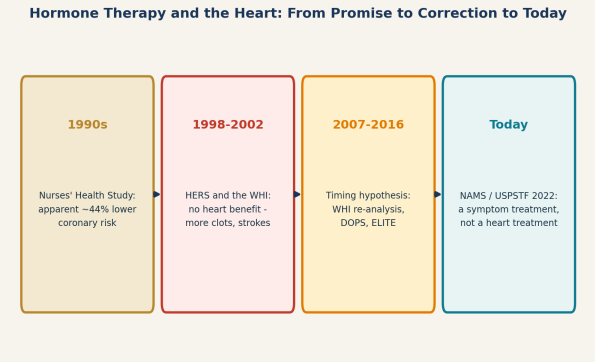
HRT: Cardiac and Vascular Health

What HRT means for coronary disease, heart failure, blood pressure, and your veins, condition by condition

Hormone therapy treats symptoms. It was never shown to protect the heart. What is safe for you depends on your own heart history.



Online: https://go.riasalimd.com/hrt-guide

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Names & Terms You Will Hear

Term	Meaning
Hormone therapy (HT), menopausal hormone therapy (MHT), hormone replacement therapy (HRT)	Estrogen, often with a second hormone, taken for menopause symptoms. MHT is today's preferred term.
Estrogen therapy (ET)	Estrogen alone, no progestogen. Used only in women without a uterus.
Estrogen-progestogen therapy (EPT)	Estrogen plus a progestogen. Used when the uterus is still there.
Systemic therapy	A pill, patch, gel, or spray. Raises estrogen levels body-wide.
Local (vaginal) therapy	A low-dose cream, tablet, ring, or insert placed in the vagina. Very little reaches the bloodstream.
Genitourinary syndrome of menopause (GSM)	Vaginal dryness and urinary symptoms from low estrogen.
Conjugated equine estrogens (CEE, brand Premarin)	An estrogen mix once made from mares' urine. The oral estrogen used in HERS and the WHI trials.
17-beta-estradiol	The estrogen your own ovaries make. Comes as a patch, gel, spray, or pill.
Estradiol valerate	A pill form of estradiol, used in some combination products.
Medroxyprogesterone acetate (MPA, brand Provera)	A man-made progestogen. Paired with CEE in Prempro and in the WHI trial.
Micronized progesterone (brand Prometrium)	A progesterone like the body's own. Often has fewer side effects.
Norethindrone acetate	A man-made progestogen used in several patches and pills.

Term	Meaning
Combination products (Prempro, Activella, Bijuva, Combipatch, Climara Pro)	Brand pills or patches with both hormones already combined.
Bazedoxifene/CEE (brand Duavee)	Estrogen paired with a SERM instead of a progestogen. No separate progestogen is needed.
Prasterone/DHEA (brand Intrarosa)	A vaginal insert for painful sex after menopause. FDA-approved.
Ospemifene (brand Osphena)	A daily pill for painful sex after menopause. A SERM, not an estrogen.
Compounded 'bioidentical' hormones and pellets	Custom-mixed hormones from a compounding pharmacy. Not FDA-approved; dosing is not standardized.
Venous thromboembolism (VTE)	A blood clot in a leg vein or in the lung. The main safety concern with pills.

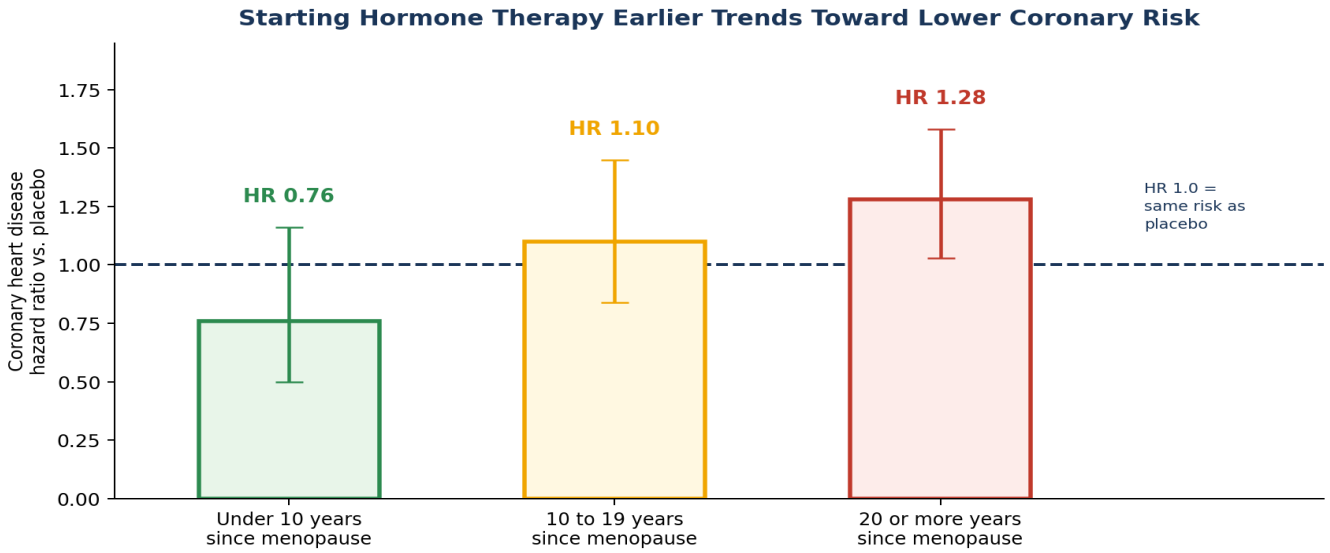
The one idea to hold onto: hormone therapy treats menopause symptoms. It was never shown to protect the heart. That belief came from data that did not hold up in later trials. What is safe for you depends on your own heart history, not a headline.

HRT: Cardiac and Vascular Health?

- Hormone therapy replaces the estrogen your ovaries stop making at menopause. If your uterus is still there, it also includes a progestogen.
- Two choices define it: whole-body (systemic) or vaginal-only (local); and estrogen alone or estrogen plus a progestogen.
- It is FDA-approved for hot flashes, night sweats, vaginal and urinary symptoms, and to prevent bone loss.
- It is not FDA-approved to prevent heart disease. No trial has ever shown that it does.
- 'Bioidentical' is mostly a marketing word. FDA-approved estradiol and progesterone ARE chemically identical to your own hormones. Compounded pellets and creams sold as 'bioidentical' are different: unregulated, with no standard dose.

Why It Matters

- In the 1990s, big studies watched women over time. The largest, the Nurses' Health Study, found women taking estrogen had about half the rate of major heart disease.
- That comparison was misleading. Women who chose hormone therapy back then were healthier to start with. This is called 'healthy-user bias.' The same bias later undid an early promise for vitamin E.
- The first randomized trial, HERS (1998), tested hormone therapy in women who already had heart disease. It found no overall benefit. It found more heart events in year one.
- The Women's Health Initiative (WHI) tested hormone therapy in healthy women. Its estrogen-plus-progestin arm stopped early, in 2002. It found more heart attacks, strokes, and blood clots. It found fewer hip fractures.
- The WHI also tested estrogen alone, in women without a uterus. That arm told a different story. Stroke and clots still rose. Heart attack risk did not. Breast cancer trended lower. Estrogen alone is not the same drug as estrogen plus progestin.
- Prescribing collapsed almost overnight after 2002. Many women stopped, even those with severe symptoms.
- One detail mattered. WHI women averaged 63 years old. Most were more than 10 years past menopause. A 2007 study looked closer. It found a hint of lower heart risk when therapy started within 10 years of menopause. It found clearly higher risk starting 20 or more years later. This is the timing hypothesis.
- Smaller trials tested timing directly. The results were mixed. None proves hormone therapy protects the heart, even started early.
- Eighteen years of WHI follow-up, published in 2017, found no difference in deaths, from any cause, the heart, or cancer, between the two groups.
- Today, The Menopause Society (2022) and the US Preventive Services Task Force (2022) agree. Hormone therapy treats symptoms. It has never been shown to protect the heart. It should not be started to try.



From the WHI's 2007 re-analysis (Rossouw et al.): heart disease risk by years since menopause at the start of therapy. Starting earlier trends toward lower risk, but this trend was not statistically significant. Stroke risk was higher no matter when therapy started.

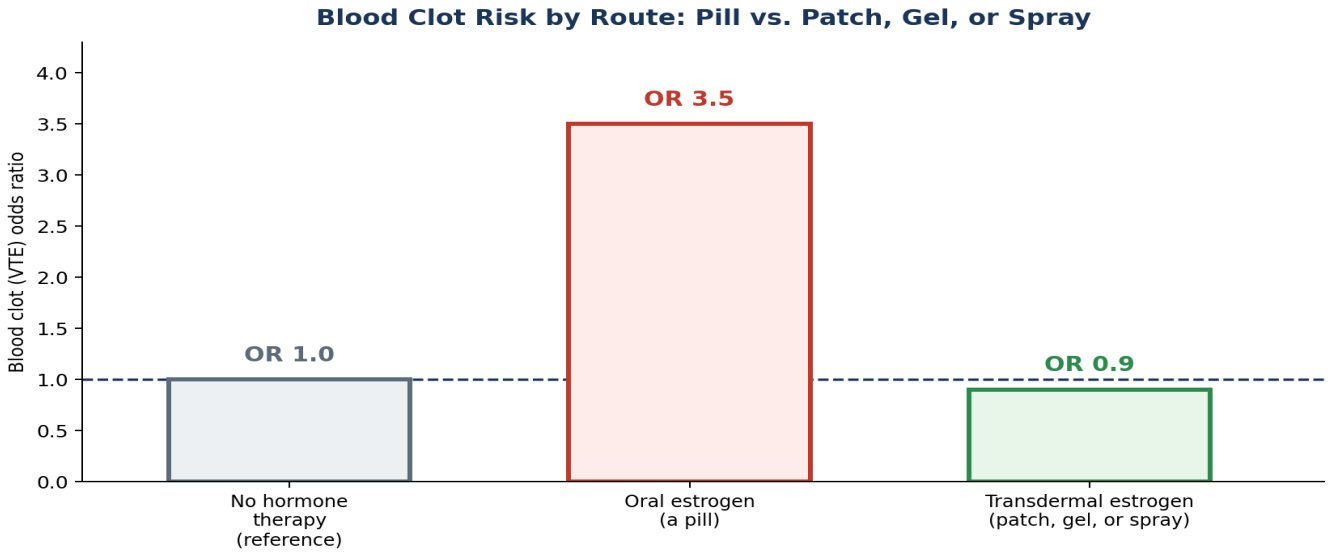
Risk Factors

Some patients are more likely to develop this condition. Knowing your risk helps your care team take extra precautions.

Risk Factor	Why It Increases Risk
Prior breast cancer or another hormone-driven cancer	Estrogen can fuel this kind of tumor. Usually avoided; always decided with oncology.
Prior stroke or TIA	The WHI found higher stroke risk at every age. Whole-body therapy is usually avoided.
Migraine with aura	Raises stroke risk on its own. A pill adds to that risk.
Active liver disease	The liver processes oral estrogen first. A patch or gel may be an option instead.
Unexplained vaginal bleeding	Must be checked before starting estrogen. It could hide a uterine problem.
Smoking	Smoking adds to estrogen's own clotting risk.
Obesity or metabolic syndrome	Raises clot risk on its own. A patch or gel is usually preferred.
Gallbladder disease	Pills raise the risk of gallstones and gallbladder surgery. A patch or gel may carry less risk.
Prior blood clot, or a clotting disorder such as factor V Leiden	Pills are usually avoided. Factor V Leiden alone multiplies clot risk about sevenfold.
Starting after 60, or more than 10 years past menopause	This group had higher heart and stroke risk in the WHI. The heart-timing window has closed.

Treatment Options

- Hormone therapy treats hot flashes, night sweats, vaginal and urinary symptoms, and bone loss. It does not protect the heart.
- For a healthy woman under 60, or within about 10 years of her last period, treating symptoms is a reasonable choice.
- Use the lowest dose that works, for as long as needed. The Menopause Society dropped its old rule to stop at 5 years or age 65 in 2022. Now you and your doctor check in on it over time.
- Route matters. A patch, gel, or spray skips the liver. It carries little or no added clot risk. A pill roughly triples clot risk.
- For vaginal or urinary symptoms alone, local (vaginal) estrogen works with very little reaching the bloodstream. This is often the lowest-dose answer.
- If your uterus is still there, estrogen is always paired with a progestogen, or in one product, a SERM. Estrogen alone can overgrow the uterine lining and raise cancer risk.
- Compounded 'bioidentical' hormones and pellets are not FDA-approved. Dosing is not standardized. There is no safety data on outcomes. They are not a safer choice.
- Once started, hormone therapy is checked again on a schedule, usually yearly. This confirms it is still needed and still the safest choice for you.



From the ESTHER study (Scarabin et al.): a pill roughly triples the odds of a blood clot. A patch, gel, or spray does not. A pill also passes through the liver first, which is why it can raise blood pressure in a few women; a patch, gel, or spray is more blood-pressure neutral.

Hormone Therapy by Heart Condition, At a Glance

Condition	Systemic HT	Vaginal estrogen	What to do instead
No heart disease	Reasonable for symptoms	Yes, for vaginal/urinary symptoms	Not needed
Coronary artery disease	Do not start to protect the heart. Continuing an existing prescription is a talk with cardiology.	Usually fine	Statin and blood pressure care. A non-hormonal medicine for symptoms.
Heart failure (HFrEF or HFpEF)	Decide with cardiology. Outcome data is essentially absent.	Usually fine	Standard heart-failure care. A non-hormonal medicine for symptoms.
High blood pressure, controlled	Not a barrier. Prefer a patch, gel, or spray. Recheck blood pressure after starting.	Usually fine	Control blood pressure first if needed.
Peripheral artery disease	No vascular benefit shown. Do not start for that reason.	Usually fine	Standard PAD care. A non-hormonal medicine for symptoms.
Prior blood clot or clotting disorder	Pills usually avoided. A patch or gel needs a careful, personal talk.	Usually fine	A non-hormonal medicine. Hematology input if a clotting disorder is known.
Varicose veins or venous insufficiency alone	Not a barrier by itself	Yes	Not needed

No Heart Disease

- With no heart disease, and within the timing window (usually under 60, or within about 10 years of your last period), hormone therapy for symptoms is a reasonable choice.
- The rule is the lowest dose that works, for as long as needed. Not an automatic stop at 5 years or age 65.
- For vaginal or urinary symptoms alone, local estrogen is the lowest-dose option. Very little reaches the bloodstream.
- Route still matters, even in a healthy woman. A patch, gel, or spray carries little added clot risk. A pill roughly triples it.
- See our Menopause and Heart Health guide for how menopause itself changes heart risk, apart from the therapy decision here.

Coronary Artery Disease (CAD)

- Whole-body hormone therapy is not recommended to protect the heart, in anyone. HERS tested this directly in women who already had heart disease. It found no benefit, and more heart events in year one.
- Never start hormone therapy to protect your heart, or because you have CAD.
- If a woman with CAD is already on hormone therapy for symptoms when heart disease is found, HERS's own authors said continuing could be reasonable, since its later years showed no added risk. This is a decision for you and your cardiologist, not a fixed rule.
- Local (vaginal) estrogen for symptoms alone is usually fine even with CAD, given how little reaches the bloodstream.
- See our Heart Disease in Women guide for more on coronary risk in women.

Heart Failure: HFrEF and HFpEF

- Outcome data on hormone therapy in women who already have heart failure is essentially absent. No major trial specifically enrolled these women.
- Estrogen can cause fluid and salt retention. That is a theoretical concern in a heart already struggling with fluid, though it has not been directly tested.
- HFpEF, the stiff-heart type, affects postmenopausal women more than others. That does not mean hormone therapy helps it. Being common in the same group is not evidence of benefit.
- See our HFpEF guide for more on this condition.
- This is a decision for you and your cardiologist, not a general guide like this one.

Hypertension and Hypertensive Heart Disease

- Controlled high blood pressure is not, by itself, a reason to avoid hormone therapy.
- Oral estrogen passes through the liver first. In a few women, that raises blood pressure. A patch, gel, or spray skips this step.
- Get your blood pressure under control before starting. Recheck it again after.
- See our High Blood Pressure guide for how to get there.
- Uncontrolled high blood pressure should be treated first. It is not a permanent barrier.

Peripheral Artery Disease (PAD)

- No trial has shown a vascular benefit from hormone therapy in PAD, or in any artery disease outside the heart.
- Do not start hormone therapy to help PAD, or any blood-vessel disease outside the heart.
- The same stroke and clotting risks elsewhere in this guide apply here too.
- See our Peripheral Artery Disease guide for standard PAD care.
- Treat PAD with its own proven tools: supervised walking, statins, blood pressure control, and not smoking.

Venous Disease: Blood Clots, Varicose Veins, and Venous Insufficiency

- Blood clots are the single biggest vascular concern with hormone therapy. Risk is highest in year one.
- A pill roughly triples clot risk. A patch, gel, or spray carries little or no added risk, based on the ESTHER study and later reviews.
- A prior blood clot, or a known clotting disorder such as factor V Leiden, usually rules out oral whole-body therapy. Factor V Leiden alone multiplies clot risk about sevenfold.
- Varicose veins and venous insufficiency are a different problem from a blood clot. They are NOT, by themselves, a reason to avoid hormone therapy. These get confused constantly, but they are not the same thing.
- See our Blood Clots (DVT) guide, Varicose Veins guide, and Venous Insufficiency guide for more on each.

Premature Ovarian Insufficiency and Early or Surgical Menopause

- Premature ovarian insufficiency (POI, before about 40) and early menopause (before about 45) are different from typical menopause. The ovaries stop working years or decades early.
- Here, the usual caution flips. Hormone therapy is usually RECOMMENDED, not just allowed, up to about age 51, the average age of natural menopause.
- Without it, these women face years of extra low-estrogen exposure. That is linked to higher long-term heart and bone risk than typical-age menopause.
- This is one of the most missed points in this whole topic. A 35-year-old after ovary removal is not the same patient as a 63-year-old, and should not get the same counseling.
- The goal is different too: replacing hormone levels that would still be circulating naturally, not adding hormones on top of normal menopause.
- The decision to eventually stop, and the dose, are still personal. But the default here leans toward treatment.

Comfort Measures at Home (No Medication Needed)

These simple steps support healing and ease symptoms. Use them alongside any medication your doctor prescribes.

- Dress in layers. Keep the bedroom cool at night.
- Know your triggers. Spicy food, caffeine, alcohol, and hot drinks are common ones.
- Try slow, paced breathing when a hot flash starts.
- Regular exercise, a healthy weight, and not smoking all ease symptoms. They protect your heart too.
- Cognitive behavioral therapy (CBT) has good evidence for hot flashes and the stress they cause.
- For dryness alone, a plain vaginal moisturizer or lubricant may be enough, with no hormone at all.

Non-Hormonal Prescription Options

- SSRIs and SNRIs: paroxetine 7.5 mg (brand Brisdelle) is the only nonhormonal medicine FDA-approved for hot flashes. Other SSRIs and SNRIs are used off-label, with good trial evidence.
- Gabapentin: an anti-seizure medicine that also eases hot flashes, especially at night.
- Oxybutynin: normally a bladder medicine. Low doses also reduce hot flashes.
- Fezolinetant (brand Veozah): FDA-approved in 2023. The first drug built just for hot flashes, not repurposed. In December 2024, the FDA added a boxed warning for rare, serious liver injury. It needs blood tests before starting, and again through the first year.
- Elinzanetant (brand Lynkuet): FDA-approved in October 2025. It blocks two receptors instead of one. Its trials found no excess liver injury, and its own safety board skipped routine monitoring. It has a shorter track record than fezolinetant.
- Each of these is a real first choice, not just a fallback, when your heart, clotting, or cancer history rules out hormone therapy.

Risks, Benefits, and Alternatives

Every choice has trade-offs. Use this table to start the shared decision conversation.

Option	Risks	Benefits	Alternatives
Whole-body hormone therapy for symptoms, in a healthy woman under 60 or within 10 years of menopause	Higher blood clot and stroke risk than a non-user. Gallbladder disease with a pill.	The most effective treatment for hot flashes and night sweats. Also protects bone; fewer hip fractures in the WHI.	A patch or gel instead of a pill. A non-hormonal medicine. No treatment if symptoms are mild.
Oral (pill) hormone therapy	Roughly triples clot risk. May raise blood pressure in a few women.	Familiar, low-cost, once-daily dosing. Decades of safety data.	A patch, gel, or spray. Little or no added clot risk.
Local (vaginal) estrogen for vaginal or urinary symptoms alone	Very small. Little reaches the bloodstream. Not the same risk as a pill or patch.	Treats vaginal dryness, irritation, and related urinary symptoms well.	A moisturizer or lubricant with no hormone. Prasterone (Intrarosa) or ospemifene (Osphena), two other non-estrogen options.
Compounded 'bioidentical' hormones or pellets	Not FDA-approved. Dosing is not standardized. No outcome data on heart, clot, or cancer risk.	None shown beyond FDA-approved products. 'Natural' is not the same as 'safer.'	An FDA-approved estradiol or progesterone product, with a known, tested dose.
A non-hormonal medicine (an SSRI/SNRI, gabapentin, fezolinetant, or elinzanetant)	Each has its own side effects. Fezolinetant carries an FDA warning for rare liver injury and needs blood tests.	Avoids hormone-related clot, stroke, and cancer risk. A real option, not just a fallback.	Hormone therapy, if nothing rules it out. Cognitive behavioral therapy. Lifestyle steps.

Common Misconceptions

Myth	Reality
Hormone therapy protects the heart.	It does not. No trial has shown that starting hormone therapy protects the heart. HERS and the WHI found no benefit, and in some groups, more risk.
The WHI proved hormones are dangerous for every woman.	The WHI tested older women, averaging 63, mostly over 10 years past menopause. Its estrogen-alone arm did not raise heart-attack risk, and breast cancer trended lower. This does not describe a 52-year-old with hot flashes.
Compounded 'bioidentical' hormones are safer because they are natural.	They are not FDA-approved. Dosing is not standardized. There is no safety data. FDA-approved estradiol and progesterone are ALSO chemically identical to your own hormones, and they ARE tested and regulated.
You must stop at 5 years, or by age 65.	That fixed rule is outdated. The Menopause Society's 2022 guidance calls for a personal decision, checked again over time, based on your symptoms and health.
Vaginal estrogen carries the same risks as a pill or patch.	Vaginal estrogen reaches the bloodstream only in small amounts. Its risk is not the same as whole-body therapy, even for many women who cannot take a pill or patch.
Varicose veins mean I cannot take hormone therapy.	Varicose veins are not blood clots. They are not, by themselves, a reason to avoid hormone therapy. A prior clot or a known clotting disorder is the real concern.
The USPSTF says never use hormone therapy.	The USPSTF's 2022 'D' grade is about using hormone therapy to PREVENT disease in a woman with no symptoms. It does not cover treating hot flashes, night sweats, or vaginal symptoms.

Possible Complications

Knowing what can go wrong helps you spot problems early. Most complications are uncommon, especially with treatment.

Where / What	What Can Happen
Cardiovascular: heart attack	Starting late, after 60 or more than 10 years past menopause, raised heart-attack risk in the WHI. Starting for symptoms within the timing window has not shown this same rise.
Cerebrovascular: stroke	Hormone therapy raised stroke risk in the WHI at every age tested. Timing does not seem to remove this risk.
Venous: blood clots (DVT, pulmonary embolism)	Oral estrogen roughly triples clot risk. Risk is highest in year one, and rises further with age, weight, and inherited clotting disorders.
Hepatobiliary: gallbladder disease	Oral estrogen raises the risk of gallstones and gallbladder surgery, confirmed in HERS.
Reproductive: uterine (endometrial) cancer	Estrogen alone, with the uterus still there, can overgrow the uterine lining and raise cancer risk. That is why a progestogen, or Duavee's SERM, is always paired with it.
Reproductive: breast cancer	Estrogen plus a progestogen raised breast-cancer risk in the WHI. Estrogen alone, in women without a uterus, trended toward lower risk, not higher.

Points to Know

If you remember nothing else, remember these key points.

- Hormone therapy treats symptoms. It has never been shown to protect the heart.
- For a healthy woman under 60, or within about 10 years of menopause, treating symptoms is a reasonable choice.
- Route matters: a pill roughly triples clot risk. A patch, gel, or spray does not.
- For vaginal or urinary symptoms alone, local estrogen is the lowest-dose option.
- A prior blood clot, stroke, hormone-driven cancer, or active liver disease usually rules out whole-body therapy. Varicose veins alone do not.
- Compounded 'bioidentical' hormones and pellets are not FDA-approved, and are not a safer choice.
- There is no fixed stop date. Check in with your doctor regularly.
- Non-hormonal medicines are real options, not just fallbacks, when hormone therapy is not safe for you.

When to Call Us - and When to Call 911

If you are not sure, call. We would rather hear from you twice than miss a real problem.

- Sudden leg pain, swelling, warmth, or redness in one leg - call us today. This can be a blood clot.
- Sudden shortness of breath, chest pain, or coughing blood - call 911. This can be a clot in the lung.
- Chest pain, pressure, or tightness - call 911.
- Sudden weakness on one side, trouble speaking, or a severe sudden headache - call 911. This can be a stroke.
- Yellow skin or eyes, dark urine, or pain in the upper right belly on a new medicine - stop it and call us. This can be a liver problem.
- Vaginal bleeding after menopause, or any new bleeding on hormone therapy - call us.
- A new breast lump or change - call us.
- Questions about hormone therapy, or a non-hormonal option, for your own heart history - call our office.

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Trusted Resources

The links below are the trusted resources Dr. Ali used to write this guide and that he recommends you visit for more information. Each is a clickable link in the digital version and a Short.io tracked URL on the printed version.

- The Menopause Society (NAMS) - Patient Education - A plain-language hub on hormone therapy from the leading US menopause society.
- Mayo Clinic - Hormone Therapy: Is It Right for You? - Candidacy, timing, and the pill-versus-patch choice, explained simply.
- Cleveland Clinic - Hormone Replacement Therapy (HRT) - An overview of forms, routes, and who should generally avoid it.
- FDA - Veozah (fezolinetant) Liver Injury Warning - The FDA's own warning on fezolinetant's boxed warning and required liver checks.

Sources Used to Build This Guide

Every recommendation in this guide is grounded in one or more of the studies, guidelines, or trusted resources below. Short links are tracked so Dr. Ali can see which references patients are reading; nothing personally identifying is captured.

- Hulley et al., Randomized Trial of Estrogen Plus Progestin for Secondary Prevention of Coronary Heart Disease in Postmenopausal Women (HERS), JAMA 1998; PMID 9718051 *[Clinical Study]*
  First RCT of hormone therapy: secondary prevention in women with established CHD. No overall benefit; more CHD events in year 1 in the hormone group; more venous thromboembolism (RH 2.89) and gallbladder disease.
- Grady et al., Cardiovascular Disease Outcomes During 6.8 Years of Hormone Therapy: HERS II, JAMA 2002; PMID 12090862 *[Clinical Study]*
  HERS open-label follow-up: the early apparent benefit in years 3-5 of HERS did not persist through 6.8 years. Hormone therapy should not be used to reduce CHD risk in women with CHD.
- Hulley et al., Noncardiovascular Disease Outcomes During 6.8 Years of Hormone Therapy: HERS II, JAMA 2002; PMID 12090863 *[Clinical Study]*
  Venous thromboembolism and gallbladder-surgery risk over the full HERS/HERS II follow-up period.
- Rossouw et al. (Writing Group for the WHI Investigators), Risks and Benefits of Estrogen Plus Progestin in Healthy Postmenopausal Women: WHI Principal Results, JAMA 2002; PMID 12117397 *[Clinical Study]*
  The WHI estrogen-plus-progestin arm, stopped early. Primary source for the CHD, breast cancer, stroke, VTE, colorectal cancer, and hip fracture hazard ratios cited throughout this guide.
- Anderson et al. (WHI Investigators), Effects of Conjugated Equine Estrogen in Postmenopausal Women With Hysterectomy: WHI Randomized Controlled Trial, JAMA 2004; PMID 15082697 *[Clinical Study]*
  The WHI estrogen-alone arm in hysterectomized women. Source for the CHD/stroke/breast-cancer asymmetry versus the combined-hormone arm.
- Cushman et al., Estrogen Plus Progestin and Risk of Venous Thrombosis, JAMA 2004; PMID 15467059 *[Clinical Study]*
  WHI venous thrombosis hazard ratio (2.06) and how age, obesity, and factor V Leiden multiply hormone-associated clot risk.
- Stampfer et al., Postmenopausal Estrogen Therapy and Cardiovascular Disease: Ten-Year Follow-Up From the Nurses' Health Study, NEJM 1991; PMID 1870648 *[Clinical Study]*
  The observational-era finding (RR 0.56 for major coronary disease in current estrogen users) that shaped decades of prescribing before HERS and WHI.
- Grodstein et al., Postmenopausal Hormone Therapy and Mortality, NEJM 1997; PMID 9187066 *[Clinical Study]*
  Nurses' Health Study mortality data illustrating the same cohort's benefit signal and its limits (attenuation with long-term use).
- Rossouw et al., Postmenopausal Hormone Therapy and Risk of Cardiovascular Disease by Age and Years Since Menopause, JAMA 2007; PMID 17405972 *[Clinical Study]*
  The WHI age-stratified reanalysis behind the timing hypothesis: CHD hazard ratio by years since menopause (under 10y, 10-19y, and 20y or more) and by age group; also shows stroke risk was not reduced by earlier timing.
- Hodis et al., Vascular Effects of Early Versus Late Postmenopausal Treatment With Estradiol (ELITE), NEJM 2016; PMID 27028912 *[Clinical Study]*

Tested the timing hypothesis directly using carotid intima-media thickness (a surrogate imaging marker, not clinical events) in early versus late postmenopausal women.

- Schierbeck et al., Effect of Hormone Replacement Therapy on Cardiovascular Events in Recently Postmenopausal Women: Randomised Trial (DOPS), BMJ 2012; PMID 23048011 *[Clinical Study]*
  Danish Osteoporosis Prevention Study: hormone therapy started early (within about a year of menopause) reduced a composite of death, heart failure admission, and MI over 10 years, without a significant rise in cancer, VTE, or stroke.
- Miller et al., The Kronos Early Estrogen Prevention Study (KEEPS): What Have We Learned?, Menopause 2019; PMID 31453973 *[Clinical Study]*
  KEEPS investigator summary: low-dose oral CEE or transdermal estradiol in recently menopausal women did not slow carotid intima-media thickness progression, but caused no severe adverse effects including no excess venous thrombosis over 4 years.
- Manson et al. (WHI Investigators), Menopausal Hormone Therapy and Long-term All-Cause and Cause-Specific Mortality: The WHI Randomized Trials, JAMA 2017; PMID 28898378 *[Clinical Study]*
  18-year cumulative follow-up of both WHI hormone trials: hormone therapy was not associated with all-cause, cardiovascular, or cancer mortality.
- The 2022 Hormone Therapy Position Statement of The North American Menopause Society (NAMS/The Menopause Society), Menopause 2022; PMID 35797481 *[Guideline]*
  Current professional-society guidance: the timing window (under 60 or within 10 years of menopause), individualized route/dose/duration, and moving away from an arbitrary stop at 5 years or age 65 toward periodic reassessment.
- US Preventive Services Task Force, Hormone Therapy for the Primary Prevention of Chronic Conditions in Postmenopausal Persons: Recommendation Statement, JAMA 2022; PMID 36318127 *[Guideline]*
  Source of the USPSTF Grade D recommendation. Critical nuance emphasized in this guide: the D grade applies to using hormone therapy to prevent chronic disease, not to treating menopausal symptoms.
- Scarabin et al., Differential Association of Oral and Transdermal Oestrogen-Replacement Therapy With Venous Thromboembolism Risk (ESTHER study), Lancet 2003; PMID 12927428 *[Clinical Study]*
  Direct comparison of oral versus transdermal estrogen and VTE risk: oral OR 3.5 vs non-users, transdermal OR 0.9 vs non-users, oral vs transdermal OR 4.0. Primary source for the route-comparison diagram.
- Pinkerton et al., Low-Dose Paroxetine (7.5 mg) Improves Sleep in Women With Vasomotor Symptoms Associated With Menopause, Menopause 2015; PMID 25137243 *[Clinical Study]*
  Confirms paroxetine mesylate 7.5 mg as the only nonhormonal medication FDA-approved for moderate-to-severe vasomotor symptoms, and its pivotal-trial design (n=591 vs 593 placebo).
- Riemma et al., Efficacy of Low-Dose Paroxetine for the Treatment of Hot Flushes: Systematic Review and Meta-Analysis of Randomized Trials, Medicina 2019; PMID 31480427 *[Clinical Study]*
  Pooled effect size for paroxetine 7.5 mg versus placebo on weekly hot-flush frequency (5 RCTs, 1,482 women).
- Lewis et al., Liver Safety of the Dual Neurokinin-1/-3 Receptor Antagonist Elinzanetant, Drug Safety 2026; PMID 41849128 *[Clinical Study]*
  Pooled phase 1-3 liver-safety data for elinzanetant (no imbalance vs placebo in ALT/AST elevations, no Hy's-Law cases); direct comparison point against fezolinetant's boxed warning.

- FDA Drug Safety Communication: FDA Adds Warning About Rare Occurrence of Serious Liver Injury With Use of Veozah (fezolinetant) *[Regulatory]*
  Primary regulatory source for fezolinetant's FDA approval (May 2023) and the boxed warning for rare serious liver injury added December 2024, including the required liver-monitoring schedule.
- The Menopause Society (NAMS) - Patient Education: Hormone Therapy *[Patient Education]*
  Plain-language patient hub from the leading US menopause professional society, cross-linked as a trusted resource.
- Mayo Clinic - Hormone Therapy: Is It Right for You? *[Patient Education]*
  Patient-facing explanation of candidacy, timing, and the oral-versus-transdermal choice.
- Cleveland Clinic - Hormone Replacement Therapy (HRT) *[Patient Education]*
  Plain-language overview of formulations, routes, and risks used for competitor benchmarking and the synonyms/route content.

About This Guide

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Reviewer note: Reviewed: The Menopause Society's patient hub, Mayo Clinic, and Cleveland Clinic. This guide adds more. It gives the real HERS, WHI, DOPS, and ELITE numbers, not a one-line verdict. It has a timing chart and an oral-versus-patch clot chart. It covers seven heart conditions, one by one. It gives real space to premature ovarian insufficiency, the most missed point in this topic. It corrects the 'USPSTF says never use it' misreading.

Disclaimer

This guide is for educational purposes only and does not replace medical advice from your physician. Recommendations may not apply to every patient. Always follow the specific instructions of Dr. Ali and your care team. In an emergency call 911 or go to the nearest emergency department.

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