여성암을 가진 비만환자, 제대로 알기

해운대백병원 가정의학과

유 선 미

Cancer Survivorship Symposium:
Advancing Care and Research

A Primary Care and Oncology Collaboration

JANUARY 15-16, 2016
SAN FRANCISCO MARRIOTT MARQUIS | SAN FRANCISCO, CALIFORNIA
survivorsym.org | #SurvOnc16

urvivorship
sis

for Survivorship Care

Patient Advocate

ancisco

PRESENTED AT: **2016 Cancer Survivorship Symposium: Advancing Care and Research**
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Presented By Diane Heditsian at 2016 Cancer Survivorship Symposium

Things I Wish Someone Had Told Me: Survivorship Begins at Diagnosis

Chase Doyle

In 2002, Diane Heditsian was 48 years old, raising 2 children, running a life science communications firm with her husband of 23 years, and planning a walking tour of Tuscany, when she was first diagnosed with breast cancer. Ms. Heditsian, now a researcher and a patient advocate at the University of California, San Francisco, shared her story at a recent Cancer Survivorship Symposium.

After undergoing a mastectomy (removal of a breast) and receiving 4 cycles of chemotherapy, she decided to travel to Italy anyway—a life-affirming trip during which she walked 20 miles daily and scoured the city for an English-speaking hairdresser willing to shave her head.

I Wish Someone Had Told Me...

1. Chemotherapy, hormone therapy, and chemical-induced menopause cause weight gain, and weight gain after breast cancer diagnosis is associated with an increased risk for cancer recurrence

    "I never realized that there are steroids in chemotherapy that have this effect."

2. Aromatase inhibitors (hormone therapies for breast cancer) **can cause joint pain, mood issues, high blood pressure, and significant hair loss, which they did for me**

    "I've had morning muscular-skeletal issues, trouble walking down the stairs, and getting out of bed; that's been resolved, although some tension issues have remained"

3. Up to 20% of patients with early-stage, node-negative breast cancer will have a recurrence, and this can happen even 20 years after diagnosis

4. Exercise as if your life depended on it, because it just might

    "I'm still working on the weight loss. I know it's going to be a life-long struggle"

5. You're not losing your mind: forgetfulness and inability to focus are normal during treatment and will likely diminish

    [partially obscured] impairment, which made it challenging to run a business. I had trouble getting organized and forgot a [...] What we call 'chemo brain' is very normal, and it will probably subside"

    [...] need some emotional/psychological/spiritual help to make sense of all this

    [...] have to deal with the cancer issue at some point, and you're going to need help doing it"

    [...] same person after breast cancer, and maybe that's a good thing

    [...] see my oncologist and get mammograms?

    [...] spelled out for me. Do I need a mammogram on the mastectomy side? Should I have diagnostic or [...] mmograms?"

    [...] breast cancer and there's "very bad" breast cancer

    [...] does not trump biology

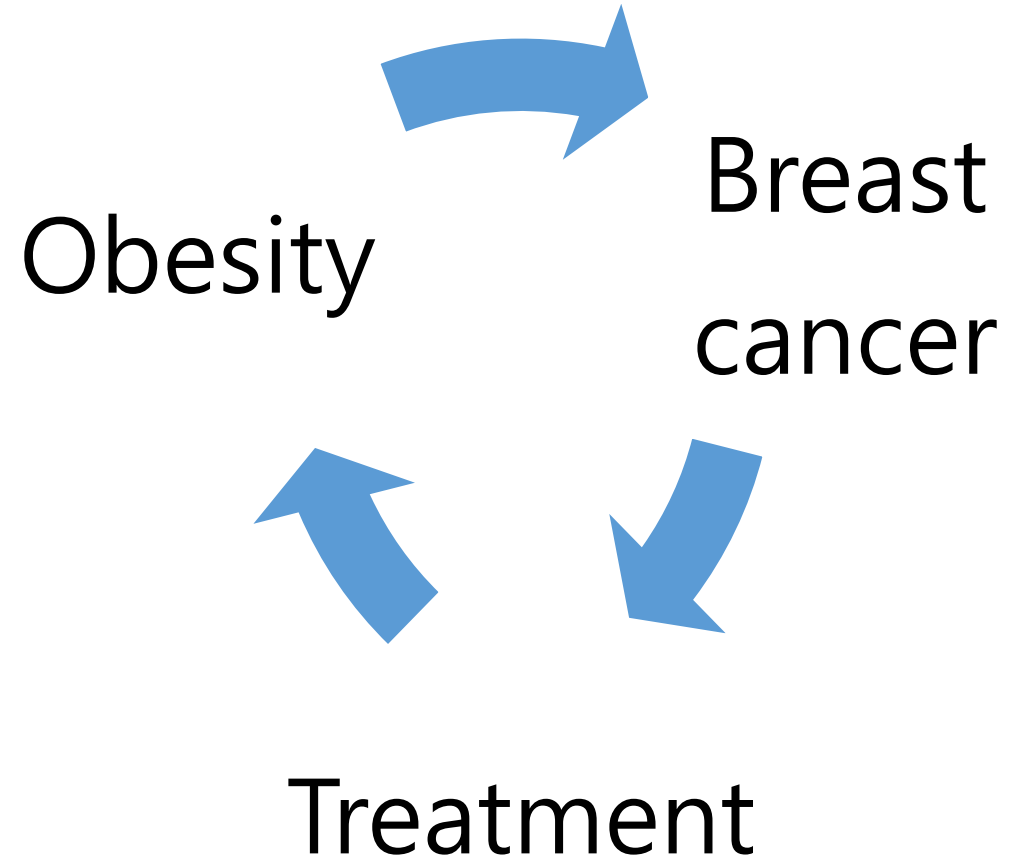[partially obscured] Since her second diagnosis and treatment, Ms. Heditsian has joined the YMCA for strength training, wears a Fitbit every day, and recently hired a lifestyle coach through an app called VitaCoach.

Chemotherapy, hormone therapy, and chemical-induced menopause cause **weight gain**, and weight gain after breast cancer diagnosis is associated with an increased risk for cancer recurrence....

Exercise as if your life depended on it.

Contents

- 위험요인
- 진단과 치료의 영향
- 예후
- 재발 예방

Obesity

Breast cancer

Treatment

국내 여성암 발생 (2021)

(단위: 명, %, 명/10만명)

순위	남자				여자				
	암종('20 순위)	발생자수	분율	조 발생률	표준화 발생률*	암종('20 순위)	발생자수	분율	조 발생률	표준화 발생률*
	모든 악성암	143,723	100.0	561.7	596.7	모든 악성암	133,800	100.0	519.7	489.5
	갑상선암 제외	134,952	93.9	527.4	562.9	갑상선암 제외	107,268	80.2	416.7	385.5
1	폐	21,176	14.7	82.8	90.5	유방	28,720	21.5	111.6	109.9
2	위	19,533	13.6	76.3	80.2	갑상선	26,532	19.8	103.1	104.0
3	대장(4)	19,142	13.3	74.8	78.7	대장	13,609	10.2	52.9	47.5
4	전립선(3)	18,697	13.0	73.1	79.3	폐	10,440	7.8	40.6	36.1
5	간	11,207	7.8	43.8	46.1	위	9,828	7.3	38.2	34.5
6	갑상선	8,771	6.1	34.3	33.9	췌장	4,280	3.2	16.6	14.5
7	신장(8)	4,775	3.3	18.7	19.0	간	3,924	2.9	15.2	13.3
8	췌장(7)	4,592	3.2	17.9	19.2	자궁체부	3,749	2.8	14.6	14.3
9	방광(10)	4,201	2.9	16.4	18.3	담낭 및 기타담도	3,532	2.6	13.7	11.5
10	담낭 및 기타담도(9)	4,085	2.8	16.0	17.7	난소(11)	3,221	2.4	12.5	12.1

*연령표준화발생률: 우리나라 2020년 주민등록연앙인구를 표준인구로 사용

유방암

France* 105.4
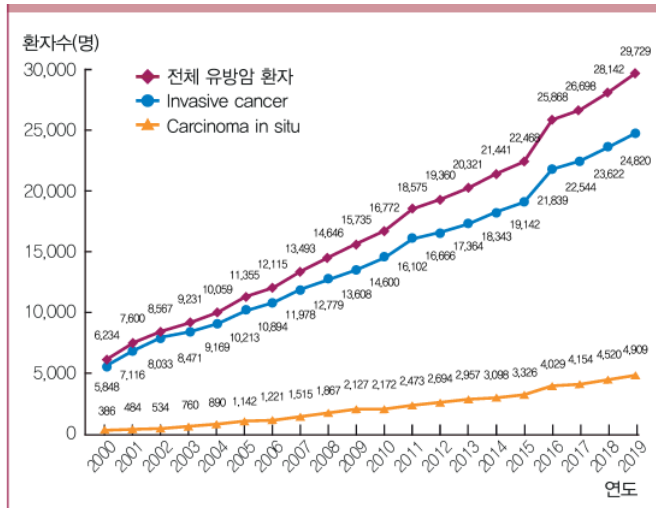Germany* 77
USA* 95.9

Japan* 74.4
China* 33
Republic of Korea 61.5
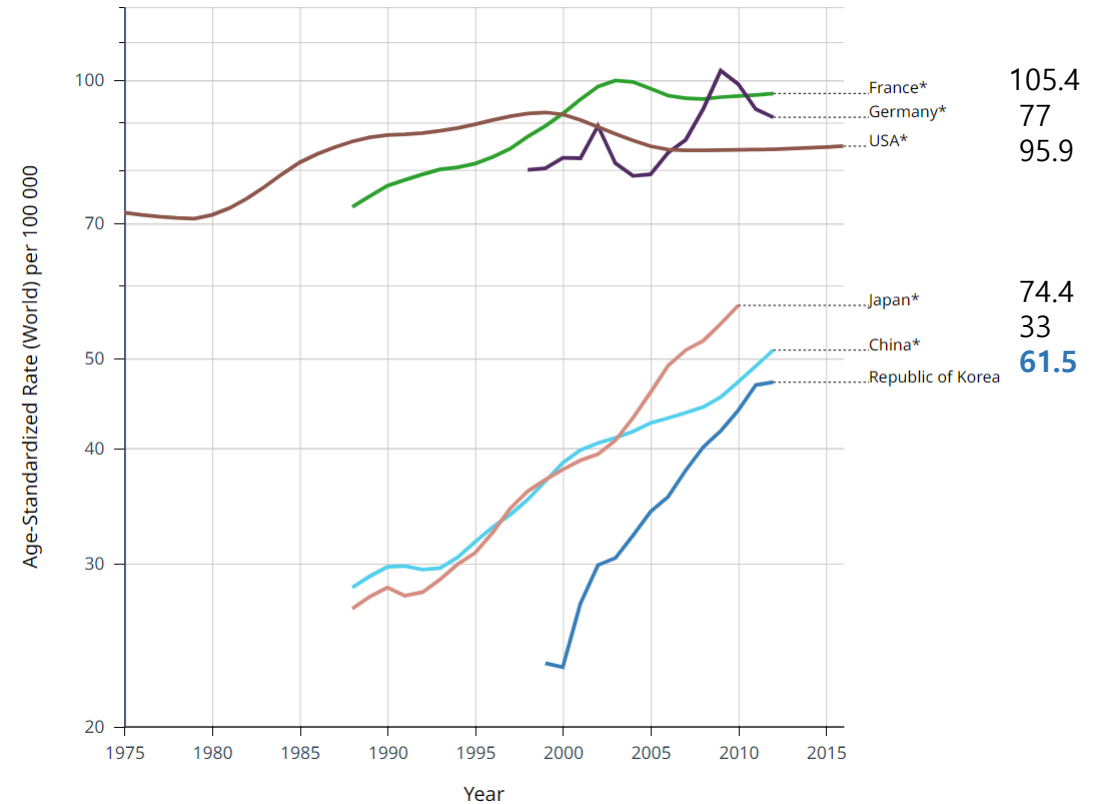
국가암정보센터. 암발생국제비교, 2021
Cancer over time. IARC WHO

우리나라 유방암 현황

2020년 약 3만명 발생

40대 후반, 50대 초반에 호발
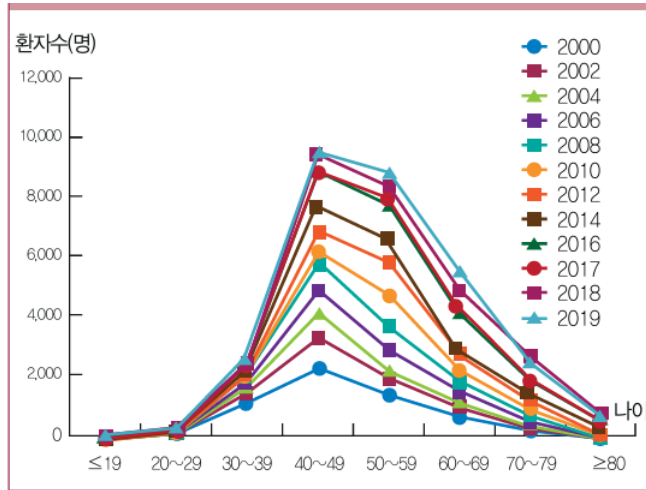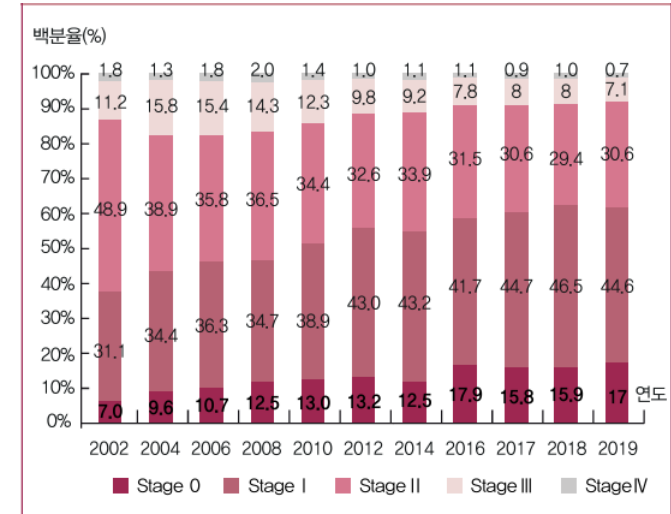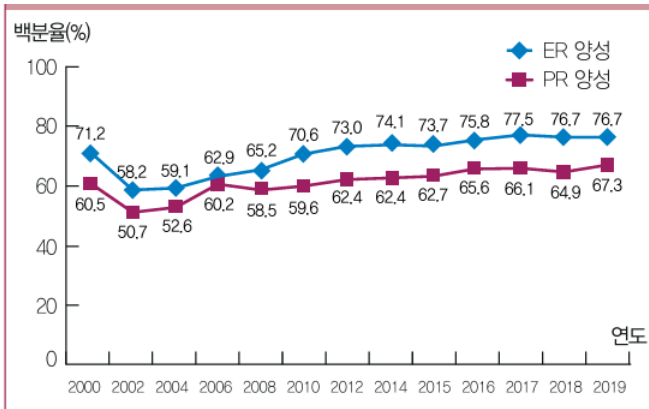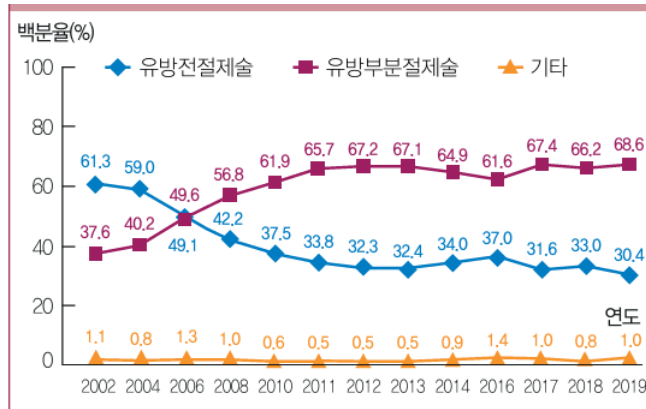
0~1기 환자가 61%

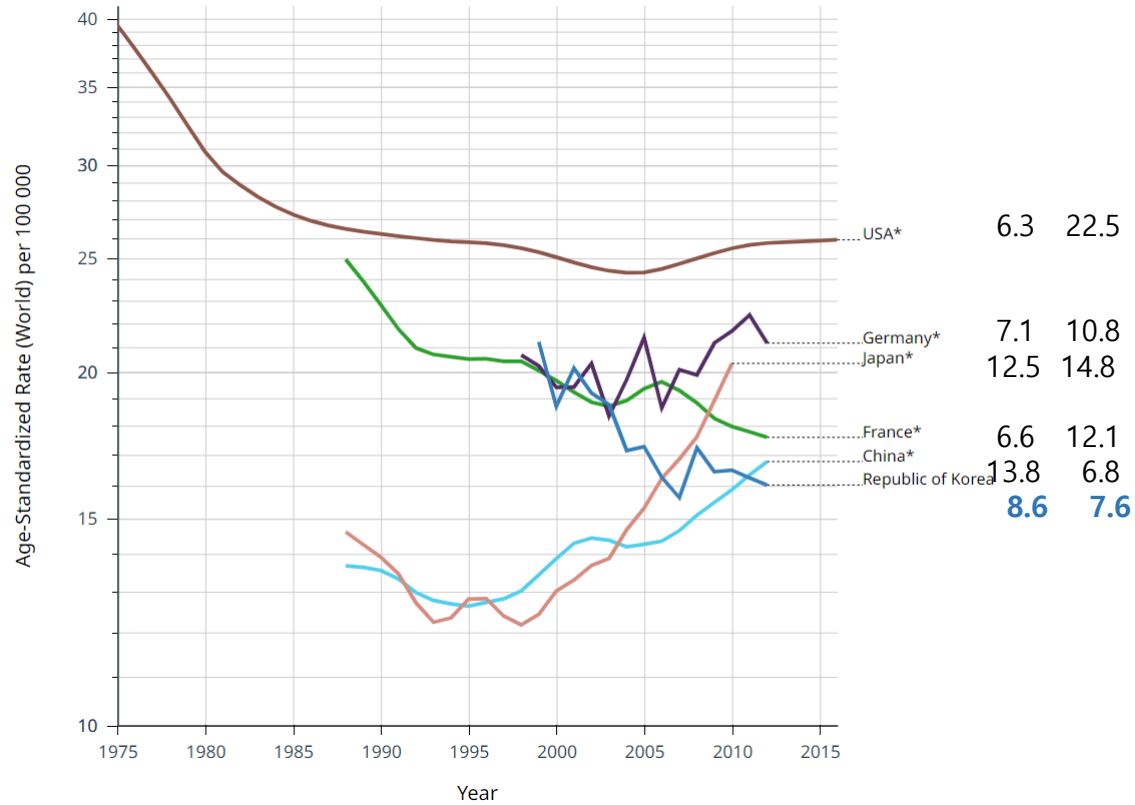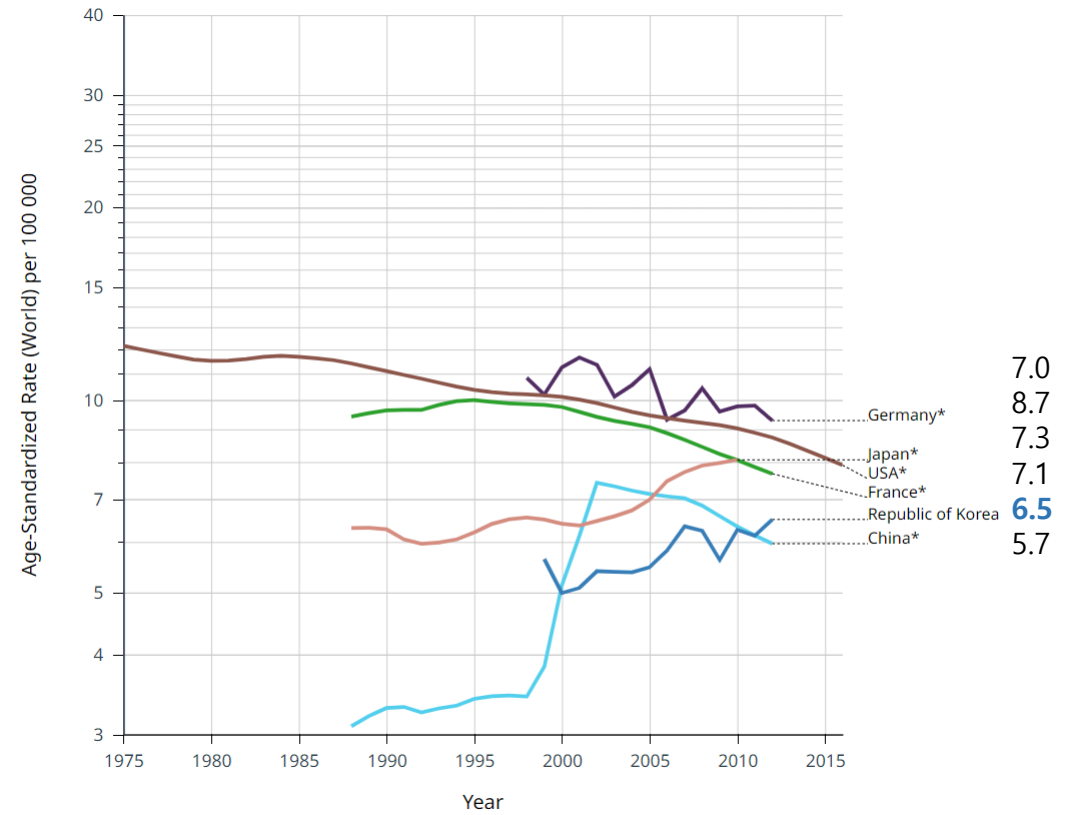
2022 유방암백서
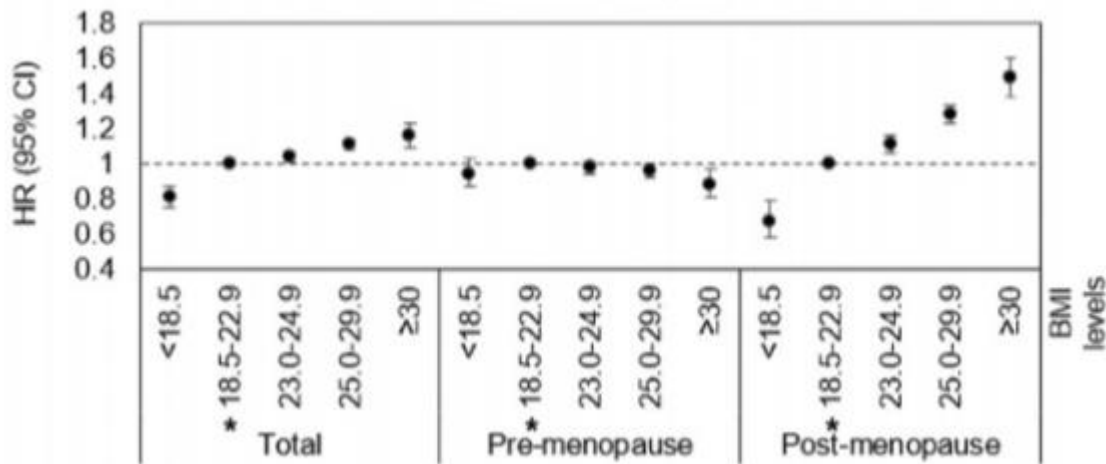
국내 여성암 발생

자궁암(경부, 체부)

난소암

Cancer over time. IARC WHO

Obesity as a risk factor for breast cancer diagnosis

Obesity as a risk factor for breast cancer diagnosis

- Risk factor in postmenopausal women, KNHIS (2.7 million, 2009, mean FU 8.4 yrs)[1]

- Obesity is associated with a more advanced breast cancer stage.[2]

BMI	Stage 0/I		Stage II/III		
	Number	%	Number	%	OR (95% CI)
Age <50					
<27.3	1378	68.7	627	31.3	
≥27.3	82	47.4	91	52.6	2.439 (1.783-3.335)
Age ≥50					
<27.3	1290	67.5	622	32.5	
≥27.3	254	60.5	166	39.5	1.356 (1.090-1.685)

1) Park I et al. Lancet Regional Health 2021:11;100146.
2) Lee Y et al. Clinical Breast Cancer 2021:21(6);e631

- Breast cancer diagnosed at a single center (N=418, 2014-2018)

- Have higher BMI
- More likely to have advanced dis

JS Lee. J Breast Dis 2020;8(2):108-114

Korean Obesity Index Standard Reference

Characteristic		< 75 percentile	≥ 75 percentile	p-value
Tumor size (cm)*		1.91 ± 1.3	2.15 ± 1.87	0.026
Positive lymph node (No.)*		1.02 ± 4.2	1.75 ± 5.0	0.011
Characteristic		No. (%) (n = 198)	No. (%) (n = 220)	p-value
Menopause	Pre-	132 (66.7)	99 (45.0)	< 0.001
	Post-	66 (33.3)	121 (55.0)	
Stage	0	42 (21.2)	41 (18.6)	0.030
	I	88 (44.4)	83 (37.7)	
	II	54 (27.3)	68 (30.9)	
	III	13 (6.6)	23 (10.5)	
	IV	1 (0.5)	5 (2.3)	
HER2	Negative	151 (76.3)	171 (77.7)	0.720
	Positive	47 (23.7)	49 (22.3)	
ER	Negative	66 (33.3)	70 (31.8)	0.840
	Positive	131 (66.2)	148 (67.3)	
PR	Negative	87 (43.9)	99 (45.0)	0.560
	Positive	107 (54.0)	113 (51.4)	
Ki-67	≥ 14%	92 (46.5)	97 (44.1)	0.650
	< 14%	98 (49.5)	110 (50.0)	

Menopause and receptor status

폐경 전

폐경 후

Picon-Ruiz M et al. CA CANCER J CLIN 2017;67:378–397
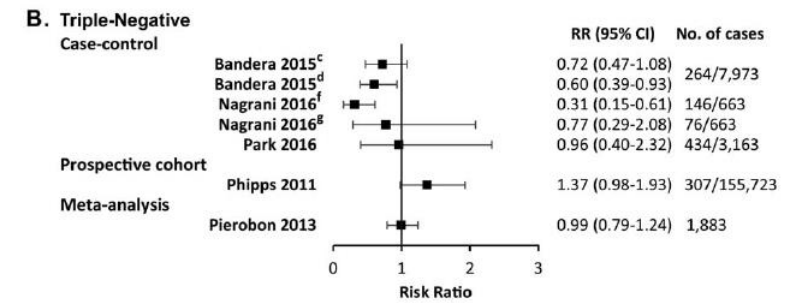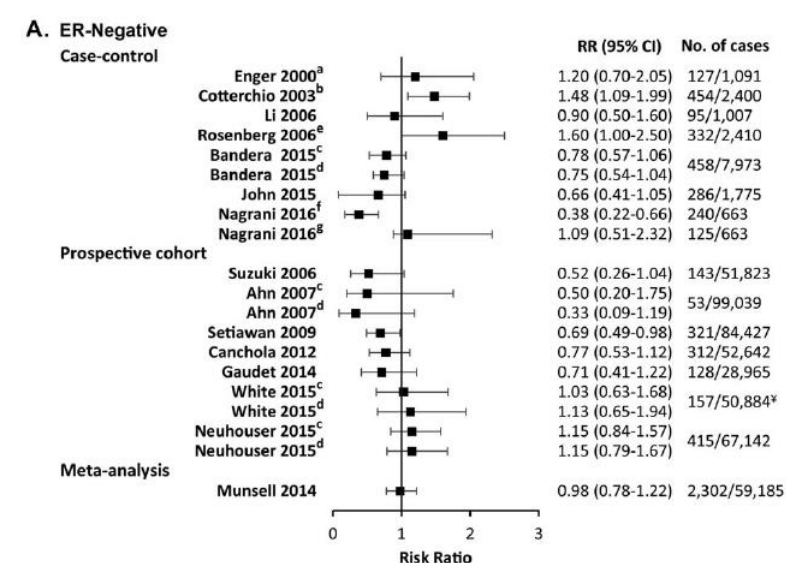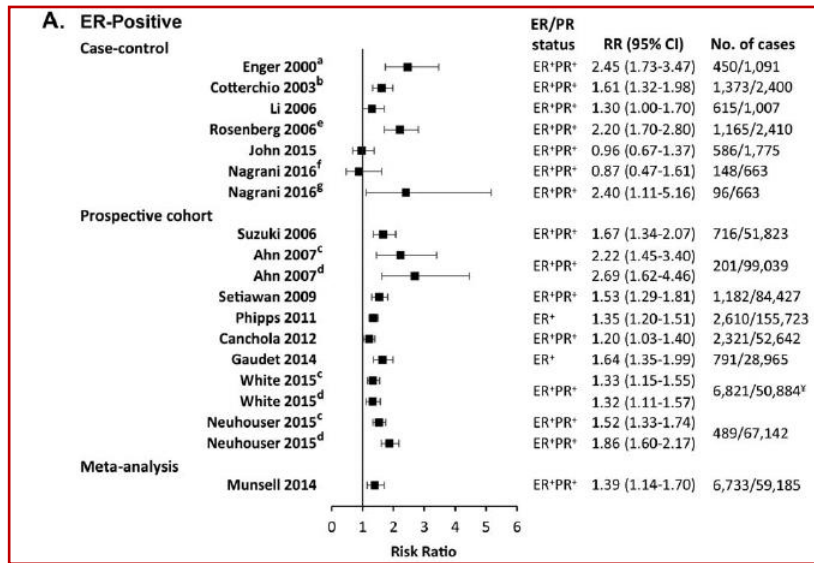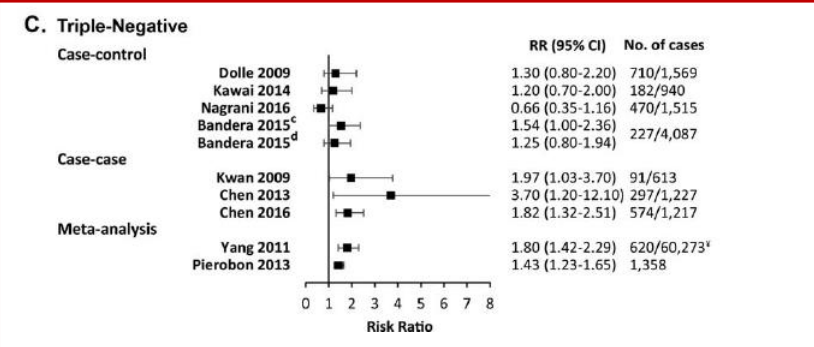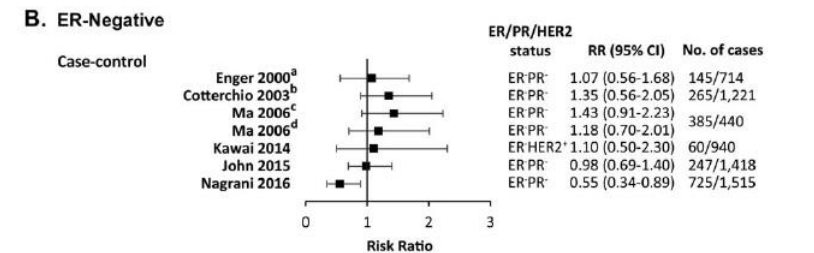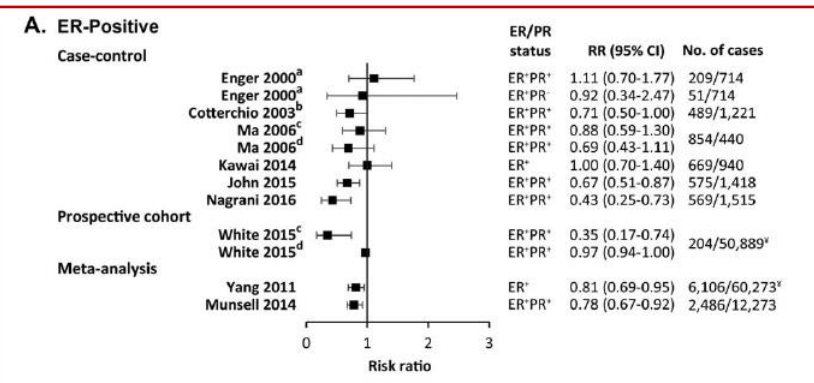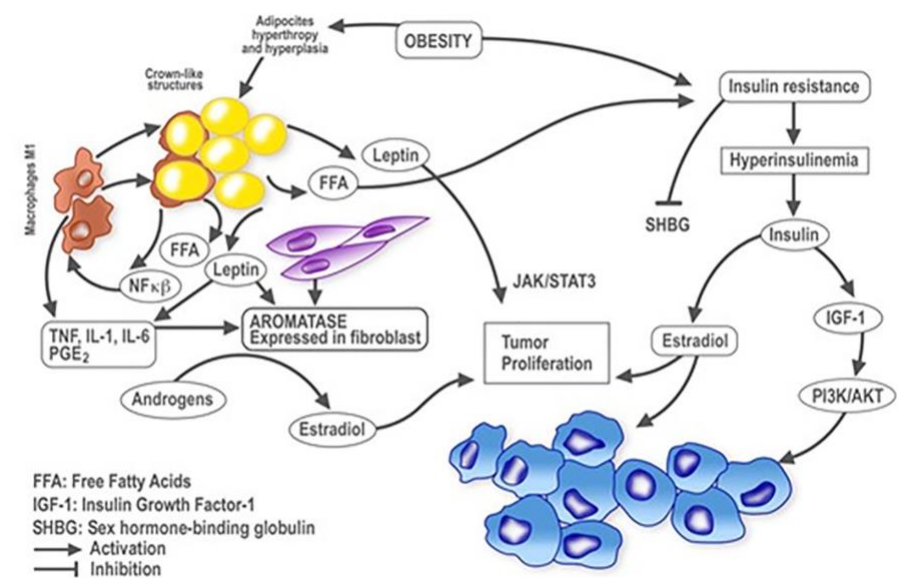
Potential mechanisms

- Difficulty of detecting a palpable mass (in low SES women)

- High estrogen d/t elevated **aromatase** transcript levels by adipose tissue
- Leptin: aromatase activity ↑
- Insulin signaling pathway
- Chronic inflammation

- Activating estrogen bioactivity by
  weakening sex hormone-binding globulin

Lee Y et al. Clinical Breast Cancer 2021;21(6):e631
García-Estevez L et al. Front Oncol 2021;11:705911

Breast cancer dx & tx
as a risk factor for obesity
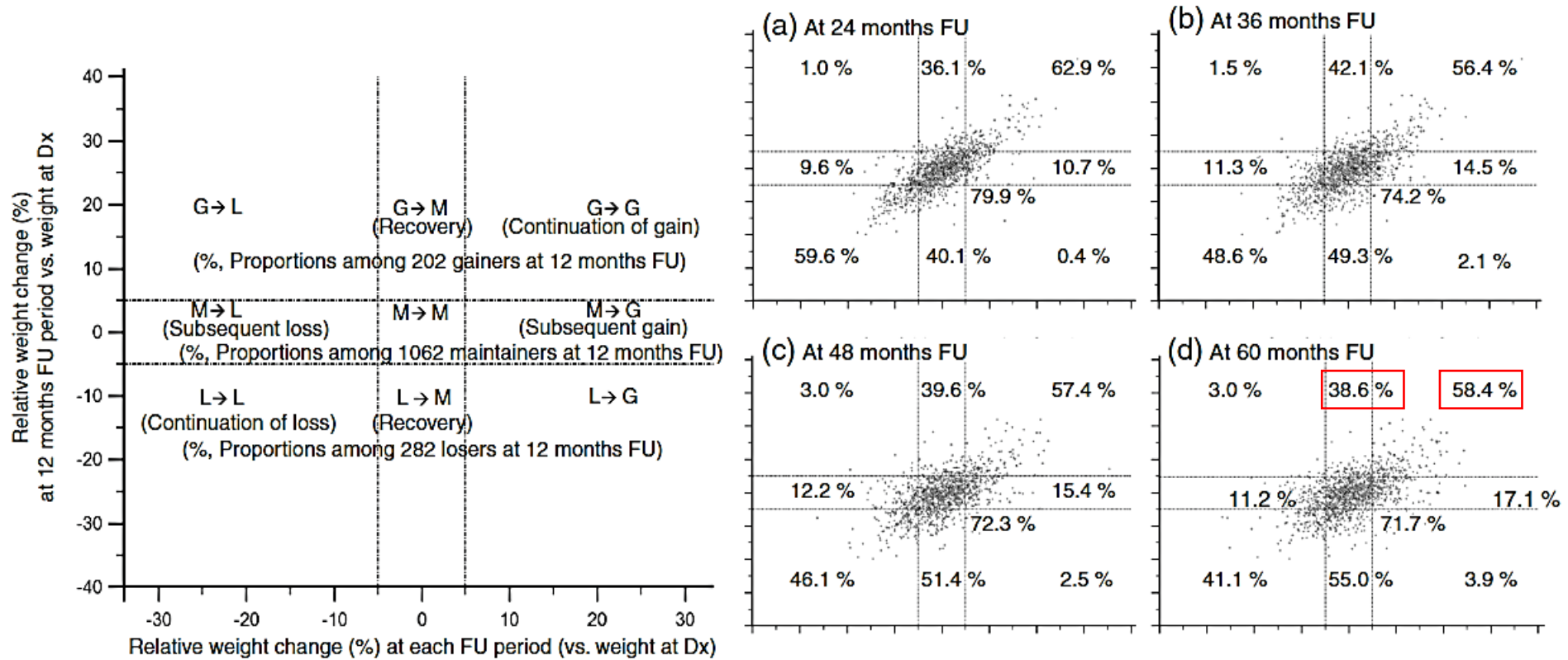# and metabolic derangement

Breast cancer survivors gain weight

- Breast cancer survivors with normal BMI @ AMC (N=1546), FU 5 yrs
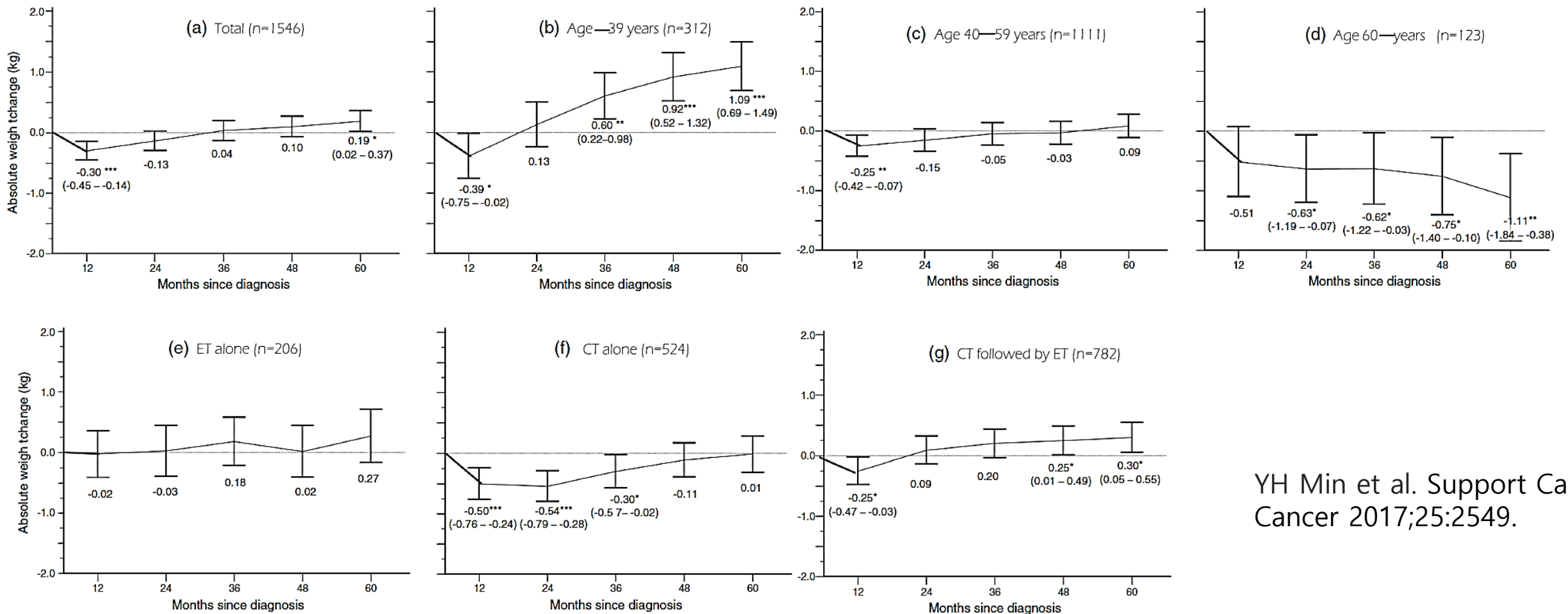
YH Min et al. Support Care Cancer 2017;25:2549.

1년 뒤 체중이 증가한 사람 중 40%는 원래 체중으로, 60%는 증가 유지

YH Min et al. Support Care Cancer 2017;25:2549.
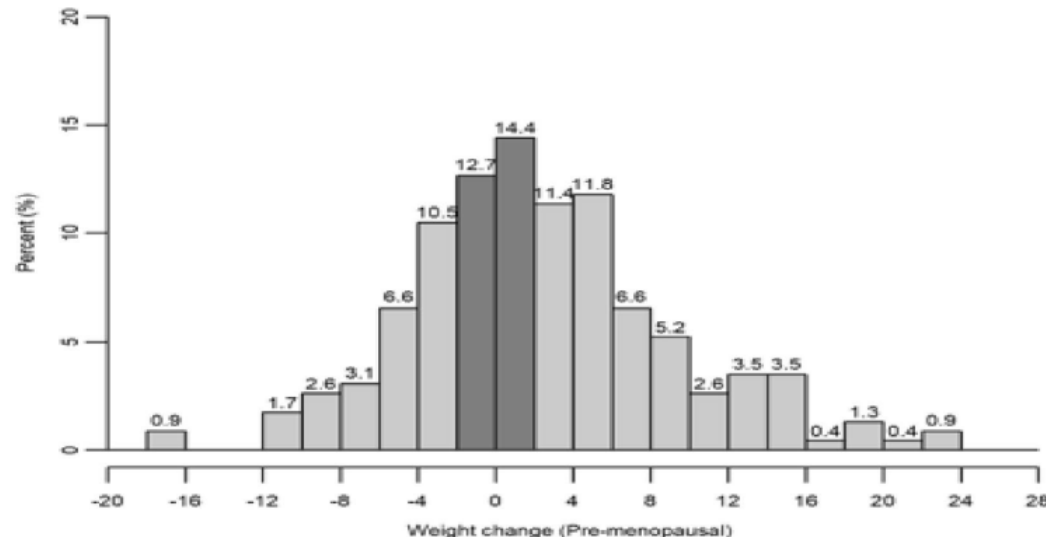
Chemotherapy may cause wt gain

- Meta-analysis (N=2620)

  2.7 kg(95% CI 2.0-7.5) 증가

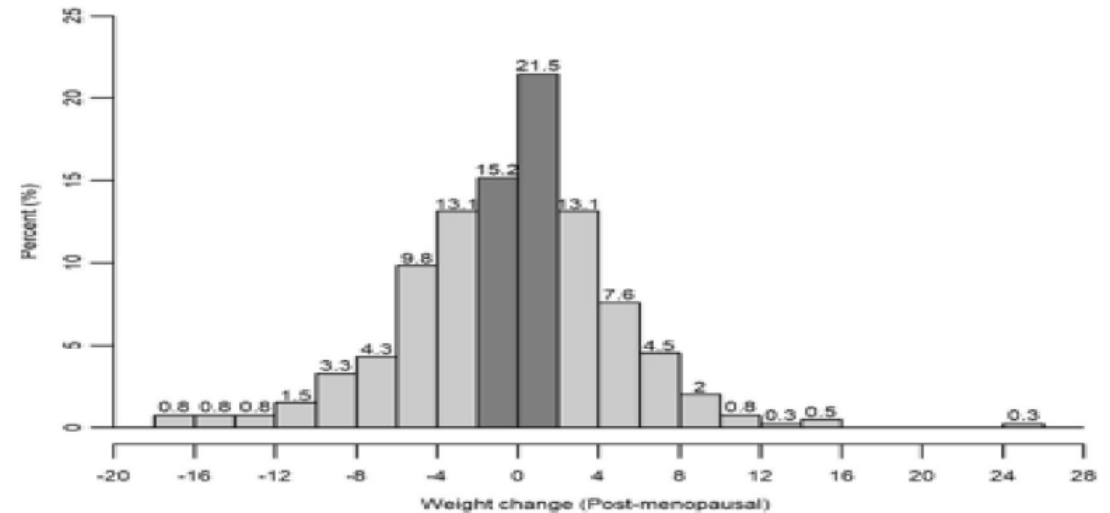- cyclophosphamide, methotrexate and 5-fluorouracil (CMF) regimes showed a greater weight gain.

Berg et al. BMC Cancer 2017;17:259.
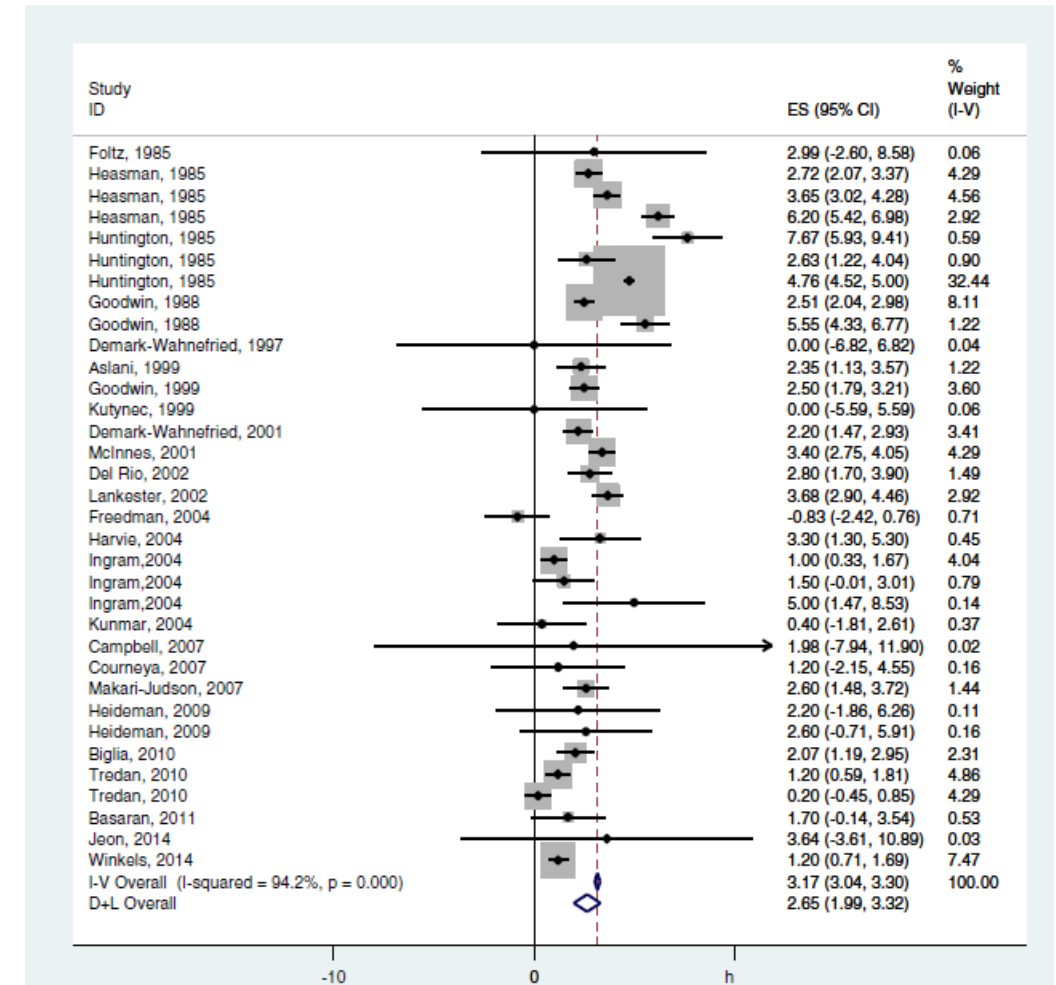
Endocrine therapy may not cause weight gain

- Early breast cancer cohort (N=625), FU 2 yrs

Pre-menopausal patients

Post-menopausal

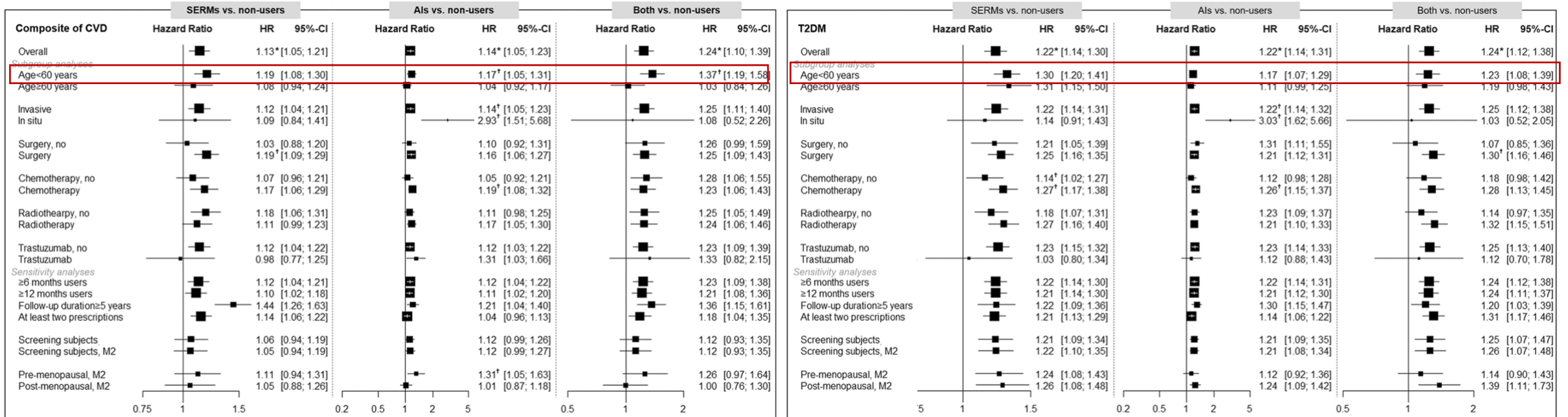- 폐경 전 여성이 체중증가를 많이 경험한다.
- Any ET RR=0.78(95% CI, 0.62-0.97)

Nyrop KA et al. *Breast Cancer Res Treat* 2020:179:709-720
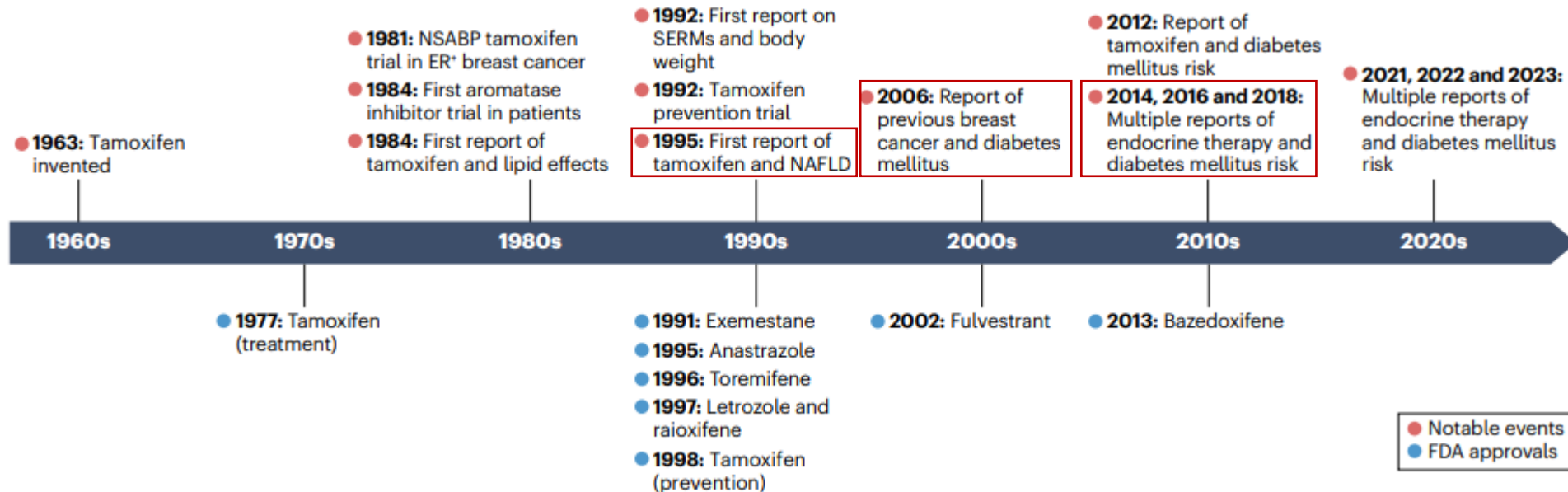
Endocrine therapy may cause CVD/T2DM

유방암 환자의 당뇨병 발생률이 높았고 EE=1.23 (1.13-1.33)

호르몬치료를 받은 유방암 환자의 당뇨병 발생률도 높았다. EE=1.23 (1.16-1.32)

Kim JE et al. J Am Heart Ass 2022:11:e026743
Jordt N et al. Breast Cancer Res Treat 2023:202(1):11-22

# Endocrine therapy and risk of metabolic disease

- Estrogens and ER activation (protecting against metabolic disease) are disrupted with breast cancer treatment.
- T2DM due to impaired hypertrophic adipose tissue expansion?

Thomas NS et al. Nature Reviews Endo 2024;20:16-26

Obesity as a prognostic factor

Recurrence of breast cancer

- Danish Breast Cancer Group cohort
  - Postmenopausal women with stage I – III, HR+, AI use (1998-2016)
  - N=13,230 FU 6.2 yrs (median), recurrence 21.4/1,000 person-yr
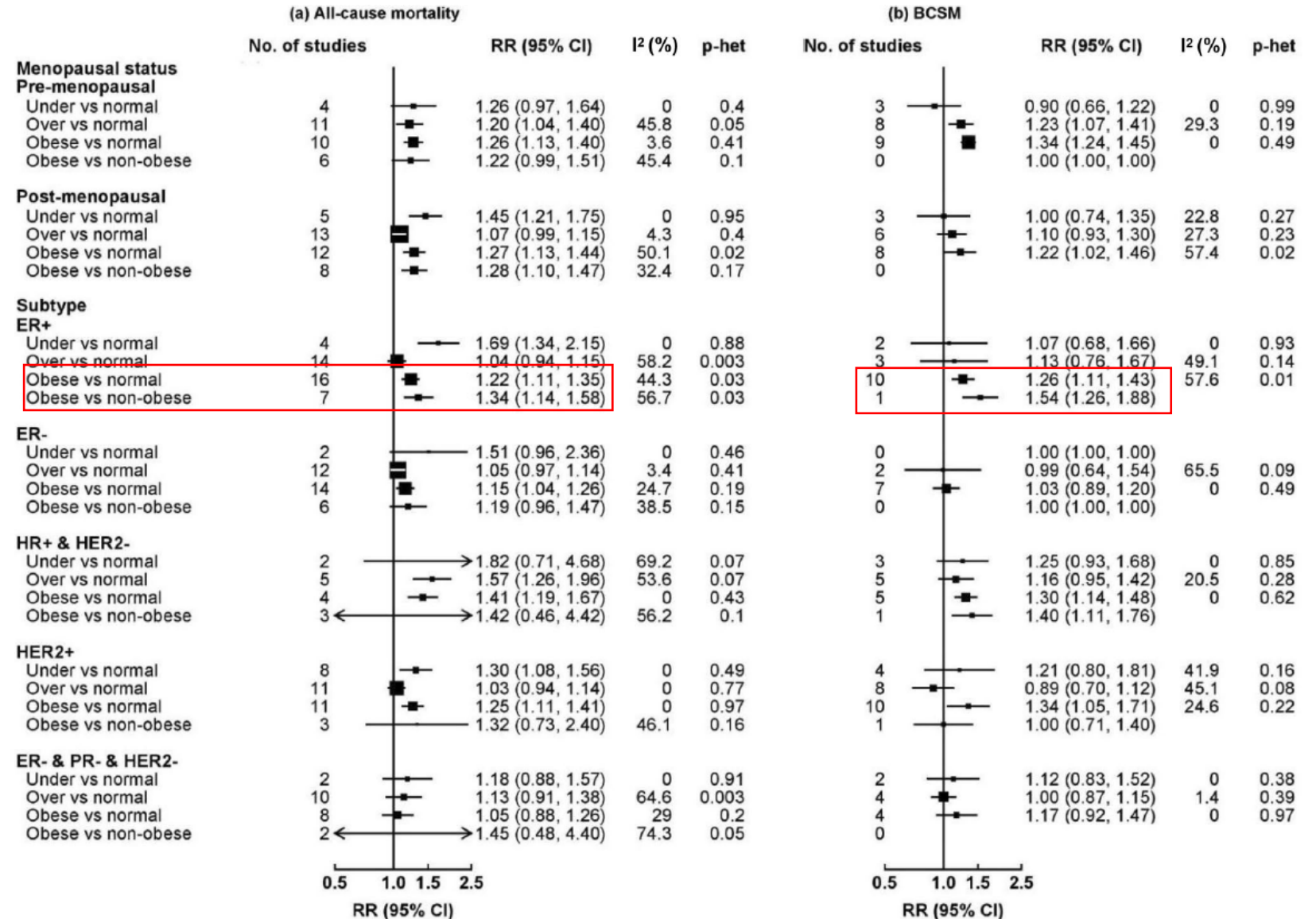

BMI 증가하면 재발 위험이 증가

Harbog S et al. JAMA Netw Open 2023
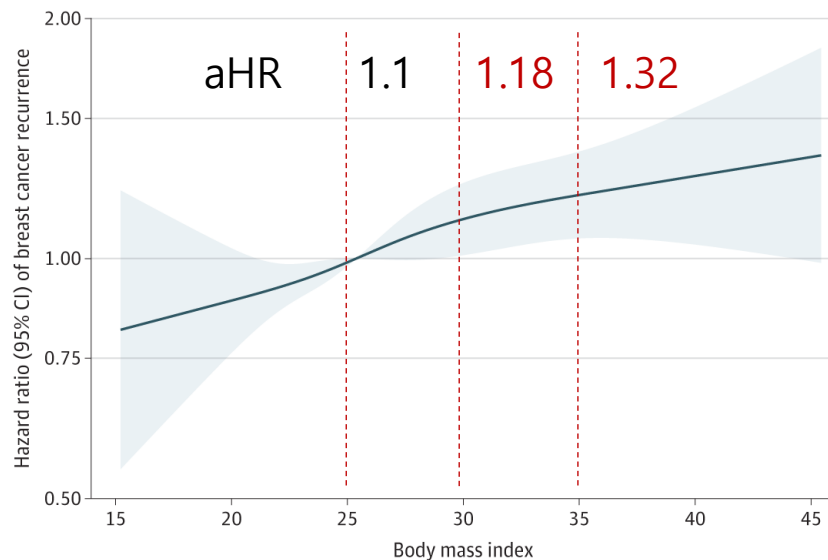
Survival and recurrence of breast cancer

- Meta analysis (N=519,544)

- 비만(진단 후 1년 미만 시점의 BMI 기준)은 총사망률, 유방암사망률, 재발의 위험요인

Pang Y et al. Breast Cancer 2022

(a) All-cause mortality / (b) BCSM — forest plot comparing RR (95% CI) by menopausal status and subtype.

Breast cancer related lymphedema

- Meta-analysis (N=8,039 pts)
  Incidence of lymphedema 26%
  BMI 25-30 vs. BMI <25   BMI 30> vs. BMI <25
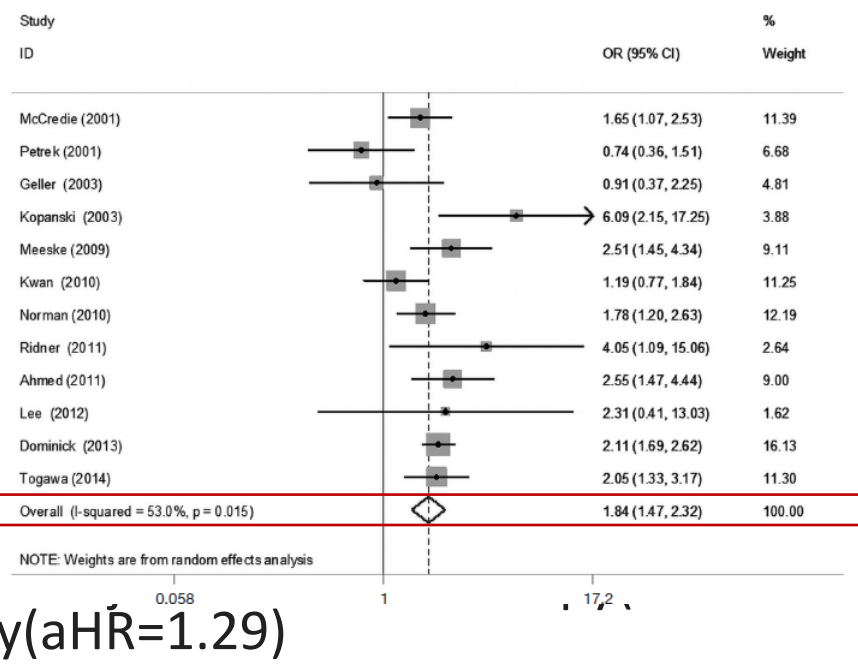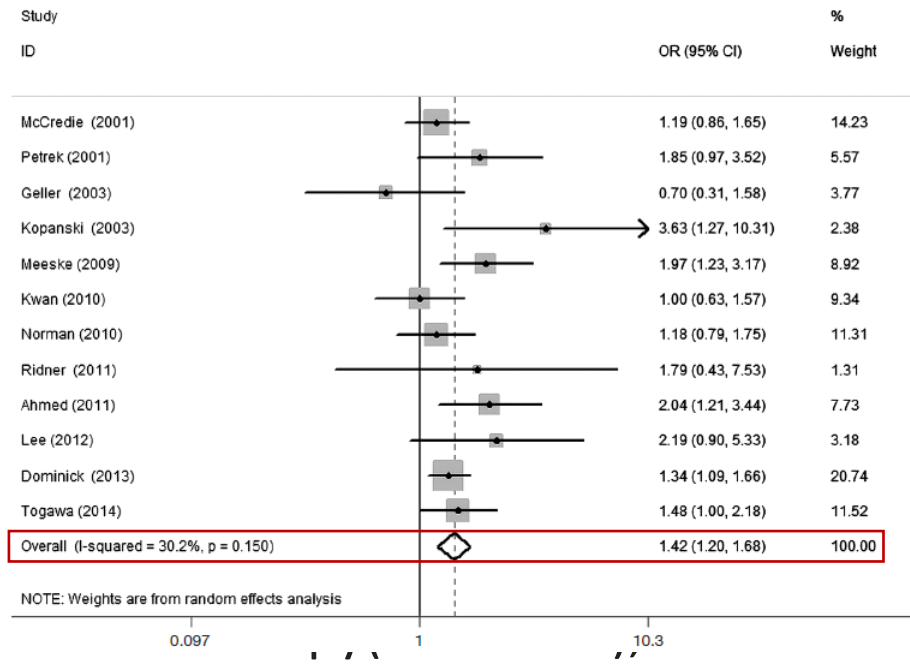
- |

), adjuvant

y(aHŔ=1.29)

Obesity on QOL of survivors

- Body images, sexual function, urinary incontinence
- Neuropathy is more common in obese patients
- Risk factor for cardiotoxicity
- Chronic fatigue

Sheng JY et al. Obese Breast Cancer Patients and Survivors: Management Considerations. Oncology 2018 Aug 15;32(8):410-7.

Obesity management as prevention for breast cancer survivors

Recommendations from major cancer organizations

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2024
Survivorship: Nutrition and Weight Management

GENERAL PRINCIPLES OF WEIGHT MANAGEMENT

- All survivors should be encouraged to achieve and maintain a BMI between 18.5 and 24.9 kg/m² and strive for metabolic health.
  ▸ Intentional weight gain should be a priority for survivors who have underweight. **(SNWM-4)**
  ▸ Intentional weight loss should be a priority for survivors who have overweight/obesity.
    ◊ Weight gain after cancer diagnosis and treatment is common and may exacerbate risk for functional decline, comorbidity, and possibly cancer recurrence or death, and may reduce quality of life.
  ▸ Weight maintenance should be a priority for survivors who have a BMI between 18.5 and 24.9 kg/m².
- In conjunction with primary care, survivors should be assessed for metabolic health and body composition independently of BMI.
- Weight management includes a three-pronged approach: caloric management, physical activity, and behavior modification.
- Providers should discuss strategies and goal setting for weight management and optimal metabolic health, including how to achieve low overall body fat and higher amounts of muscle mass.
    ◊ Practice portion control.
    ◊ Make informed food choices through routine evaluation of food labels.
    ◊ Incorporate physical activity, particularly strength training, to assure optimal lean body mass **(SPA-1)**.
    ◊ Monitor weight, diet, calories, and physical activity routines (eg, journaling, mobile phone apps).
- Referrals to registered dietitians, especially those who are Certified Specialists in Oncology Nutrition (CSO) and members of the Oncology Nutrition Dietetic Practice Group of the Academy of Nutrition and Dietetics, should be considered.[h]
- There is no current evidence to support the use of weight loss supplements in cancer survivors.

| WCRF and AICR Report on Breast Cancer, 2018[69] | • Avoid sugared beverages and processed meat, limit calorie-dense food, alcoholic beverages, salty food, and red meat
• Eat mostly food of plant origin, with a variety of non-starchy vegetables, foods containing carotenoids, and foods high in calcium
• Limit alcoholic drinks | • Aim for ≥ 150 min of moderate or 75 min of vigorous aerobic exercise per wk | • Avoid weight gain and limit body fatness by having a BMI, waist circumference, and waist-hip ratio in normal range |

Sheng JY et al. Oncology 2018 Aug 15;32(8):410-7.

Rehabilitation managing obesity-related breast cancer

Issue	Practical Approach
Weight Management	Intentional weight loss
	Lifestyle interventions (dietary modification, exercise, psychological support)
Physical Activity Recommendations	At least 150 min of moderate-intensity exercise per week
	More significant body mass index reduction with increased exercise duration
Cancer-Related Fatigue	Exercise as a pivotal element for fatigue alleviation
Cancer-Related Lymphedema	Precise assessment through innovative tools (e.g., three-dimensional assessment of lymphedema)
	Personalized self-adjusting braces and rehabilitation regimens
Surgery-Related Joint Dysfunction	Active and passive early mobilization, and upper extremity exercises after surgery
Weight-Related Joint Pain	Aquatic therapy to alleviate weight-bearing stress on joints
	Tailored exercise regimes emphasizing low-impact activities and joint-specific exercises
Small Joint Pain in Aromatase Inhibitor Treatment	Consideration of vibrating platforms to improve musculoskeletal health

Lippi L et al. Cancers 2024;16:521

Interventions for obese BCS

- Cochrane Database Systematic Reviews (2020)
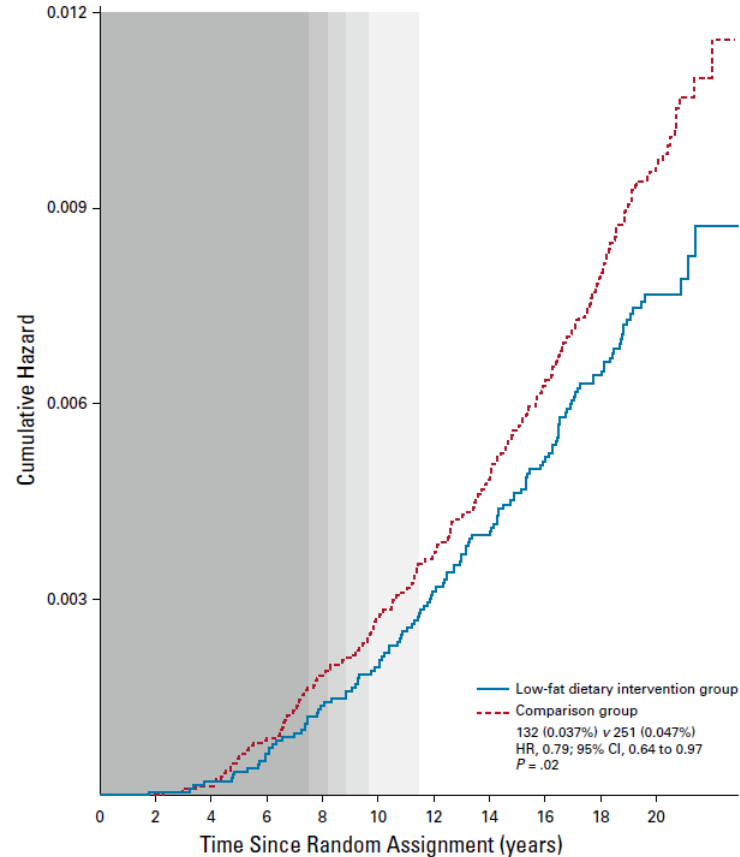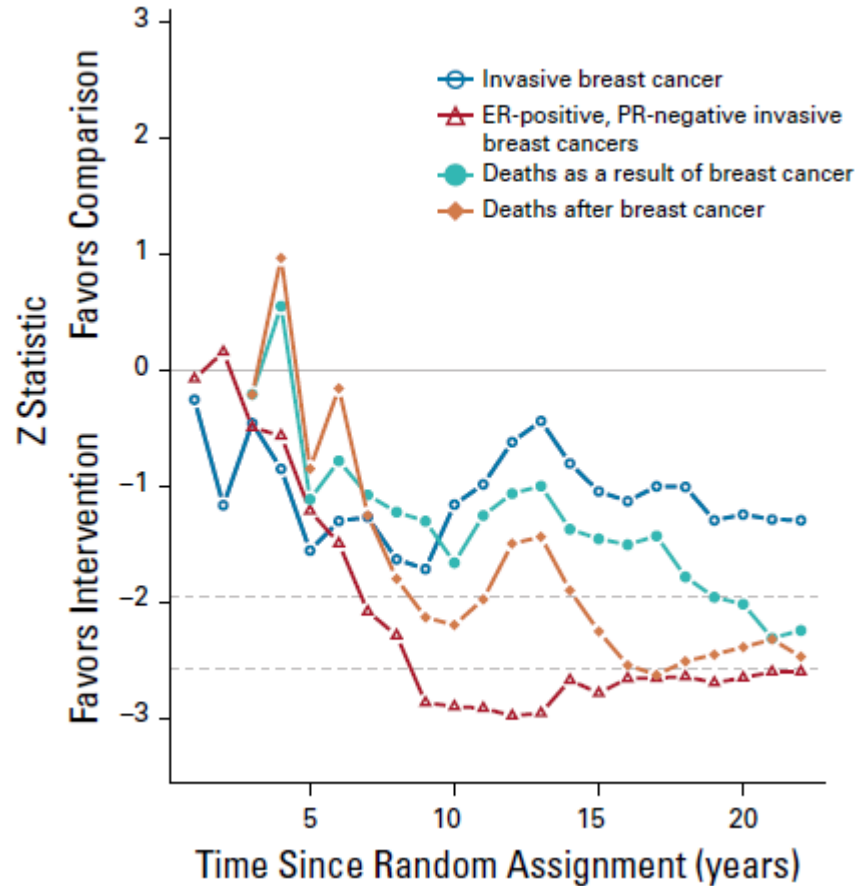 20 studies (N=2,028) intervention 2 wks-2 yrs, FU 3-36 mo

  식사, 운동, 심리적 지지를 포함하는 다학제 접근은 대조군에 비해
  체중 감소(MD: -2.25 kg, 95% CI: -3.19 to -1.3)
  BMI 감소(MD: -1.08 kg/m², 95% CI: -1.61 to -0.56)
  허리둘레 감소 (MD:-1.73 cm, 95% CI: -3.17 to -0.29)
  QOL 호전 (SMD: 0.74; 95% CI: 0.20 to 1.29) 효과를 보인다.

Shaikh H et al. *Cochrane Database of Systematic Reviews* 2020, Issue 12. Art. No.: CD012110.

Dietary modification on breast cancer occurrence and survival

· 그에 따른 사망

ble, and grain intake;

Chlebowski RT et al. J Clin Oncol 2020;38:1419-28

RCT: Lifestyle interventioin and breast ca outcome

- The LISA trial (Canadian Life Style Intervention in Adjuvant Treatment of Early Breast Cancer trial)
- N= 338 women (BMI 24-40 kg/m2), 2-year, telephone-based intervention (- 500 ~ 100 kcal/D), 8 yr FU
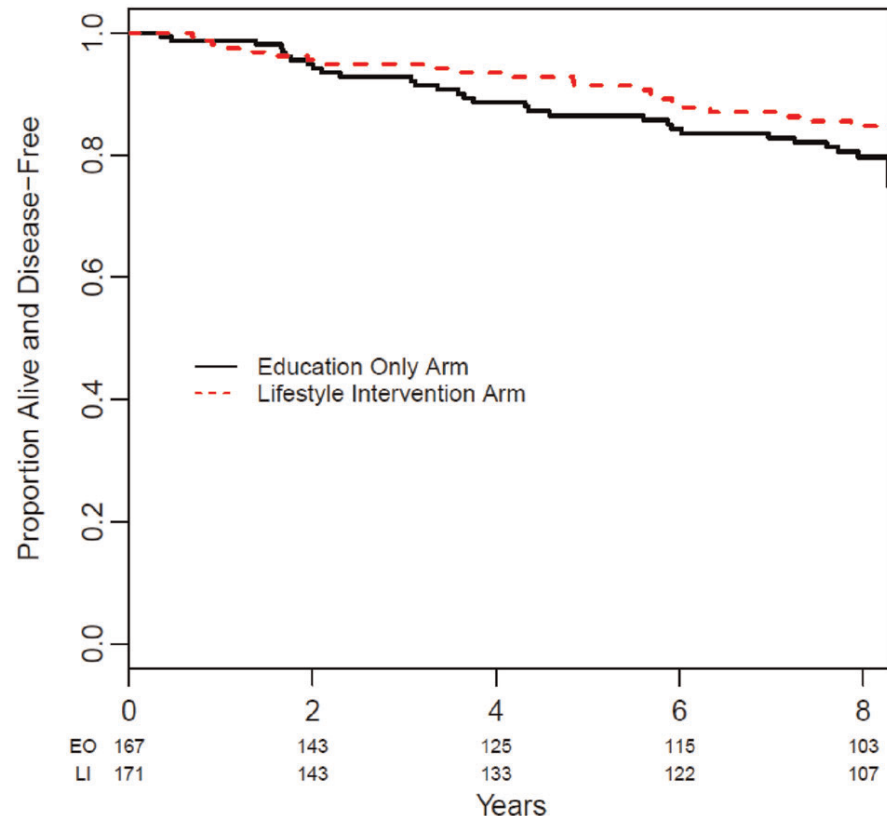
Disease free survival HR = 0.71 (CI 0.41-1.24, P=0.23)

Educ only 30/167 (18%) vs LS intervention 22/171 (12.9%)

Overall survival HR =0.86 (95% CI: 0.35–2.14, p = 0.74)

Terminated early due to loss of funding, lack of power

Goodwin PJ et al. npj Breast Cancer 2020;6:6

Anti-obesity medicine for breast cancer survivors

- **No current evidence** to support to use of wt loss supplements in cancer survivors

- Poor wt loss outcomes in breast cancer survivors on AI/AOM compared to patients without breast cancer history and not taking AIs.

- Use of GLP-1 RAs was significantly associated with a lower risk of all-cause mortality among all-type cancer survivors (HR, 0.36; 95% CI, 0.25-0.51)
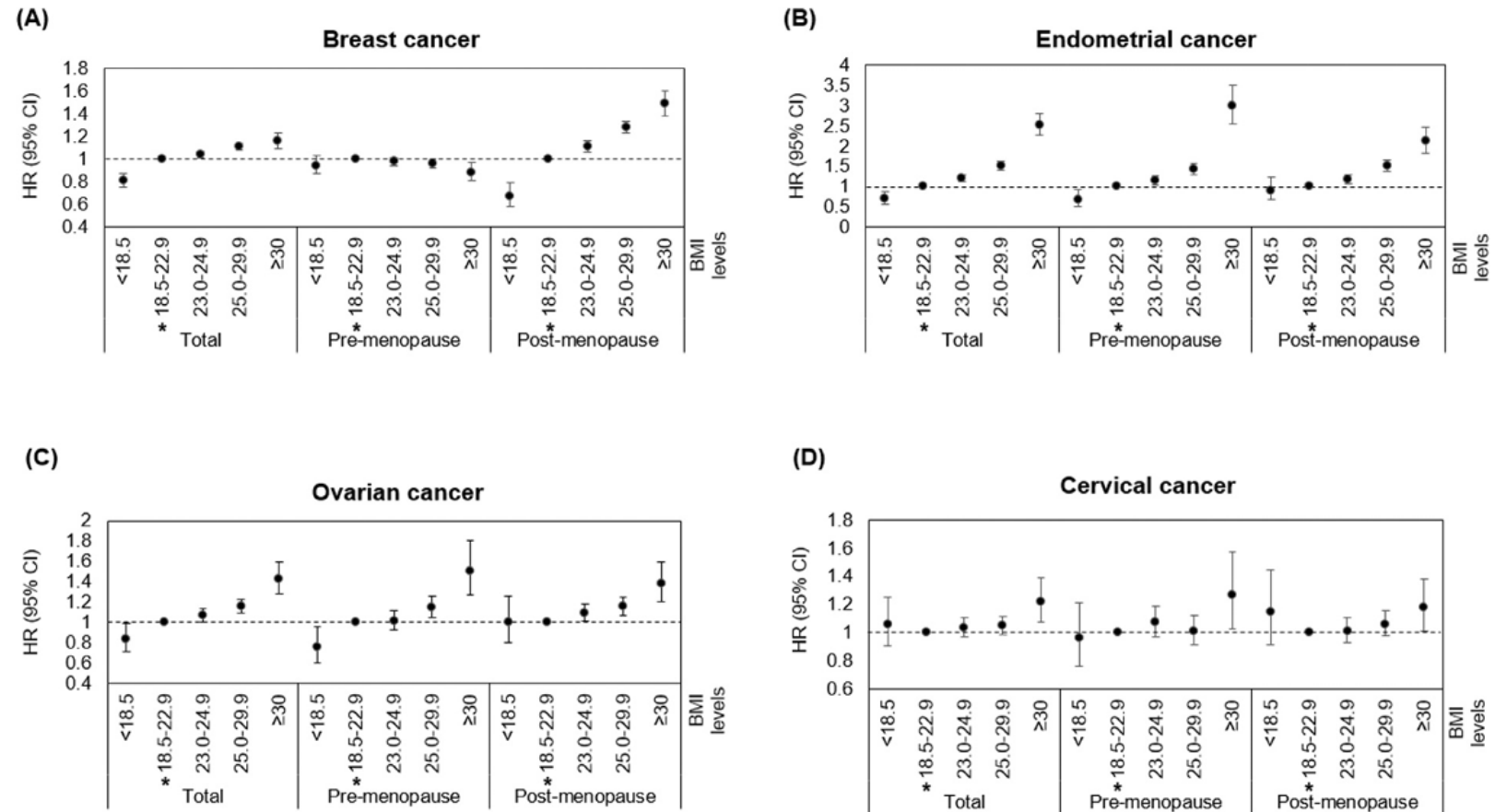
Sima Fansa et al. J Endocrine Soc 2023;7(Suppl 1) A48. Endo2023
Chen P-H et al. Cancer Res 2023;83(Suppl 7):735

Other female-specific cancers

Obesity and female-specific cancers

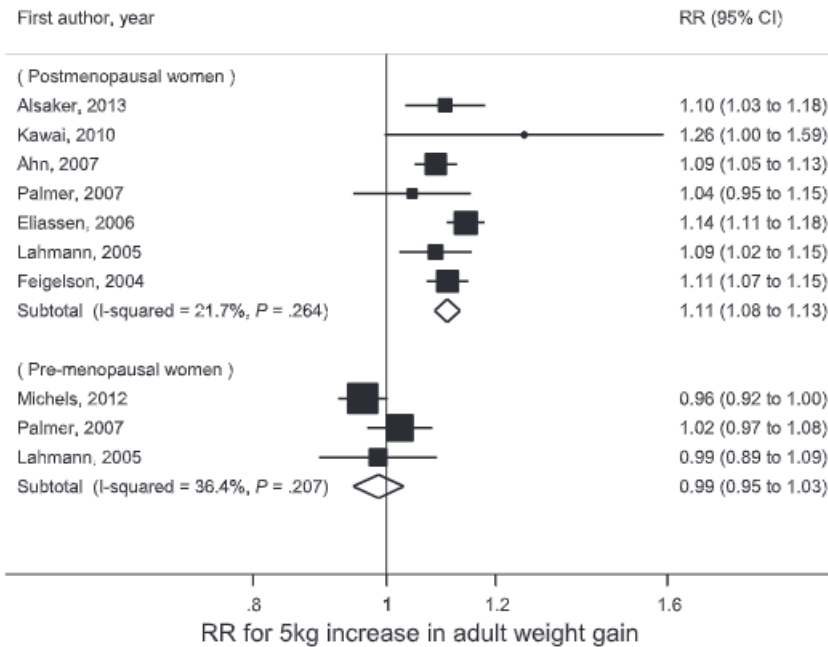Korean NHSD (N=2.7 million), FU 8.4 yrs
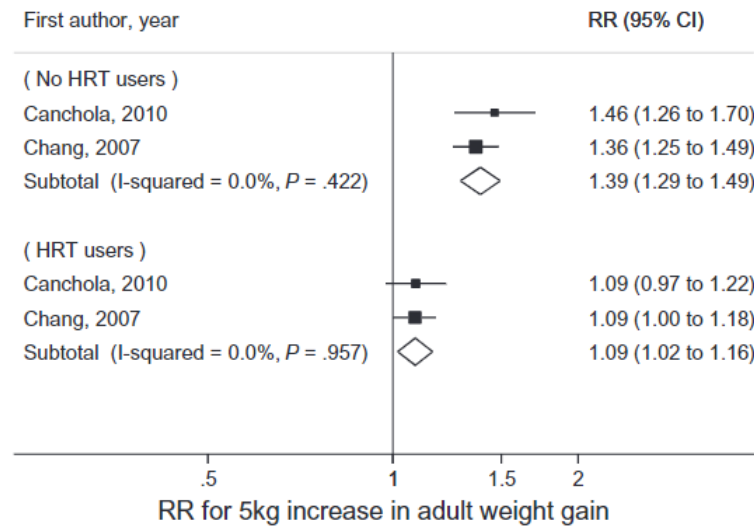
(폐경후 여성의) BMI
가 증가할수록 여성암
발생이 증가한다.
(서양과 비슷한 양상)

Park IS et al, The Lancet Regional Health 2021:11;100146.

Adult wt gain and cancer

- Meta-analysis (46 publications)
- RR for 5 kg wt gain

Keum N et al. J Natl Cancer Inst 2015
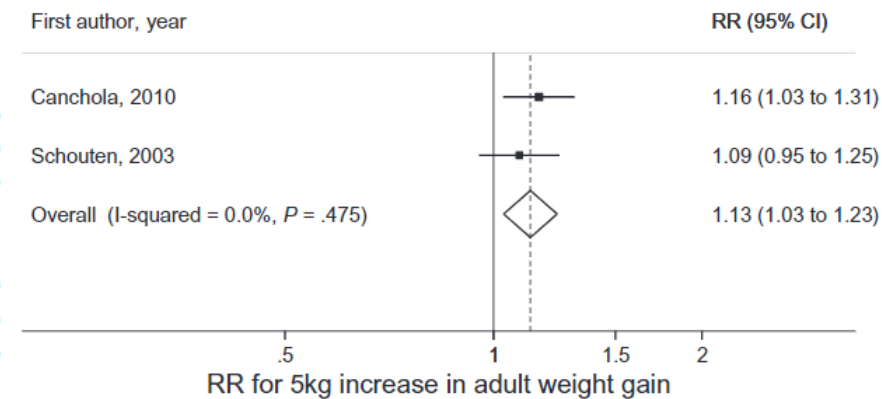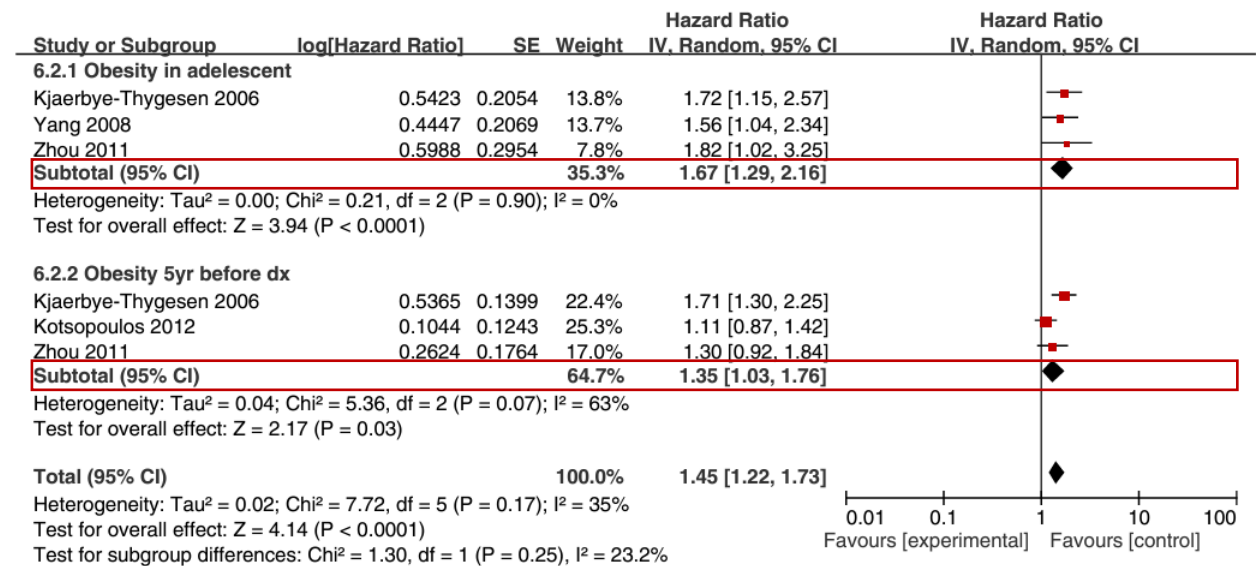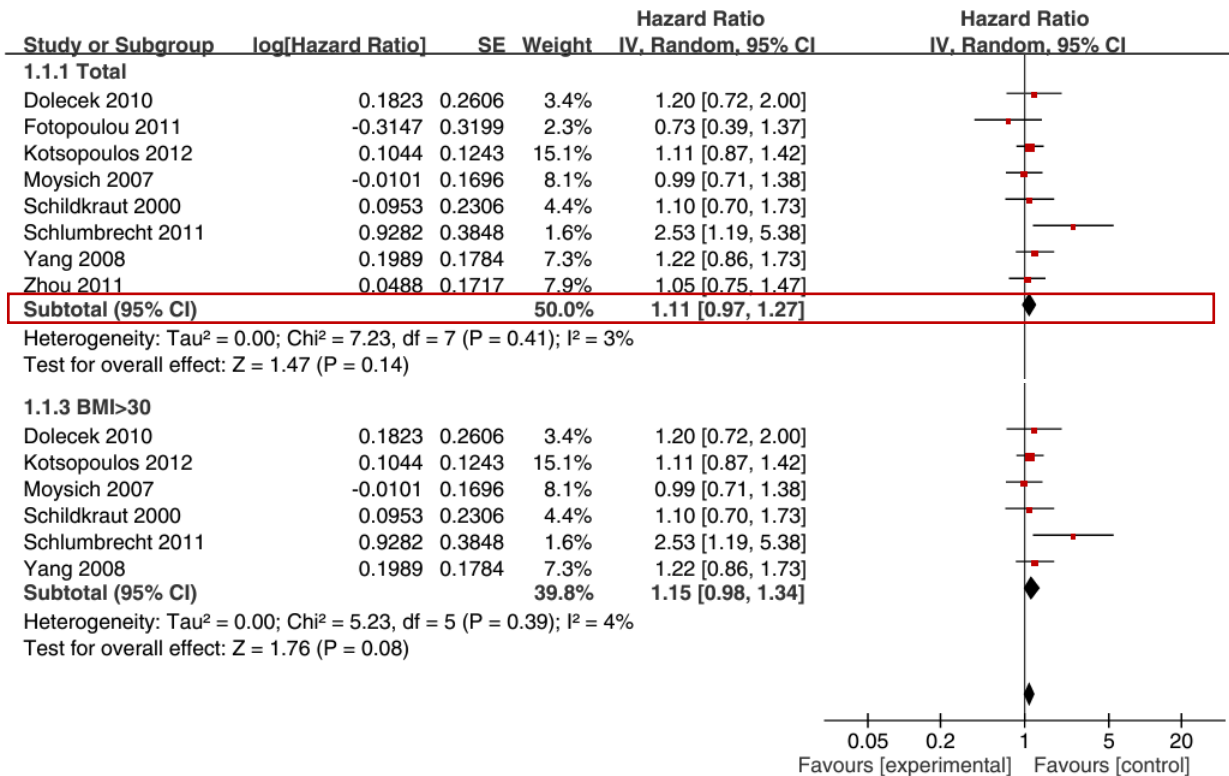
Obesity and ovarian cancer survival

- Meta-analysis (17 cohort studies)
  성인 초기 비만과 난소암 진단 5년 전 비만이 있으면 사망률이 높다.

Summary – Filling the Gap!

- 비만은 유방암, 난소암, 자궁내막암 발생의 위험요인이다.
- 유방암 치료에 사용하는 항암제는 체중 증가와 관련이 있고 호르몬 치료는 당뇨병이나 심혈관질환 발생을 증가시킨다.
- 비만인 유방암 생존자는 림프부종이 많이 발생하고 암 재발의 위험이 높고 사망 위험도 증가한다.
- 다학제 비만 중재는 체중과 허리둘레를 유의하게 줄이고 삶의 질을 향상시킨다.
- 유방암 치료 초기부터 적극적으로 체중 증가를 예방하고 비만치료를 병행하는 시도가 필요하다.