Non-High-Density Lipoprotein Cholesterol in Children with Diabetes: Proposed Treatment Recommendations Based on Glycemic Control, Body Mass Index, Age, Sex, and Generally Accepted Cut Points

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Percentile-based non-high-density lipoprotein cholesterol levels were analyzed by glycemic control, weight, age, and sex of children with type 1 diabetes (n = 26 358). Ten percent of all children and 25% of overweight adolescent girls require both immediate lipid-lowering medication and lifestyle changes to achieve non-high-density lipoprotein cholesterol levels <120 mg/dL and cardiovascular risk reduction. *(J Pediatr 2015;167:1436-9).*

Non-high-density lipoprotein cholesterol (non-HDL-C) seems to be more predictive of future cardiovascular disease than low-density lipoprotein cholesterol (LDL-C), total cholesterol, or high-density lipoprotein cholesterol (HDL-C) alone for both children and adults.[1]

In 3 previous articles, we demonstrated that the treatment rate of dyslipidemia in children with type 1 diabetes (T1D) was insufficient.[2] Moreover, we showed that cholesterol levels are influenced by age, sex, body mass index (BMI), and diabetes control.[3] Then we introduced a diagnostic algorithm for long-term monitoring of non-HDL-C, HDL-C, and LDL-C in children with diabetes and peers without diabetes.[4] The main objective of this analysis was to highlight the therapeutic significance of these findings to increase the use of lipid-lowering therapies for dyslipidemias in children with T1D. We analyzed alterations of percentile-based levels of non-HDL-C by influences of worsening glycemic control, overweight, age, and sex.

Methods

The datasets of the German-Austrian Diabetes Documentation and Quality Management System have recently been published elsewhere.[2]

For the analysis of non-HDL-C, male (53%) and female patients with T1D (n = 26 358, mean non-HDL-C 117 ± 36 mg/dL, mean hemoglobin A1c [HbA1c] 8.3% ± 1.7%) less than 18 years of age were classified into 2 age groups, ≤10 years (childhood/prepuberty) and >10 to <18 years for adolescence/puberty. Patients with LDL-C ≥190 mg/dL, lipid-lowering medication, and other forms of diabetes were excluded. BMI was calculated as body weight/(body height)^2 (kg/m^2). The individual weight status was classified as normal weight (BMI <90th percentile) or overweight (BMI ≥90th percentile) using data from a nationally representative survey of German children.[5] HbA1c levels were standardized mathematically to the Diabetes Control and Complications Trial[6] reference range (4.05%-6.05%) using the multiple-of-the-mean transformation method.[7] Three categories of HbA1c values were established (6% to <7.5%, 7.5% to 9%, and >9%), consistent with the International Society for Pediatric and Adolescent Diabetes Clinical Practice Consensus Guidelines.[8,9] Analyses of lipoproteins were performed using standard procedures in accredited laboratories subject to regular quality control according to the guidelines of the German Medical Association.[10] Non-HDL-C was calculated by subtracting HDL-C from total cholesterol. Influences of glycemic control, weight-status, age, and sex on non-HDL-C concentrations were assessed for the 25th, 50th, 75th, 90th, and 97th percentiles.

Statistical analysis was performed using SAS ver. 9.3 (SAS Institute, Cary, North Carolina). Descriptive statistics included means for continuous variables. In addition, nonparametric estimation of the 25th, 50th, 75th, 90th, and 97th percentiles for non-HDL-C was implemented using SAS proc univariate. These percentile cut-offs were also calculated for subgroups by age, BMI, sex, and HbA1c.

Results

Based on percentiles of non-HDL-C, the synoptic **Figure** illustrates the effect of rising HbA1c values from 6% to

BMI	Body mass index
HbA1c	Hemoglobin A1c
HDL-C	High-density lipoprotein cholesterol
LDL-C	Low-density lipoprotein cholesterol
non-HDL-C	Non-high-density lipoprotein cholesterol
T1D	Type 1 diabetes

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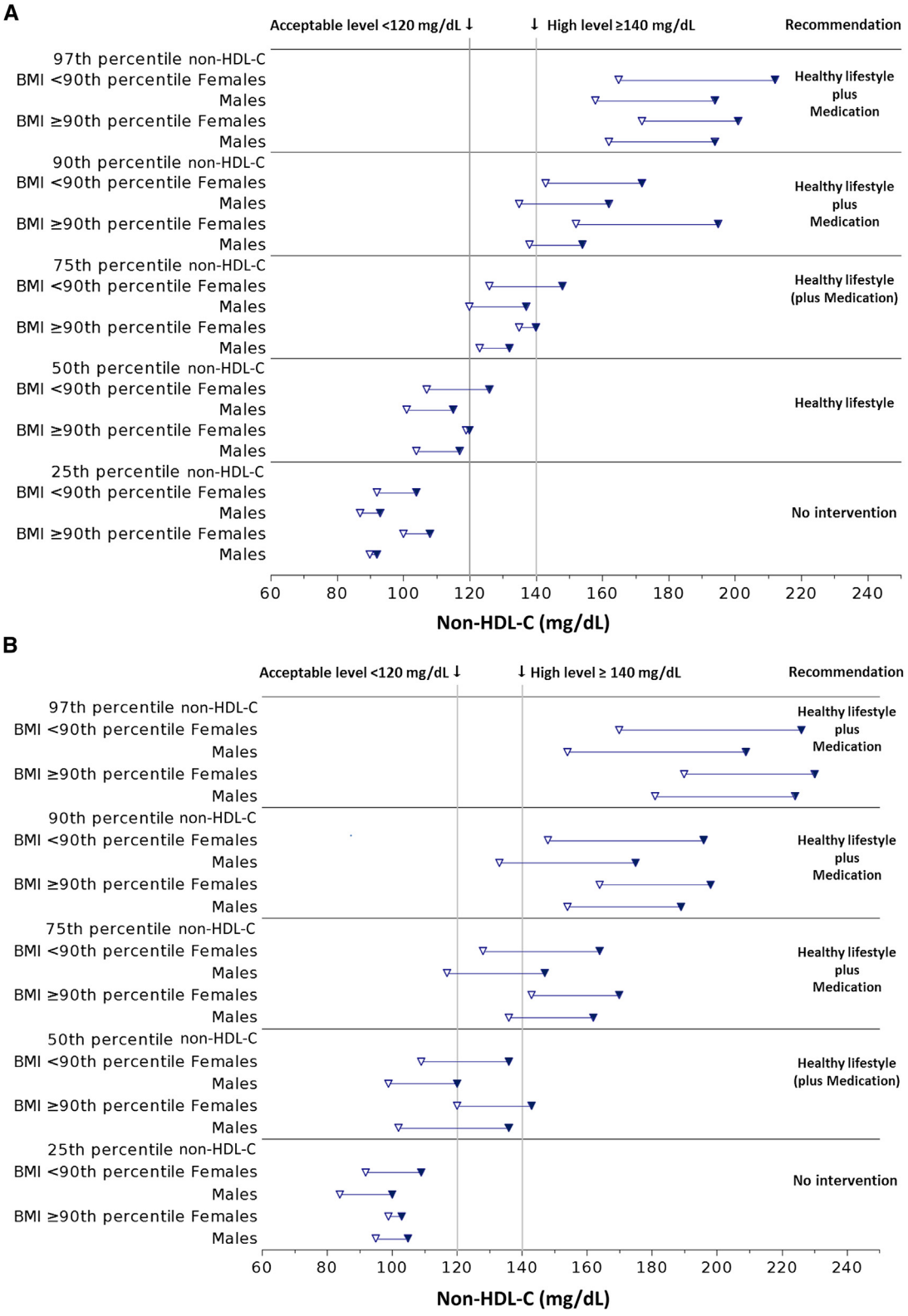

Figure. Percentile-based distribution of non-HDL-C levels related to HbA1c elevations from 6% (*open triangle*) to >9% (*black triangle*) in children with T1D; **A**, aged ≤10 years and **B**, aged >10 years. The *vertical lines* indicate the recommended acceptable (<120 mg/dL) and high (≥140 mg/dL) limit values for non-HDL-C.[1] To convert values from mg/dL to mmol/L, multiply by 0.02586.