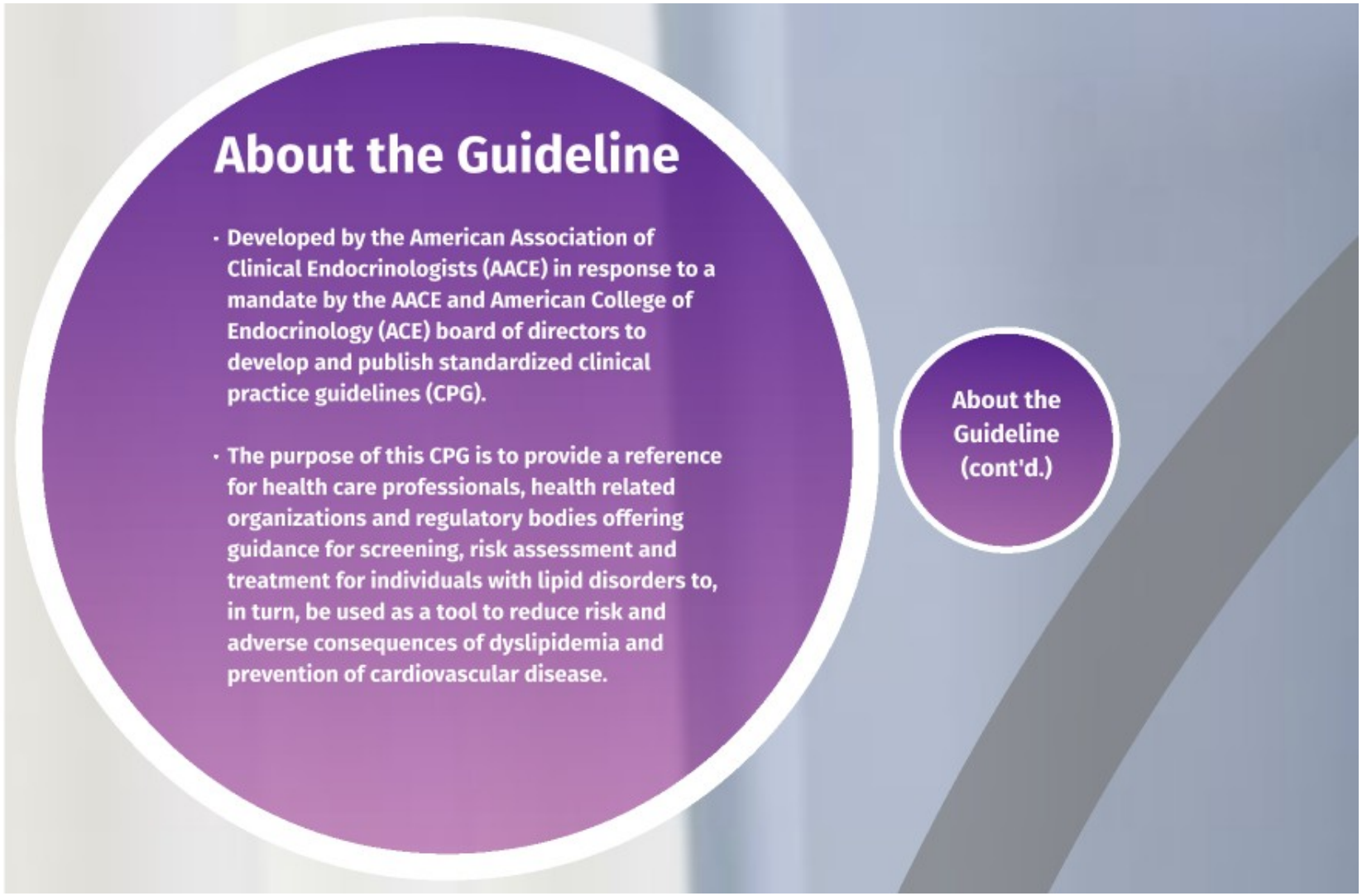
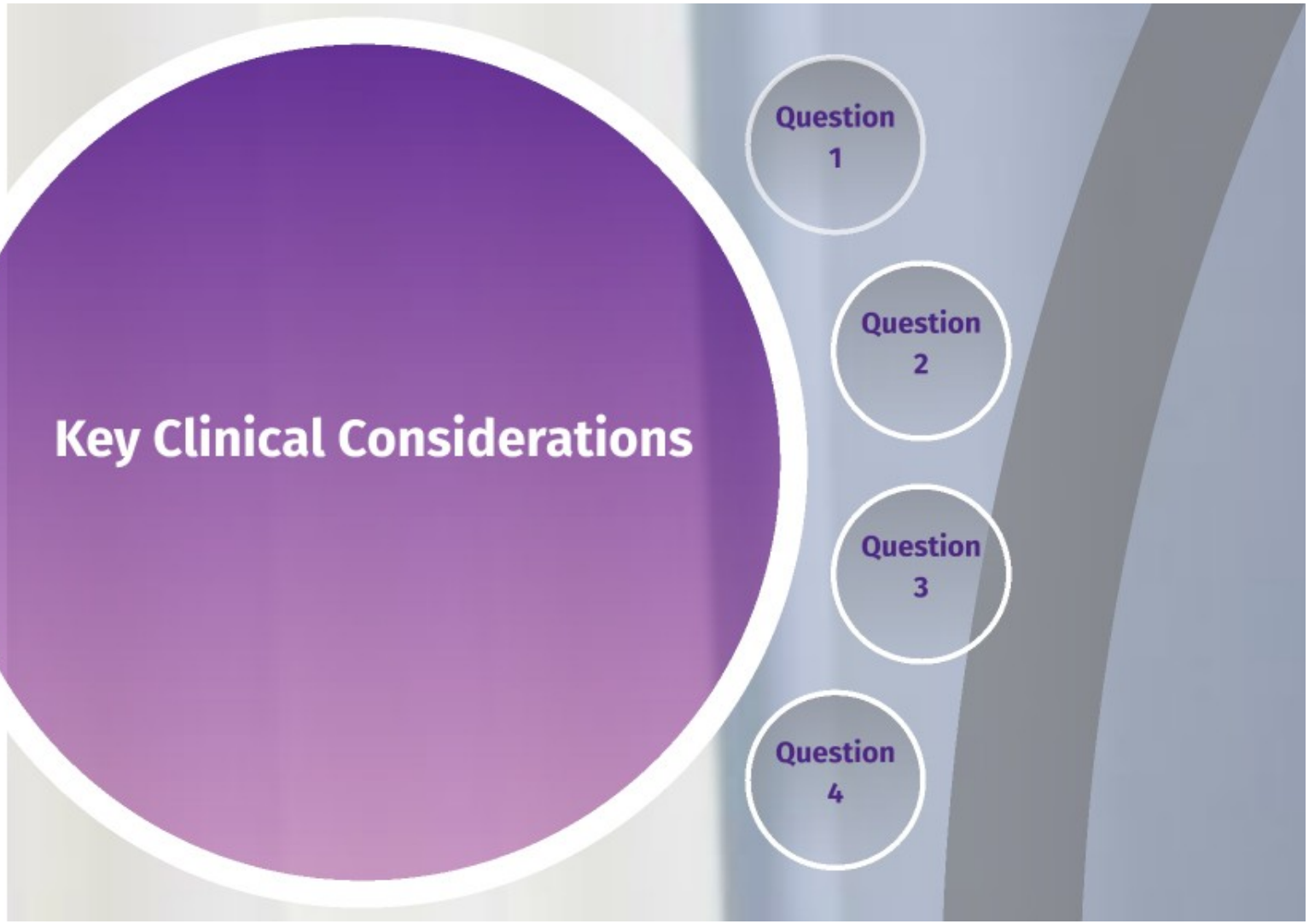

Dyslipidemia and Prevention of Cardiovascular Disease
Wolters Kluwer
Lippincott NursingCenter
Copyright © 2018, Wolters Kluwer


About the Guideline
Key Clinical Considerations
References
See More Guideline Summaries
Dyslipidemia and Prevention of Cardiovascular Disease
Guideline Summary


About the Guideline
• Developed by the American Association of Clinical Endocrinologists (AACE) in response to a mandate by the AACE and American College of Endocrinology (ACE) board of directors to develop and publish standardized clinical practice guidelines (CPG).
• The purpose of this CPG is to provide a reference for health care professionals, health related organizations and regulatory bodies offering guidance for screening, risk assessment and treatment for individuals with lipid disorders to, in turn, be used as a tool to reduce risk and adverse consequences of dyslipidemia and prevention of cardiovascular disease.
About the Guideline (cont'd.)

About the Guideline (cont'd.)

- Included in this CPG are specific recommendations for women, children and adolescents, and diabetics with lipid disorders.
- The format of the guideline is organized in four, key, specific clinical questions from which 87 recommendations were derived. Each question is listed below with a summary of relevant recommendations.


Key Clinical Considerations
Question 1
Question 2
Question 3
Question 4

Question 1

How should individuals be screened for the detection of dyslipidemia (Jellinger et al., 2017)?

Recommendations 1-8 are relevant to global risk assessment.

Based on the literature reviewed for this CPG, the following risk factor categories for ASCVD were surmised...

Major Risk Factors

- Advancing age (men > 45 years of age and women > 55 years of age)
- Increased total serum cholesterol
- Decreased non-high-density lipoprotein cholesterol (non-HDL-C)
- Increased low-density lipoprotein cholesterol (LDL-C)
- Diabetes Mellitus (DM)
- Hypertension
- Chronic kidney disease (CKD)
- Cigarette smoking
- Family history of atherosclerotic cardiovascular disease (ASCVD)

Additional Risk Factors

- Obesity, abdominal obesity
- Family history of hyperlipidemia
- Increased small, dense LDL cholesterol (referred to LDL pattern b)
    - Found in 50% of men with ASCVD; associated with high triglycerides (TG) and low HDL-C
- Increased Apolipoproteins (Apo-B)
- Increased LDL particle concentration
- Fasting/post-prandial hypertriglyceridemia
- Polycystic Ovary Syndrome (PCOS)
- Dyslipidemic triad (high TG, low HDL-C, high small, dense LDL-C)

Nontraditional Risk Factors

- Increased lipoprotein (a)
- Increased clotting factors (plasminogen activator inhibitor 1, increased fibrinogen)
- Increased inflammation markers (hsCRP, Lp-PLA2)
- Increased homocysteine levels
- Apo E4 isoform
- Increased uric acid
- Increased triglyceride remnants

5 Risk Categories Recognized by the AACE/ACE CPGs (Jellinger et al., 2017)

- **Extreme risk**
  - Those with progressive ASCVD and/or unstable angina at goal LDL-C
  - Clinical cardiovascular disease in patients with DM, CKD (stage 3 or 4), or heterozygous familial hypercholesterolemia (HeFH)
- **Very high risk**
  - Recent ACS event, coronary, carotid or peripheral vascular disease, or 10-year calculated risk for ASCVD > 20%
  - DM or CKD (stage 3 or 4) with 1 or more risk factors
- **High risk**
  - ≥ 2 risk factors and 10-year risk 10-20% for ASCVD
  - DM or CKD 3 or 4 with no risk factors
- **Moderate risk**
  - ≥ 2 risk factors and 10-year risk < 10%
- **Low risk**
  - 0 risk factors

Recommendations

Based in the above risk factors and risk categories, the following recommendations were made:

- Identify risk factors for dyslipidemia to allow for identification of lipid disorders to implement personalized and optimal treatment strategies.
- Individuals with type 2 DM should be considered very high risk for the development of atherosclerotic cardiovascular disease (ASCVD).
- Individuals with type 1 DM for more than 15 years or in type 1 diabetics with 2 or more major cardiovascular risk factors, poorly controlled DM, or insulin resistance with metabolic syndrome should be considered very high risk.
- The 10-year risk for coronary events should be assessed using one or more of the following validated assessment tools:
  - **Framingham Risk assessment tool** (D'Agostino et al., 2008).
  - **Multi-Ethnic Study of Atherosclerosis (MESA) 10-year ASCVD Risk with Coronary Artery Calcification Calculator** (McClelland et al., 2015).
  - **Reynold Risk Score** (Ridker et al., 2007).
  - **United Kingdom Prospective Diabetes Study (UKPDS) risk engine to calculate ASCVD risk in individuals with type 2 diabetes** (Stevens et al., 2001).
- Special attention should be given to screen women for 10-year risk for ASCVD; the recommended screening tools are either the Reynolds Risk Score or Framingham Risk assessment tool.
- Children and adolescents should be diagnosed and treated as early as possible to reduce risk factors in adulthood.
- Those with HDL-C levels > 60 mg/dL should have 1 risk factor equivalent subtracted from their risk profile.
- Elevated triglycerides should be included in risk assessment and treatment decisions.

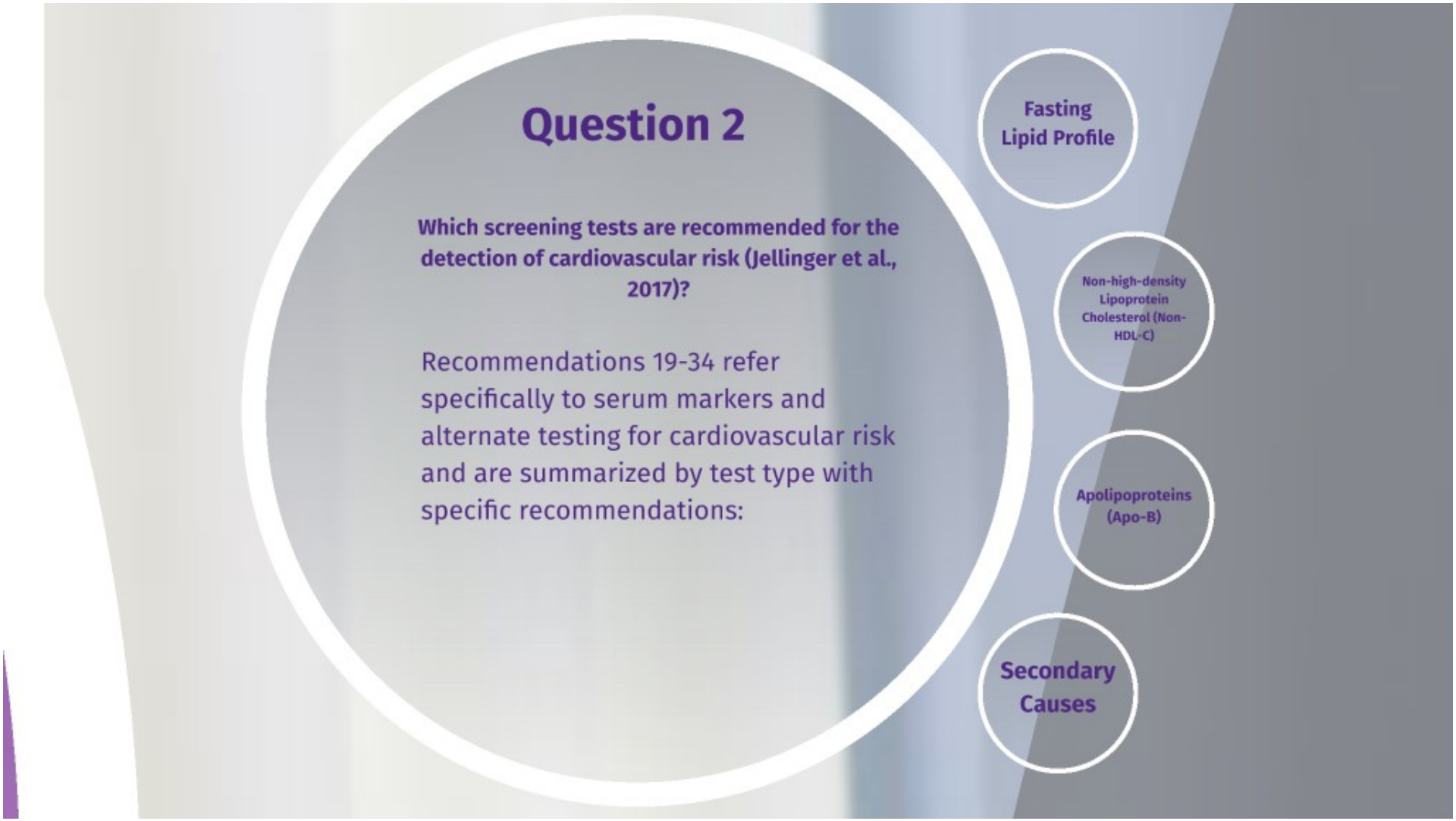
Recommendations 9-18 relate to screening specific populations for lipid disorders and include the following key groups (Jellinger et al., 2017):

- Screen for **familial hypercholesterolemia (FH)** in those with family history of premature ASCVD or elevated cholesterol.

- Screen **adults with diabetes** annually (those > 20 years of age).
  - Screen **young men (age 20-45)** and **young women (age 20-55)** every 5 years.
  - Screen **middle-aged men (age 45-65)** and **middle-aged women (age 55-65)** at least every 1-2 years and more frequently when there are risk factors for ASCVD or as judged clinically appropriate.
  - Screen **adults older than 65** years annually.

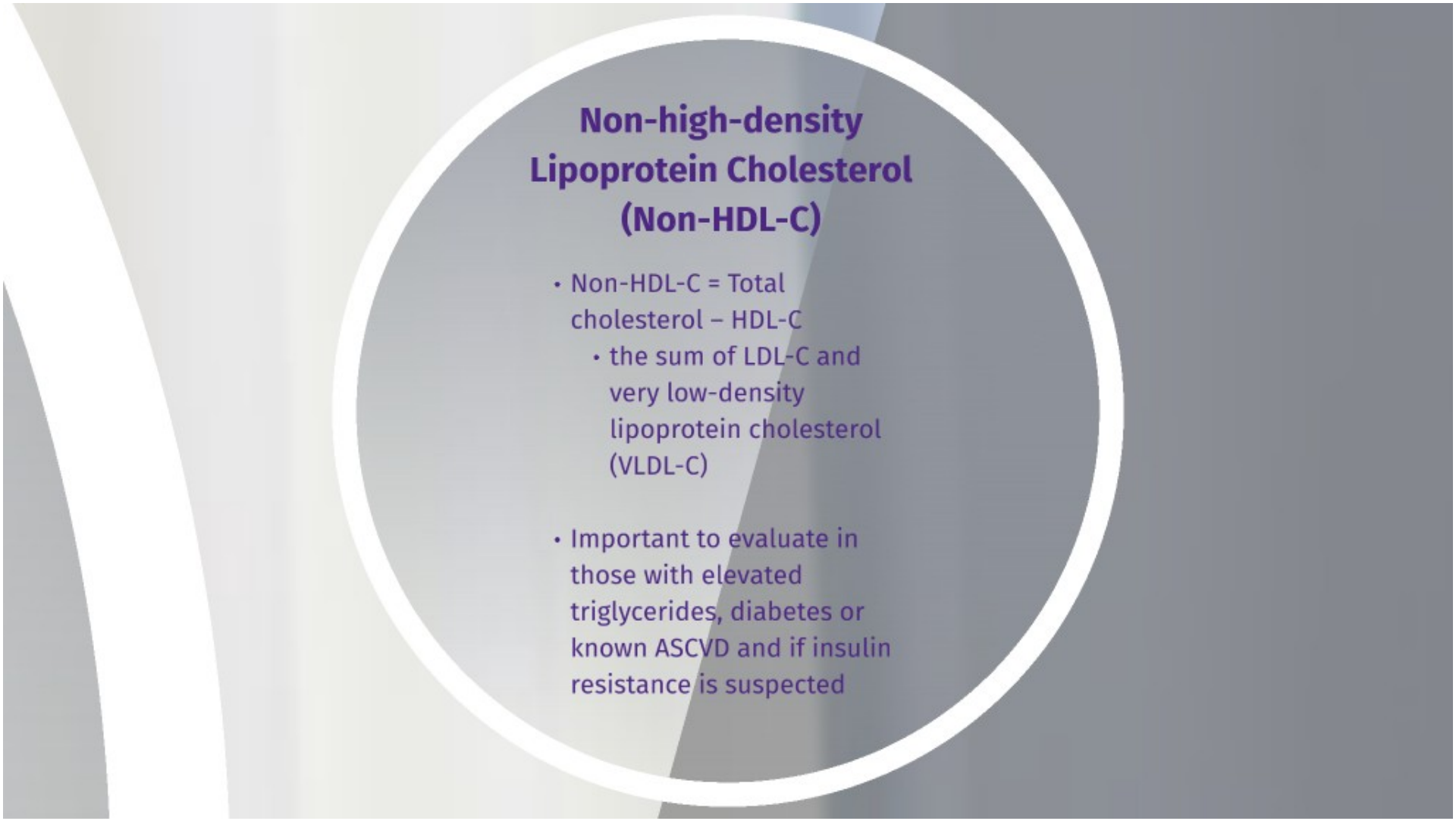
- Screen **children at risk for FH** beginning at age 3, again between ages 9 – 11, and again at age 18.

- Screen **adolescents (older than 16)** every 5 years and more frequently in those who are obese or overweight, have risk factors for ASCVD, have insulin resistance syndrome, or a family history of premature ASCVD.


Question 2
Which screening tests are recommended for the detection of cardiovascular risk (Jellinger et al., 2017)?
Recommendations 19-34 refer specifically to serum markers and alternate testing for cardiovascular risk and are summarized by test type with specific recommendations:
Fasting Lipid Profile
Non-high-density Lipoprotein Cholesterol (Non-HDL-C)
Apolipoproteins (Apo-B)
Secondary Causes

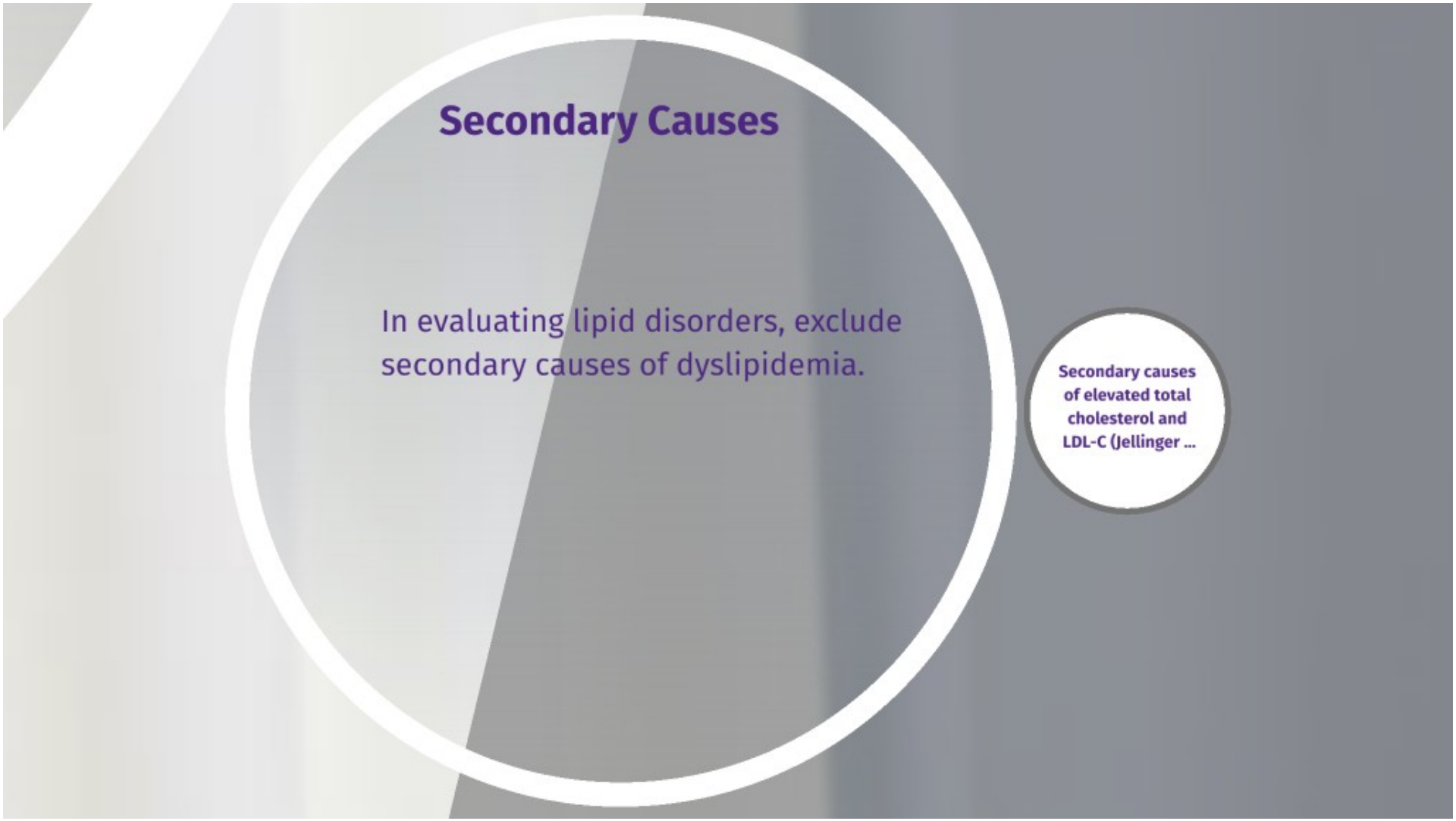
Fasting Lipid Profile

- Considered the most accurate evaluation of lipids
- Ideally performed fasting (9 -12 hours) but non-fasting acceptable if fasting not possible
- Includes measurement or calculation of the following:
  - Total cholesterol
  - Low density lipoprotein cholesterol (LDL-C)
    - Can be measured directly or calculated
    - LDL-C = (total cholesterol – HDL-C) – (TG/5)
    - Calculation most accurate during fasting state and when TG < 200 mg/dL
- Triglycerides (TG)
  - Elevated TG to HDL-C ratio is a strong predictor of insulin resistance (a risk factor for ASCVD and type 2 diabetes)
  - If marginally elevated consider measuring for LDL type B (small, dense LDL)
- High-density lipoprotein cholesterol (HDL-C)
  - Include in screening test for dyslipidemia


Non-high-density Lipoprotein Cholesterol (Non-HDL-C)
• Non-HDL-C = Total cholesterol – HDL-C
• the sum of LDL-C and very low-density lipoprotein cholesterol (VLDL-C)
• Important to evaluate in those with elevated triglycerides, diabetes or known ASCVD and if insulin resistance is suspected

Apolipoproteins (Apo-B)

- An elevated level associated with risk for early ASCVD
- May be more closely associated with insulin resistance, central adiposity, thrombosis and inflammation (Sattar et al. 2004)
- Apo-B > 130mg/dL with LDL-C < 160mg/dL with or without elevated TG considered risk for premature ASCVD


Secondary Causes
In evaluating lipid disorders, exclude secondary causes of dyslipidemia.
Secondary causes of elevated total cholesterol and LDL-C (Jellinger ...

Secondary causes of elevated total cholesterol and LDL-C (Jellinger et al., 2017):

- Hypothyroidism
- Nephrosis
- Dysgammaglobulinemia (systemic lupus erythematosus, multiple myeloma)
- Progestin or anabolic steroid treatment
- Cholostatic disease of the liver (i.e. primary biliary cirrhosis)
- Protease inhibitor use in the treatment of HIV

Secondary causes of elevated TGs and VLDL-C (Jellinger et al., 2017):

- Chronic renal failure
- Type 2 DM
- Obesity
- Excessive alcohol intake
- Hypothyroidism
- Anti-hypertensive medications (thiazide diuretics, certain beta-blockers)
- Corticosteroid use or severe stressors inducing endogenous steroid release
- Oral estrogens/progesterone therapies, pregnancy
- Protease inhibitor used in the treatment of HIV

Additional tests endorsed by the AACE/ACE CPG (Jellinger et al., 2017):

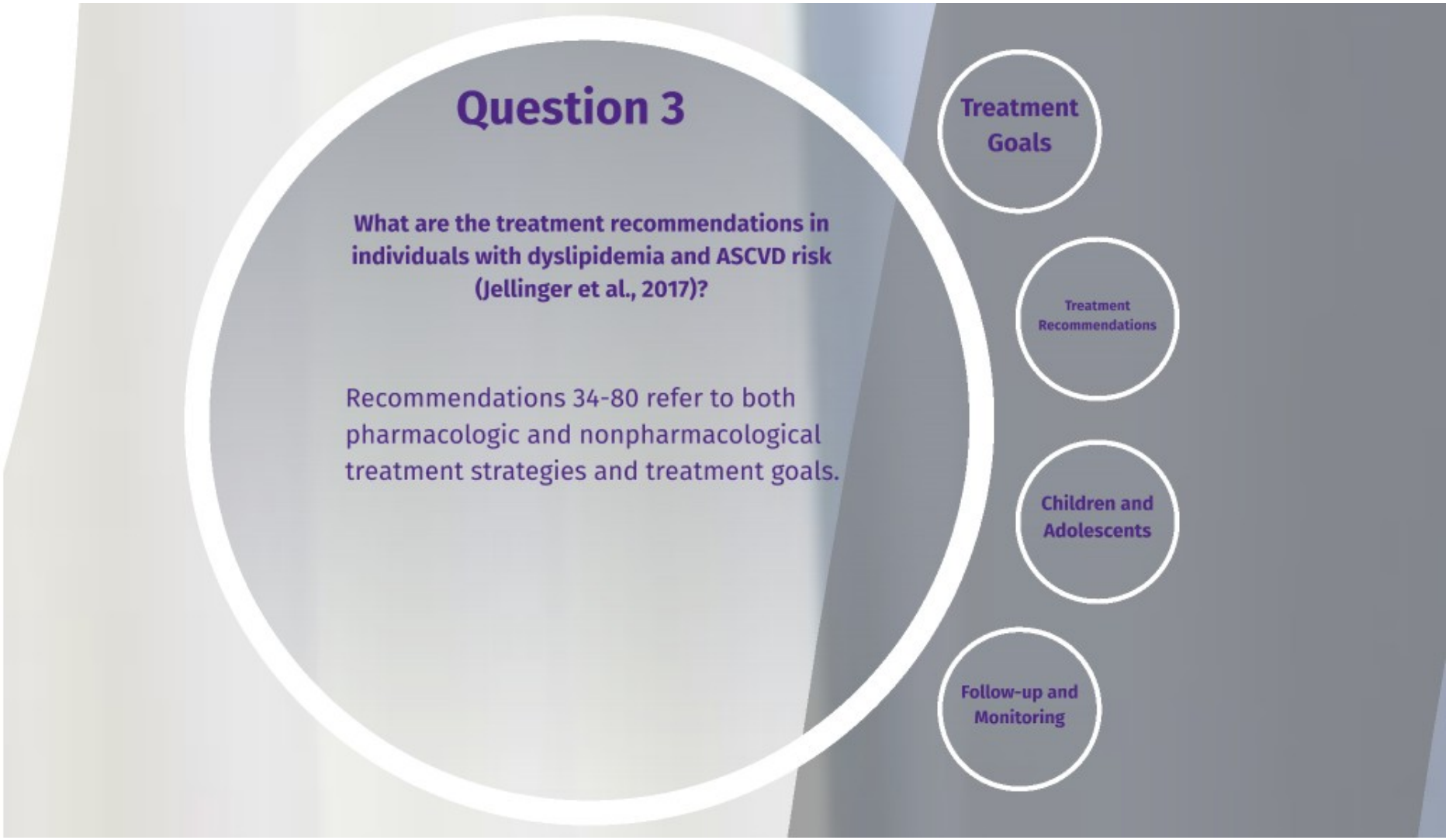
- High-sensitivity C-reactive protein (hs-CRP) measurement is recommended in those with borderline standard risk to further stratify risk.

- Lipoprotein-associated phospholipase A2 (Lp-PLA2) elevation is linked to ASCVD risk and may act synergistically with hs-CRP when both elevated; measure to further stratify risk.

- Lp-PLA2 (≥200 ng/mL) has been independently linked with coronary events (Packard et al., 2000).

- Coronary artery calcification measurement is endorsed for additional risk stratification.

- Carotid intima medial thickness (CIMT) is endorsed for additional risk stratification and treatment decisions.


Question 3
What are the treatment recommendations in individuals with dyslipidemia and ASCVD risk (Jellinger et al., 2017)?
Recommendations 34-80 refer to both pharmacologic and nonpharmacological treatment strategies and treatment goals.
Treatment Goals
Treatment Recommendations
Children and Adolescents
Follow-up and Monitoring


Treatment Goals
Treatment goals should be based on risk for ASCVD (based on the 5 risk categories described above and serum markers goals described below).
Low Risk
Moderate Risk
High Risk
Very High Risk
Extreme Risk
Children and Adolescents

Low Risk

- LDL-C < 130 mg/dL
- Total cholesterol < 200 mg/dL
- Non-LDL-C 30 mg/dL above LDL goal
- TG < 150 mg/dL

Moderate Risk

- LDL-C < 100 mg/dL
- Total cholesterol < 200 mg/dL
- Non-LDL-C 30 mg/dL above LDL goal
- TG < 150 mg/dL

High Risk

- LDL-C < 100mg/dL
- Total cholesterol < 200mg/dL
- Non-LDL-C 30 above LDL goal
- TG < 150mg/dL
- Apo B < 90 mg/dL

Very High Risk

- LDL-C < 70 mg/dL
- Total cholesterol < 200 mg/dL
- Non-LDL-C 30 mg/dL above LDL goal
- TG < 150 mg/dL
- Apo B < 80 mg/dL

Extreme Risk

- LDL-C < 55 mg/dL
- Total cholesterol < 200 mg/dL
- Non-LDL-C 25 mg/dL above LDL goal
- TG < 150 mg/dL
- Apo B < 90 mg/dL

Children and Adolescents

- LDL-C < 100 mg/dL
- Total cholesterol < 200 mg/dL
- TG < 150 mg/dL


Treatment Recommendations
(Jellinger et al., 2017)
Lifestyle Modifications

Lifestyle Modifications

- Physical activity
  - 30 minutes of moderate activity 4-6 times a week
  - May be accomplished in single session or multiple sessions throughout day (i.e. 3, 10-minute sessions)
  - Muscle strengthening 2 days/week

- Medical nutrition therapy
  - Low calorie diet with ≥ 5 servings fruit/vegetables daily and consisting of whole grains, fish, lean meats.
  - Limited intake of saturated fats, trans fats, and cholesterol and increased plant stanols/sterols (~2gm/day) and soluble fiber (10-25gm/day) which are known to reduce LDL-C.

- Smoking cessation should be encouraged and facilitated in all patients.

Pharmacologic Treatment

- Statins
  - Recommended as 1st line treatment to achieve LDL-C goals
  - Treat to risk-related LDL-C goals as described above.

- Fibrates
  - First line agents in treatment of TG > 500 mg/dL

- Omega-3 Fish Oil
  - Prescription omega-3 oil (but not dietary supplements/ over the counter) agents are recommended as dose of 2 to 4 grams daily to treat TG > 500 mg/dL

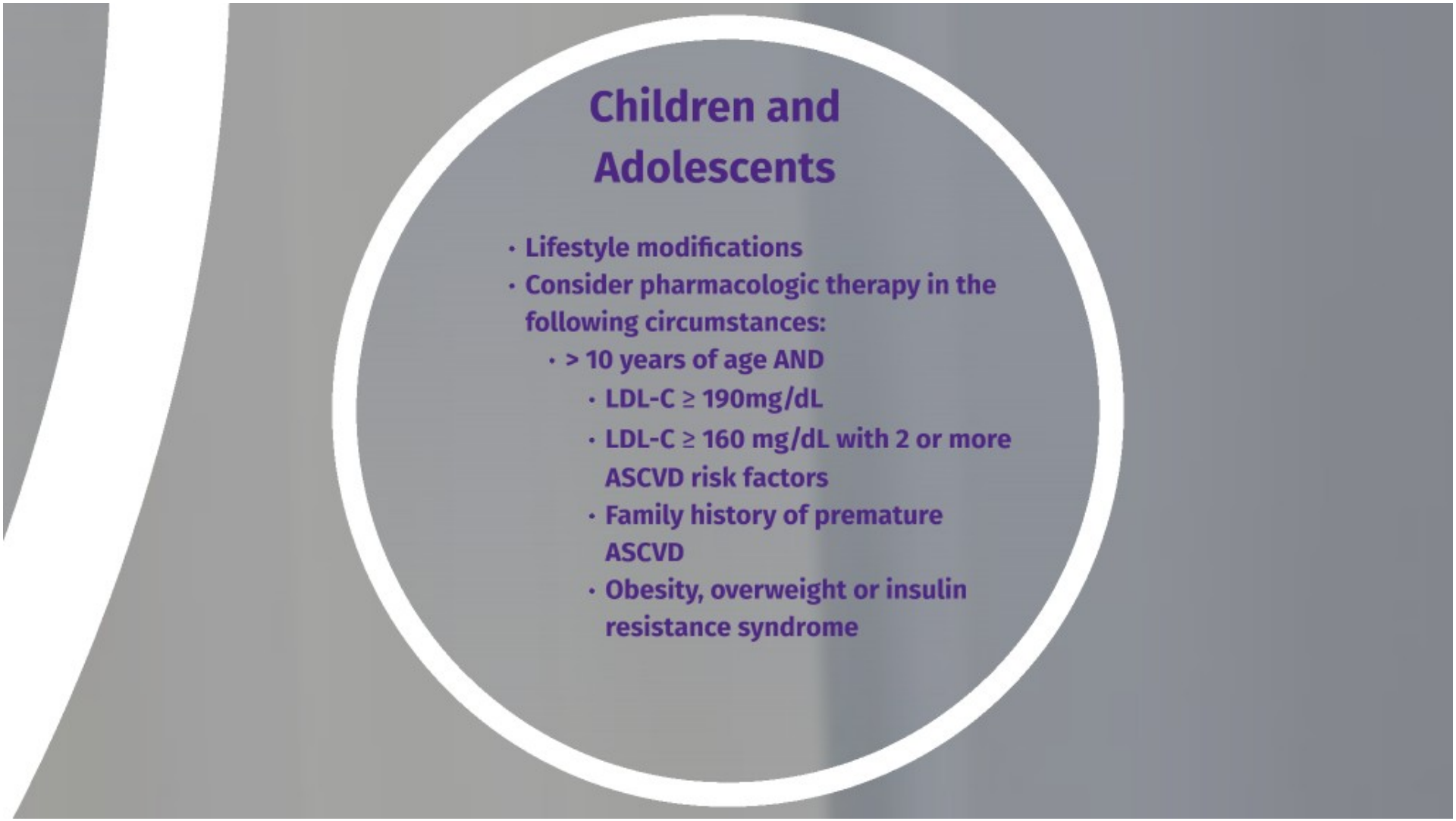
- Niacin
  - Recommended as adjunct agent for treating hypertriglyceridemia

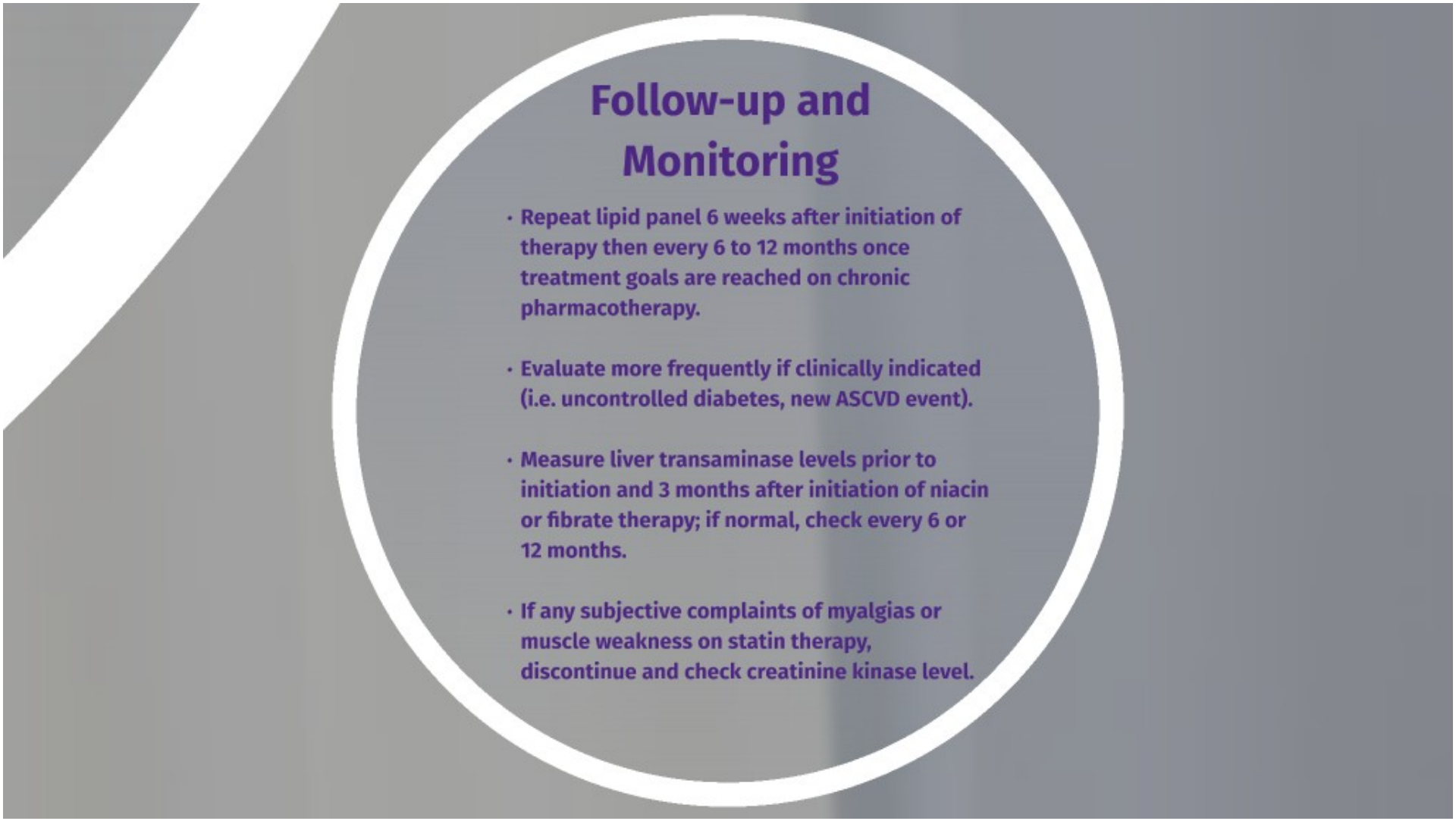
- Bile Acid Sequestrants
  - Consider as adjunct in reducing LDL-C and Apo B and increasing HDL-C
  - May increase TG level

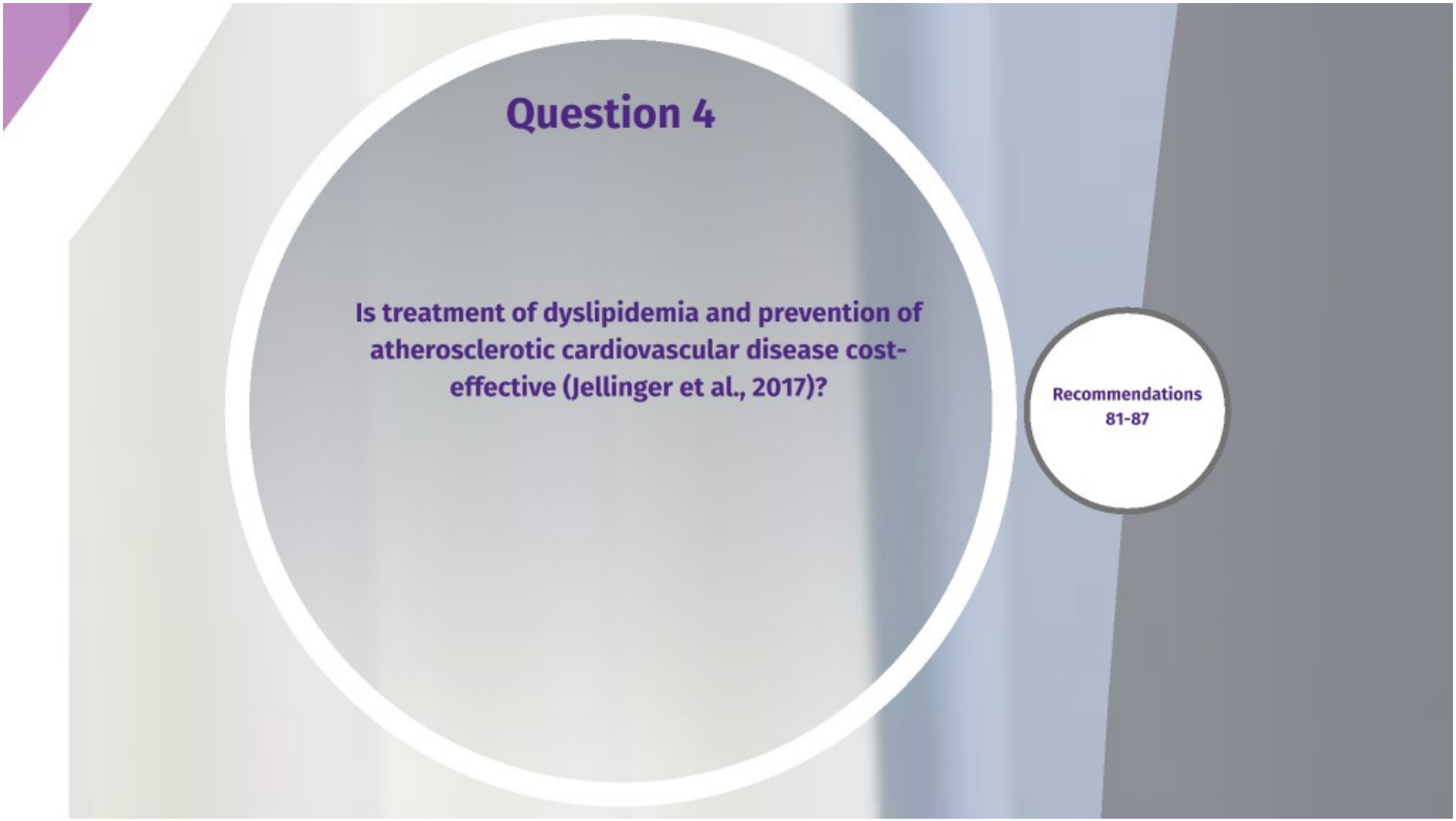
Pharmacologic Treatment (cont'd.)

- Cholesterol absorption agents
  - May be considered in statin intolerant individuals for reduction of LDL-C and Apo-B
  - May be used in combination or as monotherapy to reduce LDL-C and ASCVD risk

- Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors
  - Recommended in combination with statin to reduce LDL-C in those with familial hypercholesterolemia.
  - Add to statin therapy to achieve LDL-C/non-HDL-C goals with maximal tolerated statin dose
  - Rarely used as monotherapy


Children and Adolescents
• Lifestyle modifications
• Consider pharmacologic therapy in the following circumstances:
• > 10 years of age AND
• LDL-C ≥ 190mg/dL
• LDL-C ≥ 160 mg/dL with 2 or more ASCVD risk factors
• Family history of premature ASCVD
• Obesity, overweight or insulin resistance syndrome


Follow-up and Monitoring
• Repeat lipid panel 6 weeks after initiation of therapy then every 6 to 12 months once treatment goals are reached on chronic pharmacotherapy.
• Evaluate more frequently if clinically indicated (i.e. uncontrolled diabetes, new ASCVD event).
• Measure liver transaminase levels prior to initiation and 3 months after initiation of niacin or fibrate therapy; if normal, check every 6 or 12 months.
• If any subjective complaints of myalgias or muscle weakness on statin therapy, discontinue and check creatinine kinase level.


Question 4
Is treatment of dyslipidemia and prevention of atherosclerotic cardiovascular disease cost-effective (Jellinger et al., 2017)?
Recommendations 81-87

Recommendations 81-87 refer to the cost-effectiveness of treatment and prevention of ASCVD.

- The **most** cost-effective measures to prevent ASCVD are smoking cessation and dietary management.

- The following pharmacologic measures are considered cost-effective in moderate to high risk individuals (Jellinger et al., 2017):
  - Statin therapy is cost-effective in primary and secondary prevention of ASCVD events for those at moderate or high risk and those at low risk with LDL-C > 190 mg/dL.
  - Fibrates care cost-effective as monotherapy and as combination agent in lowering TG and raising HDL-C but not in reducing ASCVD events with exception of those with TG > 200 mg/dL and HDL-C < 40 mg/dL.
  - Bile acid sequestrants are not a cost-effective alternative to statins as their ability to lower LDL is not as good.
  - Ezetimibe has not been evaluated effectively to make a recommendation.

References

D'Agostino, R. B, Vasan, R. S., Pencina, M. J., Wolf, P.A., Cobain, M., Massaro, J. M., & Kannel, W. B. (2008). General Cardiovascular Risk Profile for Use in Primary Care. The Framingham Heart Study. Circulation, 117(6), 743-753. doi: 10.1161/CIRCULATIONAHA.107.699579

Jellinger, P. S., Handelsman, Y., Rosenbilt, P. D., Bloomgarden, Z. T., Fonseca, V. A., Garber, A. J., Grunberger, G.,...Bush, M. A. (2017). American Association of Clinical Endocrinologists and American College of Endocrinology Guidelines for Management of Dyslipidemia and Prevention of Cardiovascular Disease. Endocrine Practice, 23(Suppl. 2), 1-87. doi: 10.4158/EP171764.APPGL

McClelland, R. L., Jorgensen, N. W., Budoff, M., Blaha, M. J., Post, W. S., Kronmal, R. A., Bild, D. E., ...Burke, G. L. (2015). 10-Year Coronary Heart Disease Risk Prediction Using Coronary Artery Calcium and Traditional Risk Factors: Derivation in the MESA (Multi-Ethnic Study of Atherosclerosis) With Validation in the HNR (Heinz Nixdorf Recall) Study and the DHS (Dallas Heart Study). Journal of the American College of Cardiology, 66(15), 1643-53. doi: 10.1016/j.jacc.2015.08.035.

Packard, C. J., O'Reilly, D. S., Caslake, M. J., McMahon, A. D., Ford, I., Cooney, J., Macphee, C. H.,...Lowe, G.D. (2000). Lipoprotein- associated phospholipase A2 as an independent predictor of coronary heart disease. West of Scotland Coronary Prevention Study Group. New England Journal of Medicine, 343(16), 1148- 1155. doi:10.1056/NEJM200010193431603

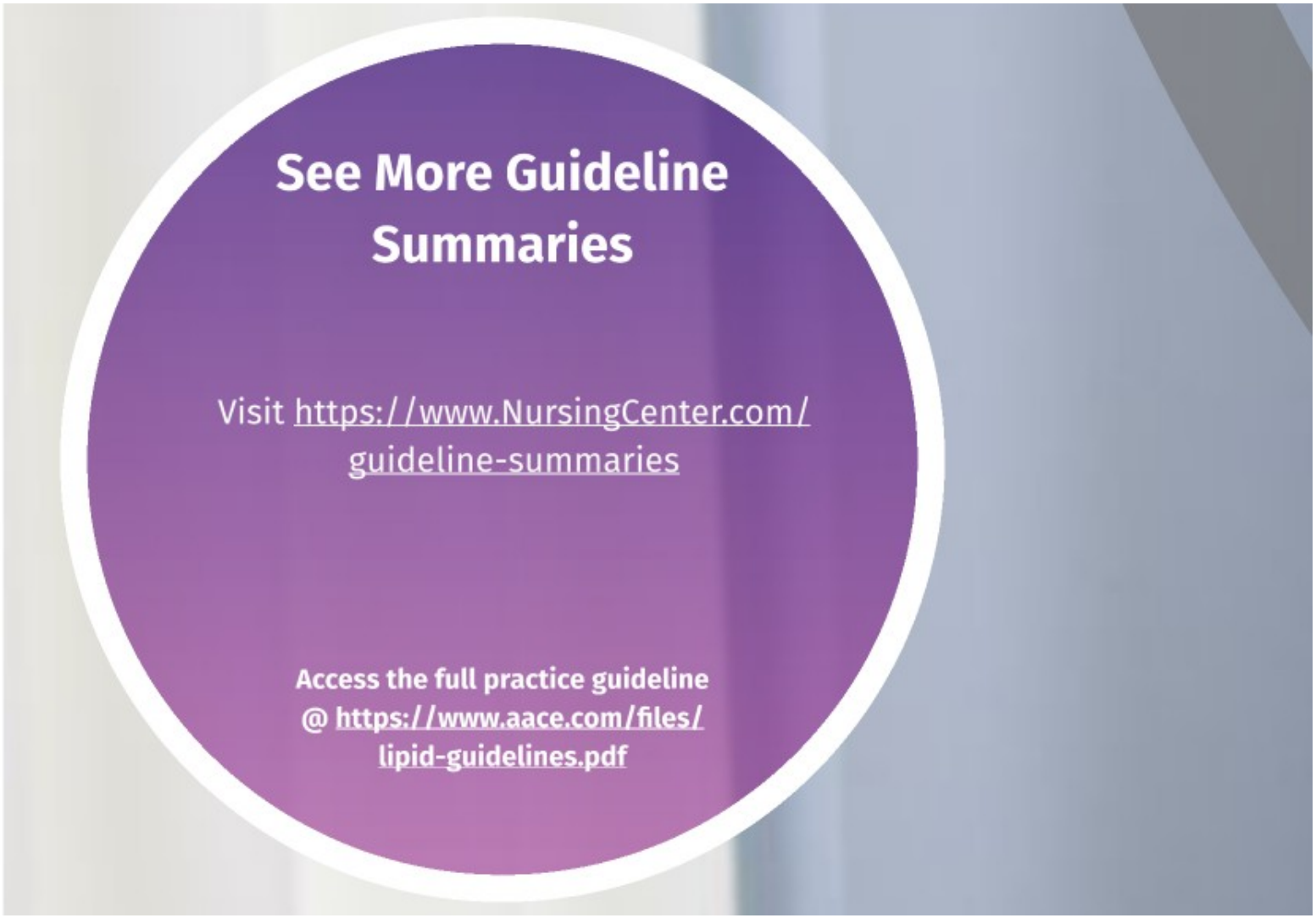
References (cont'd.)

References (cont'd.)

Ridker, P. M., Buring, J. E., Rifai, N. & Cook, N. R. (2007). Development and validation of improved algorithms for the assessment of global cardiovascular risk in women: The Reynolds Risk Score. Journal of the American Medical Association, 297(6), 611-619. doi:10.1001/jama.297.6.611

Sattar, N., Williams, K., Sniderman, A. D., D'Agostino, R., & Haffner, S. M. (2004). Comparison of the associations of apolipoprotein B and non-high-density lipoprotein cholesterol with other cardiovascular risk factors in patients with the metabolic syndrome in the Insulin Resistance Atherosclerosis Study. Circulation, 110(17), 2687-2693. doi:10.1161/01.CIR.0000145660.60487.94

Stevens, R .J., Kothari, V., Adler, A. I. & Stratton, I. M. (2001). The UKPDS Risk Engine: a model for the risk of coronary heart disease in type 2 diabetes; United Kingdom Prospective Diabetes Study (UKPDS) Group. Clinical Science, 101(6), 671-679. doi:10.1042/cs1010671


See More Guideline Summaries
Visit https://www.NursingCenter.com/guideline-summaries
Access the full practice guideline @ https://www.aace.com/files/lipid-guidelines.pdf


Dyslipidemia and Prevention of Cardiovascular Disease
Wolters Kluwer
Lippincott NursingCenter
Copyright © 2018, Wolters Kluwer