Presentation to the Clinical Utility of Treating Patients with Compounded "Bioidentical Hormone Therapy"

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Objectives

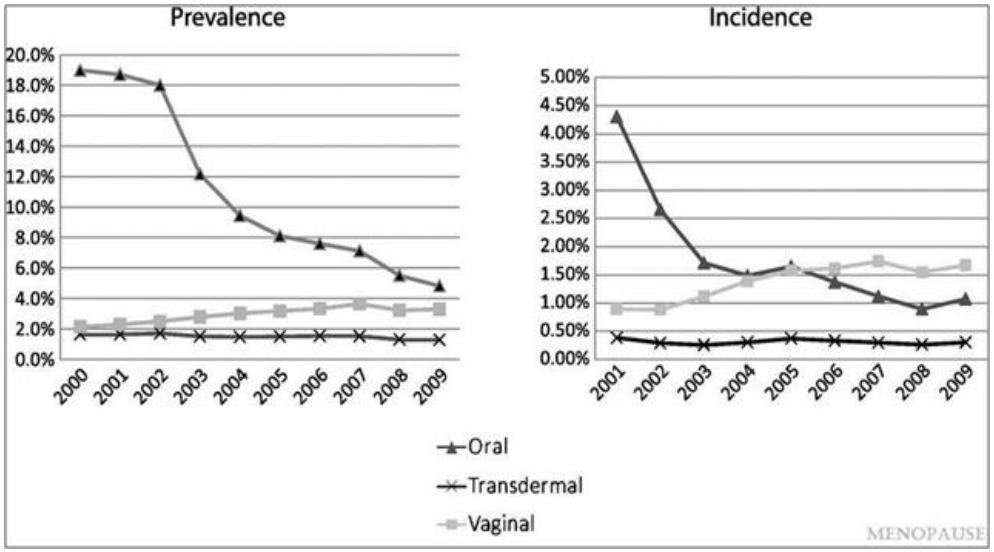
- Discuss the impact of the WHI study on current use of hormone therapy.
- Discuss reasons why women may be turning to bioidentical hormone therapy.
- Highlight the promotion and marketing of bioidentical hormone therapy on the internet.
- Discuss the common questions patients ask about bioidentical hormone therapy.

Introduction

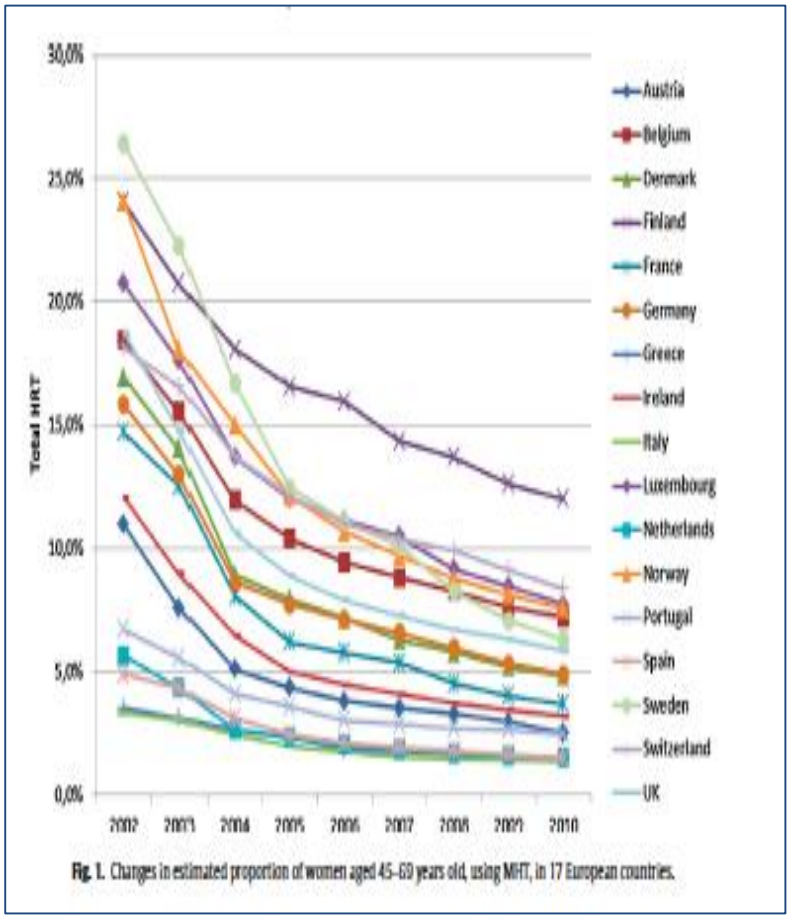
- HT most effective agent for managing menopausal symptoms.
- Despite this, there is a significant care gap in prescribing HT.
  - Women have reservations in taking HT.
  - Health care providers are reluctant to prescribe.
- Impact of the WHI study initial study findings continues to this day.

Changes in HT Use Worldwide

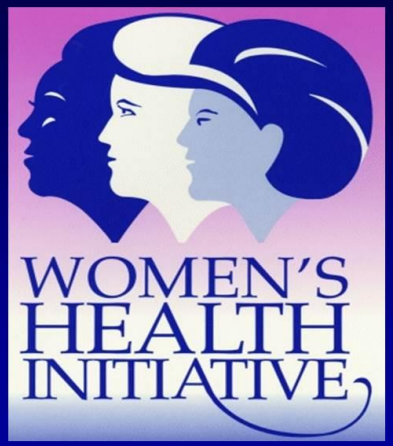
HT use declined dramatically worldwide after the WHI EPT arm initial results, from ~50 – 80% decline (~10 – 16% worldwide).



Steinkellner et al. Menopause. 2012;19:616-621



Ameye et al Maturitas. 2014;79(3):287–291.



NIH National Heart, Lung, and Blood Institute

WHI Hormone Therapy trials:

- Estrogen and Progestin Trial: 16,608 women
- Estrogen Alone Trial: 10,739 women with hysterectomy

Objectives: To assess the effects of HT on CVD (primary outcome) and breast cancer (secondary outcome)

https://www.whi.org/SitePages/WHI%20Home.aspx

WHI initial results: increased risks (cardiovascular, breast cancer) outweighed preventive benefits (↓ fractures).

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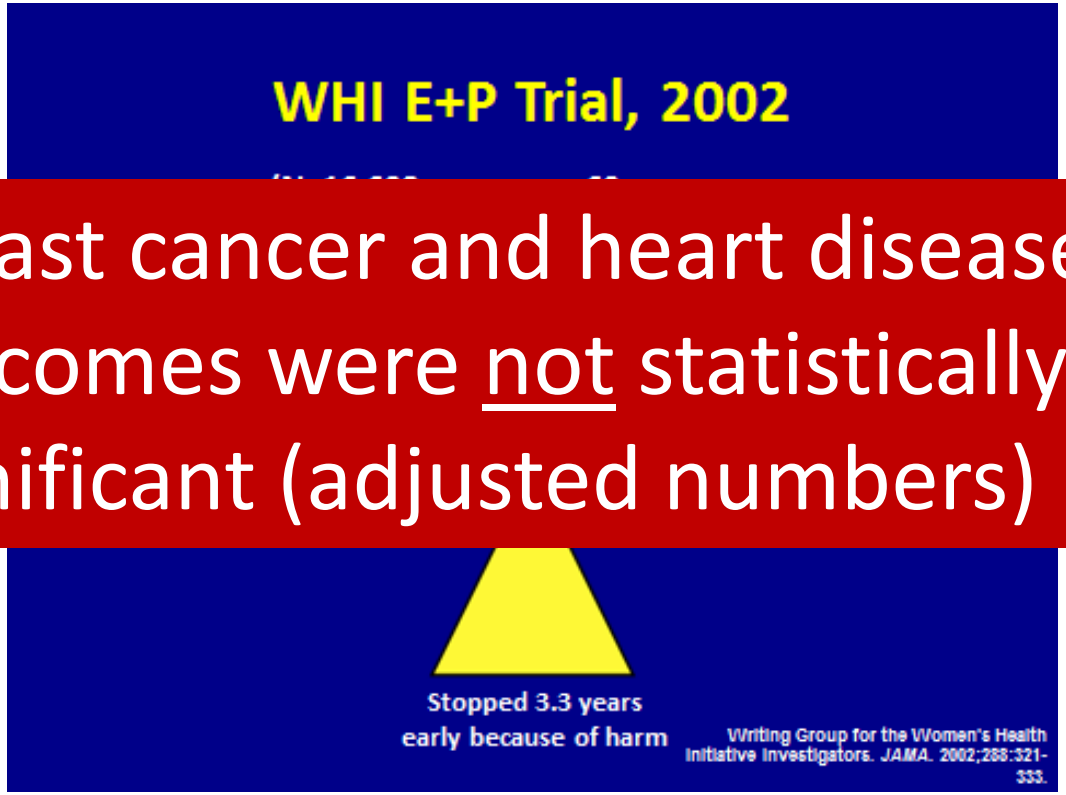


WHI initial results: increased risks (cardiovascular, breast cancer) outweighed preventive benefits (↓ fractures).

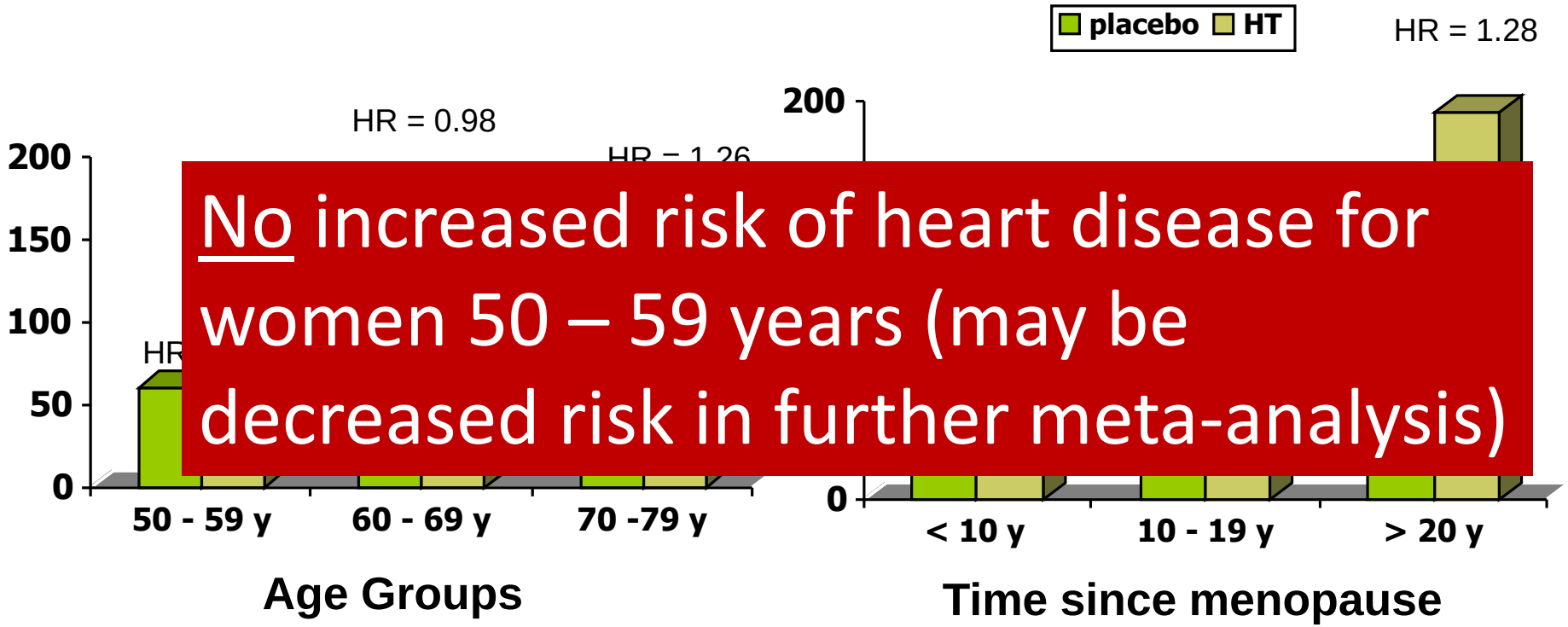
And 2/3rd of women were over 60 years of age (ave 63 years)

The WHI estrogen alone: No increased risk of breast cancer or heart disease with estrogen

SIGMA slide set 2012

Note: VTE not statistically significant

Reanalysis of WHI data showed that CHD risk was in older women, ≥ 10 years after menopause



No increased risk of heart disease for women 50 – 59 years (may be decreased risk in further meta-analysis)

CHD Outcomes

Rossouw et al, JAMA 2007;297:1465 - 77

Current Role of Hormone Therapy

Menopause: The Journal of The North American Menopause Society
Vol. 24, No. 7, pp. 000-000
DOI: 10.1097/GME.0000000000000921

POSITION STATEMENT

The 201
Menopa

Systemic HT is a safe, effective option to initiate in healthy women <60 years of age or less than 10 years after menopause.

2016 IMS Recommendations on women's midlife health and menopause hormone therapy

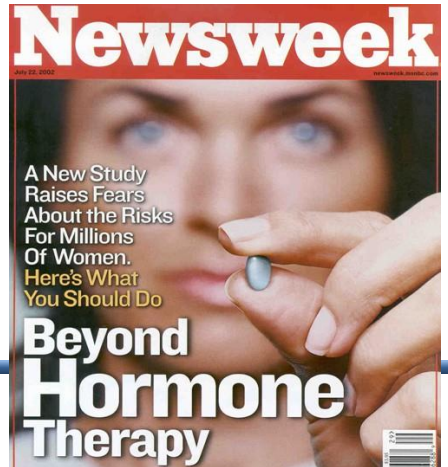
R. J. Baber, N. Panay & A. Fenton the IMS Writing Group

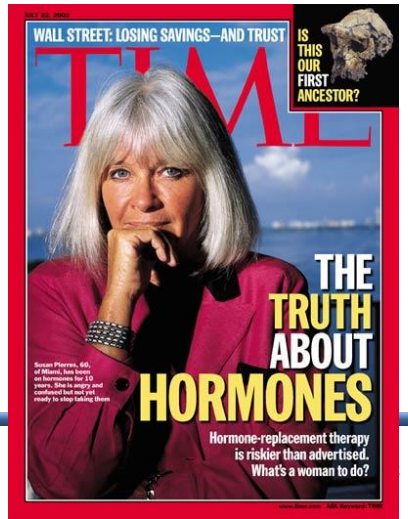
anaging
enopause

Chapter 1: Assessment and Risk Management of Menopausal Women ... S6
Chapter 2: Cardiovascular Disease ... S16
Chapter 3: Menopausal Hormone Therapy and Breast Cancer ... S23
Chapter 4: Vasomotor Symptoms ... S31
Chapter 5: Urogenital Health ... S35
Chapter 6: Prescription Therapeutic Agents ... S42
Chapter 7: Ongoing Management of Menopausal Women and Those With Special Considerations ... S51
Chapter 8:

Changes in HT use

- The publicity on the results of the WHI dramatically changed perceptions on HT.
  - Unfortunately generalized to all menopausal women
- The media messaging after the initial results of the WHI played up risks, especially breast cancer.
- Led to confusion, as well as mistrust by both patients and health care professionals.





Recently the handling of the results by the WHI writing group and media has been criticized

CLIMACTERIC, 2017
VOL. 20, NO. 2, 91–96
http://dx.doi.org/10.1080/13697137.2017.1280251

Taylor & Francis
Taylor & Francis Group

REVIEW

The evidence base for HRT: what can we believe?

R. D. Langer

Principal Scientist, Jackson Hole Center for Preventive Medicine, Jackson, WY, USA; Associate Dean for Clinical and Translational Research and Professor of Family Medicine, University of Nevada Reno School of Medicine, Reno, NV, USA

https://cmajnews.com/2017/04/12/landmark-trial-overstated-hrt-risk-for-younger-women-109-5421/

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NAMS
THE NORTH AMERICAN MENOPAUSE SOCIETY

Misinterpretation of WHI Results Decreased Use of Hormones, Even In Women Not at Risk

A new study analyzed SWAN data to document decrease in hormone therapy initiation and continuation; many younger symptomatic women needlessly went without relief

https://www.menopause.org/docs/default-source/press-release/whi-impact-on-hormone-therapy-trends-1-9-19.pdf

Risk Perception

- Uncertainty or diversity in scientific information or by "experts" can lead to fear and mistrust.
- Risks can be perceived to be higher if publicized more frequently. *"What we hear is what we know"*
- Public perception of risk is greatly influenced by media, social media and celebrities.
  - These draw on our emotional and subjective opinions.

Gluckman PD. PMCSA Series Part 2. November 2016, Lewandosky et al, PLOS One 2013;8(10), Kortenkamp Sci Communication 37(3):287-313

Decision Making with Menopause

- Menopause decisions are complex and emotionally driven, especially with hormone therapy.
- Vast amount of information about HT can make it difficult to decipher.
- Allows for discourse of HT information in the media, internet and social media.

Carpenter et al Maturitas. 2011;70(1):10–15, Pines Climacteric 2008;11(6):443-446, Colombo et al Eur J Obstet Gynec Reprod Biol 2010:153:56-61

Impact of the WHI

- WHI results provided an environment to promote hormones that were different than used in the WHI, ie bioidentical hormones
  - More like our own "molecular structure"

- Hormones used in WHI: conjugated equine estrogen and medroxyprogesterone.
  - conjugated equine estrogen: mixture of estrogens not all "identical" to human body
  - medroxyprogesterone: synthetic progesterone.

A few comments about BHT

- Bioidentical hormones are available in both commercial and compounded HT products.
  - Often term used for custom compounded BHT including estrogen (estriol, estradiol, estrone), progesterone, testosterone, DHEA

- Bioidentical hormones do not meet the definition of "natural".
  - Bioidentical hormones need to be chemically synthesized from a natural starting material to be the same molecular structure as humans

A few comments about BHT

- There may be unique benefits with some bioidentical hormones (ie transdermal estradiol, micronized progesterone – which are all commercially available)
  - However this evidence is still evolving
- Compounding of pharmaceuticals provides an important role in our health system.

A few comments about BHT

The issue is how BHT is promoted at many levels – "disconnect" between peer review literature and how these may be advertised/promoted to patients

Why are Women Choosing BHT?

- Want something “natural” – perception that natural is better.
- Appeal of how BHT is marketed as “individualized” or “customized” care.
- Control over their own decision making about their health – want to be own advocates.
- Health care provider not comfortable in prescribing HT and/or patient not satisfied with care.

Why are Women Choosing BHT?

- The allure of a “special ingredient” not commercially available (for example estriol)
- Believe that cBHT are FDA approved
- Their social network – their friends are using
- Celebrity endorsements may make it particularly appealing
- What they see on the internet – attractive direct to consumer advertising

Menopause from Different Standpoints

Thompson et al, 2017, Qualitative Study on Motivations for Using cBHT

Most significant appeal was not the actual cBHT itself but the clinical care associated with it.

Women want to be listened to and their symptoms validated!

Thompson et al. BMC Women's Health 2017;17:97, Fishman et al. Social Scie Med 2015;132:79-87

Position Statements on cBHT*

	Year	
NAMS	2017	"cBHT should be avoided…lack of efficacy and safety studies" Only recommended if women cannot tolerate commercial HT or not available dose/formulation.
IMS	2016	"Prescribing of compounded bioidentical hormone therapy is not recommended"
SOGC	2014	"The safety and effectiveness of such preparations have not been assessed in the way that preparations approved by regulatory bodies must be assessed…"[2]
ACOG	2018	"Conventional HT is recommended over compounded BHT given the available data"
Endocrine society	2017	"Concerned that patients may be receiving misleading or false information about cBHT"
AACE	2017	"No evidence supports the safety or efficacy of cBHT."
AACP	2014	"Insufficient evidence to support the safety or efficacy of cBHT products over traditional HT products"

*cBHT – compounded BHT

McBane et al. Pharmacotherapy 2014/doi:10.1002/phar. 1394
Reid et al. J Obstet Gynaecol Can 2014;36(9 eSuppl A):S1-S80

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DOI: 10.1097/GME.0000000000000901

Promotion and marketing of bioidentical hormone therapy on the internet: a content analysis of websites

Nese Yuksel, BScPharm, PharmD, FCSHP, NCMP,[1] Laetitia Treseng, BScPharm, PharmD,[2] Bushra Malik, BScPharm,[3] and Ubaka Ogbogu, LLB, BL, LLM, SJD[1,4]

Quantitative content analysis, n=100 websites promoting BHT services or products

Objectives

- To assess the quality of information presented and the claims made on websites offering BHT products or services.
- To describe the marketing strategies employed by these websites.

Yuksel et al, Menopause 2017;24(10):1129-35

Characteristics of Websites

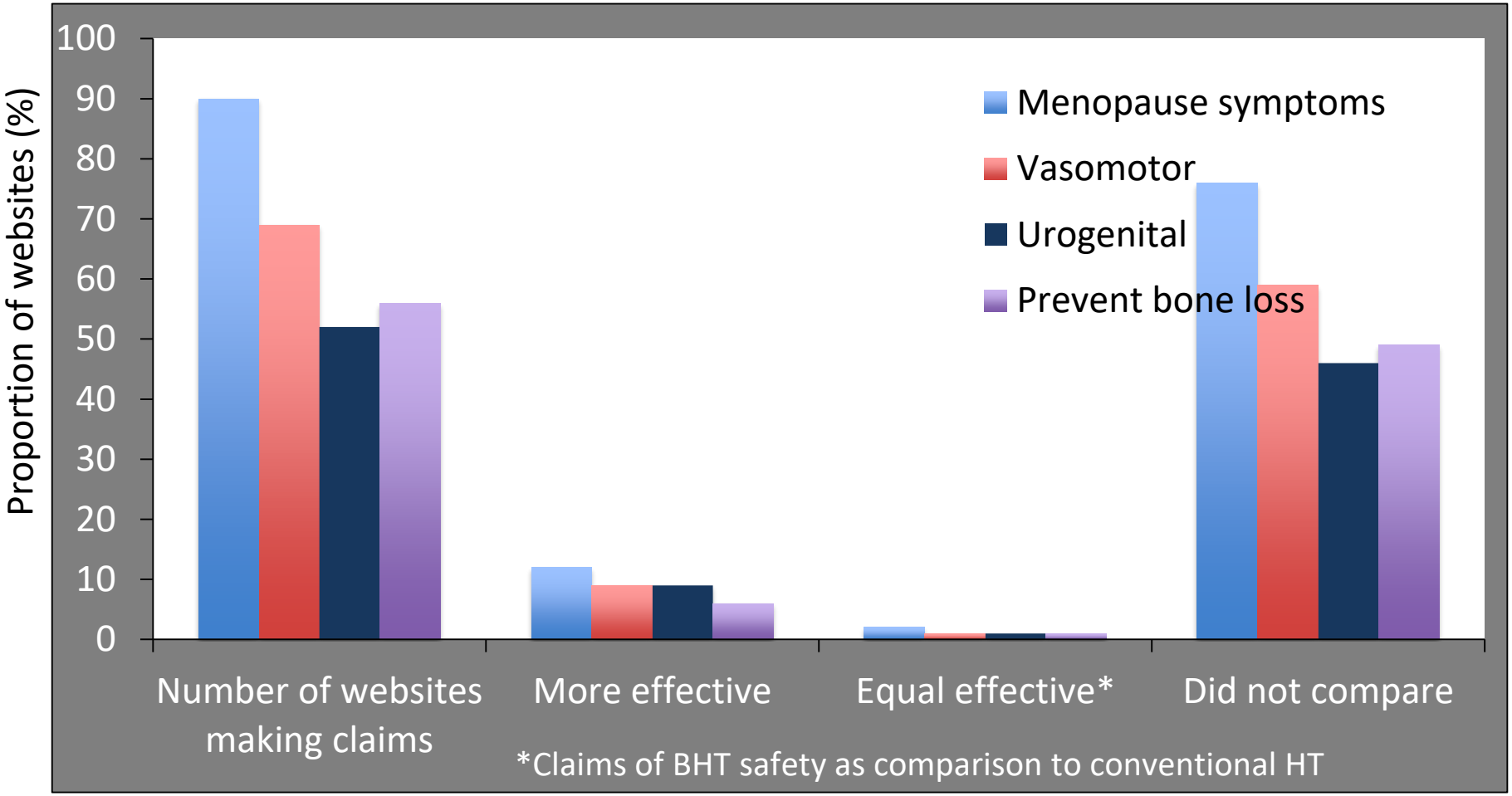
Characteristics	n = 100
Region, n (%)	
Canada	59
United States	38
United Kingdom	2
Type of website , n (%)	
Medical Clinic	47
Compounding pharmacy	19
Homeopathic/Naturopathic	16
Selling BHT online*	14
Health care professional, n (%)	
Physician	50
Pharmacist	19
Naturopath	4
Nurse	2

* OTC progesterone cream

Yuksel et al, Menopause 2017;24(10):1129-35

BHT Efficacy Presented on Websites

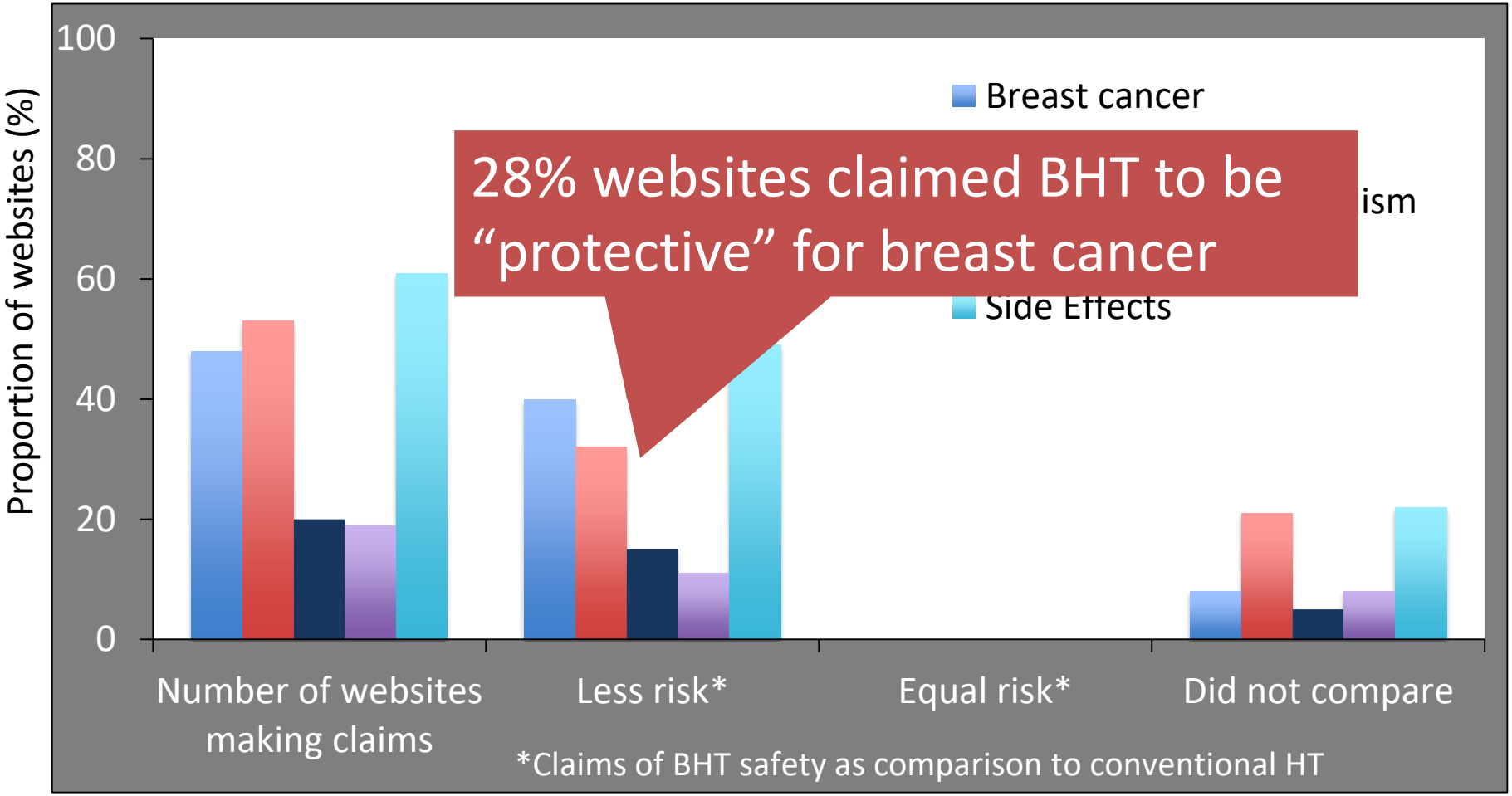
Quantitative content analysis of websites (n=100)



Yuksel et al, Menopause 2017;24(10):1129-35

BHT Safety Presented on Websites

Quantitative content analysis of websites (n=100)



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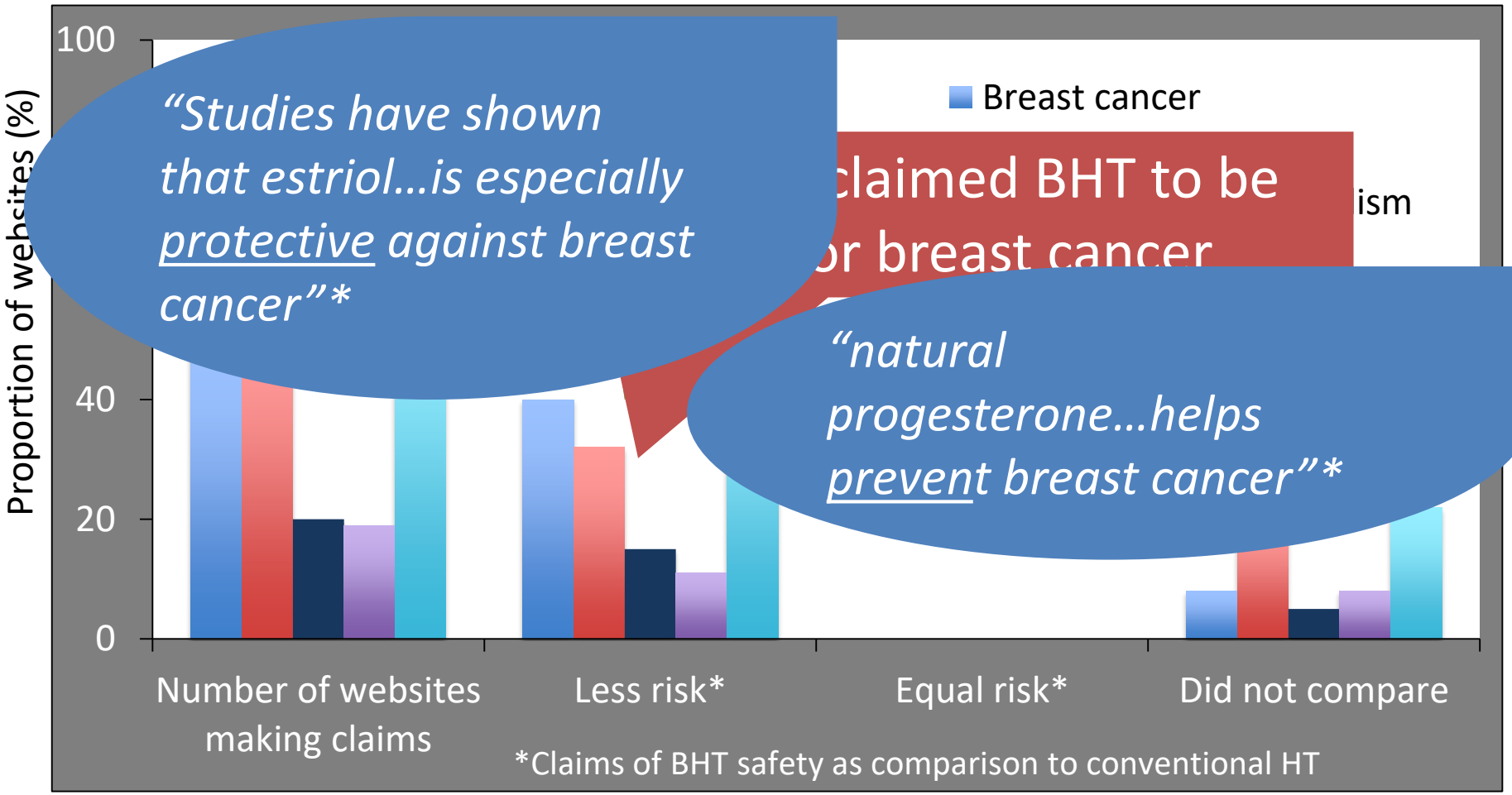
BHT Safety Presented on Websites

Quantitative content analysis of websites (n=100)



Yuksel et al, Menopause 2017;24(10):1129-35

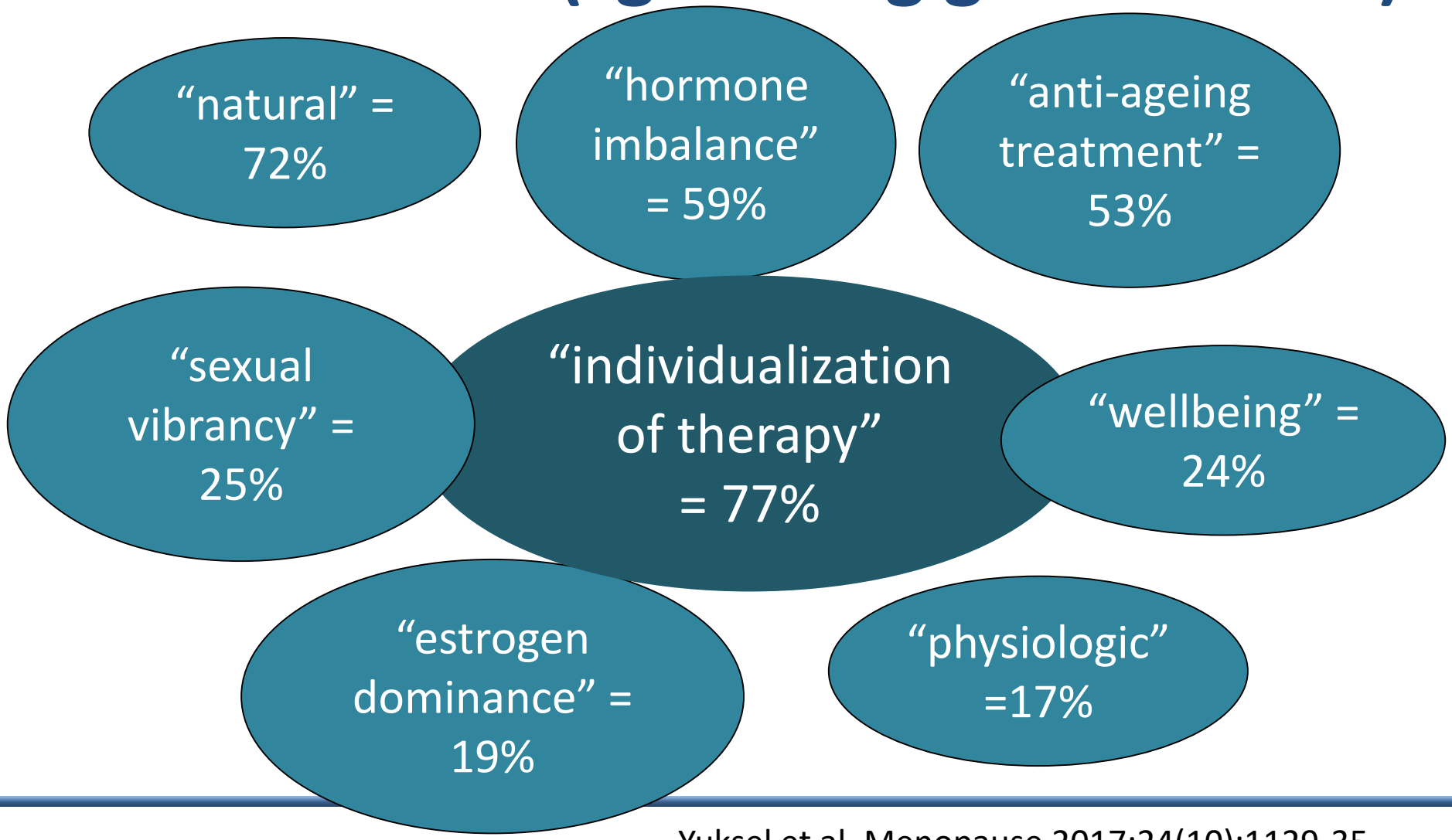
Targeted Audience

Targeted gender	N=100
Female	99
Male	62

Medical conditions targeted	N=100
Menopause	95
Perimenopause	54
Andropause	54
PMS	24
Weight loss	14
Infertility	10
Osteoporosis	8
Others	6

Yuksel et al, Menopause 2017;24(10):1129-35

Marketing Strategies: Descriptors Used to Promote BHT ("glittering generalities")



Yuksel et al, Menopause 2017;24(10):1129-35

Final Points

- Websites promoted BHT to be safer compared to conventional HT.
- Claims on breast cancer risk were misleading, ~quarter of websites using words such as “protective” or “prevents”.
- Marketing targets white, middle to upper class, with varying advertising techniques:
  - “glittering generalities”
  - playing on fear of conventional HT

Yuksel et al, Menopause 2017;24(10):1129-35

What Questions are Patients Asking?

What is bioidentical hormone therapy?

Is cBHT natural? physiologic?
Will it "balance" my hormones?

Will cBHT help me with my symptoms?
Is it better than other HT?

Is cBHT safe? Is it safer than other HT

Does cBHT have less risk of breast cancer?

What are the side effects?

Can you check my hormone levels?

What Questions are Patients Asking?

What is BHT anyway?

"The term 'bioidentical hormones' rose as a marke
refers to the use of any hormone that is 'identical
often extracted from plant sources and synthesize
produced in the body.

"Bioidentical hormones include estrogen such as

Where do I find BHT?

"Bioidentical hormones are actually in many commercial hormone therapy products that have been approved by Health Canada, as well as formulations that are compounded by pharmacies that specialize in compounding (formulations not available in conventional hormone therapy).

"Bioidentical hormones found in commercial HT products include 17 β-estradiol (pills, patches, gels, vaginal products), estrone (vagina) and micronized progesterone."

What are compounded BHT?

folio

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June 27, 2017

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What you need to know about bioidentical hormone therapy

UAlberta pharmacy researcher addresses the big questions around BHT.

https://www.folio.ca/what-you-need-to-know-about-bioidentical-hormone-therapy/

SIGMA-Canadian Menopause Society

Answers to Your Questions on Bioidentical Hormone Therapy

Yuksel N Pharm D, Edmonton **Derzko C** MD, FRCSC Toronto

https://www.sigmamenopause.com/sites/default/files/pdf/publications/SIGMABHTBrochureCombinedDerzkoYukselNov_2017Final.pdf

What Concerns do Women Have?

- Costs associated with cBHT and often not always covered by third party payers
- Conflicting information on hormone therapy (both commercial HT and cBHT)
- Confusion on “who” to believe or trust – different messaging from health care providers
- Not having more studies in the area to help guide women

Individualization of Therapy

- cBHT is often promoted for “individualizing” of therapy.
- However conventional HT is also ”individualized” to patient needs and response to therapy.
- Hormone levels, either saliva or blood testing are <u>not</u> useful for titrating hormone therapy.
  - Perimenopause – hormones can fluctuate
  - Therapeutic endpoint of use of hormone therapy is improvement in symptoms

Conclusion

- Substantial gap exists between recommendations from professional organizations and how BHT is promoted.
- Mixed messaging on online websites may lead to patient confusion regarding hormone therapy in general.
- *What I would like to see in the report:*
  - *Summary of evidence for claims on safety in comparison to commercial HT*
  - *Guidance on the types of claims that could be made and how these agents can be marketed or promoted*
  - *Better regulation on the internet*

Questions