CV Risk and Menopause Hormone Treatment

Katie Bensching MD FACP

Primary Care Clinician

OHSU CWH Menpause Program

Associate Professor OHSU

Department of Medicine

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33rd Annual Internal Medicien Review

Agenda

- Brief review
  - Menopause Symptoms / Indications for Systemic Estrogen
  - Menopause and ASCVD Risk
  - Menopause Hormonal Therapy and ASVD Risk (including 'timing hypothesis'
  - CV Risk Assessment

  (ASCVD vs PREVENT , NEW 2026 ACC/AHA et al Management of Dyslipidemia)
- Individualized CV risk assessment when considering MHT
  - Cho et al
  - D'Costa et al
  - UpToDate
  - Cross walk all above and 2026 dyslipidemia guideline
- Cases

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Menopause

- Average age Menopause - Final Menstrual Period - 52yo
- Early Menopase Onset < 45 yo (1 %)
- Premature menopause aka Primary Ovarian Insufficiency (POI) <40 yo

- Hormone Replacement Therapy (HRT) - Estrogen for POI
  - true replacement therapy
- Menopausal Hormone Theray (MHT) -
  - to palliate symptoms of menopause

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Systemic Estrogen – MHT
Strong Indication vs Intermediate vs Not indicated

STRONG INDICATION

- VMS - moderate to severe
- Insomnia
- Mood

POSSIBLE INDICATION

- Joint aches

NOT INDICATION

- Genitourinary symptoms only
- Skin changes
- Weight loss

Table 1 Effects of menopause and menopausal hormone therapy on cardiovascular risk factors: A summary of clinical and metabolic changes

From: Cardiovascular Risk Associated with Menopause and Menopause Hormone Therapy: A Review and Contemporary Approach to Risk Assessment

Risk Factor	Effect of Menopause	Effect of MHT
Blood Pressure (BP)	– Systolic BP ↑ 4–7 mm Hg – Diastolic ↑ 3–5 mm Hg – Accelerated age-related BP ↑	– Oral estrogen ↓ SBP by 1–6 mm Hg – Combined therapy ↑ SBP – Transdermal estrogen ↓ DBP by up to 5 mm Hg
Weight, Adiposity, and BMI	– ↑ Visceral and pericardial fat – ↑ BMI and waist circumference linked to CHD and mortality	– Modest ↓ visceral fat – ↓ BMI (~ 1 kg/m^2) – Preserves lean tissue mass
Insulin Resistance	– ↑ Insulin resistance (OR 1.40–1.59) – ↑ HbA1c by ~ 5%	– ↑ Insulin sensitivity – ↓ HbA1c by up to 0.6% – ↓ Fasting glucose by ~ 20 mg/dL
Lipid Profile Changes (HLD)	– ↑ total cholesterol (10–14%) – ↑ LDL (10–20 mg/dL) – ↑ApoB (8–15%) – ↑ Initially, then ↓ HDL	– ↓ LDL (9–18 mg/dL) – ↑ HDL – Transdermal estrogen is more favorable for triglycerides (less elevation than oral) – No overall CVD risk ↓
Lipoprotein(a) [Lp(a)]	– ↑ by ~ 25% during menopause – ↑ ASCVD risk with Lp(a) > 50 mg/dL – ↑↑ ASCVD risk with Lp(a) > 100 mg/dL (doubled)	– ↓ Lp(a) by 20–30%, oral > other forms – Does not ↓ CVD events
Coronary Artery Calcification (CAC)	– ↑ CAC scores (OR 2.37) Mean CAC = 53	– Oral estrogen ↓ CAC – Transdermal may↑ CAC
Carotid Atherosclerosis	– ↑ CIMT progression – Independent predictor of stroke and CHD	– Early initiation may slow CIMT – No benefit with lower dose or delayed start
Physical Activity, Smoking, and Diet	– ↓ Physical activity – ↓ Dietary quality – No change in smoking status	– No direct effect on physical activity, diet, or smoking habits
Myocardial Infarction (MI) Risk	– ↑ MI risk (accumulation of other CV risk factors)	– CEE + MPA formulation ↑ MI risk (HR 1.29) – Transdermal formulation is safer
Stroke Risk	– ↑ Ischemic stroke risk (HR 1.1–2.0) – ↑↑ in early-onset menopause	– Oral estrogen ↑ stroke risk (~ 40%) – Transdermal < 50 mcg is safer – Risk unaffected by initiation timing

Menopause , MHT and CV risk

- CV risk increases with age
- CV risk increases with menopause, independent of age.

- MHT has not been shown to prevent or stabilize or reverse CVD
  - Except in observational studies (baik et al)

- 4 Major North American professional societies agree :

  MHT is not indicated for prevention of CVD (primary prevention) or reversal of CVD (secondary prevention)

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MHT and ASCVD Risk

- May reduce CV risk in low risk women when started early in menopause and < 60
- More risk when also using MPA and maybe other progesterones
- Women with CVD or at high risk for CVD on MHT are at increased risk for stroke and thromboembolism

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Timing hypothesis

MHT when used in early menopuse

- Is very low risk for Stroke ,VTE
- May even prevent CVD in low risk women,
  - Potential beneficial effect on normal endothelium

HOWEVER

MHT when used in late menopause

- Increases risk for Stroke , VTE
  - Mechanism Detrimental effect on endothelium with plaques

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NAMS (The Menopause Society) Position Statement 2022

The initiation of hormone therapy by menopausal women older then 60 yrs requires careful consideration of individual risks and benefits (LEVEL I)

Long-term use of hormone therapy, including women over 60 yo, may be considered in healthly women at low risk for CVD …(LEVEL III)

Factors that should be considered are … underlying risk of .. CHD, CVA …

Hormone therapy does not need to be routinely discontinued in women aged older then 60 or 65 (LEVEL III)

Mitigation of risk through use of lowest effective dose and potentially non oral route of administration becomes increasingly important as women age with longer duration of therapy (LEVEL III)

Longer durations or extened use beyond age 65 should include periodic reevaluations of comorbidities and consideration of periodic trials of lowering or discontinuing hormone therapy.

FDA Black Box Warning Removed
Makary et al JAMA Nov 10 2025

Removed boxed warnings for cardiovascular disease, stroke, breast cancer, and probable dementia.

All of the underlying adverse event info remains on the package insert.

Remove of recommendation to rx lowest effective dose for shortest duration but rather treatment decisions should be individualized and fall within the clinical judgement

Tailored safety info instead of applying identical class based language

Updated guidance on starting rx in women younger than 60 yo or within 10 yrs of menopause onset

https://jamanetwork.com/journals/ajama/fullarticle/2841321

WHI Safety Committee Response

Wittes et al
Jama April 16 2026

“ process … highly unusual”

Table. A US Food and Drug Administration (FDA) Advisory Committee vs the Menopause Expert Panel

Topic	FDA advisory committee	Expert panel on postmenopausal hormones
Governing rule	FACA	No formal rule
Type of meeting	By FACA mandate, meetings are open to the public	Each expert gave a 5-minute presentation, a short discussion among the panelists followed, then the panel convened for a closed session not open to the public
Comments by the public	May send written comments and present views publicly	May send written comments; no public presentation
Charter	Open to the public	No public charter
Membership	Physicians, scientists, statisticians, epidemiologists, patient advocates, and other experts in the field; standing members of the committee attend, plus ad hoc members if needed to address specific issues	A group of experts appeared to be chosen because they wanted the box warnings to be removed
Administration	General Services Administration provides regulations and guidance	Appeared to be run by the FDA director
Database	FACA has a public database with committee documents (eg, charters and meeting minutes)	No public database
Notice of meeting	FDA must publish notification of advisory committee meetings at least 15 days before meeting date in the Federal Register	No formal rule for notification
Background materials	FDA generally makes background materials available on its website at least 2 days before the meeting	No background materials were available to the public
Conflicts of interest	Each prospective panel member fills out a detailed conflict of interest statement	No apparent conflict of interest statements recorded
Length of meeting	Meetings last 4 to 10 hours to ensure full discussion by committee, sponsor, and FDA; entire meeting open to the public	Meeting lasted 2 hours

Abbreviation: FACA, Federal Advisory Committee Act.

Summary
MHT and ASCVD Risk

- May reduce CV risk in low risk women when started early in menopause and < 60
- More risk when using progestogens also
- Women with CVD or at high risk for CVD on MHT are at increased risk for stroke and thromboembolism
- 4 Major North American professional societies agree : MHT is not indicated for prevention of CVD (primary prevention) or reversal of CVD (secondary prevention)

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CV Risk Assessment

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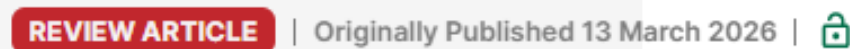
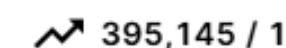
Circulation



2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

Writing Committee Members, Roger S. Blumenthal, MD, FACC, FAHA, FASPC, FNLA, Chair, Pamela B. Morris, MD, FACC, FAHA, FASPC, FNLA, Vice Chair, Mario Gaudino, MD, FAHA, FACC, JC Liaison, Heather M. Johnson, MD, MS, FAHA, FACC, FASPC, JC Liaison, Timothy S. Anderson, MD, MAS, Vera A. Bittner, MD, MSPH, FACC, FAHA, MNLA, MAACVPR, ... SHOW ALL ... , and John T. Wilkins, MD, MSc, FAHA | AUTHOR INFO & AFFILIATIONS

Circulation • New online • https://doi.org/10.1161/CIR.0000000000001423



PREVENT (new items in red)

REQUIRED

- AGE
- SBP (not DBP)
- Total Cholesterol
- HDL Cholesterol
- eGFR
- BMI
- DM ?
- Current Smoker
- On Lipid lowering med?
- On AntiHTN med?

OPTIONAL

UACR (urinary albumin / Cr Ratio)

Hba1c

Zip Code

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Blumenthal, R.S., Morris, P.B., et al. 2026 ACC/AHA Guideline on the Management of Dyslipidemia. *Circulation*.

About the PREVENT Equations | Online Calculator

CVD | ASCVD | Heart Failure

Sex*
Male / Female

Age (years)*
30-79

SBP (mmHg)*
90-200

Total Cholesterol (mg/dL)*
130-320

HDL Cholesterol (mg/dL)*
20-100

eGFR (mL/min/1.73m²)*
15-140

BMI (kg/m²)*
18.5-39.9

Diabetes
Any history of diabetes.
No / Yes

Current Smoking
Any cigarette use within the last 30 days
No / Yes

Lipid-lowering medication
Current use of statin medication to lower cholesterol
No / Yes

Anti-hypertensive medication
Current use of any medication for hypertension
No / Yes

The following three predictors are optional for further personalization of risk assessment. When they are clinically indicated or available,

If available or indicated, select "Yes" and enter the value.

UACR (mg/g)
UACR is clinically indicated for individuals with chronic kidney disease, diabetes, or hypertension
No / Yes
0 to 25000 mg/g

HbA1C
HbA1c is clinically indicated for individuals with diabetes, prediabetes, overweight, or obesity, or those with history of gestational diabetes
No / Yes
3 to 15 %

Zip Code
valid 5-digit zip code is needed to estimate social deprivation index [SDI]
No / Yes
Enter zip code

Calculate | Reset

https://professional.heart.org/en/guidelines-and-statements/prevent-calculator

OLD Poole Cohort E vs New PREVENT –ASCVD Calculator

RISK	POOLED COHORT EQUATIONS	PREVENT-ASCVD
Low	<5%	<3%
Borderline	5 - <7.5%	3 to <5%
Intermediate	7.5 - <20%	5 to <10%
High	≥20%	≥10%

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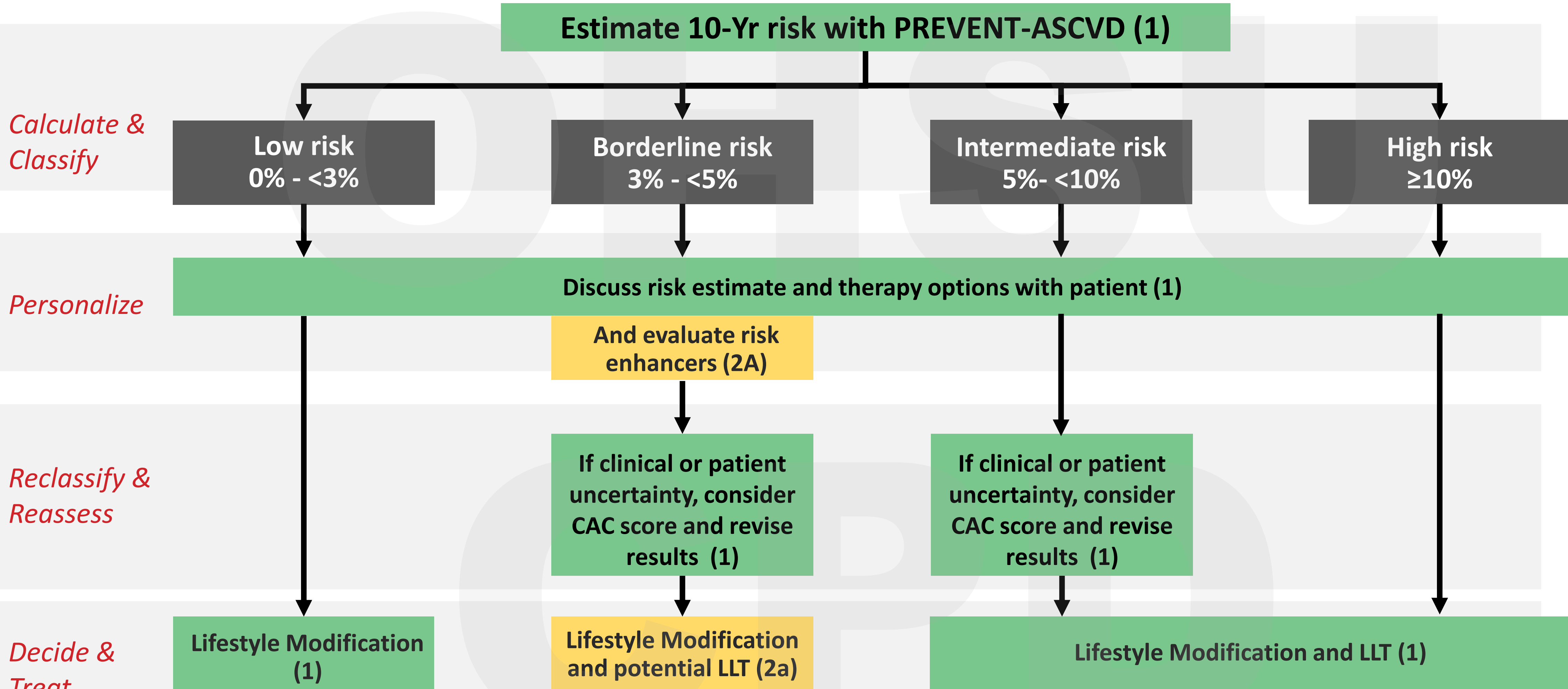
American Heart Association.

Calculate, Personalize, Reclassify (CPR) Framework



Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease; CAC, coronary artery calcium; LLT, lipid-lowering therapy; and PREVENT, Predicting Risk of cardiovascular disease EVENTS.

American Heart Association.

Blumenthal, R.S., Morris, P.B., et al. 2026 ACC/AHA Guideline on the Management of Dyslipidemia. *Circulation*.

Lipoprotein Goals for ASCVD Risk Reduction

Patient population	LDL-C <100 mg/dL (2.6 mmol/L) Non-HDL-C <130 mg/dL (3.4 mmol/L)	LDL-C <70 mg/dL (1.8 mmol/L) Non-HDL-C <100 mg/dL (2.6 mmol/L)	LDL-C <55 mg/dL (1.4 mmol/L) Non-HDL-C <85 mg/dL (2.2 mmol/L)
Primary prevention	PREVENT-ASCVD < 10% • If TG ≥ 150 mg/dL to 499 mg/dL, apoB goal: <90 mg/dL	PREVENT-ASCVD ≥ 10% • If TG ≥ 150 mg/dL to 499 mg/dL, apoB goal: <70 mg/dL	N/A
Severe hypercholesterolemia	**Without** FH, ASCVD risk factors, and subclinical atherosclerosis	**With** FH, ASCVD risk factors, and subclinical atherosclerosis	Severe hypercholesterolemia or HeFH with clinical ASCVD
Diabetes	**Without** ASCVD risk factors or diabetes-specific risk modifiers • apoB goal: <90 mg/dL	**Without** ASCVD risk factors or diabetes-specific risk modifiers • apoB goal: <70 mg/dL	N/A
Subclinical atherosclerosis	CAC = 1-99 AU and <75th percentile for age, sex, and race	• CAC ≥ 100 to 299 AU or ≥75th percentile for age, sex, and race • CAC ≥ 300 to 999 AU – Optional goal: LDL-C <55 mg/dL, non-HDL-C <85 mg/dL, and consider apoB goal <55 mg/dL	CAC ≥ 1000 AU
Hypertriglyceridemia	<50 y old with no additional risk enhancers	• With clinical ASCVD not at very high risk – apoB goal: <70 mg/dL • Age 40-75 y with ≥1 ASCVD risk factor – apoB goal: <70 mg/dL	• With clinical ASCVD at very high risk – apoB goal: <55 mg/dL
Clinical ASCVD	N/A	Not at very high risk • Optional goal: LDL-C <55 mg/dL, non-HDL-C <85 mg/dL, and consider apoB goal <55 mg/dL	• At very high risk – apoB goal: <55 mg/dL • With CKD

Abbreviations: ApoB indicates apolipoprotein B; ASCVD, atherosclerotic cardiovascular disease; AU, Agatston units; CAC, coronary artery calcium; CKD, chronic kidney disease; FH, familial hypercholesterolemia; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; and TG, triglycerides.

American Heart Association.

Blumenthal, R.S., Morris, P.B., et al. 2026 ACC/AHA Guideline on the Management of Dyslipidemia. *Circulation*.

Lipoprotein Goals for ASCVD Risk Reduction

Patient population	HIGH RISK*	HIGHER RISK*	EXTREMELY HIGH RISK *
Primary prevention	PREVENT-ASCVD < 10% • If TG ≥ 150 mg/dL to 499 mg/dL, apoB goal: <90 mg/dL	PREVENT-ASCVD ≥ 10% • If TG ≥ 150 mg/dL to 499 mg/dL, apoB goal: <70 mg/dL	N/A
Severe hypercholesterolemia	**Without** FH, ASCVD risk factors, and subclinical atherosclerosis	**With** FH, ASCVD risk factors, and subclinical atherosclerosis	Severe hypercholesterolemia or HeFH with clinical ASCVD
Diabetes	**Without** ASCVD risk factors or diabetes-specific risk modifiers • apoB goal: <90 mg/dL	**With** ASCVD risk factors or diabetes-specific risk modifiers • apoB goal: <70 mg/dL	N/A
Subclinical atherosclerosis	CAC = 1-99 AU and <75th percentile for age, sex, and race	• CAC ≥ 100 to 299 AU or ≥75th percentile for age, sex, and race • CAC ≥ 300 to 999 AU – Optional goal: LDL-C <55 mg/dL, non-HDL-C <85 mg/dL, and consider apoB goal <55 mg/dL	CAC ≥ 1000 AU
Hypertriglyceridemia	<50 y old with no additional risk enhancers	• With clinical ASCVD not at very high risk – apoB goal: <70 mg/dL • Age 40-75 y with ≥1 ASCVD risk factor – apoB goal: <70 mg/dL	• With clinical ASCVD at very high risk – apoB goal: <55 mg/dL
Clinical ASCVD	N/A	Not at very high risk • Optional goal: LDL-C <55 mg/dL, non-HDL-C <85 mg/dL, and consider apoB goal <55 mg/dL	• At very high risk – apoB goal: <55 mg/dL • With CKD

Abbreviations: ApoB indicates apolipoprotein B; ASCVD, atherosclerotic cardiovascular disease; AU, Agatston units; CAC, coronary artery calcium; CKD, chronic kidney disease; FH, familial hypercholesterolemia; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; and TG, triglycerides.

Blumenthal, R.S., Morris, P.B., et al. 2026 ACC/AHA Guideline on the Management of Dyslipidemia. *Circulation*.

* My addition

Individualized CV Risk Assessment When Considering Systemic MHT

- UpToDate
- Rethinking MHT Cho et al Circulation 2023 (ACC CV Disease in Women)
- Cardiovascular Risk Associated with Menopause and MHT - D'Costa et al Curr Atheroscler Rep 2025

ALL BASED on " OLD" ASCVD Calculator

UpToDate 4/7/26
Use an ASCVD Risk Calculator

UpToDate® menopause hormone therapy

Back

Evaluating CVD risk in females contemplating MHT

10-year CVD risk		Years since menopause onset
		<10 years
Low (<5%)	?<3% Prevent	MHT ok
Moderate (5 to 10%)	?>3->57% Prevent	MHT ok (choose transdermal)
High (>10%)*	?>=5% Prevent	Avoid MHT

CVD risk calculated by ACC/AHA Cardiovascular Risk Calculator. Methods to calculate risk and risk stratification vary among countries.

CVD: cardiovascular disease; MHT: menopausal hormone therapy; ACC: American College of Cardiology; AHA: American Heart Association.

* High risk includes known myocardial infarction (MI), stroke, peripheral artery disease, etc.

Adapted from:

1. *Manson JE. Current recommendations: what is the clinician to do? Fertil Steril 2014; 101:916.*
2. *Stuenkel CA, Davis SR, Gompel A, et al. Treatment of symptoms of the menopause: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 2015; 100:3975.*

Graphic 107770 Version 4.0

Cho et al
Rethinking Menopausal Hormone Therapy
Circulation 2023

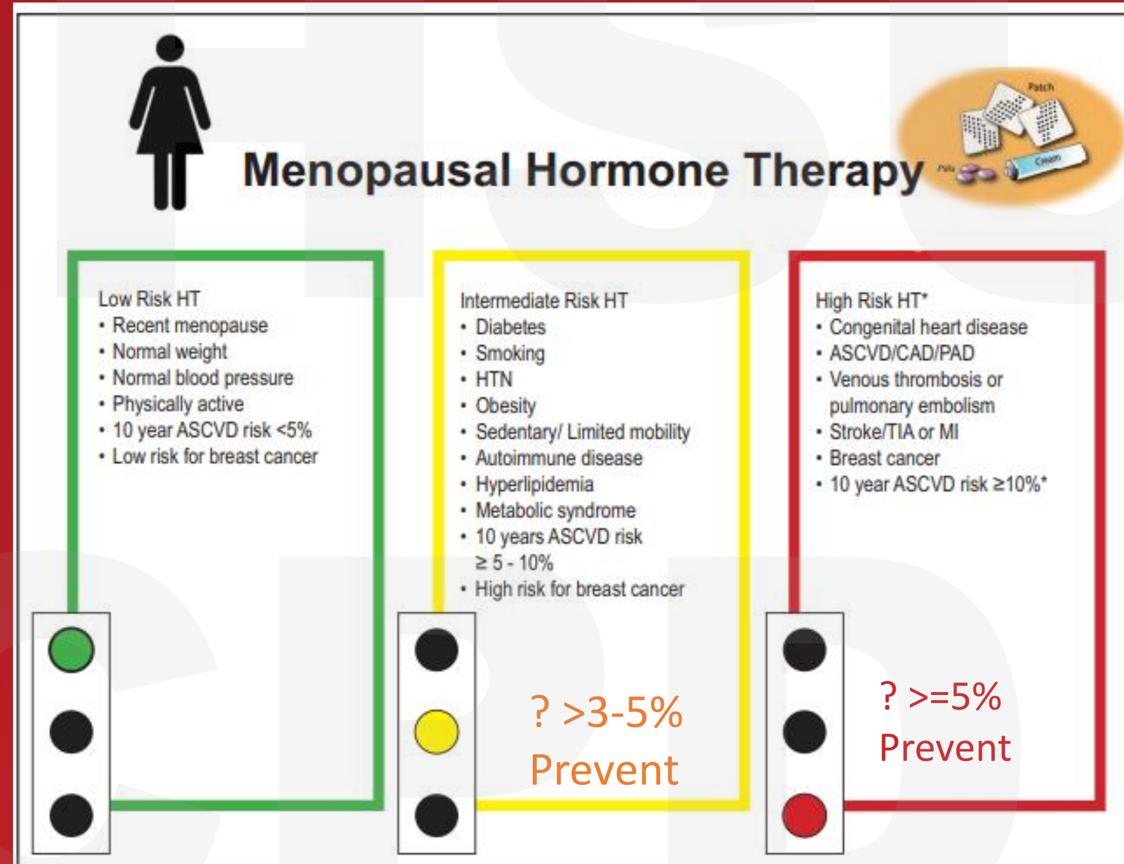


Figure 3. Menopausal hormone therapy recommendation by patient risk.
*In general, it is advised to avoid systemic hormone therapy. Consider alternative therapy, and if severe vasomotor symptoms persist, individualized, shared decision-making is recommended. All women are candidates for low-dose vaginal estrogen therapy for genitourinary symptoms of menopause. ASCVD indicates atherosclerotic cardiovascular disease; CAD, coronary artery disease; HTN, hypertension; MI, myocardial infarction; PAD, peripheral artery disease; and TIA, transient ischemic attack.

Approximate Equivalent Ranges of 10-yr ASCVD Risk Estimates

RISK	POOLED COHORT EQUATIONS	PREVENT-ASCVD
Low	<5%	<3%
Borderline	5 - <7.5%	3 to <5%
Intermediate	7.5 - <20%	5 to <10%
High	≥20%	≥10%

LOW RISK < 3%

BORERLINE 3 - >5%

INTERMEDIATE
5-<10%
HIGH >=10%

Table 6. Atherosclerotic Cardiovascular Disease Risk Score and Years Since Menopause Onset for Initiating HT

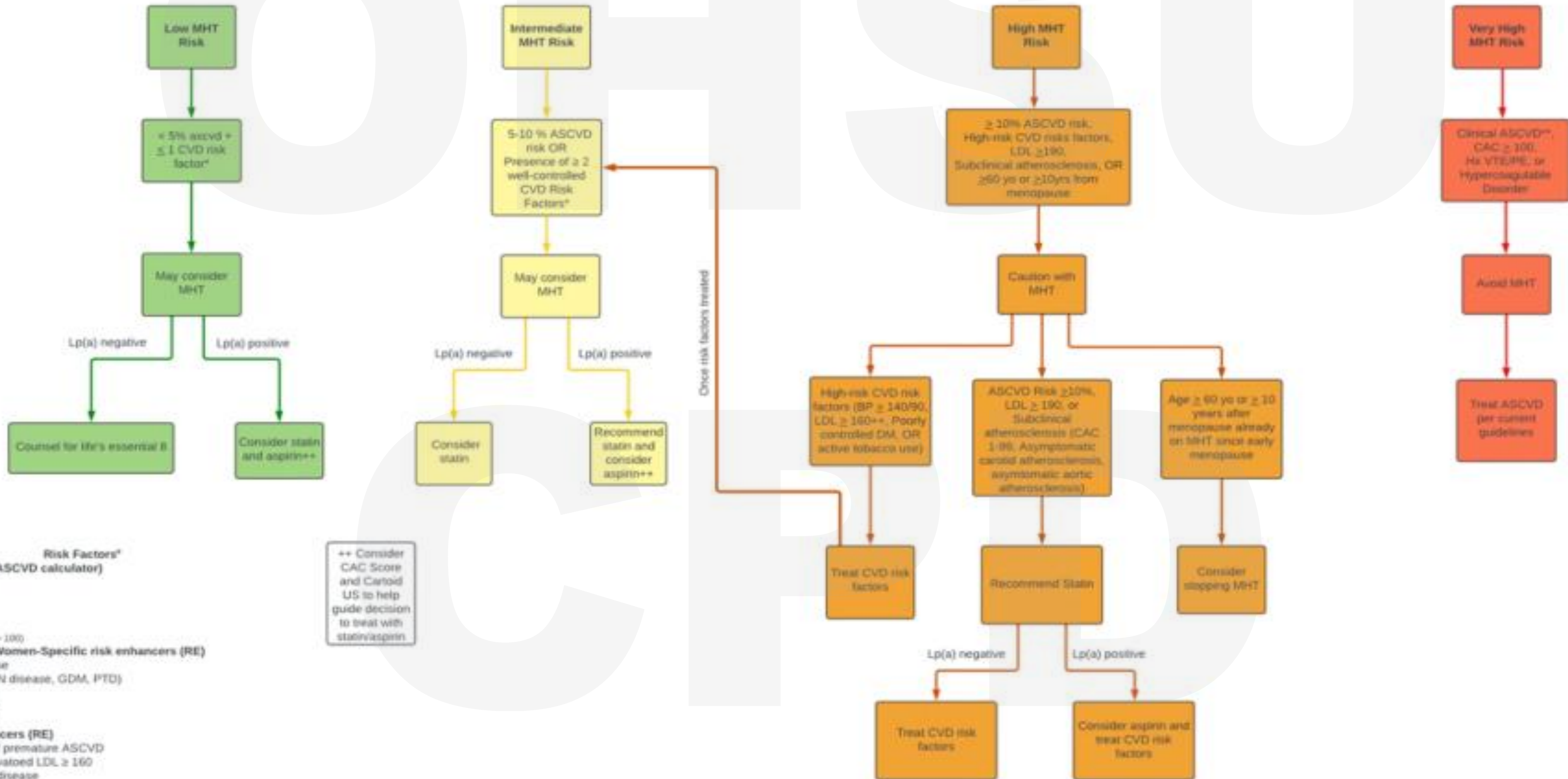
Cardiovascular disease risk over 10 years American College of Cardiology/American Heart Association atherosclerotic cardiovascular disease risk score	Years since menopause onset		
	≤5	6–10	≥10
Low risk (<5%)	HT acceptable	HT acceptable	Consider alternatives; HT acceptable with individualized, shared decision-making
Intermediate risk (≥5.0% to <10%)	HT acceptable. Consider transdermal HT depending on risk factors	HT acceptable. Consider transdermal HT depending on risk factors	Generally advised to avoid systemic HT. Consider alternative therapy, and if severe VMS persist, individualized, shared decision-making
High risk (≥10%)	Generally advised to avoid systemic HT. Consider alternative therapy, and if severe VMS persist, individualized, shared decision-making	Generally advised to avoid systemic HT. Consider alternative therapy, and if severe VMS persist, individualized, shared decision-making	Avoid HT. Consider alternative therapy, and if severe VMS persist, individualized, shared decision-making

HT indicates hormone therapy; and VMS, vasomotor symptoms.

Circulation. 2023;147:597–610. DOI: 10.1161/CIRCULATIONAHA.122.061559 February 14, 2023 605

From: Cardiovascular Risk Associated with Menopause and Menopause Hormone Therapy: A Review and Contemporary Approach to Risk Assessment

D'Costa et al , Current Atherosclerosis Reports 8/2025



Risk Factors*

1. **Traditional RF (ASCVD calculator)**
   a. HTN
   b. DM
   c. smoking
   d. BMI>25
   e. High LDL (LDL > 100)
2. **Non-traditional Women-Specific risk enhancers (RE)**
   a. early menopause
   b. APO (LBW, HTN disease, GDM, PTD)
   c. breast cancer
   d. autoimmune dz
   e. VMS
3. **Other risk enhancers (RE)**
   a. family history of premature ASCVD
   b. persistently elevatoed LDL ≥ 160
   c. chronic kidney disease
   d. metabolic syndrome
   e. Ethnicity - south asian
   f. Persistently elevated TG≥ 175
   g. Lp(a) ≥ 50 mg/dL or ≥ 125 nmol/L

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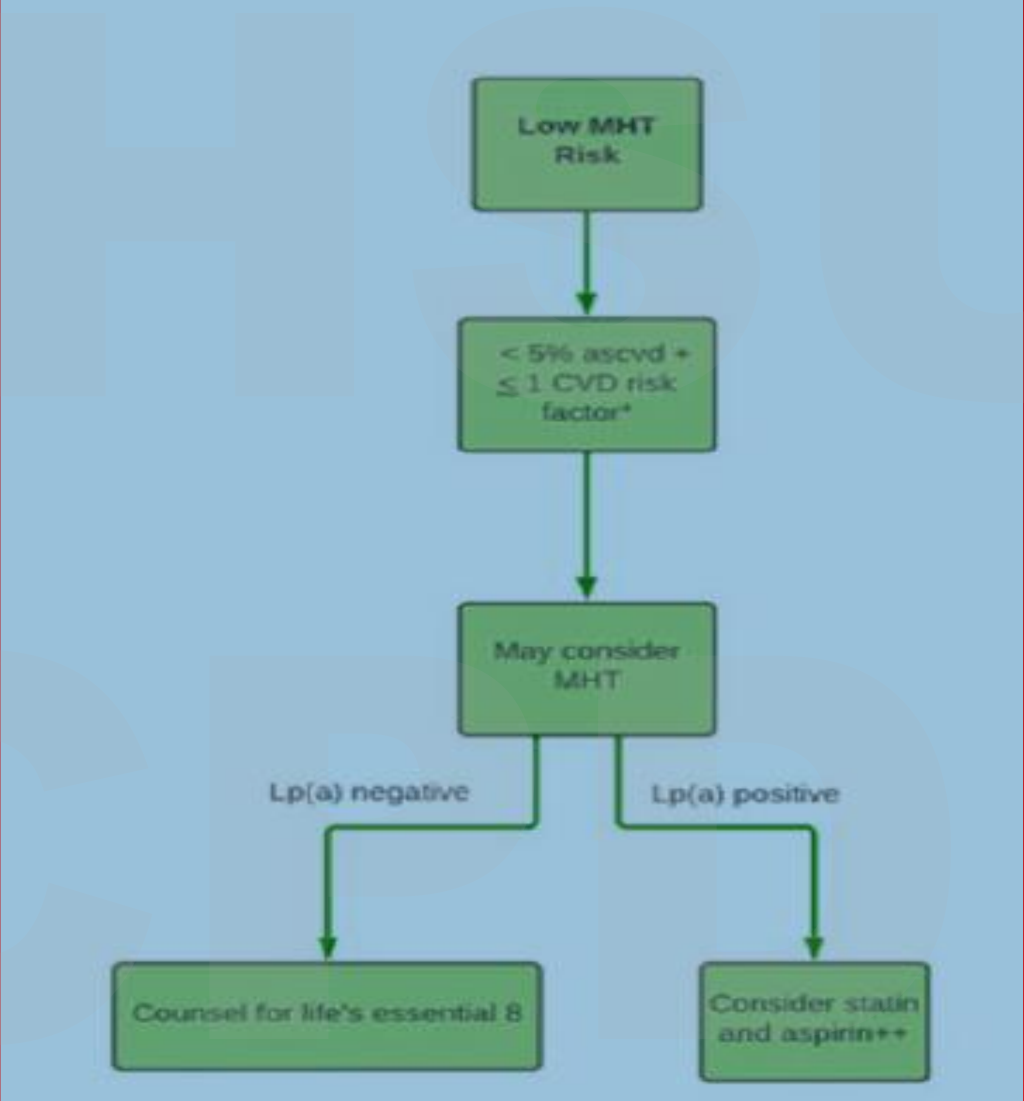
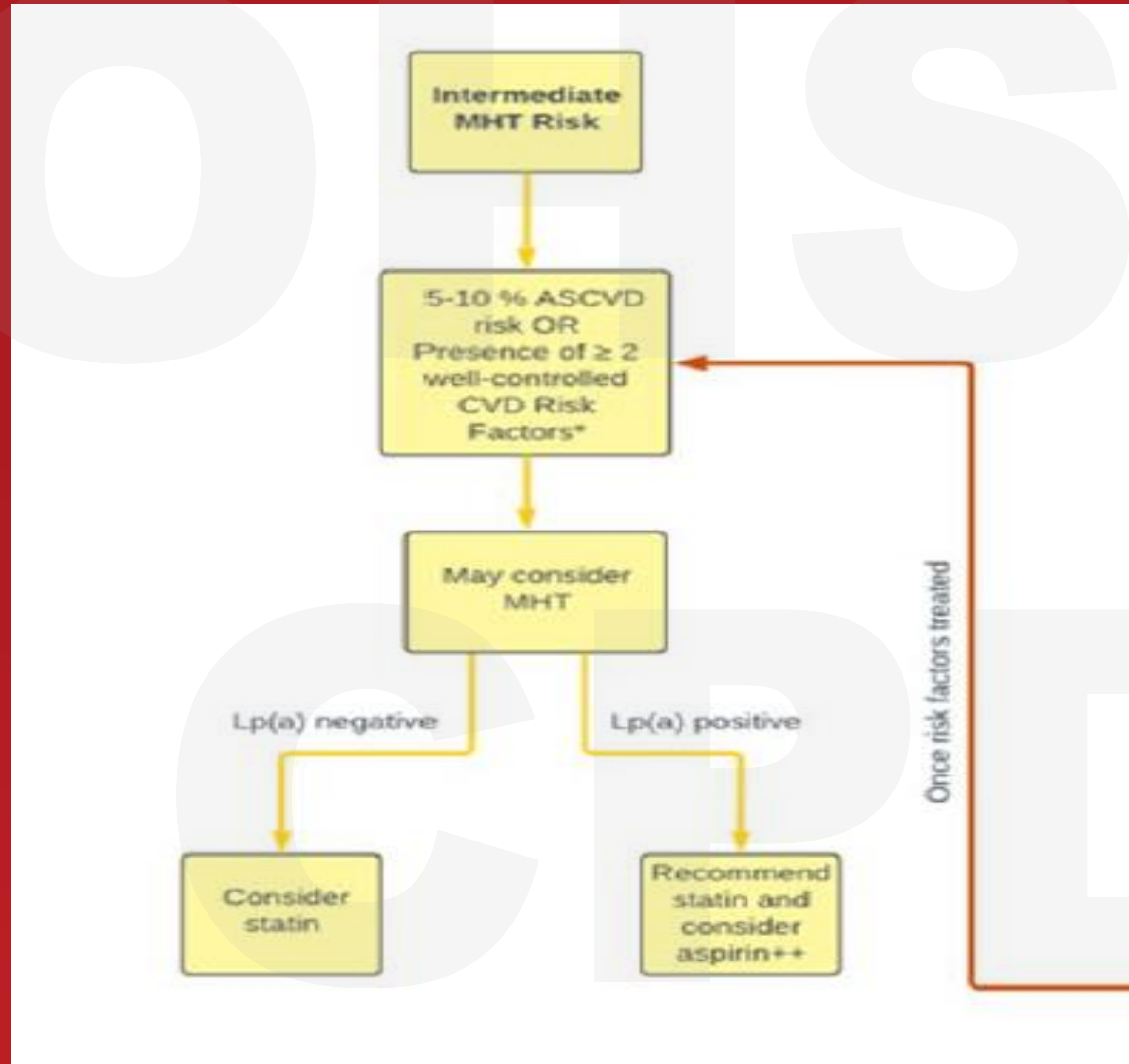
LOW RISK – MAY CONSIDER MHT



INTERMEDIATE RISK – MAY CONSIDER MHT



++ Consider CAC Score and Cartoid US to help guide decision to treat with statin/aspirin

HIGH RISK – CAUTION WITH MHT

High MHT Risk

≥ 10% ASCVD risk, High-risk CVD risks factors, LDL ≥190, Subclinical atherosclerosis, OR ≥60 yo or ≥10yrs from menopause

Caution with MHT

- High-risk CVD risk factors (BP ≥ 140/90, LDL ≥ 160++, Poorly controlled DM, OR active tobacco use) → Treat CVD risk factors
  - Once risk factors treated → back to High MHT Risk
- ASCVD Risk ≥10%, LDL ≥ 190, or Subclinical atherosclerosis (CAC 1-99, Asymptomatic carotid atherosclerosis, asymptomatic aortic atherosclerosis) → Recommend Statin
  - Lp(a) negative → Treat CVD risk factors
  - Lp(a) positive → Consider aspirin and treat CVD risk factors
- Age ≥ 60 yo or ≥ 10 years after menopause already on MHT since early menopause → Consider stopping MHT

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VERY HIGH RISK – AVOID MHT

Very High MHT Risk

↓

Clinical ASCVD**, CAC $\geq$ 100, Hx VTE/PE, or Hypercoagulable Disorder

↓

Avoid MHT

↓

Treat ASCVD per current guidelines

**Defined as: prior MI/PCI/CABG, Angina, Ischemia, prior stroke, symptomatic PAD

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Lipoprotein Goals for ASCVD Risk Reduction

Patient population	HIGH RISK*	HIGHER RISK*	EXTREMELY HIGH RISK *
Primary prevention	PREVENT-ASCVD < 10% • If TG ≥ 150 mg/dL to 499 mg/dL, apoB goal: <90 mg/dL	PREVENT-ASCVD ≥ 10% • If TG ≥ 150 mg/dL to 499 mg/dL, apoB goal: <70 mg/dL	N/A
Severe hypercholesterolemia	**Without** FH, ASCVD risk factors, and subclinical atherosclerosis	**With** FH, ASCVD risk factors, and subclinical atherosclerosis	Severe hypercholesterolemia or HeFH with clinical ASCVD
Diabetes	**Without** ASCVD risk factors or diabetes-specific risk modifiers • apoB goal: <90 mg/dL	**With** ASCVD risk factors or diabetes-specific risk modifiers • apoB goal: <70 mg/dL	N/A
Subclinical atherosclerosis	CAC = 1-99 AU and <75th percentile for age, sex, and race	• CAC ≥ 100 to 299 AU or ≥75th percentile for age, sex, and race • CAC ≥ 300 to 999 AU – Optional goal: LDL-C <55 mg/dL, non-HDL-C <85 mg/dL, and consider apoB goal <55 mg/dL	CAC ≥ 1000 AU
Hypertriglyceridemia	<50 y old with no additional risk enhancers	• With clinical ASCVD not at very high risk – apoB goal: <70 mg/dL • Age 40-75 y with ≥1 ASCVD risk factor – apoB goal: <70 mg/dL	• With clinical ASCVD at very high risk – apoB goal: <55 mg/dL
Clinical ASCVD	N/A	Not at very high risk • Optional goal: LDL-C <55 mg/dL, non-HDL-C <85 mg/dL, and consider apoB goal <55 mg/dL	• At very high risk – apoB goal: <55 mg/dL • With CKD

Abbreviations: ApoB indicates apolipoprotein B; ASCVD, atherosclerotic cardiovascular disease; AU, Agatston units; CAC, coronary artery calcium; CKD, chronic kidney disease; FH, familial hypercholesterolemia; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; and TG, triglycerides.

Blumenthal, R.S., Morris, P.B., et al. 2026 ACC/AHA Guideline on the Management of Dyslipidemia. *Circulation*.

* My addition

Other Contraindications

- BP > 180/110 (likely increased risk CVA)
- TG > 400 (Estrogen increases TG level)

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Guidance for HT Decision Making in Women w CV RF and a strong indication for HT

ADDRESS MODIFIABLE RISKS and RECONSIDER?

H. Hirsch and J.E. Manson *Maturitas 161 (2022) 1–6*

Table 2
Guidance for Hormone Therapy (HT) Decision Making Among Women with Cardiovascular Risk Factors and a Strong Indication for HT.

DIAGNOSIS	Hypertension	Dyslipidemia	Diabetes	Obesity	Metabolic Syndrome
CONTROLLED	Oral or transdermal	Transdermal	Transdermal	Transdermal	Transdermal
UNCONTROLLED	Transdermal Or non-hormonal options	Efforts should be made to control DLD and reduce LDL < 190 (preferably <130) mg/dL or use non-hormonal options	Efforts should first be made to reduce A1c between 7 and 8% or use non-hormonal options	Transdermal	Efforts should be made to gain control of metabolic syndrome or use non-hormonal options

Definitions:.
Controlled BP: Average blood pressure of less than 120/80 mmHg.
Uncontrolled BP: Average blood pressures of greater than 140/90 mmHg.
Abbreviations:
HT: Hormone Therapy
A1c: Glycated Hemoglobin
References: [16–18].

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Who is LOW risk for CVD ?

NO History of CVD

- No MI, ACS, Unstable Angina, Stable Angina, Medically Managed Angina
- No Ishemic Stroke, TIA
- No Peripheral Vascular disease

NO Evidence of Subclinical CVD

- Coronary Calcium Score 0
- No Finding of CAD, CVD, PAD on imaging
  - (US, CT, MRI, Plain XR)

NO History of Diabetes, CKD3 or higher, HIV , Lipid Disorder

PREVENT Calculator INTERMEDIATE Risk	10 yr risk of CVD 5 -<10% and CAC score 0
PREVENT Calculator BORDERLINE RISK	10 yr risk CVD 3- <5 % and NO risk enhancer *
PREVENT Calculator LOW RISK	10 yr risk CVD <3%

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Who is at higher risk for CVD ?

History of CVD

MI, ACS, Unstable Angina, Stable Angina, Medically Managed Angina,

Stroke, TIA

Peripheral Vascular Disease (including AAA)

Evidence of Subclinical CVD

Coronary Calcium Score > 0 , >100 A ,

Finding of CAD, CVD, PAD on imaging

(US, CT, MRI, ?Plain XR)

History of Diabetes, CKD3 or higher, HIV , Lipid Disorder, Lp(a) > 50 mg/dl

PREVENT Calculator HIGH Risk	10 yr risk of CVD >= 10 %
PREVENT Calculator INTERMEDIATE Risk	10 yr risk of CVD 5 -<10% (can consider CAC to clarify risk)
PREVENT Calculator BORDERLINE RISK	10 yr risk CVD 3- <5 % and risk enhancer

*? Consider "Other Risk Enhancers" (f hx pcvd in FDR <55 M / < 65 F, high risk ancestry, high polygenic risk, chronic inflammatory diseases, Lp(a)>50 mg/dl , hsCRP >=2 > once and no secondary cause, CKM syndrome, reproductive risk markers (premature menopause, preeclampsia, gest DM, gest HTN, preterm delivery)

Cho et al
Rethinking Menopausal Hormone Therapy
American College of Cardiology CV Disease in Women Committee

Table 1. Recommendations for Hormone Therapy From 4 Different Medical Societies

Aspect of treatment	American College of Obstetricians and Gynecologists[10]	North American Menopause Society[13]	American Association of Clinical Endocrinology and American College of Endocrinology[11]	Endocrine Society[12]
Principal indication	Menopause symptoms	Menopause symptoms	Menopause symptoms	Menopause symptoms
Prevention of coronary heart disease	Not recommended	Not recommended	Not recommended	Not recommended
Special considerations	None	Consideration of age and time from menopause onset	Consideration of age, time from menopause onset, and risk of cardiovascular disease, with lipid profile, smoking history	Consideration of age, time from menopause onset, and baseline risks of cardiovascular disease and breast cancer
Dose and route of administration	Lowest effective dose	Appropriate dose to manage symptoms with consideration of route	Lowest effective dose	Shared decision-making to determine formulation, dose, and route
Duration of use	Shortest period based on risk-benefit analysis, with recommendation against routine discontinuation in patient ≥65 y of age	May be extended for persistent vasomotor symptoms, prevention of bone loss, or quality of life after attempt at stopping; reassess benefits and risks regularly	Recommended for ≤5 y with reduction of dose if continuing	Shortest total duration consistent with the treatment goals and evolving risk assessment of the individual woman

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Annual Reassessment

- New health history or family history?
- Reassess CV risk (and other risks) for MHT
- Review with pt increased risk for CV event on MHT as age
- If on oral estrogen , consider transition to transdermal
- Consider taper or stop MHT (no literature to favor either method)
- You won't know your pt still is benefiting from MHT unless you taper or stop it. Ask patient if they have missed any doses and if so noted any recurrence of symptoms

OHSU CPD

Case 1 a
These hot flashes are awful.
But there’s lots of heart disease in my family

Early post menopausal 52 yo , moderately severe HF , fatigue, poor mood. No libido. Function impacted at work/ home.

Wants to avoid hormones, but is really struggling.

Fhx cad - mother at 75 yo just had an MI and father died of MI at 80 yo.

Pmhx - tah but ovaries intact - fibroid bleeding at 45 yo , no hx cad, mi, pad, cva, tia

Meds - loratidine

Non smoker

PREVENT score -- > low risk < 3 % 10 yr risk.

OHSU
CPD

Case 1 a
These hot flashes are awful.
But there's lots of heart disease in my family

Early postmenopausal

Strong indication

Low CV Risk (even tho family hx CAD)

UTX removed

We have many options for treatment of VMS

Systemic Estrogen is the most effective treatment.

(review other treatments)

→Benefits of systemic estrogen >> Harms CV disease

OHSU CPD

Case 1 b
These hot flashes are awful.
But there's lots of heart disease in my family

Early postmenopausal

Strong indication

Low CV Risk (even tho family hx CAD)

UTX intact

We have many options for treatment of VMS

Systemic Estrogen is the most effective treatment. Must take Progestogen also.

(review other treatments)

→Benefits of systemic estrogen >> Harms CV disease

OHSU CPD

Case 1 c
These hot flashes are awful.
But there's lots of heart disease in my family

Early postmenopausal

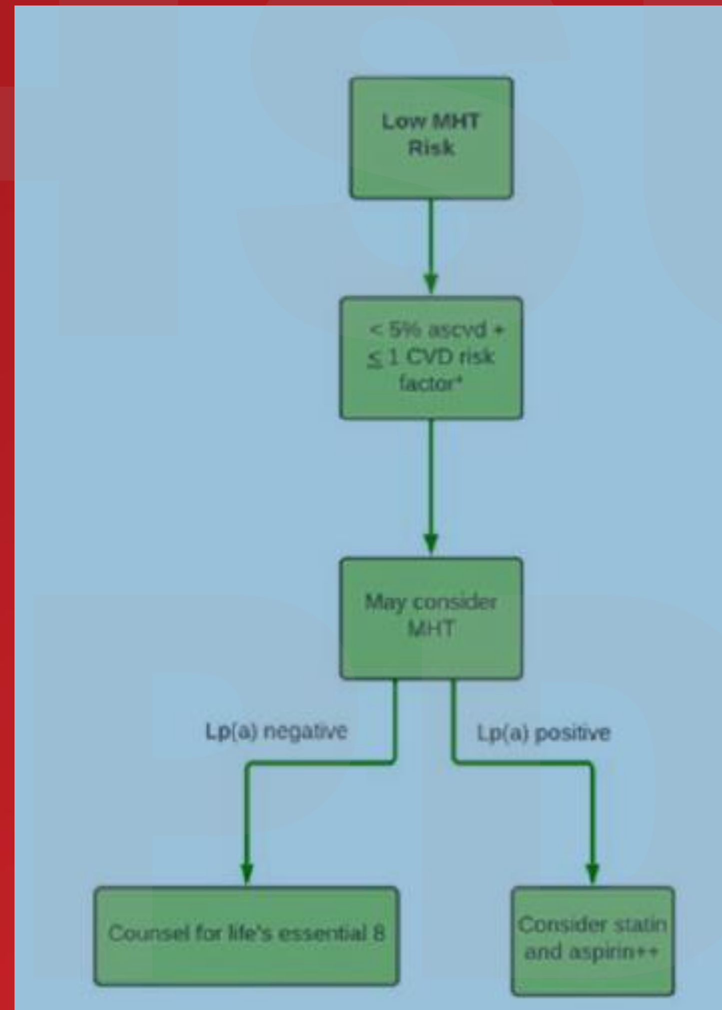
Strong indication

Low CV Risk (even tho family hx CAD) EXCEPT Lipoprotein (a) > 50 mg/ dl

UTX intact

OHSU CPD

CASE 1 C - LOW RISK – MAY CONSIDER MHT



Case 1 d
These hot flashes are awful.
But there's lots of heart disease in my family

Early postmenopausal

Strong indication

Low CV Risk (even tho family hx CAD) EXCEPT Lipoprotein (a) > 50 mg/ dl

UTX intact

We have many options for treatment of VMS

Systemic Estrogen is the most effective treatment. Must take Progestogen also.

(review other treatments)

Consider CAC scan to clarify her risk futher

IF CAC > 0 →

IF CAC 1-99 →

IF CAC > 100 →

OHSU CPD

OHSU CPD

Case 2a
Intermediate Risk –

- 55 Yo female with severe VMS
- No clinical ASCVD
- PREVENT 7.5 %
- Lp(a) 10 mg/ dl
- No other RF

- No CAC done

OHSU CPD

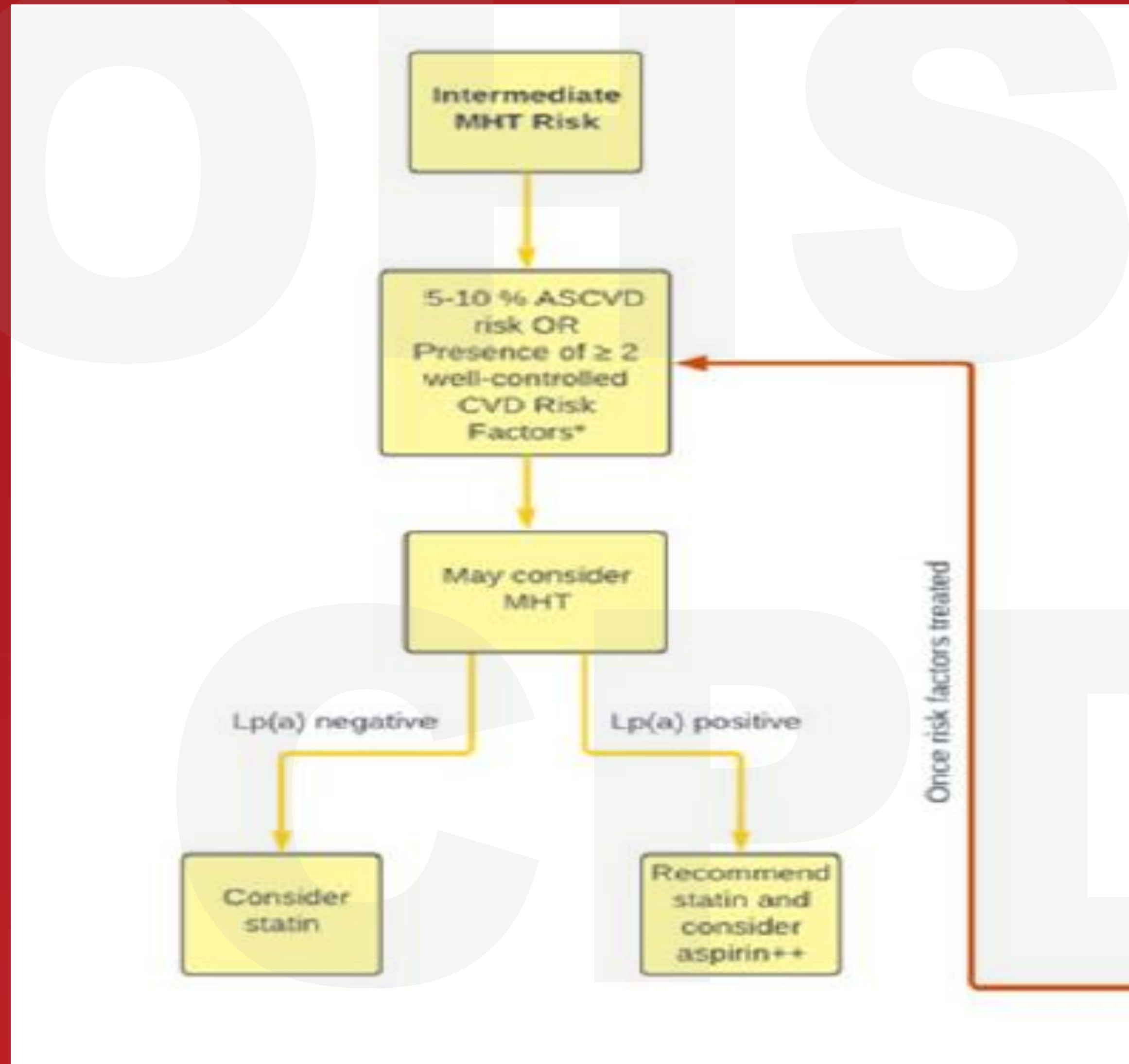
American Heart Association.

Risk Factors*

1. Traditional RF (ASCVD calculator)
   a. HTN
   b. DM
   c. smoking
   d. BMI>25
   e. High LDL (LDL > 100)
2. Non-traditional Women-Specific risk enhancers (RE)
   a. early menopause
   b. APO (LBW, HTN disease, GDM, PTD)
   c. breast cancer
   d. autoimmune dz
   e. VMS
3. Other risk enhancers (RE)
   a. family history of premature ASCVD
   b. persistently elevatoed LDL ≥ 160
   c. chronic kidney disease
   d. metabolic syndrome
   e. Ethnicity - south asian
   f. Persistently elevated TG≥ 175
   g. Lp(a) ≥ 50 mg/dL or ≥ 125 nmol/L

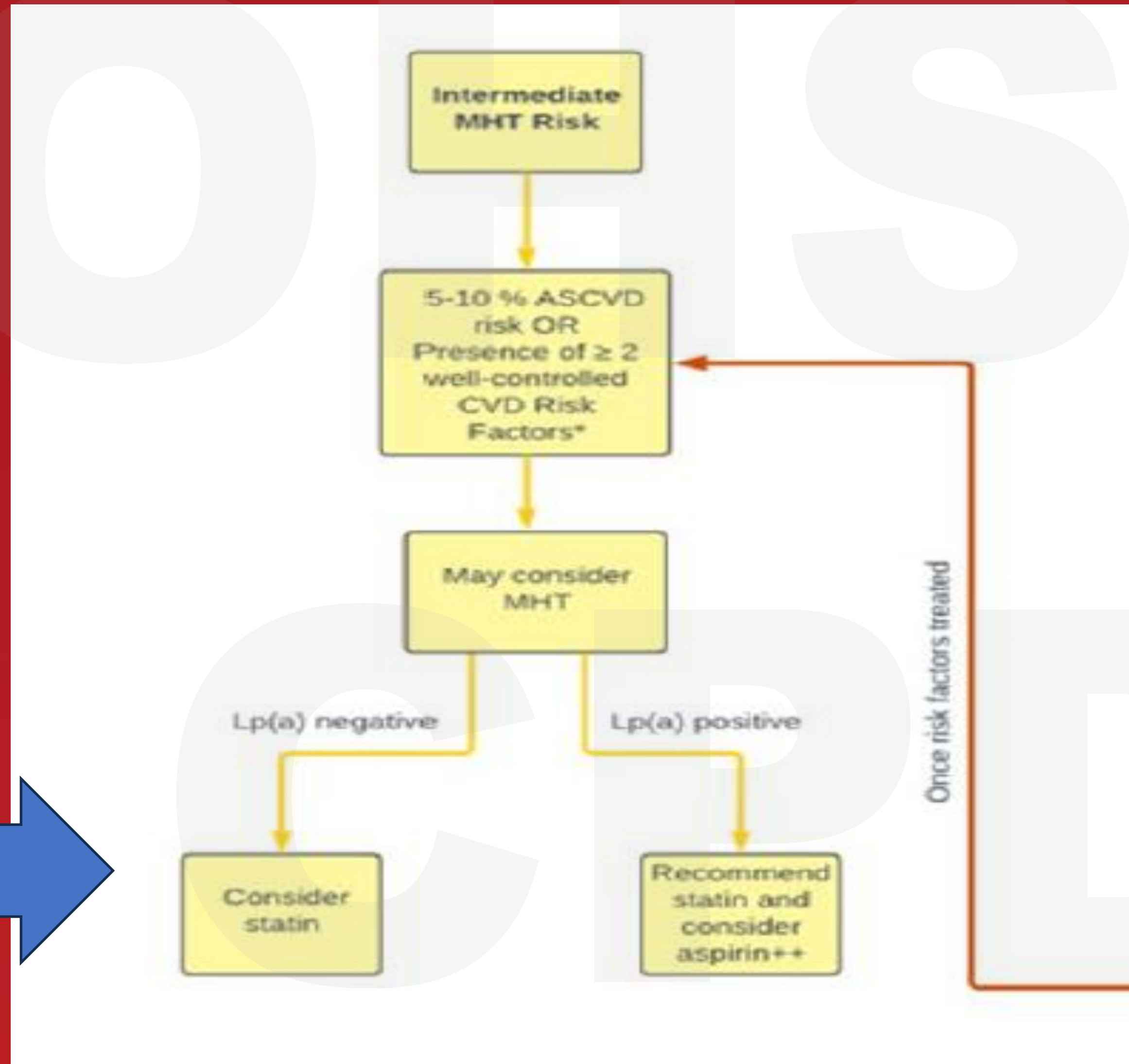
OHSU CPD

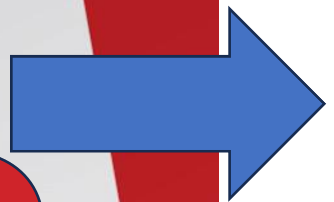
INTERMEDIATE RISK – MAY CONSIDER MHT



++ Consider CAC Score and Cartoid US to help guide decision to treat with statin/aspirin

INTERMEDIATE RISK – MAY CONSIDER MHT





++ Consider CAC Score and Cartoid US to help guide decision to treat with statin/aspirin

OHSU CPD

Case 2b
Intermediate Risk –

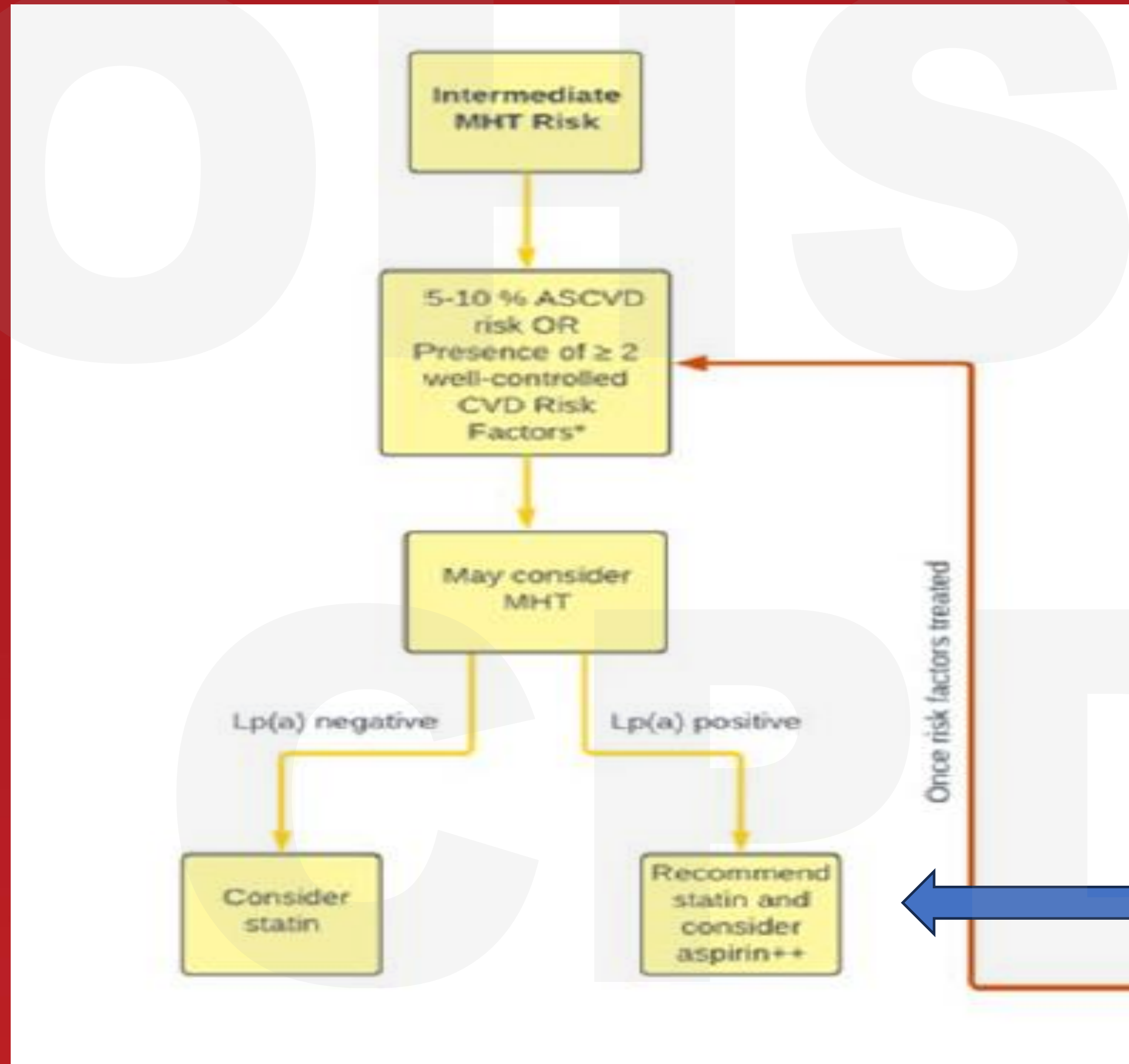
- 55 Yo female with severe VMS
- No clinical ASCVD
- PREVENT 7.5 %
- Lp(a) 60 mg/ dl
- No other RF

- No CAC done

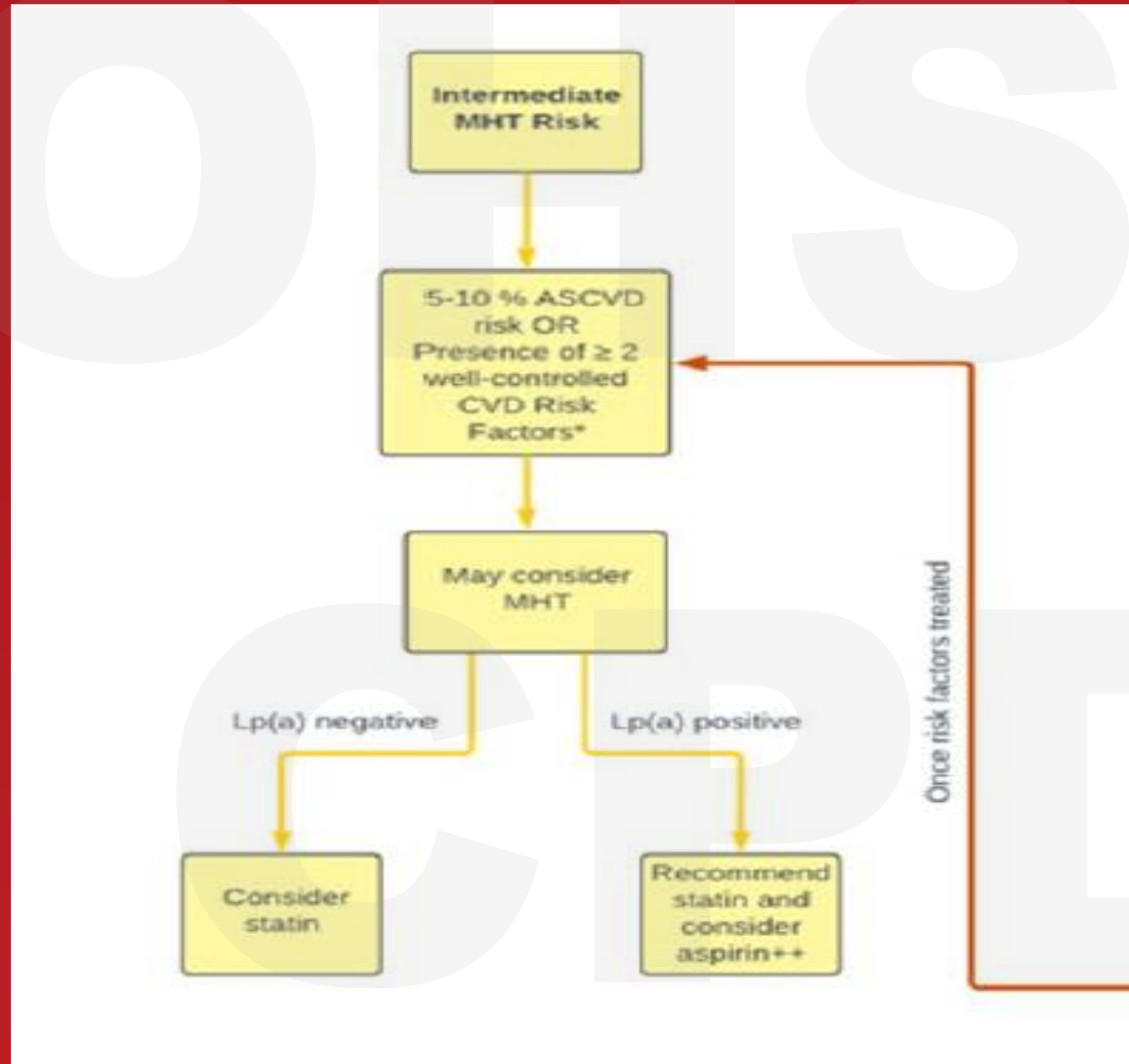
OHSU CPD

American Heart Association.

INTERMEDIATE RISK – MAY CONSIDER MHT



INTERMEDIATE RISK – MAY CONSIDER MHT



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OHSU CPD

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American Heart Association.

Case 3
EXTENDED USE of MHT after 60yo?

- 60 yo women hx severe HF on MHT for 8 years with good result
- Never trialed non hormonal rx.
- Transdermal Estradiol 0.05 twice weekly and micronized progesterone 100 mg daily.
- Do I need to stop it? Do I need to taper? How long can it take it? Will you still prescribe it?

OHSU CPD

American Heart Association.

Extended use of MHT

Over 40% of women 60-65 have Hot Flashes that can impair sleep and QOY

TMS and ACOG agree

- do not dc MHT based on age alone
- use an individualized approach
- can continue if pt and clinician agree benefit on QOL> risk

OHSU CPD

Approximate Equivalent Ranges of 10-yr ASCVD Risk Estimates

RISK	POOLED COHORT EQUATIONS	PREVENT-ASCVD
Low	<5%	<3%
Borderline	5 - <7.5%	3 to <5%
Intermediate	7.5 - <20%	5 to <10%
High	≥20%	≥10%

LOW RISK < 3%

BORERLINE 3 - >5%

INTERMEDIATE
5-<10%
HIGH >=10%

Table 6. Atherosclerotic Cardiovascular Disease Risk Score and Years Since Menopause Onset for Initiating HT

Cardiovascular disease risk over 10 years American College of Cardiology/American Heart Association atherosclerotic cardiovascular disease risk score	Years since menopause onset		
	≤5	6–10	≥10
Low risk (<5%)	HT acceptable	HT acceptable	Consider alternatives; HT acceptable with individualized, shared decision-making
Intermediate risk (≥5.0% to <10%)	HT acceptable. Consider transdermal HT depending on risk factors	HT acceptable. Consider transdermal HT depending on risk factors	Generally advised to avoid systemic HT. Consider alternative therapy, and if severe VMS persist, individualized, shared decision-making
High risk (≥10%)	Generally advised to avoid systemic HT. Consider alternative therapy, and if severe VMS persist, individualized, shared decision-making	Generally advised to avoid systemic HT. Consider alternative therapy, and if severe VMS persist, individualized, shared decision-making	Avoid HT. Consider alternative therapy, and if severe VMS persist, individualized, shared decision-making

HT indicates hormone therapy; and VMS, vasomotor symptoms.

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OHSU CPD

61 YO still VMS – never on MHT

I hear it is safe to use Estrogen over 60…

DELAYED INITIATION OF MHT?

OHSU CPD

61 YO still VMS – never on MHT
I hear it is safe to use Estrogen over 60…
DELAYED INITIATION OF MHT

OHSU
CPD

- Trial of non hormonal treatments is first line
- Avoid MHT , even if low risk for CVD

OHSU

CPD

Case 5
79 yo female
I feel miserable
I need Estrogen

- 79 yo female
  - Severe VMS after TAH at 45 yo, controlled with estrogen for 15 years.
  - Off MHT for 19 years . No VMS for years
  - Ischemic CVA a year ago, tob (2 cigs / day)
  - Depression exacerbation moderate , started on SNRI
  - Get message from her Gyne who prescribed her Transdermal estrogen

OHSU CPD

Case 5
79 yo female
I feel miserable
I need Estrogen

- 79 yo female
  - Severe VMS after TAH at 45 yo, controlled with estrogen for 15 years.
  - Off MHT for 19 years . No VMS for years
  - Ischemic CVA a year ago,   tob (2 cigs / day)
  - Depresison exacerbation moderate , started on SNRI , but she stopped it
  - Get message from her Gyne who prescribed her Transdermal estrogen

Wants to start estrogen because of poor energy, and dry skin and because helped her so much at time of surgical menopause.

OHSU CPD

Case 5
79 yo female
I feel miserable
I need Estrogen

- 79 yo female

POOR INDICATION MHT
HIGH RISK MHT

I know you want to feel better, and you felt great on estrogen in your 40s, but this is a different situation.   MHT is unlikely to help your depression and has risks.

Do not recommend you use it.   Let's try ….. Instead.

OHSU CPD

OHSU CPD

Case 6
New pt to you
78 yo on MHT

- 78 yo - anxiety , new radicular back pain, lymphocytic colitis, GERD, vulvar lichen sclerosis followed by gyne, on oral estradiol 1 mg

- After several visits and improvement in her radicular pain, you decide to delve into her MHT use.

OHSU CPD

Case 6
New pt to you
78 yo on MHT

- 78 yo - anxiety , new radicular back pain, lymphocytic colitis, GERD, vulvar lichen sclerosis followed by gyne, on oral estradiol 1 mg, s.p tah
- After several visits and improvement in her radicular pain, you decide to delve into her MHT use.
- NO hot flashes for years, even with missed dosesof estrogne . No insomnia when anxiety is controlled. On same dose for over 10 years.
- You suggest taper of estrogen and change to transdermal delivery.
- She is amenable has tapers to .05 mg transdermal Estradiol, and at next visit she reports no VSM

OHSU CPD

OHSU

CPD

Who is LOW risk for CVD ?

NO History of CVD

No MI, ACS, Unstable Angina, Stable Angina, Medically Managed Angina

No Ishemic Stroke, TIA

No Peripheral Vascular disease

NO Evidence of Subclinical CVD

Coronary Calcium Score 0

No Finding of CAD, CVD, PAD on imaging

(US, CT, MRI, Plain XR)

NO History of Diabetes, CKD3 or higher, HIV , Lipid Disorder

PREVENT Calculator INTERMEDIATE Risk 10 yr risk of CVD 5 -<10% and CAC score 0

PREVENT Calculator BORDERLINE RISK 10 yr risk CVD 3- <5 % and NO risk enhancer *

PREVENT Calculator LOW RISK 10 yr risk CVD <3%

Who is at higher risk for CVD ?

History of CVD

MI, ACS, Unstable Angina, Stable Angina, Medically Managed Angina,

Stroke, TIA

Peripheral Vascular Disease (including AAA)

Evidence of Subclinical CVD

Coronary Calcium Score > 0 , >100 A ,

Finding of CAD, CVD, PAD on imaging

(US, CT, MRI, ?Plain XR)

History of Diabetes, CKD3 or higher, HIV , Lipid Disorder, Lp(a) > 50 mg/dl

PREVENT Calculator HIGH Risk — 10 yr risk of CVD >= 10 %

PREVENT Calculator INTERMEDIATE Risk — 10 yr risk of CVD 5 -<10% (can consider CAC to clarify risk)

PREVENT Calculator BORDERLINE RISK — 10 yr risk CVD 3- <5 % and risk enhancer

*? Consider “Other Risk Enhancers” (f hx pcvd in FDR <55 M / < 65 F, high risk ancestry, high polygenic risk, chronic inflammatory diseases, Lp(a)>50 mg/dl , hsCRP >=2 > once and no secondary cause, CKM syndrome, reproductive risk markers (premature menopause, preeclampsia, gest DM, gest HTN, preterm delivery)

NAMS (The Menopause Society) Position Statement 2022

The initiation of hormone therapy by menopausal women older then 60 yrs requires careful consideration of individual risks and benefits (LEVEL I)

Long-term use of hormone therapy, including women over 60 yo, may be considered in healthly women at low risk for CVD …(LEVEL III)

Factors that should be considered are … underlying risk of .. CHD, CVA …

Hormone therapy does not need to be routinely discontinued in women aged older then 60 or 65 (LEVEL III)

Mitigation of risk through use of lowest effective dose and potentially non oral route of administration becomes increasingly important as women age with longer duration of therapy (LEVEL III)

Longer durations or extened use beyond age 65 should include periodic reevaluations of comorbidities and consideration of periodic trials of lowering or discontinuing hormone therapy.

THE END

Thanks to the OHSU CWH Menopause Team

lead by Emily Griffin MD