

October 27, 2010

## Screening and management of dyslipidemia in diabetic patients

### Clinical Question

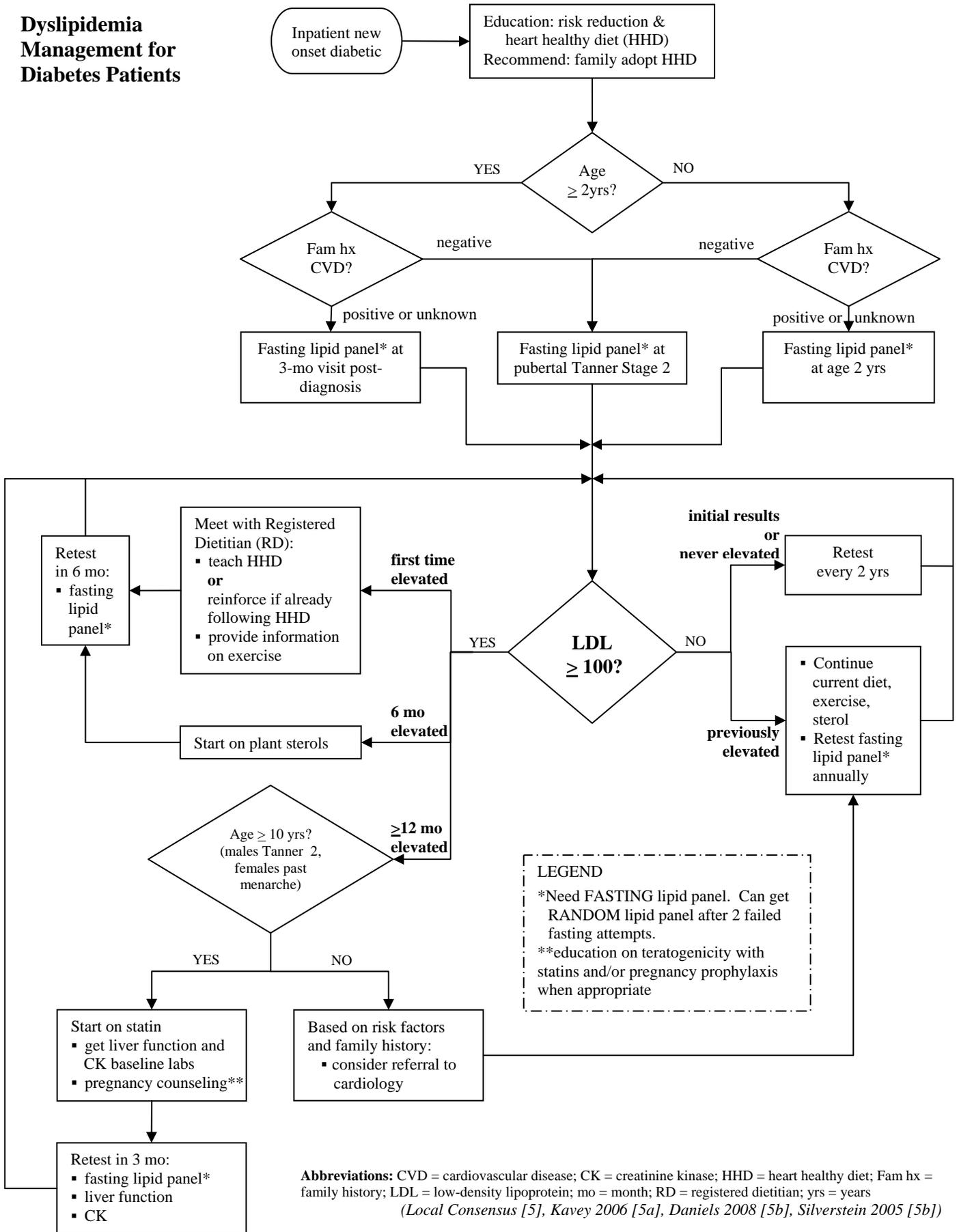
- P (population/problem) In pediatric patients with diabetes  
I (intervention) what is the optimal screening for dyslipidemia  
O (outcome) to reduce risk of cardiovascular complications.

**Target Population:** Pediatric patients with diabetes

### Recommendations (See Table of Recommendation Strength following references)

1. It is recommended that diabetes patients be screened for dyslipidemia following the algorithm below (*Local Consensus [5], Kavey 2006 [5a], Daniels 2008 [5b], Silverstein 2005 [5b]*).  
**Note:** Timing for the first screening is based on age (at least two years), family history for cardiovascular disease (negative history delays need for screening), and puberty (all patients screened not later than puberty regardless of family history) (*Local Consensus [5], Kavey 2006 [5a], Daniels 2008 [5b], Silverstein 2005 [5b]*).
2. It is recommended that patients with fasting low-density lipoprotein (LDL) levels greater than 100 mg/dL (milligrams per deciliter) be initially managed with a heart healthy diet, exercise, and monitoring of LDL levels (*Local Consensus [5], Kavey 2006 [5a], Silverstein 2005 [5b]*).
3. It is recommended that patients following a heart healthy diet with fasting LDL levels that persist for six months above 100 mg/dL be educated on the inclusion of plant sterols into their diet (*Local Consensus [5], Robinson 2009 [5a], Law 2000 [5a], Daniels 2008 [5b]*).
4. It is recommended that patients who continue to have LDL levels > 100 mg/dL after following a heart healthy diet and exercise for 12 months, and plant sterols for 6 months:
  - if age  $\geq$  10 years: start on statins (males Tanner 2, females past menarche):
  - if age < 10 years: be considered for referral to cardiology, based on risk factors and family history(*Local Consensus [5], Kavey 2006 [5a], Silverstein 2005 [5b]*).
5. It is recommended that patients with persistently elevated LDL levels be managed following the algorithm below (*Daniels 2008 [5b], Silverstein 2005 [5b]*).  
**Note:** Referral to cardiology may be appropriate based on age, family history for cardiovascular disease and other risk factors (*Local Consensus 2010 [5]*).

# Dyslipidemia Management for Diabetes Patients



## Discussion/summary of evidence

Because cardiovascular disease (CVD) is the leading cause of death in patients with diabetes and because dyslipidemia is an important CVD risk factor, a search was performed to identify screening and management guidelines for children and adolescents with diabetes. Three main guidelines were identified, 1) the American Heart Association Scientific Statement that addresses Cardiovascular Risk Reduction in High-Risk Pediatric Patients, 2) A Statement from the American Diabetes Association regarding the Care of Children and Adolescents with type 1 diabetes and 3) The American Academy of Pediatrics reporting on Lipid Screening and Cardiovascular Health in Childhood (*Kavey 2006 [5a], Daniels 2008 [5b], Silverstein 2005 [5b]*). These guidelines were appraised using the AGREE (Appraisal of Guidelines for Research and Evaluation) instrument and the results by domain were:

AGREE Domains	AHA (Kavey 2006 [5a])	ADA (Silverstein 2005 [5b])	AAP (Daniels 2008 [5b])
Scope and Purpose	100 %	85 %	63 %
Stakeholder Involvement	53 %	64 %	56 %
Rigor of Development	59 %	38 %	40 %
Clarity and Presentation	81 %	78 %	72 %
Applicability	15 %	22 %	15 %
Editorial Independence	100 %	0 %	0 %

AHA = American Heart Association, ADA = American Diabetes Association, AAP = American Academy of Pediatric

These three guidelines have clear pediatric-focused recommendations that are not directly based on evidence-based outcome data but were generated by consensus expert opinion or extrapolated from adult data. The recommendations developed for this BEST are primarily based on a combination of local consensus and recommendations from the AHA guideline.

## References/citations (evidence grade in [ ]; see *Table of Evidence Levels following references*)

**Note:** When using the electronic version of this document,  indicates a hyperlink to the PubMed abstract. A hyperlink following this symbol goes to the article PDF when the user is within the CCHMC network.

1. **Daniels, S. R.; Greer, F. R.; and Committee on, N.:** Lipid screening and cardiovascular health in childhood. *Pediatrics*, 122(1): 198-208, 2008, [5b] [\\_\\_\\_\\_\\_](#)  [\\_\\_\\_\\_\\_](#).
2. **Kavey, R.-E. W. et al.:** Cardiovascular risk reduction in high-risk pediatric patients: a scientific statement from the American Heart Association Expert Panel on Population and Prevention Science; the Councils on Cardiovascular Disease in the Young, Epidemiology and Prevention, Nutrition, Physical Activity and Metabolism, High Blood Pressure Research, Cardiovascular Nursing, and the Kidney in Heart Disease; and the Interdisciplinary Working Group on Quality of Care and Outcomes Research: endorsed by the American Academy of Pediatrics. *Circulation*, 114(24): 2710-38, 2006, [5a] [\\_\\_\\_\\_\\_](#)  [\\_\\_\\_\\_\\_](#).
3. **Law, M.:** Plant sterol and stanol margarines and health. *BMJ*, 320(7238): 861-4, 2000, [5a] [\\_\\_\\_\\_\\_](#)  [\\_\\_\\_\\_\\_](#).
4. **Local Consensus:** During Best Evidence Statement development timeframe. 2010, [5] .
5. **Maahs, D.; Wadwa, R.; Bishop, F.; Daniels, S.; Rewers, M.; and Klingensmith, G. J.:** Dyslipidemia in youth with diabetes: to treat or not to treat? *J Pediatr.*, 153(4): 458-65., 2008, [5b] [\\_\\_\\_\\_\\_](#)  [\\_\\_\\_\\_\\_](#).
6. **Micromedex® Healthcare Series:** [intranet database] Version 5.1 Accessed: August, 2010. *Thomson Reuters (Healthcare) Inc:* Greenwood Village, Colo. 2010, [5]  [\\_\\_\\_\\_\\_](#).
7. **Robinson, M. T.:** Nutrition evidence-based guidelines for treating hyperlipidemia in children with type 1 diabetes: a case presentation. *Diabetes Educator*, 35(3): 408-19, 2009, [5a] [\\_\\_\\_\\_\\_](#)  [\\_\\_\\_\\_\\_](#).
8. **Silverstein, J. et al.:** Care of children and adolescents with type 1 diabetes: a statement of the American Diabetes Association. *Diabetes Care*, 28(1): 186-212, 2005, [5b] [\\_\\_\\_\\_\\_](#)  [\\_\\_\\_\\_\\_](#).

Note: Full tables of evidence grading system available in separate document:

- [Table of Evidence Levels of Individual Studies by Domain, Study Design, & Quality](#) (abbreviated table below)
- [Grading a Body of Evidence to Answer a Clinical Question](#)
- [Judging the Strength of a Recommendation](#) (abbreviated table below)

**Table of Evidence Levels** (see note above)

<b>Quality level</b>	<b>Definition</b>
1a† or 1b†	Systematic review, meta-analysis, or meta-synthesis of multiple studies
2a or 2b	Best study design for domain
3a or 3b	Fair study design for domain
4a or 4b	Weak study design for domain
5a or 5b	Other: General review, expert opinion, case report, consensus report, or guideline

†a = good quality study; b = lesser quality study

**Table of Recommendation Strength** (see note above)

<b>Strength</b>	<b>Definition</b>
“Strongly recommended”	There is consensus that benefits clearly outweigh risks and burdens (or visa-versa for negative recommendations).
“Recommended”	There is consensus that benefits are closely balanced with risks and burdens.
No recommendation made	There is lack of consensus to direct development of a recommendation.
<b>Dimensions:</b> In determining the strength of a recommendation, the development group makes a considered judgment in a consensus process that incorporates critically appraised evidence, clinical experience, and other dimensions as listed below.	
<ol style="list-style-type: none"> <li>1. Grade of the Body of Evidence (see note above)</li> <li>2. Safety / Harm</li> <li>3. Health benefit to patient (<i>direct benefit</i>)</li> <li>4. Burden to patient of adherence to recommendation (<i>cost, hassle, discomfort, pain, motivation, ability to adhere, time</i>)</li> <li>5. Cost-effectiveness to healthcare system (<i>balance of cost / savings of resources, staff time, and supplies based on published studies or onsite analysis</i>)</li> <li>6. Directness (<i>the extent to which the body of evidence directly answers the clinical question [population/problem, intervention, comparison, outcome]</i>)</li> <li>7. Impact on morbidity/mortality or quality of life</li> </ol>	

## Health Benefits, Side Effects and Risks

The American Heart Association and the American Diabetes Association emphasize the importance of early recognition of elevation of low density lipoproteins in children with Diabetes (Kavey 2006 [5a], Silverstein 2005 [5b]). Cardiovascular disease, cerebrovascular disease and peripheral vascular disease resulting from atherosclerosis are leading causes of morbidity and mortality among adults with Type 1 diabetes and there is unequivocal evidence that atherosclerosis is well established in adolescence with dyslipidemia being the major risk factor (Silverstein 2005 [5b]). Early education regarding cardiovascular health and early intervention in children with LDL elevation is critical to improving long term outcomes.

Risks associated with treatment of hyperlipidemia are minimal. The recommendations reserve introduction of pharmacotherapy for patients who do not respond to diet, exercise and plant sterols. Side effects of plant sterols are indigestion, constipation and diarrhea. Although plant sterols are not currently part of the dietary treatment recommendations from the American Diabetes Association in children, the American Heart Association’s recommendations suggest plant sterols may be a useful adjunct to therapy (Kavey 2006 [5a]). A review of randomized controlled trials of adult participants adding plant sterols to their diet reported a reduction in serum concentration of LDL cholesterol that would be expected to reduce the risk of heart disease by about 25% at an intake of 2 gm per day (Law 2000 [5a]).

Pharmacotherapy with statins, such as atorvastatin, is FDA approved in children over 10 years of age. Side effects with statin therapy include diarrhea, arthralgia, and nasopharyngitis. There is also discussion about a risk of elevated liver enzymes (0.2% to 2.3%) (Micromedex® Healthcare Series [5]). The recommendations address this risk with measurement of liver enzymes at baseline and then monitoring every 3 months after starting on statin therapy.

## Supporting information

### Introductory/background information

There are an estimated 1.5 million people with type 1 diabetes and 20 million with type 2 diabetes in the U.S., including 150,000 persons under age 20 years (*Maahs 2008 [5b]*). Cardiovascular disease is the leading cause of death in persons with either form of diabetes (*Maahs 2008 [5b]*). Studies have demonstrated CVD risk in childhood correlates with abnormalities in surrogate markers for atherosclerosis in childhood (carotid intima-media thickness and arterial elasticity) (*Maahs 2008 [5b]*). Despite the acknowledgement that dyslipidemia is a potentially modifiable risk factor in this high-risk population, screening and management of dyslipidemia have been inconsistent within the diabetes population. There is a lack of data regarding the treatment of dyslipidemia on which to base clinical care in children. Therefore, current recommendations in published guidelines are generated by consensus expert opinion or are extrapolated from adult data. For these reasons this BESt statement was created to assist the clinician in the screening and management of dyslipidemia in children and adolescents with diabetes.

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### Search strategy

#### 1. Initial search

- **DATABASE:** Ovid: MedLine
- **OVID FILTERS**
  - Publication dates: 1996 to May 21, 2010
  - Limits: English language  
all child (0 to 18 years)
- **SEARCH TERMS & MeSH TERMS**
  - exp \*Diabetes Mellitus/ AND exp Dyslipidemias/  
search results filtered for: diagnosis subheading OR treatment outcome.mp.

#### 2. Search for synthesized evidence

- **DATABASE:** Ovid: MedLine
- **OVID FILTERS**
  - Publication dates: 1996 to Mar 3, 2010
  - Limits: English language  
all child (0 to 18 years)
  - Publication type: (guideline or meta analysis or practice guidelines or systematic review).pt. or "the cochrane library".jn. or "cochrane database of systematic reviews".jn.
- **SEARCH TERMS & MeSH TERMS**
  - exp Diabetes Mellitus/ or Diabetes Mellitus, Experimental/ or Diabetes, Gestational/ or Diabetes Insipidus, Neurogenic/ or Diabetes Complications/ or Diabetes Insipidus, Nephrogenic/ or Diabetes Mellitus, Lipoatrophic/ or "National Institute of Diabetes and Digestive and Kidney Diseases (U.S.)"/ or Diabetes Insipidus/

## Applicability issues

Measures that are proposed to be audited:

- Percentage of diabetes clinic patients 2 years of age or older with a diabetes diagnosis and also a positive or unknown family history of hyperlipidemia who have a documented lipid panel ordered by 3 months after first visit
- Percentage of diabetes clinic patients with fasting LDL values <100 in the last 13 months
- Percentage of diabetes clinic patients in Tanner Stage 2 to 5 (adrenarche) of pubertal development and with LDL values greater than or equal to 100 who have discussed plant sterols and lifestyle modifications with an RD or other healthcare provider

Copies of this Best Evidence Statement (BESt) are available online and may be distributed by any organization for the global purpose of improving child health outcomes. Website address: <http://www.cincinnatichildrens.org/svc/alpha/h/health-policy/ev-based/default.htm>

Examples of approved uses of the BESt include the following:

- copies may be provided to anyone involved in the organization's process for developing and implementing evidence-based care;
- hyperlinks to the CCHMC website may be placed on the organization's website;
- the BESt may be adopted or adapted for use within the organization, provided that CCHMC receives appropriate attribution on all written or electronic documents; and
- copies may be provided to patients and the clinicians who manage their care.

Notification of CCHMC at [HPCEInfo@cchmc.org](mailto:HPCEInfo@cchmc.org) for any BESt adopted, adapted, implemented or hyperlinked by the organization is appreciated.

*For more information about CCHMC Best Evidence Statements and the development process, contact the Diabetes Center at: 513-636-2444; <http://www.cincinnatichildrens.org/svc/alpha/d/diabetes/contact.htm>.*

## Note

**This Best Evidence Statement addresses only key points of care for the target population; it is not intended to be a comprehensive practice guideline. These recommendations result from review of literature and practices current at the time of their formulation. This Best Evidence Statement does not preclude using care modalities proven efficacious in studies published subsequent to the current revision of this document. This document is not intended to impose standards of care preventing selective variances from the recommendations to meet the specific and unique requirements of individual patients. Adherence to this Statement is voluntary. The clinician in light of the individual circumstances presented by the patient must make the ultimate judgment regarding the priority of any specific procedure.**

**Reviewed against quality criteria by 2 independent reviewers**