

Pregnancy-associated **breast cancer**

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A pregnant woman in a white dress is shown from the waist up, holding a large yellow flower to her belly. The background is a light pink gradient.

**Pregnancy-associated
breast cancer**

Scope of problem

Characteristics

Diagnosis and **treatment**

Pregnancy after breast
cancer



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Definition of PABC

Breast cancer diagnosed during pregnancy

or in the first postpartum year

“Dual effect” of pregnancy

pregnancy has a protective effect on BC risk

recent pregnancy increases the risk of BC

(esp, ≥ 35 years)

Incidence of PABC

Rare

Occurs 1 in 3000 pregnancies

0.2% ~ 3.8% of all breast cancer

Only 6.5% of all BC diagnosed in fertile women

< 40 years

Johannsson O, et al. Lancet 1998;352:1359-60

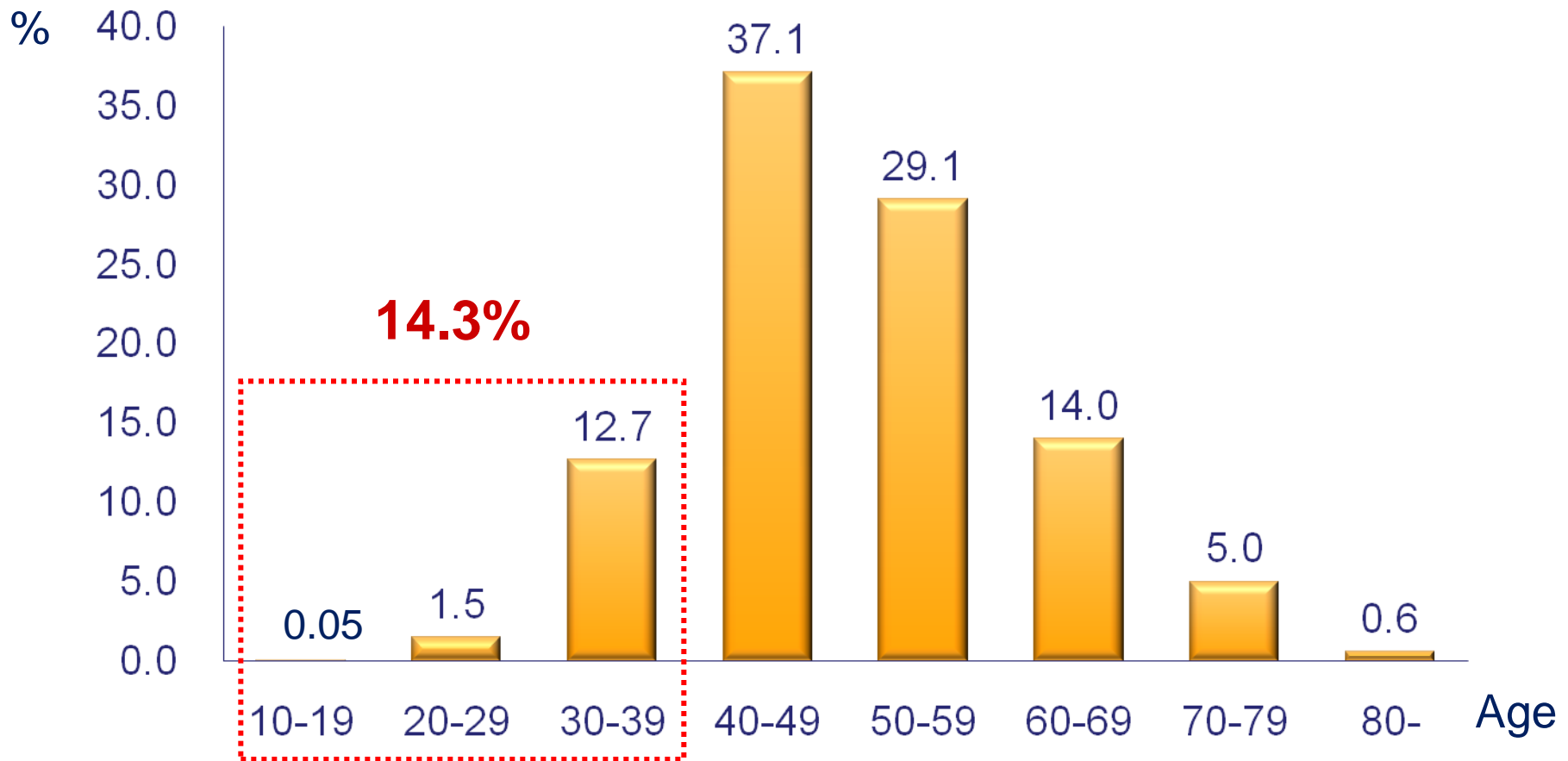
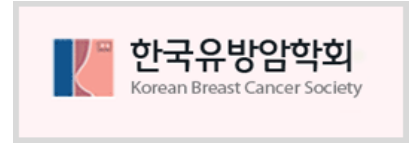
Smith LH, et al. Am J Obstet Gynecol 2003;189:1128-35

Van Nes JG, et al. Breast 2006;15:3-10

Beadle BM, et al Cancer 2009;115:1174-84

Breast cancer in Korea

According to age (2010)

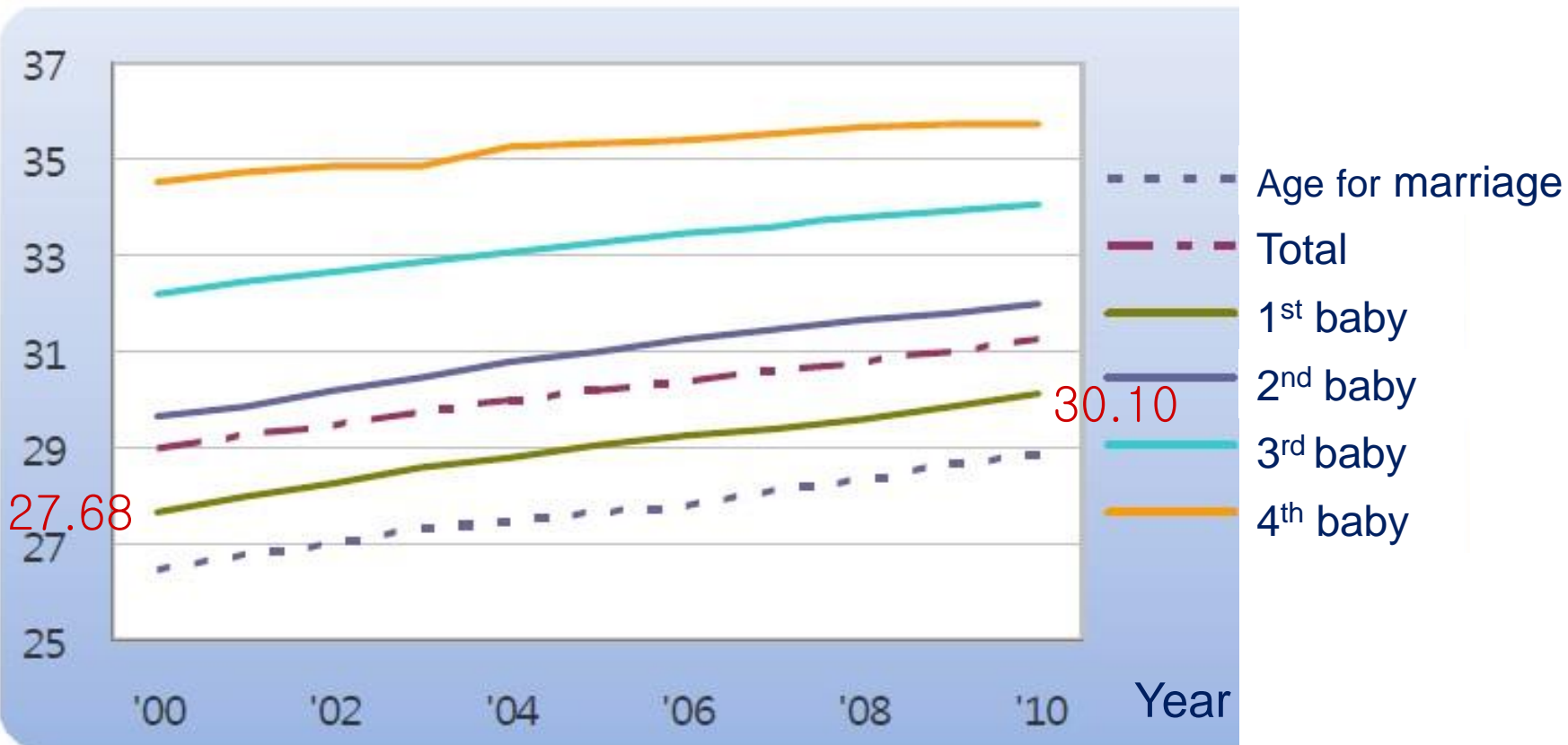


Birth statistics in Korea

Average birth age (2010)

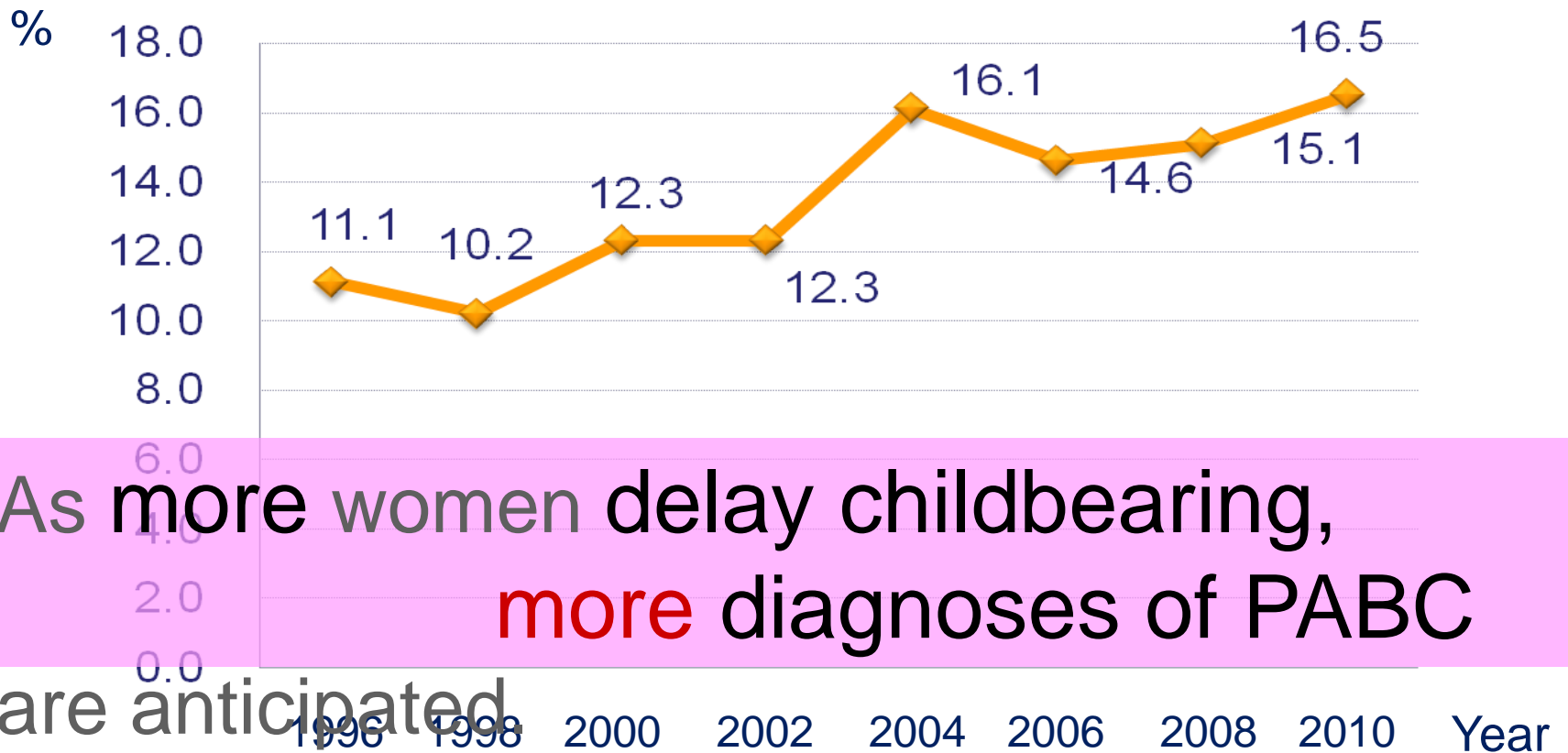
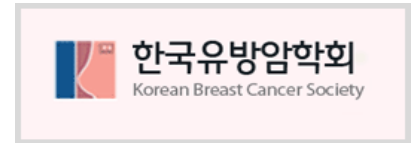


Age



Breast cancer in Korea

Late first-delivery : ≥ 30
years (2010)



Mechanism of PABC

Exposure to high endogenous estrogen

Breast differentiation & involution
(microenvironment)

Suppression of the immune system during
pregnancy

Woo JC, et al. Arch Surg 2003;138:91-8

Russo J, et al. Clin Cancer Res 2005;11:931-6

Yager ID, et al. NEJM 2006;354:270-82

Mc Daniel SM, et al. Am J Pathol 2006;168:608-20



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Characteristics of PABC

More likely to have a family history? **N**

White TT, et al. **O** Ann Surg 1956;144:384-93
Ali SA, et al. Breast J 2012;18:139-44

Higher risk for bilateral breast cancer? **Yes**

Haagensen CD, et al. **S** Am J Obstet Gynecol 1967;98:141-9
DiFronzo LA, et al. Surg Clin North Am 1996;76:267-8

Characteristics of PABC

BRCA mutations

Average age of PABC women: 32-38 years

BC related to BRCA mutation is diagnosed in

young women
→ PABC in BRCA mutations may be

coincidental

Characteristics of PABC

Controversial results

BRCA 1 : increase risk for PABC

Johannsson O, et al. Lancet 1998;352:1359-60

BRCA 1 : 38% decrease in PABC risk

BRCA 2 : significantly increase risk

Cullinane CA, et al. Int J Cancer 2005;117:988-91

BRCA 1 & 2 : similar reduction risk as

non-carriers

Andrieu N, et al. JNCI 2006;98:535-44

Genetic counseling should be offered to
PABC patients

Characteristics of PABC

Hormone receptor status

Increased incidence of HR-negative BC

Reed W, et al. Virchows Arch 2003;443:44-50

Middleton LP, et al. Cancer 2003;98:1055-60

Jacobs IA, et al. Am Surg 2004;70:1025-9

Ives AD, et al. Breast 2005;14:276-82

due to ...

high circulating estrogen competing with the
binding assay

negative feedback effect of estrogen,

Characteristics of PABC

Adverse pathologic features

Larger tumor

Increased number of metastatic lymph node

Higher histologic grade

Increased frequency of TNBC

Pentheroudakis G, et al. Eur J Cancer 2006;42:4126-40

Navrozoglou I, et al. EJSO 2008;34:837-43

Pilewskie M, et al. Ann Surg Oncol 2012;19:1167-73



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Diagnosis of PABC

Clinical examination

Painless mass found by the patient herself

'Milk-rejection sign'

Molckovsky A, et al. BCRT 2008;108:333-8

Theriault R, et al. Curr Oncol Rep 2007;9:17-21

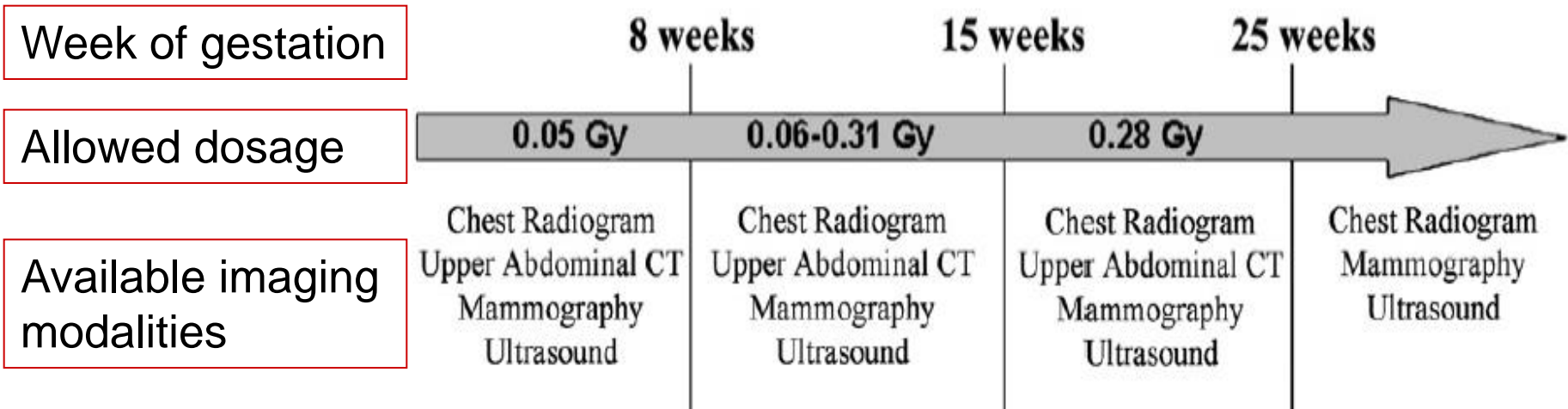
Saber A, et al. Am Surg 1996;62:998-9

→ Delays are likely to be due to pregnancy-induced

physiological change such as

Diagnosis of PABC

Imaging modalities



Chest radiography:

0.0001 Gy

Upper abdomen CT:

0.0036 Gy

Lower abdomen CT:

0.089 Gy

Diagnosis of PABC

Imaging modalities

Ultrasonography has high sensitivity and specificity

is considered the standard method

Parente JT, et al. Obstet Gynecol 1988;71:861-4

Theriault R, et al. Curr Oncol Rep 2007;9:17-21

method

MRI has not been established whether it is safe or not

should be avoided in the 1st trimester

Shellock FG, et al. J Magn Reson Imaging 1999;10:477-84

Diagnosis of PABC

Pathologic diagnosis

FNA has low sensitivity due to atypical
cytomorphologic findings

Sorosky JI, et al. Obstet Gynecol Clin North Am 1988;25:353-63

Core needle biopsy is more sensitive and
specific

has increased risk of milk fistula
and infection

Petrek JA, et al. Cancer 1994;74:518-27

Treatment of PABC

Local treatments : Surgery

MRM is the treatment of choice

BCS is an option for PABC diagnosed late in pregnancy

Kuerer HM, et al. Surgery 2002;131:108-10

Jacobs IA, et al. Am Surg 2004;70:1025-9

The efficacy and safety of SLNBx has **yet** to be evaluated

→ **ALND** is the gold standard method

Navrozoglou H, et al. EJSO 2008;34:837-43

Treatment of PABC

Local treatments : Radiotherapy

Contraindicated in pregnancy

embryonic death in implantation period

mental retardation, neoplasm, hematologic disorder

in 1st trimester

Antypas C, et al. IJROBP 1998;40:959-9

Behrman RH, et al. Radiology 2007;243:605

To date, no evidence exists

to support any novel mode of

radiotherapy

Treatment of PABC

Systemic treatments : Chemotherapy

Not recommended in 1st trimester

spontaneous abortion, teratogenesis, or fetal malformation

Espie M, et al. Drug Saf 1988;18:135-42

Anti-metabolites (methotrexate): contraindicated

Anthracyclines: acceptable - tx of choice

Taxanes & vinorelbine: not recommended

Trastuzumab: related to anhydroamniosis, cardiac development

Cardonick E, et al. Lancet Oncol 2004;5:283-91

Molckovsky A, et al. BCRT 2008;108:333-8

Treatment of PABC

Systemic treatments : Chemotherapy

If CTx is initiated during pregnancy,

fetal monitoring should be

performed

Azim HJ, et al. Breast 2011;20:1-6

Must cease 3 weeks prior to labor

avoiding fetus with neutropenia, infection, or

hemorrhage

Ring A, et al. JCO 2005;23:4192-7

Lactation: prohibited during CTx

only allowed 4 weeks after the last

administration

Egan PC, et al. Cancer Treat Rep 1985;69:1387-9

Treatment of PABC

Systemic treatments : Endocrine therapy

Should be delayed until pregnancy is over

Tamoxifen: teratogenic, fetal malformation

Aromatase inhibitors: no evidence

GnRHa: teratogenic

Barthelmes L, et al. Breast 2004;13:446-51

Ring AE, et al. Ann Oncol 2005;16:1855-60

Loibl S, et al. Cancer 2005;106:237-46

Treatment of PABC

Systemic treatments : Supporting agents

G-CSF: safe in pregnancy

Serotonin receptor antagonist: safe in pregnancy

Corticosteroid: safe after 2nd trimester

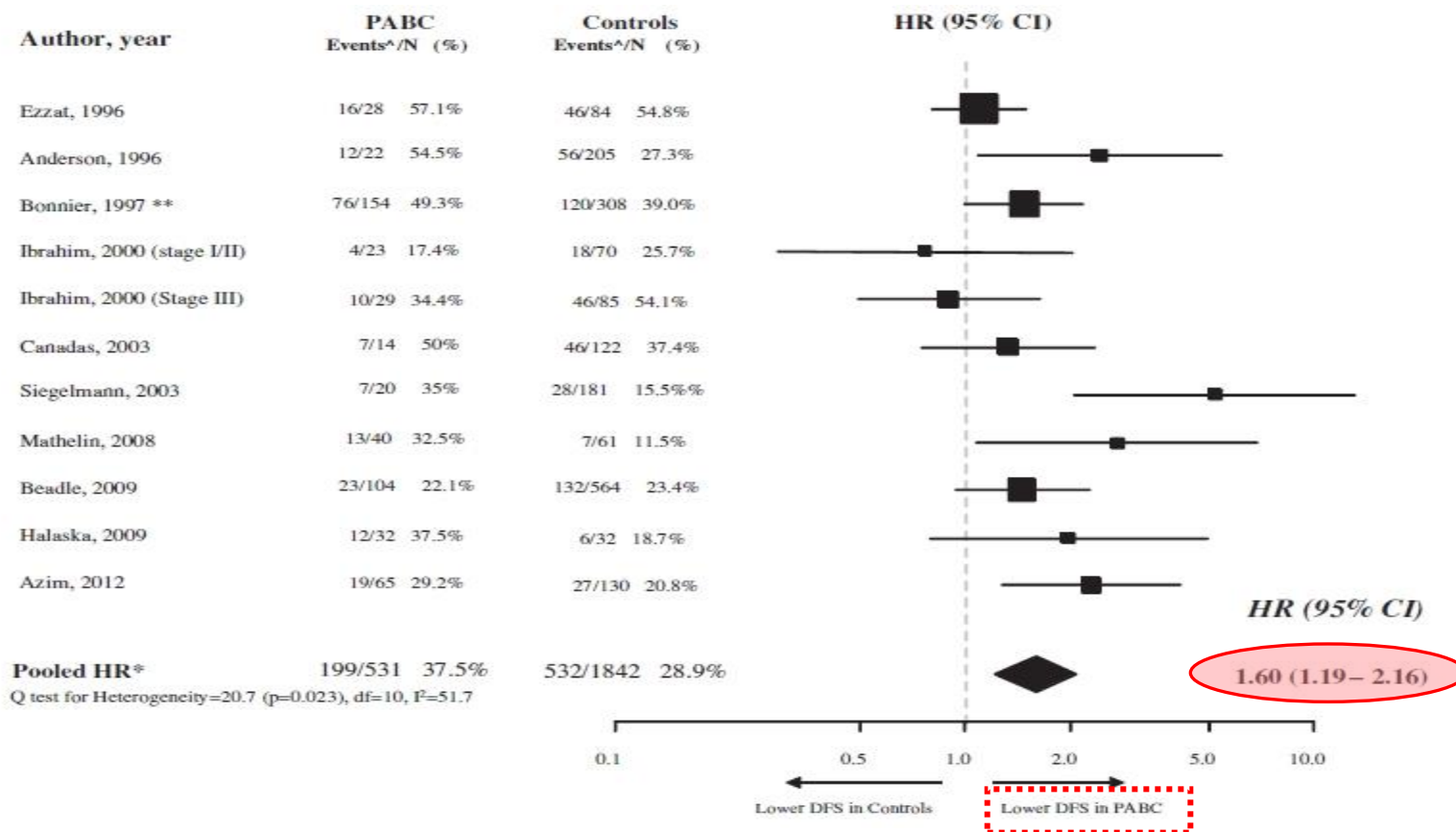
Molinsky A, et al. BCRT 2008;108:333-8
Lennard MS, et al. Crit Rev Oncol Hematol 2008;67:196-203

Bisphosphonates: no evidence

Prognosis of PABC

Controversy

Prognosis of pregnancy-associated breast cancer: A meta-analysis of 30 studies



Prognosis of PABC

Poor

It is unclear whether this is due to

aggressiveness of tumor
delayed diagnosis
lower treatment intensity
promotion by hormonal

factors

tumor promoting

microenvironment

Rodriguez AO, et al. Obstet Gynecol 2008;112:71-8

Stensheim H, et al. JCO 2009;27:45-51



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Safety of pregnancy after breast cancer

Many young breast cancer survivors **fear** pregnancy

Why ?

increase of estrogen

reactivation & growth of tumor cells

recurrence or progress of the disease

breast cancer risk for

Safety of pregnancy after breast cancer

Protective effect of a subsequent pregnancy after BC

“Healthy mother effect”

more likely to be disease-free at the time of conception

women who feel well will pursue a pregnancy

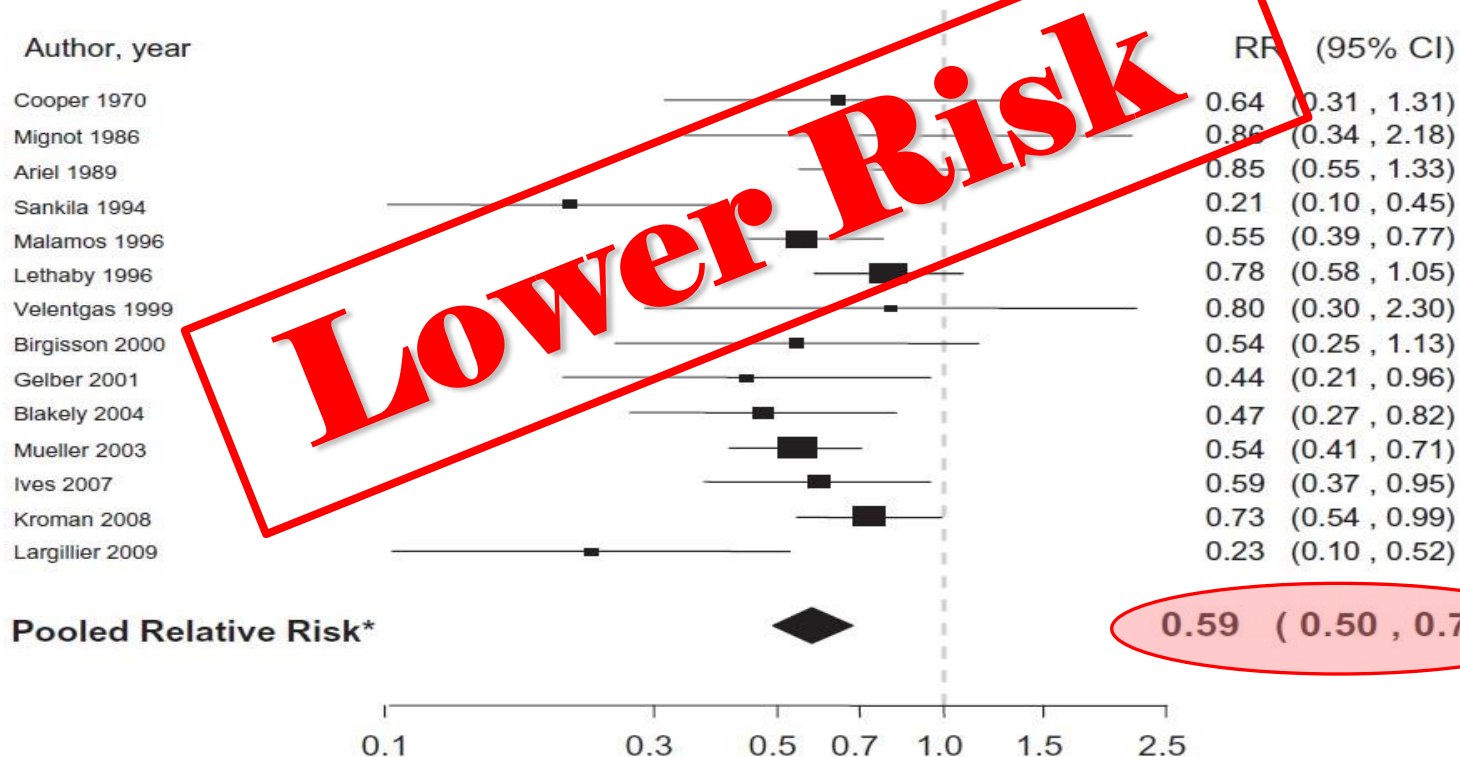
Determine whether the **survival benefit** reflects a

self-selection bias or an **unknown biological mechanism**

Safety of pregnancy after breast cancer

Safety of pregnancy following breast cancer diagnosis: A meta-analysis of 14 studies (1,244 cases & 18,415 controls)

Overall survival



Optimal interval before pregnancy

Current Recommendation: **2-3 years**

Why ?

Recurrences are seen most commonly in 2-3 years

Second line therapies can complicate the pregnancy

Pregnancy can interrupt detection of secondary BC

Optimal interval before pregnancy

Reasonable Recommendation

When adjuvant treatment is indicated

...

chemotherapy or hormonal tx: 6 months

radiation therapy: 12 months

In case of increased recurrence risk

...

2 years may be appropriate



Conclusion

Incidence of PABC is **rare**, however, it will increase
Diagnosis of PABC is usually **delayed** due to

Tailored treatment pregnancy-induced for mother and fetus is breast change required

Prognosis of PABC is considered to be **poor**

Pregnancy seems **not** to have a negative impact

on survival of breast

Thank you for your attention!

