness of the initial screening at any point within the recommended age range. The longer mean sojourn time for acceptable non−HDL-C than that of normal BMI[11] and blood pressure[12] likely reflects their divergent developmental trajectories—lipids tend to decline before puberty, whereas BMI and blood pressure rise with growth. It may also reflect the stronger genetic determination,[13] lower random measurement variability, and stronger tracking of non−HDL-C.[10]

Children with borderline-high or high non−HDL-C had a shorter mean sojourn time and a lower estimated probability of maintaining their initial classification than those with acceptable non−HDL-C, suggesting that more frequent follow-ups may be needed for these higher-risk groups. The NHLBI guideline recommends confirming abnormal non−HDL-C with a repeated fasting sample within at least 2 weeks and within 3 months before making treatment decisions.[1]

Prior studies have demonstrated a positive association between BMI and LDL-C in children.[14] Children in more severe non−HDL-C classifications had higher mean BMI (Appendix Table 3, available online). Sex-related differences in lipid profiles have also been reported, with prepubertal girls exhibiting higher LDL-C than boys.[13] In line, this study showed that girls consistently had higher non−HDL-C than boys at both Grades 4 and 6; however, these differences became less pronounced with age (Appendix Table 2, available online). Females were more likely than males to regress from borderline-high or high non−HDL-C to lower classifications. A possible explanation is that non−HDL-C tends to decline with biological maturation,[2] and puberty typically begins earlier in girls, which may contribute to earlier reductions in non−HDL-C among girls. This study estimated natural stability at the population level, but future research incorporating pubertal staging, BMI, and sex-specific lipid metabolism could enhance individual-level risk assessment.[2,15] These factors are not currently considered within the screening window on the basis of chronological age.

Limitations

This Japanese cohort with non−HDL-C measurements at ages 9−11 years within the same individual enabled estimates of natural transitions within the NHLBI-recommended screening window. Population differences in ethnicity, dietary patterns,[16,17] physical activity,[18] and healthcare access[19] compared with Western populations may limit generalizability and should be considered when interpreting the findings in the context of U.S. guidelines. Nevertheless, the prevalence of high non−HDL-C was only slightly lower in this Japanese cohort (Appendix Table 2, available online) than in U.S. children aged 8−12 years (4.6%−6.5% vs 6.9% overall).[20] These comparable prevalence and similar age-related lipid patterns[15,21] suggest the potential applicability of this study's findings to U.S. pediatric populations. The time-homogeneous Markov model assumes that transition intensities remain constant over time, which enables estimation of mean sojourn time beyond the observed follow-up period but cannot fully capture time-varying lipid dynamics, particularly during puberty when biological maturation can alter lipid trajectories.

CONCLUSIONS

The estimated mean sojourn time exceeded 2 years across non−HDL-C classifications. These model-based estimates suggest the stability of non−HDL-C within this screening window at a population-level, supporting the guideline recommendation for screening between ages 9 and 11 years.[1,8,9]

ACKNOWLEDGMENTS

The authors thank the participants, volunteers, and study staff involved in all aspects of this Japanese Study.

Disclaimer: The contents of the published material are solely the responsibility of the individual authors and do not reflect the views of the National Health and Medical Research Council.

Funding: AM has been cofunded by the European Union's Horizon Europe Framework program for research and innovation 2021−2027 under the Marie Skłodowska-Curie grant

agreement Number 101126611. CGM was supported by a National Health and Medical Research Council investigator grant (APP1176494) during the development and drafting of this work.

Declaration of interest: None.

CREDIT AUTHOR STATEMENT

Yaxing Meng: Conceptualization, Methodology, Software, Validation, Formal analysis, Writing - original draft, Visualization, Funding acquisition. Tetsuhiro Kidokoro: Investigation, Resources, Data curation, Writing- Reviewing and Editing. Natsuko Imai: Investigation, Resources, Data curation, Writing - reviewing & editing. Russell J. Thomson: Formal analysis, Software. Grant R. Tomkinson: Writing - reviewing & editing. Costan G. Magnussen: Writing - original draft, Writing - reviewing & editing, Visualization, Project administration, Supervision, Funding acquisition.

SUPPLEMENTAL MATERIAL

Supplemental materials associated with this article can be found in the online version at https://doi.org/10.1016/j.amepre.2025.108243.

REFERENCES

1. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents, National Heart, Lung, and Blood Institute. Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: summary report. *Pediatrics.* 2011;128(suppl 5):S213–S256. https://doi.org/10.1542/peds.2009-2107C.
2. Eissa MA, Mihalopoulos NL, Holubkov R, Dai S, Labarthe DR. Changes in fasting lipids during puberty. *J Pediatr.* 2016;170:199–205. https://doi.org/10.1016/j.jpeds.2015.11.018.
3. Berenson GS, Srinivasan SR, Cresanta JL, Foster TA, Webber LS. Dynamic changes of serum lipoproteins in children during adolescence and sexual maturation. *Am J Epidemiol.* 1981;113(2):157–170. https://doi.org/10.1093/oxfordjournals.aje.a113080.
4. Jackson C. Multi-state models for panel data: the msm package for R. *J Stat Softw.* 2011;38:1–28. https://doi.org/10.18637/jss.v038.i08.
5. Lartey ST, Si L, Otahal P, et al. Annual transition probabilities of overweight and obesity in older adults: evidence from World Health Organization Study on global AGEing and adult health. *Soc Sci Med.* 2020;247:112821. https://doi.org/10.1016/j.socscimed.2020.112821.
6. Moreira C, Meira-Machado L, Fonseca MJ, Santos AC. A multistate model for analyzing transitions between body mass index categories during childhood: the generation XXI birth cohort study. *Am J Epidemiol.* 2019;188(2):305–313. https://doi.org/10.1093/aje/kwy232.
7. Welton NJ, Ades AE. Estimation of Markov chain transition probabilities and rates from fully and partially observed data: uncertainty propagation, evidence synthesis, and model calibration. *Med Decis Making.* 2005;25(6):633–645. https://doi.org/10.1177/0272989X05282637.
8. American Academy of Pediatrics. *Bright Futures Guidelines for Health Supervision of Infants, Children, and Adolescents*. 2017. https://doi.org/10.1542/9781610020237.
9. Correction to: 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice guidelines. *Circulation.* 2019;139(25):e1178–e1181. https://DOI.ORG/10.1161/CIR.0000000000000699.
10. Meng Y, Niinikoski H, Rovio SP, et al. The influence of dietary counseling over 20 years on tracking of non-high-density lipoprotein cholesterol from infancy to young adulthood. *J Pediatr.* 2024;264:113776. https://doi.org/10.1016/j.jpeds.2023.113776.
11. Häkkänen P, But A, Ketola E, Laatikainen T. Weight transitions and psychosocial factors: a longitudinal cohort study of Finnish primary school children with overweight. *Prev Med Rep.* 2020;20:101239. https://doi.org/10.1016/j.pmedr.2020.101239.
12. Meng Y, Sharman JE, Iiskala F, et al. Tracking and transition probability of blood pressure from childhood to midadulthood. *JAMA Pediatr.* 2025;179(1):34–45. https://doi.org/10.1001/jamapediatrics.2024.4368.
13. Kafol J, Becker M, Cugalj Kern B, et al. Sex differences in cholesterol levels among prepubertal children. *Atherosclerosis.* 2025;410:120484. https://doi.org/10.1016/j.atherosclerosis.2025.120484.
14. Sustar U, Kordonouri O, Arens S, et al. Evaluation of body mass index, overweight and obesity status, and cholesterol levels in younger children. *JAMA Netw Open.* 2023;6(4):e238141. https://doi.org/10.1001/jamanetworkopen.2023.8141.
15. Okada T, Murata M, Yamauchi K, Harada K. New criteria of normal serum lipid levels in Japanese children: the nationwide study. *Pediatr Int.* 2002;44(6):596–601. https://doi.org/10.1046/j.1442-200x.2002.01634.x.
16. La Vecchia C, Serra Majem L. Evaluating trends in global dietary patterns. *Lancet Glob Health.* 2015;3(3):e114–e115. https://DOI.ORG/10.1016/S2214-109X(15)70011-2.
17. Fabiani R, Naldini G, Chiavarini M. Dietary patterns and metabolic syndrome in adult subjects: a systematic review and meta-analysis. *Nutrients.* 2019;11(9):2056. https://doi.org/10.3390/nu11092056.
18. Owen CG, Nightingale CM, Rudnicka AR, Cook DG, Ekelund U, Whincup PH. Ethnic and gender differences in physical activity levels among 9−10-year-old children of white European, South Asian and African-Caribbean origin: the Child Heart Health Study in England (CHASE Study). *Int J Epidemiol.* 2009;38(4):1082–1093. https://doi.org/10.1093/ije/dyp176.
19. Aspalter C, Gauld R. *Health Care Systems in Europe and Asia*. London, United Kingdom: Routledge, 2012. https://doi.org/10.4324/9780203157992.
20. Kit BK, Kuklina E, Carroll MD, Ostchega Y, Freedman DS, Ogden CL. Prevalence of and trends in dyslipidemia and blood pressure among U.S. children and adolescents, 1999−2012. *JAMA Pediatr.* 2015;169(3):272–279. https://doi.org/10.1001/jamapediatrics.2014.3216.
21. Cook S, Auinger P, Huang TT. Growth curves for cardio-metabolic risk factors in children and adolescents. *J Pediatr.* 2009;155(3)(suppl 6):S6.e15−S6.e26. https://doi.org/10.1016/j.jpeds.2009.04.051.