



Impact of hormone replacement therapy on patients after endometrial cancer: a global comparison

Priya Patel, Swetha Sajan PharmD Candidates¹
Abby A. Kahaleh², PhD, MS, BPharm, MPH

^{1,2}Roosevelt University College of Pharmacy



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Purpose

- To conduct a study to analyze existing studies on the risk of recurrence of endometrial cancer (EC) with hormone replacement therapy (HRT) by comparing global recurrence rates in North America, Asia, and Europe using the economic, clinical and humanistic outcomes (ECHO) model.

Background

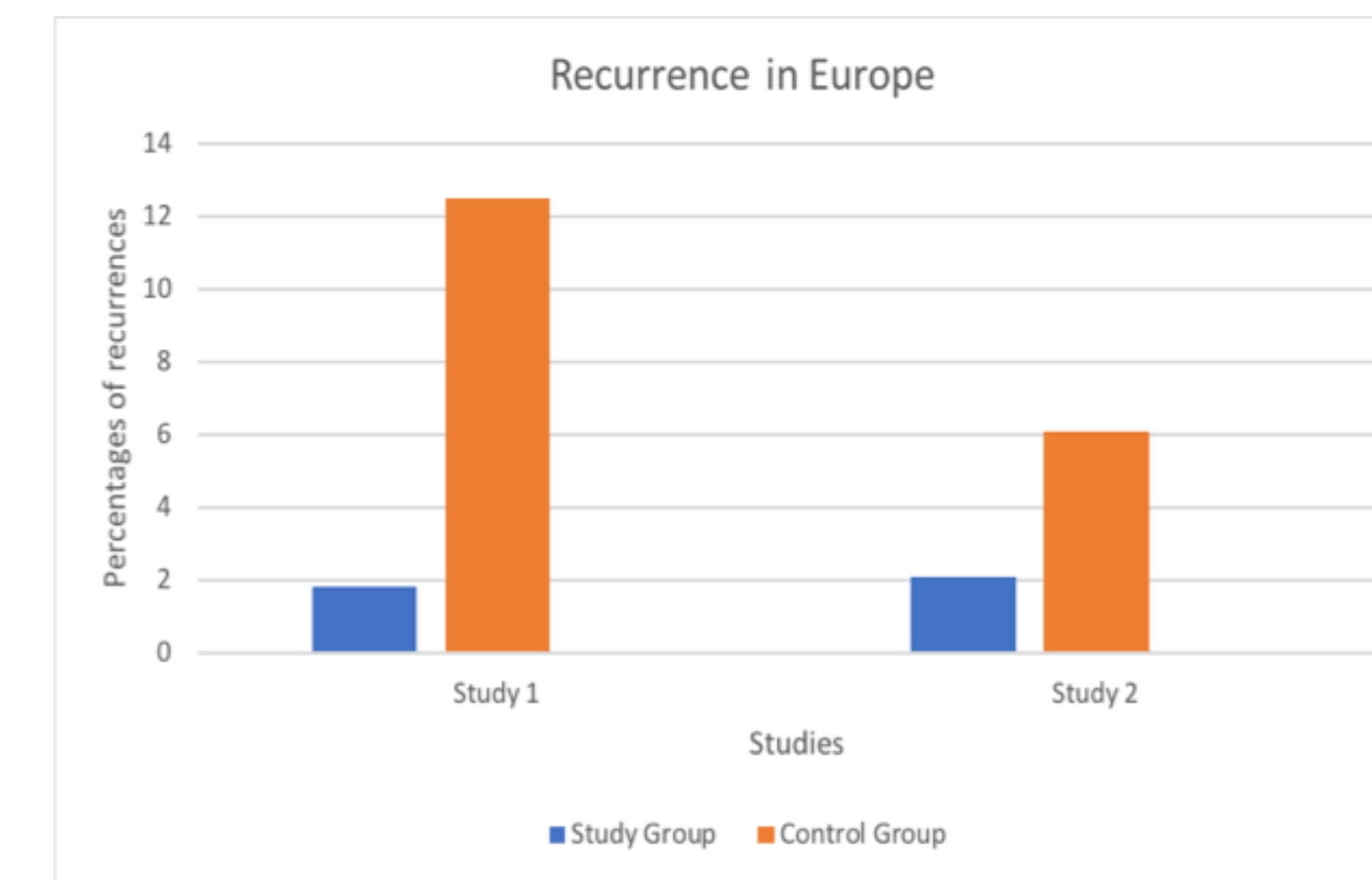
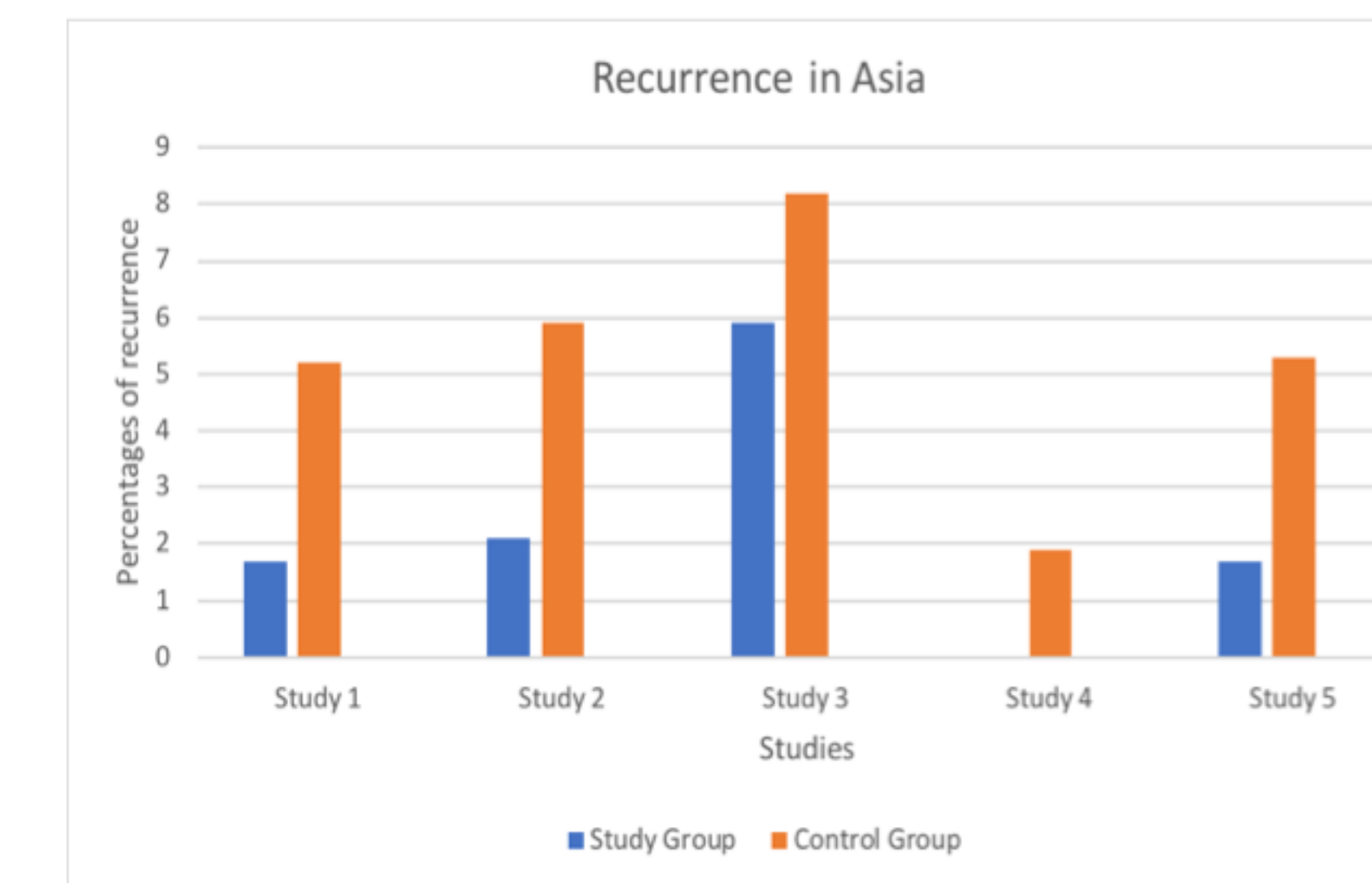
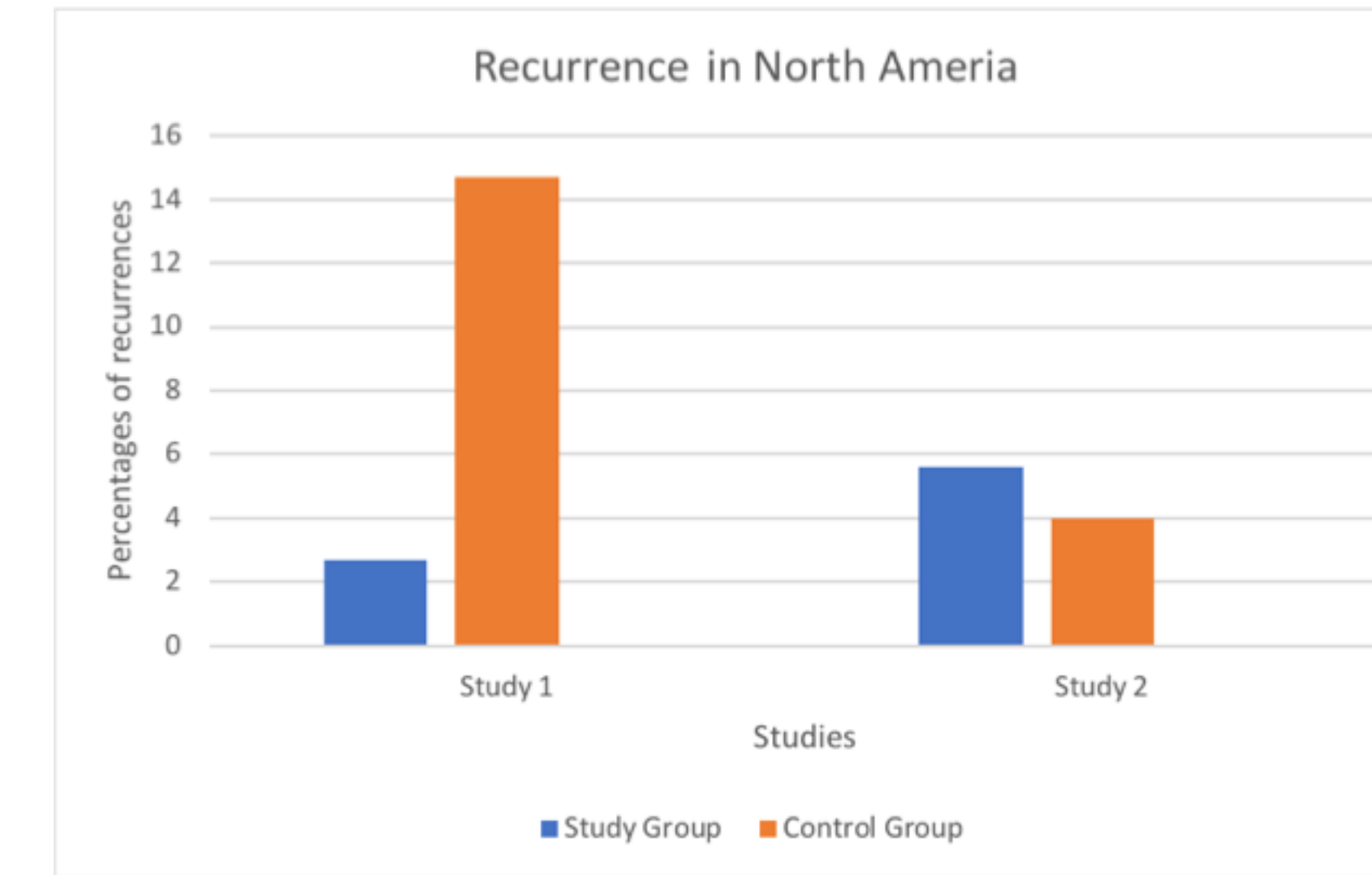
- More than 600,000 women in the United States are survivors of EC.¹
- The average age of women diagnosed with EC is 60 years old, mostly post-menopausal women.¹
- In younger women who are diagnosed with EC, a hysterectomy is performed to treat the cancer, which leads to surgically induced menopause.
- The use of combined progestin and estrogen therapy is commonly prescribed for the treatment of menopausal symptoms such as hot flashes and sleep disorders and to improve quality of life (QOL).⁶
- Many of these women suffer from climacteric menopausal symptoms but they are not given the option of HRT to alleviate these symptoms because of a misinterpretation by the Women's Health Initiative (WHI) Study from 2004.¹¹

Methods

- Studies published in English in 2000-2019
- 11 studies conducted in North America, Asia, and Europe
- Terminology: EC; HRT; HRT and EC; HRT recurrence for EC; recurrence of EC; HRT in postmenopausal women; HRT QOL EC; and cost effectiveness HRT in EC
- Search engines: Cochrane, Google Scholar, PubMed, EBSCO Host online database
- RCTs, meta-analysis, retrospective and prospective case controls, article reviews, and matched control studies
- Participants: women who underwent hysterectomy and survived EC in North America, Asia, and Europe.
- Primary outcome: Impact of HRT on the frequency of recurrence in women who survived EC
- Secondary outcome: Impact of HRT on reducing symptoms of menopause in women who survived EC, improving patient's quality of life and direct cost

Results: Clinical Outcomes

Study Title	Authors	Description	Findings/ Results	Conclusions
North America^{2,3}				
Study 1: Estrogen Replacement Therapy in Endometrial Cancer Patients: A Matched Control Study	Suriano KA, Mchale M, Mclaran CE, et al.	Impact of estrogen replacement therapy on recurrence and death in women with a history of endometrial cancer. A matched control study at the University of California, Irvine Medical Center and Long Beach Memorial Medical Center in Irvine, California, US. N = 150. Follow-up: 83 months (study group); 69 months (control group)	2.7% (2/75) recurrences in study group, 10.7% (8/75) local recurrences and 4% (3/75) recurrences in distant sites in control group	Estrogen therapy with or without progestins did not increase the risk of recurrence in endometrial cancer survivors. Furthermore, a longer disease-free interval was observed in patients who received ERT than in control group.
Study 2: Randomized Double-Blind Trial of Estrogen Replacement Therapy Versus Placebo in Stage I or II Endometrial Cancer: A Gynecologic Oncology Group Study	Barakat RR, Bundy BN, Spirios NM, et al.	Studied the effects of ERT on recurrence rate and survival in women who went through hysterectomy for stage I or II endometrial cancer. A double-blind, randomized, phase III noninferiority trial by the Gynecologic Oncology Group. N = 556. Initiation: 20 weeks post-surgery. Duration: 3 years. Follow-up: 2 years	5.6% (14/251) recurrences in the ERT group 4% (12/305) in control group (only compliant participants included).	Although the study was closed prematurely, there was a low rate of recurrence in the low-risk population.
Asia⁴⁻⁸				
Study 1: The influence of hormone therapy with drospirenone-estradiol on endometrial type endometrial cancer patients	Lim S, Kim YH, Lee K, Lee J	To examine the adverse effects of drospirenone/estradiol (Angeliq) on stage I and II endometrial cancer survivors. This retrospective case control took place in multiple university hospitals in Korea. N = 174. Initiation: 8 weeks post-surgery. Follow-up: 64 months (study group); 36 months (control group)	1.7% (1/58) recurrence in HRT group, 2.6% (3/116) recurrences and 2.6% (3/116) deaths in the control group.	Patients who require HRT post-surgery should be able to receive it. The study showed no significant adverse effect on recurrence or death with the use of HRT in EC survivors.
Study 2: Effects of hormone replacement therapy on the rate of recurrence in endometrial cancer survivors: A meta-analysis	Shim S, Lee SJ, Kim S	A meta-analysis that reviewed literature to study recurrence of EC in survivors who used HRT. The study was done at the Konkuk University School of Medicine, Seoul, Republic of Korea. Studies included were one randomized trial, and five observational studies. N = 1,975. Duration: 2-132 months	2.1% (19/896) recurrences among HRT users, 5.9% (64/1079) recurrences in non-users across 6 studies.	No significant increase in risk of EC with the use of HRT in Stage III survivors. Population bias may be involved because of recruitment of relatively healthier and younger women for post-EC HRT treatment, which may have resulted in the protective effect shown in the oestrogen + progestin group.
Study 3: Effects of hormone therapy on recurrence in endometrial cancer survivors: a nationwide study using the Korean Health Insurance Review and Assessment Service database	Cho H, Ouh Y, Lee JK, Hong JH	Korean Health Insurance Review and Assessment Service (HIRA) database was used to study the effects of Hormone Replacement Therapy on recurrence rate of patients who underwent surgery between 2010 to 2013. N = 5,667. Initiation: 11 months. Mean Duration: 15.7 months (recurrence); 23.7 months (no recurrence). Mean Follow-up: 47.5 months	5.9% (50/847) HRT users faced recurrences while 8.2% (396/4820) faced recurrence in control group.	Post-operative use of HRT did not cause significant increase in recurrence rate of EC.
Study 4: Does immediate hormone replacement therapy affect the oncologic outcome in endometrial cancer survivors?	Ayhan A, Taskiran C, Simsak S, Sever A	This prospective case-control study determined the effect immediate hormone replacement therapy had on endometrial cancer survivors in Turkey. N = 102. Initiation: 4-8 weeks post-surgery. Mean Duration: 48.1 months. Follow-up: duration of therapy	Of the 50 patients who were receiving immediate hormone therapy, none of the patients experienced recurrence. On the other hand, 1.9% (1/52) patients in the control group experienced pelvic recurrence.	The study concluded that the risk of recurrence of EC was not increased with the use of HRT. In addition, EC survivors should be followed up closely if they are using HRT.
Study 5: Hormone Replacement Therapy After the Treatment of Cancer	Tangjilgamol S, Manusinivithaya S, Hanprasertpong J, Kavanagh J	Literature review that studied effects of estrogen or hormone replacement therapy on endometrial cancer survivors in Bangkok, Thailand. N = 2,003	In the HRT group, there were 1.7% (16/924) of patients who experienced recurrence. In the control group, there were 5.3% (57/1,079) of patients who experienced pelvic recurrence.	Overall, it was observed that recurrence rate was lower in study group compared to control group. However, it should also be noted that there has not been an adequate amount of data to explain the safety of using HRT after treatment of endometrial cancer.
Europe^{9,10}				
Study 1: Hormone Replacement Therapy after endometrial cancer	Mueck AO, Seeger H	Studied the impact of HRT through a literature review that included 5 controlled studies. The study also questions the recent practice of using low-dose oestrogen therapy as opposed to the continuous combined estrogen progestone therapy in treating menopausal symptoms after EC. N = 637	1.8% (4/228) of recurrences occurred in the study group. In the control group, 12.5% (51/409) of patients experienced recurrence.	Existing studies do not show a higher risk of recurrence of endometrial cancer in patients who use HRT after survival of EC. Patients should be educated on risks and benefits of HRT as well as alternative forms of therapy.
Study 2: Safety of hormone replacement therapy in gynaecological cancer survivors	Billatis I, Thomakos N, Rodolakis A, et al.	Studied the effects of HRT risk of gynaecological cancer recurrence across English literature. This literature review was done at the University of Athens, Greece and included retrospective and prospective case control studies. N = 1,976	In the HRT group, 2.1% (19/896) of patients experienced recurrences, and in the control group, 6.1% of patients experienced recurrences. (66/1,080)	The use of HRT in endometrial cancer survivors seemed to not show a risk of recurrence. The study suggested that patients should be aware of the lack of strong evidence on the use of HRT in endometrial cancer.



Results: Economic Outcomes

- Two studies focused on examining economic outcomes were conducted in Europe. HRT was found to be cost effective based on individual study thresholds.
- The study conducted in UK used a threshold of £30,000 to be considered cost effective and the cost was £205 per QALYS gained.
- The study that was conducted in Sweden used a threshold of 600,000 kronas to be cost effective and the cost per QALY was 8,000 kronas.

Results: Humanistic Outcomes

- Symptoms were better controlled in patients using HRT than placebo^{5,6,12}
- Overall increase in quality adjusted life years (QALY)²
- The study conducted in UK indicated an increase in quality adjusted life years by 1.23.
- The study conducted in Sweden revealed an increase in life expectancy of about 3.5 days in women using oestrogen only therapy.

Conclusions

Clinical:

- Prescribers should not be dismissing the option
- Individualized care

Economic:

- Economically favorable based on QALY
- Not enough data

Humanistic:

- Studies showed that there was a gain in life years based on QALY
- Not enough data
- Improved post-menopausal symptoms

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Disclosure

Priya Patel: Nothing to disclose
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