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Research

Evaluating the prevalence of lipid assessments in children in Alberta, Canada

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Abstract

Background: Familial hypercholesterolemia is a common, inherited, life-threatening and treatable condition that is characterized by marked elevations of low-density lipoprotein cholesterol (LDL-C), resulting in a high risk of cardiovascular disease, but treatment starting in childhood dramatically reduces this risk. We sought to evaluate the prevalence of pediatric lipid assessments among children in Alberta.

Methods: We reviewed laboratory and administrative data from Alberta Health between Apr. 1, 2012, and Dec. 31, 2021. We evaluated 2 pediatric cohorts (children aged 2–10 yr and children aged 9–17 yr) to allow for longitudinal assessments throughout the pediatric period. We also reviewed annual frequencies of lipid assessment for all children between 2013 and 2021.

Results: Pediatric lipid assessments were performed for 1972 (4.3%) of 46 170 children aged 2–10 years and for 8158 (19.9%) of 40 926 children aged 9–17 years. Female children (aged 2–10 yr) and those living in rural communities were significantly less likely to have a lipid assessment, compared with male children and those in nonrural communities. Among those with lipid assessments, 23 (1.2%) and 86 (1.1%) children aged 2–10 years and 9–17 years, respectively, had an LDL-C level suggestive of probable familial hypercholesterolemia (≥ 4.0 mmol/L). Statin therapy was prescribed in 16 children during the study period. The frequency of lipid assessments was relatively stable, with the exception of a decrease in 2020.

Interpretation: Rates of pediatric lipid assessment in Alberta are suboptimal. These findings highlight the need to increase awareness of the benefits of early diagnosis and treatment of familial hypercholesterolemia with regard to long-term health and identify and overcome barriers to diagnosis and treatment.

Pediatric lipid disorders are common, with about 20% of children having abnormal levels of 1 or more lipid values.[1,2] The presence and severity of dyslipidemia in childhood is associated with atherosclerotic burden and future cardiovascular risk.[3,4] The most severe forms of pediatric dyslipidemia are typically the result of a monogenic inherited disorder, such as familial hypercholesterolemia.[5] Familial hypercholesterolemia is common, with a world-wide prevalence of about 1 in 250 to 1 in 300 people, and an even higher prevalence in some regions, such as Quebec, because of the founder effect.[5,6] Pediatric lipid screening is a simple and effective tool to identify children with an inherited lipid disorder, such as familial hypercholesterolemia.[7] If untreated, people with familial hypercholesterolemia have an 18-fold increased risk of cardiovascular disease.[8] Early diagnosis is paramount and treatment starting in childhood dramatically reduces atherosclerotic progression and subsequent risk for manifesting cardiovascular disease.[9] To this end, since 2011, the National Heart, Lung, and Blood Institute (NHLBI) in the United States has recommended universal lipid screening for all children aged 9–11 years and again between ages 17 and 21 years.[10] However, familial hypercholesterolemia is diagnosed in less than 10% of affected people, and less than 5% of pediatricians in Canada report routinely performing lipid assessments in healthy children.[7,11] The real-world practice patterns of primary care physicians with respect to pediatric lipid assessments for children in Canada requires evaluation to gain insights regarding the current detection of familial hypercholesterolemia and other inherited lipid disorders. Thus, we sought to evaluate the prevalence of pediatric lipid assessments among children in Alberta and factors associated with lipid assessment.

Methods

Data sources and cohorts

We retrieved data from 5 Alberta Health databases including the Provincial Registry, the Laboratory Database, the Pharmaceutical Information Network, the Discharge Abstract Database, Vital Statistics and the National Ambulatory Care

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Reporting System. Individuals are assigned a unique identification number that permits linking across the databases. Extracted data for each data source are described in Appendix 1, Supplementary Table 1, available at www.cmajopen.ca/content/11/5/E820/suppl/DC1. We excluded children from all data sets if they had an underlying diagnosis (based on codes from the *International Classification of Diseases and Related Health Problems, 10th Revision* in inpatient or emergency department records) — such as hypothyroidism, diabetes or chronic kidney disease — that would predispose them to routine lipid screening, independent of universal screening practice. A full list of the excluded diagnoses is provided in Appendix 2, Supplementary Table 2, available at www.cmajopen.ca/content/11/5/E820/suppl/DC1.[10] We also excluded children without 9 full years of follow-up data (i.e., children that moved out of province or died before the end of the study period) using data from Vital Statistics.

We used administrative, pharmaceutical and laboratory data, including lipid parameters between Apr. 1, 2012 (onset of data availability), and Dec. 31, 2021. Because laboratory data were only available for 10 years (Apr. 1, 2012, onwards), we evaluated 2 separate pediatric cohorts to allow for longitudinal assessments throughout the pediatric period. The first cohort comprised children born between Apr. 1, 2010, and Dec. 31, 2010 (follow-up from 2–10 yr), and the second cohort comprised children born between Apr. 1, 2003, and Dec. 31, 2003 (follow-up from 9–17 yr). There was thus a 2-year overlap in age between the 2 cohorts: children in the younger cohort were 9 and 10 years of age between 2019 and 2021 and children in the older cohort were 9 and 10 years of age between 2012 and 2014. This allowed for the evaluation of an era effect of lipid assessment patterns across the 2 cohorts. We evaluated initial lipid profile data, including total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), non-HDL-C and triglycerides. We also collected data on sex, residence (rural v. nonrural, whereby we defined rural as having a 0 in the second character of the postal code)[12] and age at initial lipid assessment.

Statin dispensation from a community pharmacy (outpatient), including date, were recorded for lovastatin, pravastatin, fluvastatin, simvastatin, atorvastatin and rosuvastatin using their respective anatomic therapeutic chemical code.

Data analysis

We presented continuous variables as medians with 25th and 75th percentiles, and categorical variables as counts and percentages. We defined lipid assessment as the reporting of an LDL-C or total cholesterol value. We considered an LDL-C level of 4.0 mmol/L or higher as indicative of severe hypercholesterolemia or probable familial hypercholesterolemia, in accordance with the simplified Canadian definition for familial hypercholesterolemia.[6] We considered a total cholesterol level of 5.2 mmol/L or higher as abnormal.[10]

We used logistic regression to evaluate the relationship between lipid assessment and sex and residence (rural v. nonrural). We calculated the percentage of initial lipid assessments at each age using an adjusted denominator (subtracting the number of children who had previously had an initial lipid assessment). For each longitudinal cohort, we used a logistic regression model, adjusting for sex and residence, to assess the relationship between lipid assessment and age. We also reviewed annual trends in lipid assessment (i.e., the total number of pediatric lipid assessments per year) between Jan. 1, 2013, and Dec. 31, 2021, for all children aged 2–18 years in Alberta to assess whether there were calendar year effects.

We performed statistical analyses using Stata 17.0 (StataCorp) and SAS version 9.4 (SAS Institute). Given the large sample, a p value of less than 0.0001 defined statistical significance.

Ethics approval

All data were deidentified and research ethics board approval was obtained through the University of Alberta.

Results

The study cohorts included 46 170 children aged 2–10 years and 40 926 children aged 9–17 years. We excluded children with a diagnosis that may influence lipid metabolism (n = 346 and n = 455 in the younger and older cohorts, respectively).

Demographic data for each cohort are described in Table 1. At least 1 lipid assessment (total cholesterol or LDL-C level) was performed in 1972 (4.3%) of children aged 2–10 years and 8158 (19.9%) of children aged 9–17 years. Male children in the younger cohort had 1.32 (95% confidence interval [CI] 1.20–1.45) times the odds of having a lipid assessment, compared with female children, whereas male children in the older cohort had 0.90 (95% CI 0.86–0.95) times the odds of having an assessment, compared with female children. Children living in rural areas in both cohorts were less likely to have a lipid assessment, compared with children living in nonrural communities (children aged 2–10 yr: odds ratio [OR] 0.56, 95% CI 0.48–0.66; children aged 9–17 yr: OR 0.60, 95% CI 0.55–0.65).

Total cholesterol was 5.2 mmol/L or higher for 112 (6.5%) of 1723 children aged 2–10 years and 448 (6.2%) of 7185 children aged 9–17 years; 23 (1.2%) of 1826 children in the younger cohort and 86 (1.1%) of 7517 children in the older cohort had an LDL-C value of 4.0 mmol/L or higher (Table 2).

Three (13.0%) of the 23 children in the younger cohort with LDL-C levels 4.0 mmol/L or higher had a statin dispensed. Thirteen children in the older cohort had a statin dispensed; 8 of these children had an LDL-C value of 4 mmol/L or higher within the study period (9.3% of the 86 children with LDL-C ≥ 4 mmol/L) and 1 child had no LDL-C value reported but had a total cholesterol level of 5.14 mmol/L. Although 4 children had a statin dispensed with an initial LDL-C level less than 4.0 mmol/L and a total cholesterol level less than 5.2 mmol/L, the date of the statin dispensation was several years after the initial lipid assessment was performed.

The percentage of children having their first lipid assessment increased based on age, with only 0.1% of 2-year-olds

Table 1: Cohort characteristics

Characteristic	No. (%) of children in younger cohort (aged 2–10 yr)		No. (%) of children in older cohort (aged 9–17 yr)	
	Screening *n* = 1972	No screening *n* = 44 198	Screening *n* = 8158	No screening *n* = 32 768
Sex				
Male	1146 (5.1)	21 546 (94.9)	4024 (19.1)	16 992 (80.1)
Female	826 (3.5)	22 652 (96.5)	4134 (20.8)	15 776 (79.2)
Rurality				
Rural	177 (2.6)	6585 (97.4)	863 (13.7)	5429 (86.3)
Nonrural	1795 (4.6)	37 611 (95.4)	7195 (20.8)	27 339 (79.2)
Age at initial lipid screening, yr, median (IQR)	8 (6–10)	NA	15 (13–16)	NA

Note: IQR = interquartile range, NA = not applicable.

Table 2: Summary of lipid screening results

Variable	No. (%) of children*	
	Younger cohort (aged 2–10 yr) *n* = 1972	Older cohort (aged 9–17 yr) *n* = 8158
Total cholesterol, mmol/L, median (IQR)	4.02 (3.60–8.44)	3.89 (3.43–4.43)
LDL-C, mmol/L, median (IQR)	2.15 (1.79–2.54)	2.09 (1.70–2.53)
HDL-C, mmol/L, median (IQR)	1.33 (1.12–1.56)	1.25 (1.07–1.47)
Non-HDL-C, mmol/L, median (IQR)	2.66 (2.27–3.10)	2.58 (2.14–3.10)
Triglycerides, mmol/L, median (IQR)	0.97 (0.66–1.49)	0.97 (0.70–1.39)
Total cholesterol > 5.2 mmol/L†	112 (6.5)	448 (6.2)
LDL-C > 3.5 mmol/L‡	71 (3.9)	228 (3.0)
LDL-C > 4.0 mmol/L‡	23 (1.2)	86 (1.1)
LDL-C > 5.0 mmol/L‡	7 (0.4)	18 (0.2)
Statin prescribed	3 (0.2)	13 (0.2)

Note: HDL-C = high-density lipoprotein cholesterol, IQR = interquartile range, LDL-C = low-density lipoprotein cholesterol
*Unless indicated otherwise. The denominator of the proportion of children with total cholesterol or LDL-C levels is of the total.
†Of 1723 children in the younger cohort and 7185 children in the older cohort with total cholesterol assessments.
‡Of 1826 children in the younger cohort and 7517 children in the older cohort with LDL-C assessments.

having an initial lipid assessment, compared with 4.8% of 17-year-olds (Figure 1). The odds of receiving a lipid assessment was 1.33 per additional year of age in the younger cohort (95% CI 1.31–1.36) and 1.21 per additional year of age in the older cohort (95% CI 1.20–1.22). Both cohorts included children aged 9–10 years. The odds of 9- and 10-year-old children having a lipid assessment did not differ significantly between the 2 cohorts (OR 1.07, 95% CI 0.98–1.18).

The number of annual lipid assessments was relatively constant over time, with the exception of a slightly lower number in 2020, followed by a return to assessment rates in keeping with previous years in 2021 (Figure 2).

Interpretation

Inherited lipid disorders such as familial hypercholesterolemia are common and are typically clinically silent throughout childhood.[13] Thus, systematic strategies that incorporate universal, targeted and cascade screening are needed to optimize diagnosis.[14] Screening approaches that centre around universal screening with implementation of genetic testing and cascade screening are cost effective and efficient in identifying familial hypercholesterolemia, not only among children but also their affected relatives.[15] The findings in this study indicate that lipid assessments are infrequently performed in children in Alberta; only 4% of children had a lipid assessment

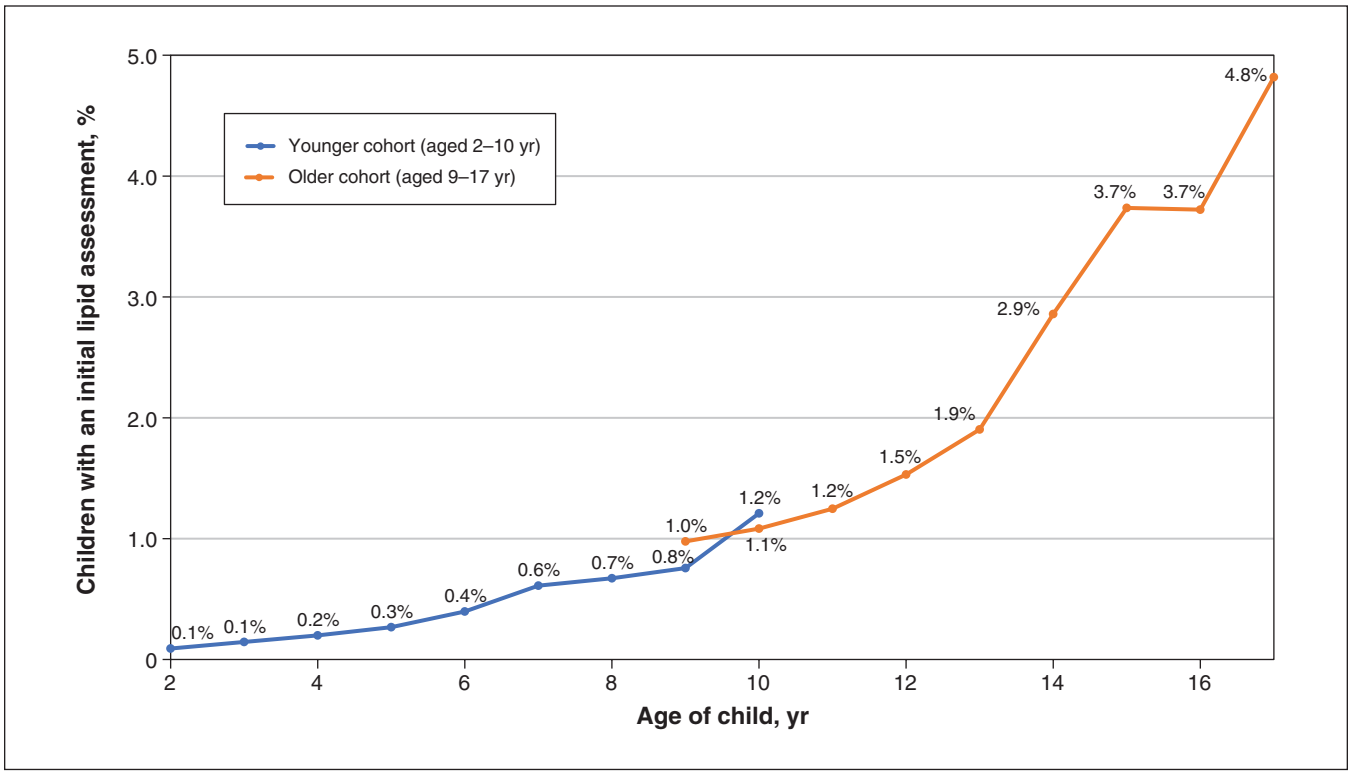

Figure 1: Percentage of children with initial lipid assessments.

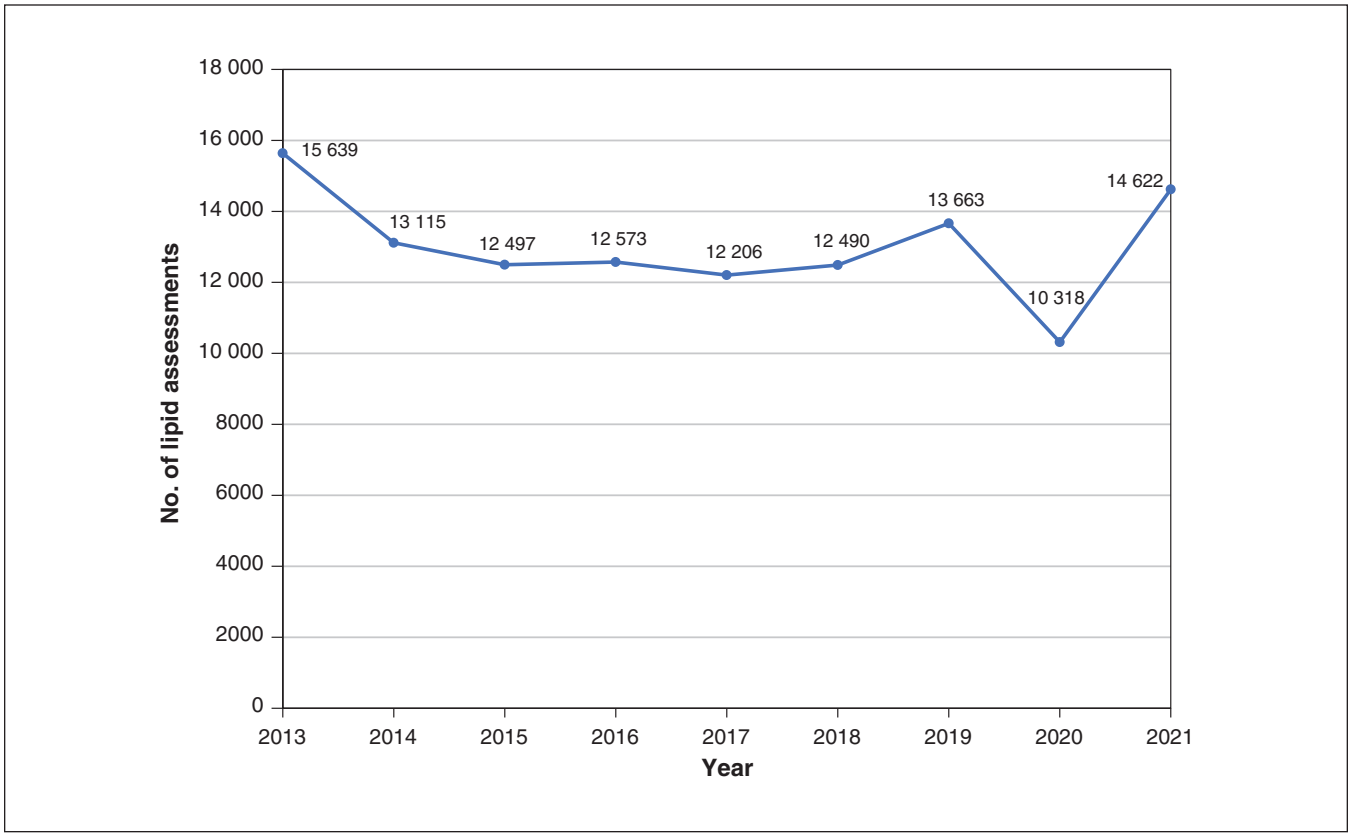

Figure 2: Number of lipid assessments performed for all children aged 2–18 years between 2013 and 2021.

performed between 2 and 10 years of age and 20% between 9 and 17 years of age. These suboptimal assessment rates are not aligned with current recommendations for universal lipid screening from the NHLBI between ages 9 and 11 years or recent recommendations from the Canadian Cardiovascular Society to screen between ages 2 and 10 years.[3,10] Although around 1% of children with lipid assessments had an LDL-C level that was severely elevated and suspicious of familial hypercholesterolemia, only 10% of these children were treated with statins. These findings — from a well-defined geographic population and publicly funded health care system — highlight the need for dedicated strategies to promote the early and systematic detection of inherited lipid disorders among children in Canada. Moreover, efforts must be made to promote the evidence-based treatment of identified patients.

The finding of infrequent lipid assessments in the first decade of life is well aligned with previous work. In a survey administered through the Canadian Pediatric Surveillance Program, only about 3% of Canadian pediatricians who provide primary care reported performing lipid screening on otherwise healthy 9- to 11-year-old children most or all of the time.[11] In the United States, although some studies have shown lipid screening rates of around 20%,[16,17] other analyses have identified lower rates (2%–7%) in otherwise healthy children.[18–21]

Although we were unable to determine the reason for lipid assessment in the present study, it is reasonable to assume that a substantial proportion of assessments were performed as part of a selective screening approach related to the presence of other cardiovascular risk factors or the diagnosis of premature cardiovascular disease in family members.[14] Supporting this, the frequency of initial lipid assessment increased gradually with age, from 0.1% among 2-year-old children to 4.8% among 17-year-old adolescents, suggesting that assessments may have been performed owing to the presence of other risk factors that accumulated with time. Our finding that lipid assessments were relatively consistent between 2013 and 2019 supports the notion that increasing age rather than year was the factor influencing lipid assessment practices. Moreover, assessments were more common among males than females between the ages of 2 and 11 years, which may be related to the increased prevalence of obesity among school-aged boys compared with girls.[22,23]

An important finding in the present study was the observation that children in rural communities underwent lipid assessments less frequently than their urban counterparts. This may be owing to a lack of access to primary care in geographically dispersed and under-resourced locations. Previous work has similarly shown that limited access to care impedes routine health assessments, including pediatric lipid assessments.[17,21] Strategies are thus needed to improve rates of lipid screening in vulnerable communities with reduced access to primary care.[22]

We leveraged an overlap of ages between the 2 cohorts (9- and 10-year-old children) to evaluate changes in lipid assessment practices between the cohort periods (2012–2014 for those from the older cohort v. 2019–2021 for those from the younger cohort). Lipid assessment patterns were similar across consistent age groups (9- and 10-year-old children) and over the time period from 2013 to 2019, showing that screening has not improved over these 8 years. Slightly lower rates of lipid assessment were observed in 2020, which may have been related to the COVID-19 pandemic and decreased health care assessments during this period.

Among children who underwent screening, about 1% in both cohorts had an initial LDL-C value of 4 mmol/L or higher (109 children in total) indicating a high likelihood of familial hypercholesterolemia.[6] Despite this, and evidence supporting the beneficial long-term effects of early treatment for children with familial hypercholesterolemia,[9,24,25] only 11 of these children across the 2 cohorts were provided statin therapy. The low rates of statin therapy are consistent with previous survey data that indicated that 7% of general pediatricians routinely prescribe statins in children with severe and persistent elevations in LDL-C.[15] This highlights that, in addition to strategies aimed at improving the detection of pediatric dyslipidemia, efforts must be made to both enable primary care physicians in management and improve access to pediatric lipid specialists in Canada.[3]

Limitations

Lipid assessment patterns in Alberta may not be representative of those in other provinces or territories across Canada. Given limitations with regard to when collection of provincial administrative data began, we were unable to evaluate longitudinal lipid assessment patterns across the full pediatric age range for a given child (from age 2 yr to 18 yr). Therefore, we generated 2 cohorts to evaluate screening practices between ages 2 and 10 years and 9 and 17 years. We were unable to ascertain the purpose of lipid assessments (e.g., if it was part of a universal screening approach or targeted, selective screening). We were also unable to assess if children had lipid assessments performed outside the available data period (< 2 yr in the younger cohort and < 9 yr in the older cohort). Thus, although lipid assessments before 2 years of age were likely uncommon, it is possible that children in the older cohort had assessments before their ninth birthday and were not captured in the present study. As a result, we were not able to determine the true prevalence of lipid screening (i.e., initial lipid assessment) and, thus, refer to assessment practices instead. Further, a lack of administrative data before 2012 prevents us from evaluating changes in patterns of lipid assessment as a result of the 2011 NHBLI guidelines.[10]

We did not evaluate repeat assessments of dyslipidemia over time and as a result the true prevalence of dyslipidemia; moreover, responses to therapy cannot be determined from the available data. In addition, we were unable to determine if the cause of severe hypercholesteremia was familial hypercholesterolemia or secondary to another condition.

Finally, administrative data captured dispensing of statins from outpatient pharmacies. Although unlikely, children may have had prescriptions dispensed as an inpatient or parents may have chosen not to fill a prescription provided by their child's physician.

Conclusion

The proportion of pediatric lipid assessments among children and adolescents in Alberta is suboptimal, particularly in the first decade of life and among children living in rural communities. Assessment practices have not changed substantially in the last 8 years, apart from a noticeable decrease in assessments in 2020. Children identified to have severe dyslipidemia appear to be undertreated, although further evaluation of this population of children on a more granular level is needed. To optimize the primary prevention of cardiovascular disease, it is imperative that a combination of strategies is incorporated to improve the detection and management of children with dyslipidemia, particularly those with inherited lipid disorders.

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