

The WHI hormone trial was designed to answer questions about preventing life-threatening diseases

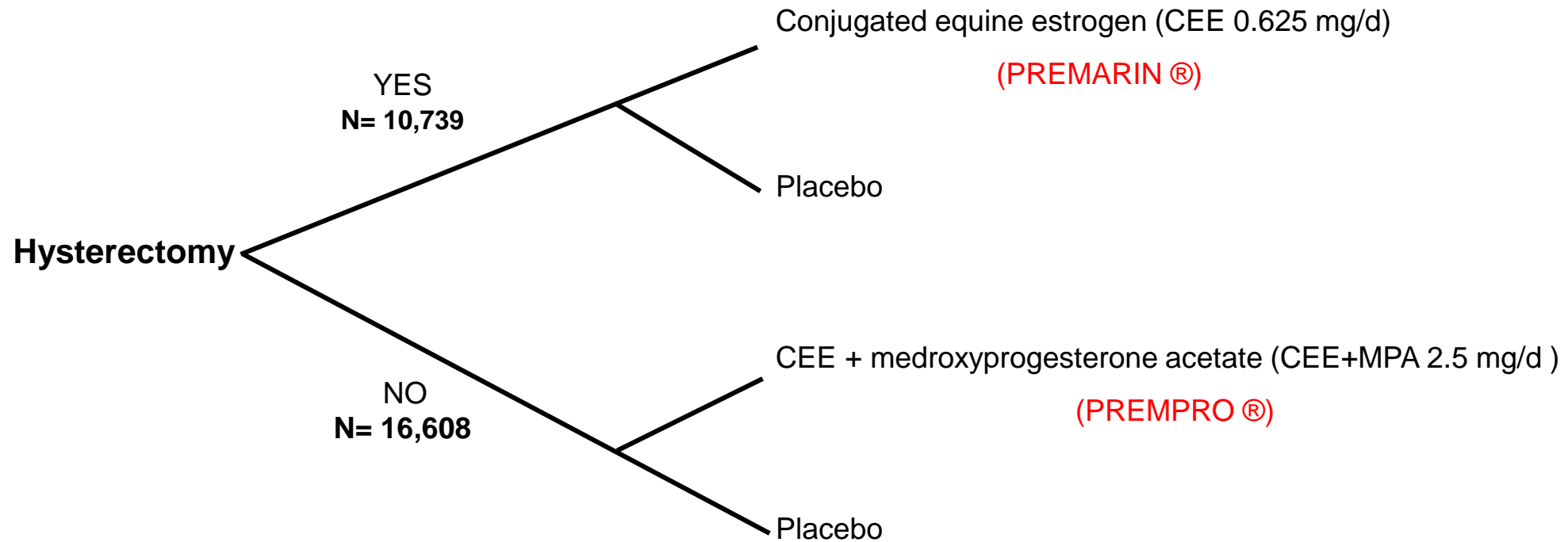


1: Does hormone therapy reduce the risk of heart?

2: Does hormone therapy reduce the risk of hip fractures?

Safety: Does hormone therapy increase the risk of breast cancer?

- Prior studies had suggested we could expect to see a 22% or greater reduction in CHD risk over 9 years
- There was concern that hormones would increase breast cancer rates, by about 14% over a longer timeframe



WHI Study Group. Control Clin Trials. 1998;19(1):61-109;
Stefanick et al, Ann Epidemiol. 2003 Oct;13(9 Suppl):S78-86.

WHI Hormone Therapy trial was really 2
separate trials done in parallel



Both trials were stopped early by an independent committee of experts who were monitoring the trial.

Risk and benefits of hormones, informed by WHI

Hormone therapy benefits

Relieve menopausal symptoms

Prevent fractures

Reduce endometrial cancer risk (combined hormones only)

May reduce colorectal cancer risk (combined hormones only)

May reduce breast cancer risk (estrogen only)

Hormone therapy risks

Increase stroke risk

Increase blood clot rates

Increase risk of mild cognitive impairment and dementia (in older women)

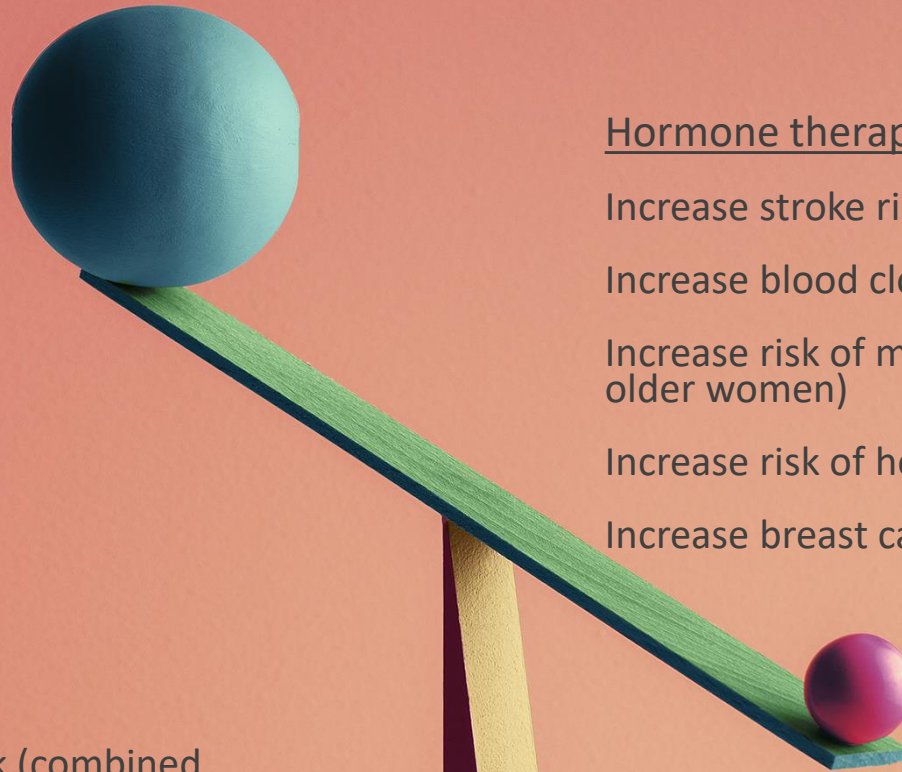
Increase risk of heart disease (combined hormones only)

Increase breast cancer risk (combined hormones only)

Conclusions:

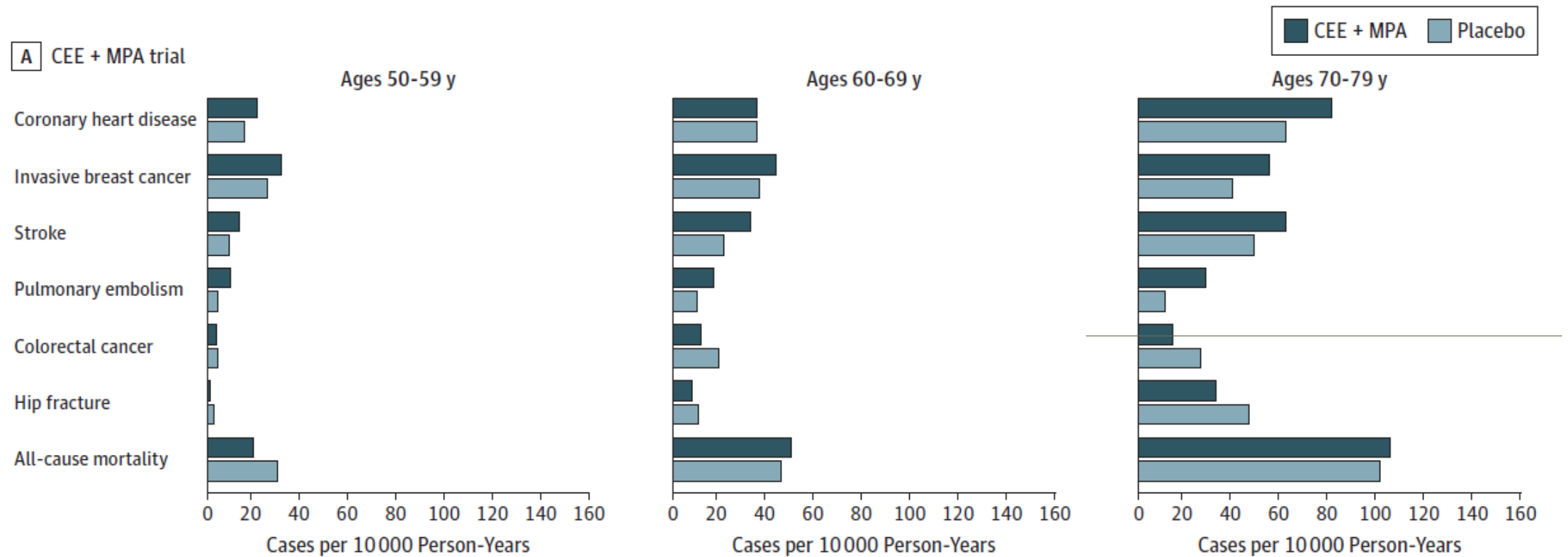
These risk/benefit profiles do not support hormone therapy use for disease prevention.

It is reasonable for women with moderate to severe menopausal symptoms to consider use (lowest dose, duration needed) to relieve symptoms, depending on their risk of other conditions.

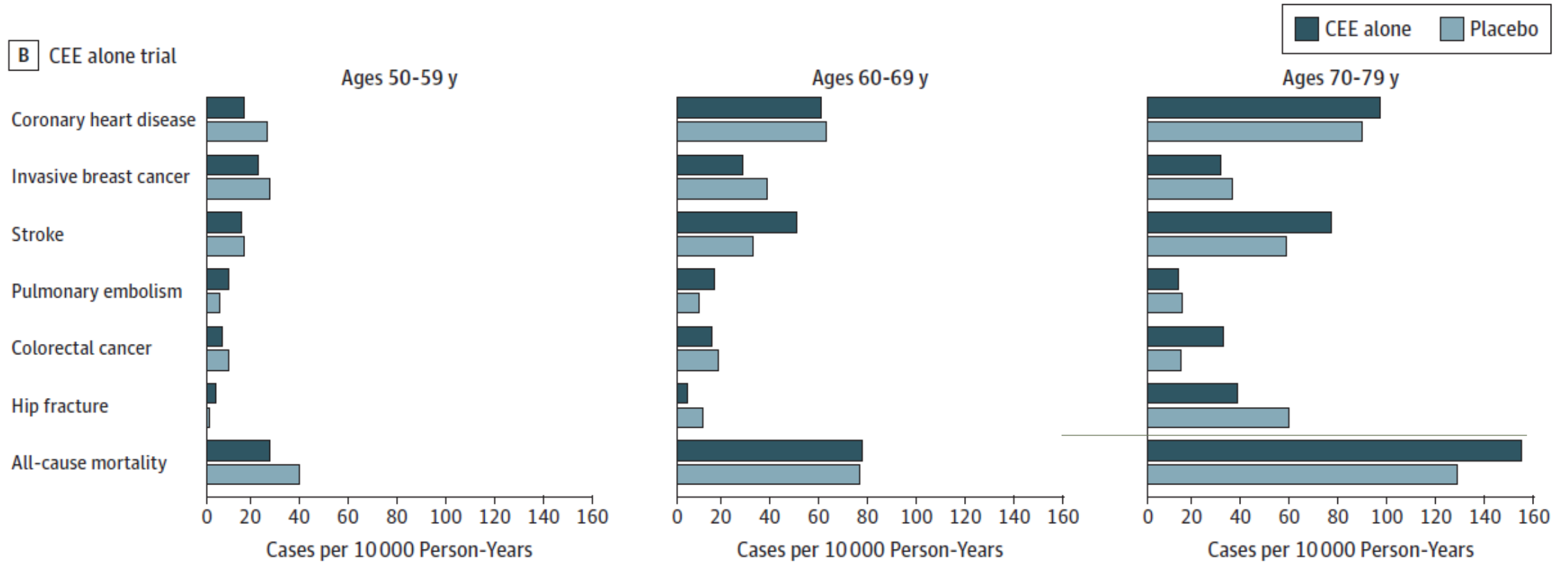


Disease rates increase with age but Estrogen + Progestin seems to have the same effect in each age-group

Figure 3. Absolute Risks of Health Outcomes by 10-Year Age Groups in the Women's Health Initiative Hormone Therapy Trials During the Intervention Phase



Estrogen alone was somewhat beneficial for younger women but was unsafe for older women



None of the age interactions were statistically significant (at the $P < .05$ level), except for colorectal cancer, all-cause mortality, myocardial infarction, and the

global index in the CEE alone trial (details appear in Figure 5). CEE indicates conjugated equine estrogens; MPA, medroxyprogesterone acetate.

The timing of hormone use matters:

- Age at starting, duration of use, and time since last use all influence hormone effects . . . And these effects vary by disease
 - Hormone therapy increased the risk of heart disease in the first couple of years of use, and then this increased risk diminished
 - Estrogen plus progestin increased the risk of breast cancer; the longer the use, the greater the risk
 - Most benefits and risks seemed to go away rather quickly after women stopped using them,
 - Breast cancer effects persisted long after women stopped using hormones



Impact of the estrogen plus progestin trial results

By 2012, there were

- 4.3 million fewer users of estrogen plus progestin
- 126,000 fewer breast cancer cases
- 76,000 fewer cases of cardiovascular disease
- 263,000 more fractures
- 145,000 more quality adjusted life years

These changes reduced direct medical expenditures in the US by an estimated \$35.2 billion

WHI results have . . .

- Informed us of the complex nature of hormone therapy impact on women's bodies
- Changed clinical practice
- Improved women's health
- Saved money
- Improved some of our scientific methods.

Resurgence of the WHI criticism, misinformation, and misdirection

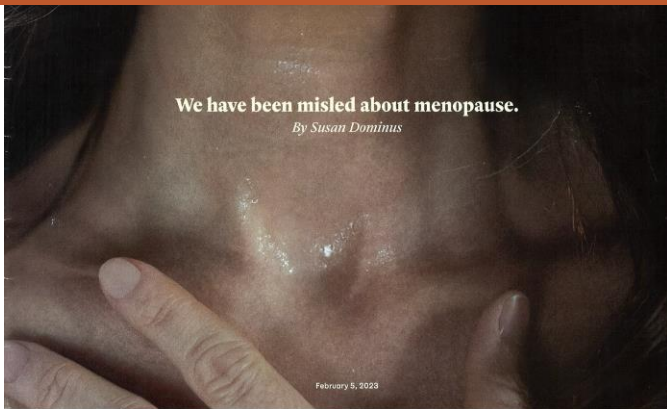


“We have been misled about menopause.”

By Susan Dominus

14 page article (available online and in print)

You asked the wrong question!



Regarding the WHI, the author states that “the study itself was designed with what would come to be seen as a major flaw. W.H.I. researchers wanted to be able to measure health outcomes – how many women had strokes, heart attacks, or cancer – but those ailments may not show up until women are in their 70s or 80s . . .”

The heavily edited WHI response appeared only in print on February 26, 2023

The objective of the W.H.I was never to test the use of menopausal hormone therapy for treating menopausal symptoms; its purpose was to focus on other unanswered questions

...

WHI definitively established that menopausal hormone therapy should not be used to prevent heart disease, stroke and other chronic diseases, an increasingly common practice at the time [of study initiation.

The Thread

Readers respond to our stories.

RE: SZA'S RUINATION BROUGHT HER EVERYTHING *Danyel Smith profiled the pop star.*

This is a stunningly well-written article, not just about the amazing SZA, but about (Black) women in R.&B., in general — one of the best pieces I've ever read about the (recent) history of R.&B. and hip-hop. I will definitely get a copy of the author's book! Kudos to both her and the brave, beautiful artist who is SZA!
James Spencer, Virginia

I'd only listened to SZA in my daughter's car, but this brilliantly written piece compelled me to fire up Spotify and listen to both "Ctrl" and "SOS" — beautiful music that touches me, a 65-year-old-plus white lady. It's in my rotation now. Danyel Smith is a powerful illustrator in words of a vibe, a feeling, a mood.
Cara, Minneapolis

As an old guy who likes young music, I have to say, I'm behind the curve. I had seen the initials but not — consciously — heard the music, but Danyel Smith's writing knocked me out. Those punchy verbs alone, and how it takes Smith three packed paragraphs before she even gets to SZA — brilliant writing.
Netsuke, Montreal



RE: WOMEN HAVE BEEN MISLED ABOUT MENOPAUSE

Susan Dominus wrote about the risks and benefits of menopausal hormone therapy.

Susan Dominus's article brings a personal perspective to the very real struggles some women experience with menopause. As



members of the Women's Health Initiative Steering Committee, however, we believe the article did not adequately characterize critical aspects of a landmark large-scale national study from our organization that increased understanding of chronic disease risk and prevention in women.

When the W.H.I. was launched in 1993, the effectiveness of estrogen-based therapies for relief of menopausal symptoms was already well established. It continues to be F.D.A.-approved and recommended by professional societies for this purpose. The objective of the W.H.I. was never to test the use of menopausal hormone therapy for treating menopausal symptoms; its purpose was to focus on other unanswered questions.

The W.H.I. menopausal hormone therapy trials were rigorously designed and conducted to test the benefits and risks of specific hormonal therapies for chronic diseases. They definitively established that menopausal hormone therapy should not be used to prevent heart disease, stroke and other chronic diseases, an increasingly common practice at the time. The resulting worldwide decrease in their use in older women, often many years after menopause, undoubtedly has saved millions of lives and billions of U.S. health care dollars. Understandably, these raised questions for younger, perimenopausal women, who were not the focus of the W.H.I. hormone trials. We agree that the benefit of symptom relief may well outweigh any small risks in perimenopausal women, particularly for estrogen alone, which had fewer adverse effects than estrogen plus progestin preparations.

We wholeheartedly agree with the theme of the article that our society must stop discounting women's health concerns and must invest in high-quality research



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to address them. The W.H.I. investigators, and many thousands of loyal participants in the study, are part of that effort and will continue to offer valuable insights to women as they journey through life.
Cynthia Thomson, Tucson, Ariz., and Garnet Anderson, Seattle, for the Women's Health Initiative Steering Committee

RE: MIEKO KAWAKAMI

Joshua Hunt profiled the author of "Breasts and Eggs."

What a tender and thoughtful article. I've taught Kawakami's brilliant novel "Heaven" a couple of times in my world-literature course at Fordham University. Students love her passionate ruthlessness, and see often in her novels' conclusion a kind of refusal to close the subject of meaning down. I'm dying to see what Kawakami's new manuscript offers our classroom discussions. What a superstar.
Skip Thompson, Brooklyn, N.Y.

"Breasts and Eggs" stunned me, and "All the Lovers in the Night" broke my heart. These were two of the most vibrant, vital works that I read during the pandemic, and for which I am so, so grateful. What an incredible writer — I can't wait until her next book.
Name Withheld, Kentucky

I loved this beautifully written, tender profile. The mention of the novelist's clothing I found especially germane. With few illusions and grounded in her past, Kawakami wields her Hermès handbag and Gucci dress like well-sharpened weapons.
Michael Ashford, Los Angeles



'Our society must stop discounting women's health concerns and must invest in high-quality research to address them.'

Send your thoughts to magazine@nytimes.com.