MEME KANSERİNDE KEMOPREVANSİYON

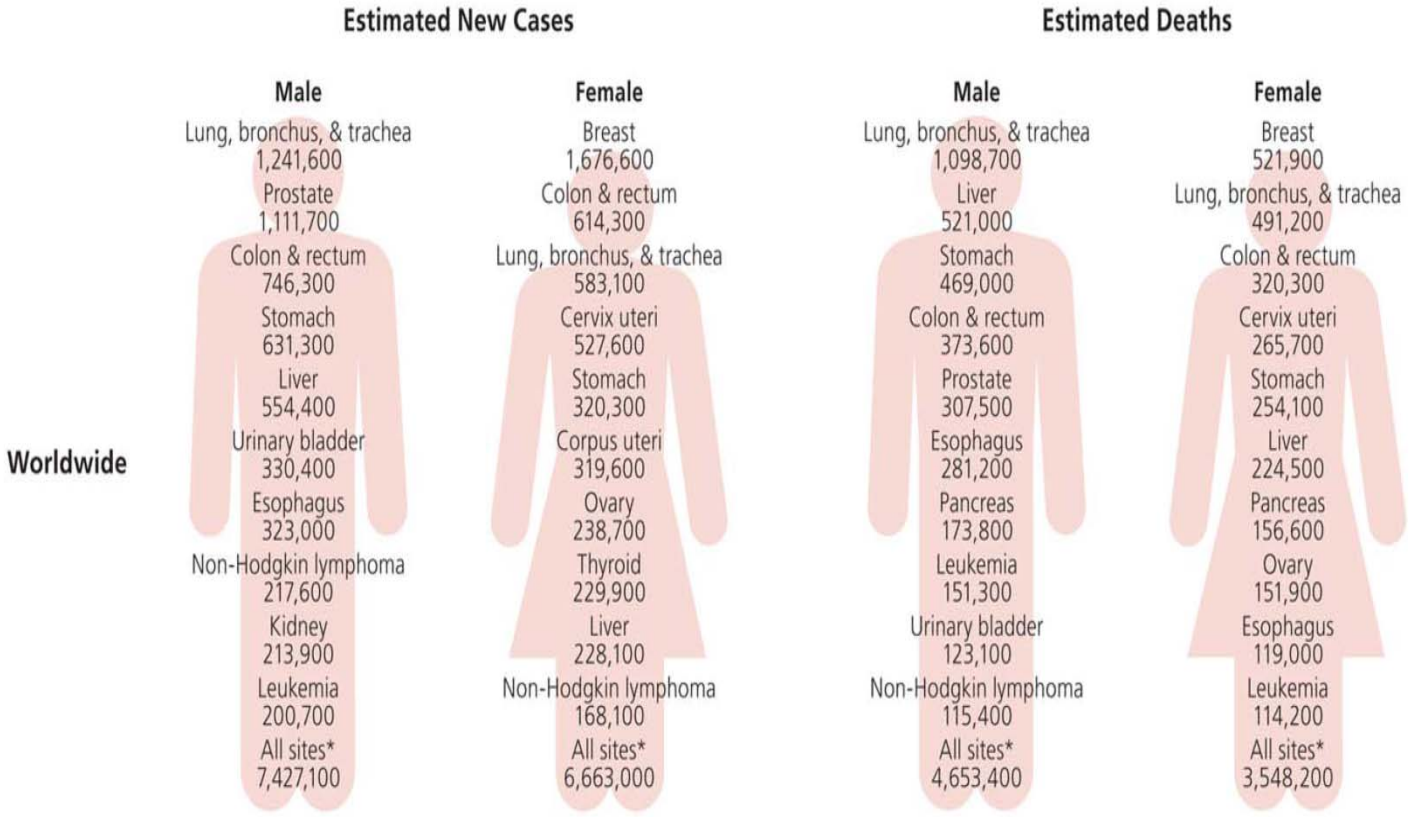
Doç. Dr. Gökhan ERDEM

LİV Hospital Ankara Hastanesi, Tıbbi Onkoloji

Prof. Dr. İ. Lale ATAAN Anısına...

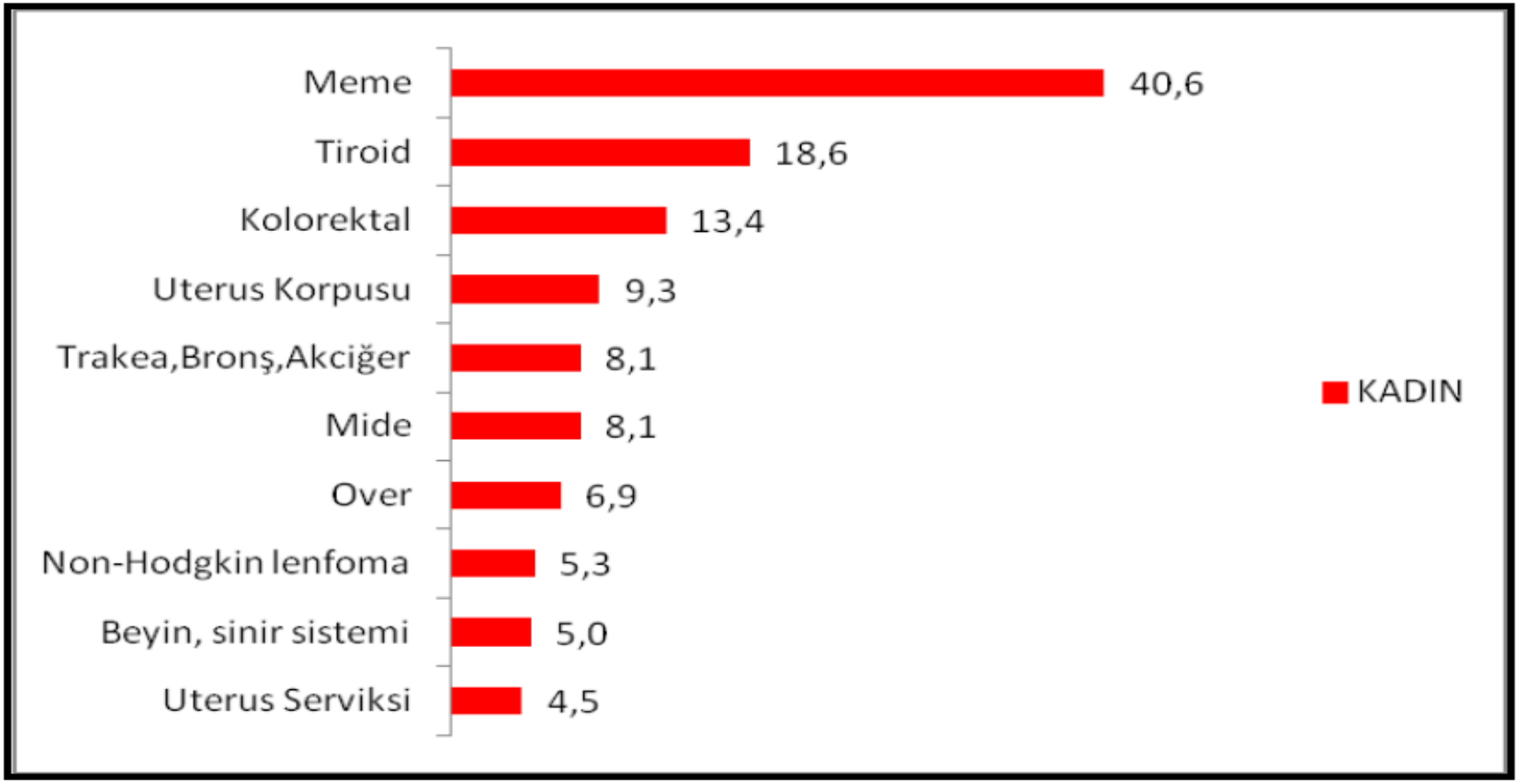
Meme Kanserinde Yüksek Risk Tanımı
ve Herediter Meme Kanseri Kursu
Ankara 28.03.2015

NEDEN ÖNEMLİ?



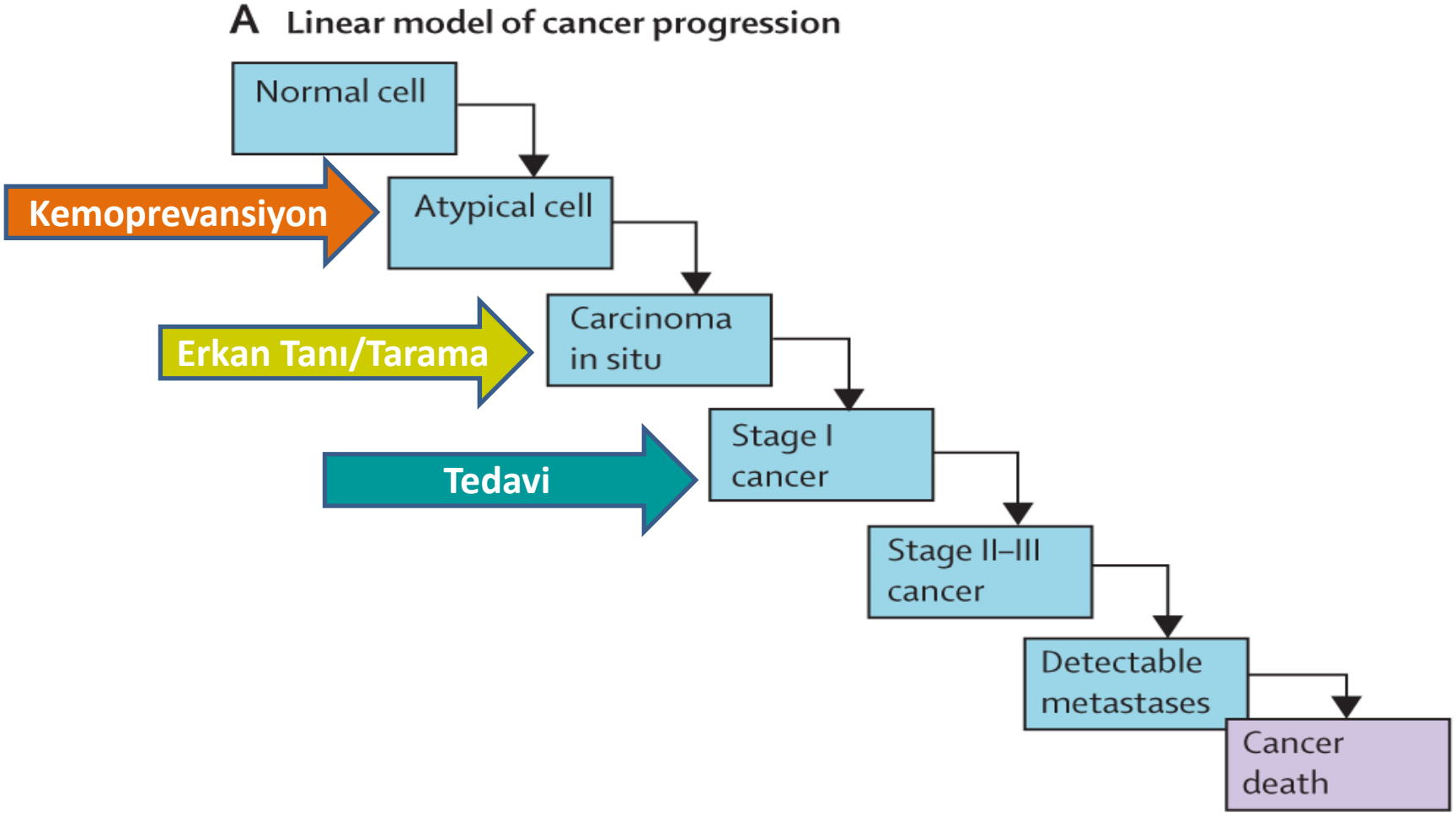
CA CANCER J CLIN 2015;65:87-108.

NEDEN ÖNEMLİ?

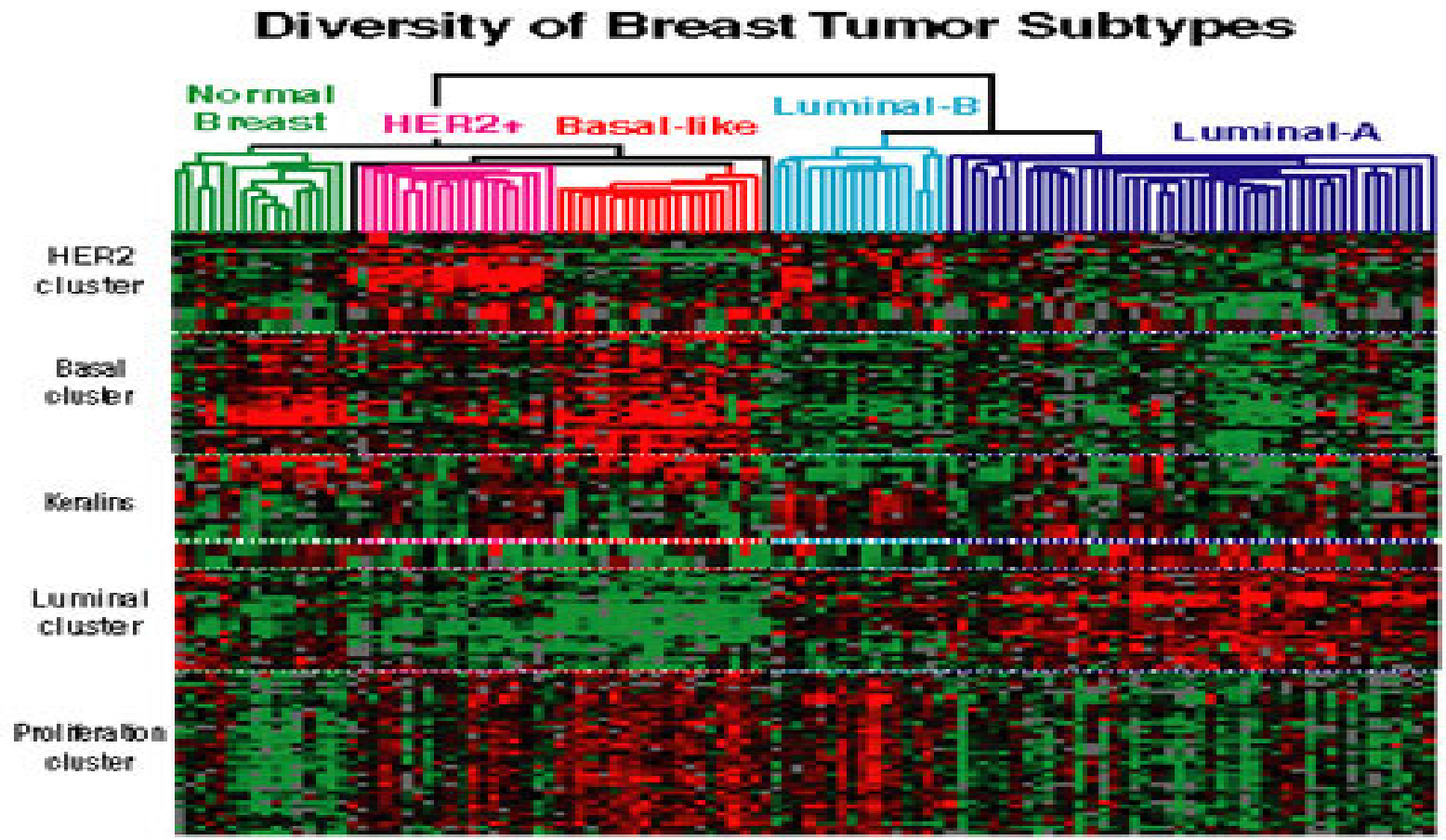


Türkiye'de 2009 verilerine göre kadınlarda en sık görülen 10 kanser

ÇÖZÜM?


A Linear model of cancer progression
Normal cell
Kemoprevansiyon
Atypical cell
Erkan Tanı/Tarama
Carcinoma in situ
Tedavi
Stage I cancer
Stage II–III cancer
Detectable metastases
Cancer death

SÜREÇ.....

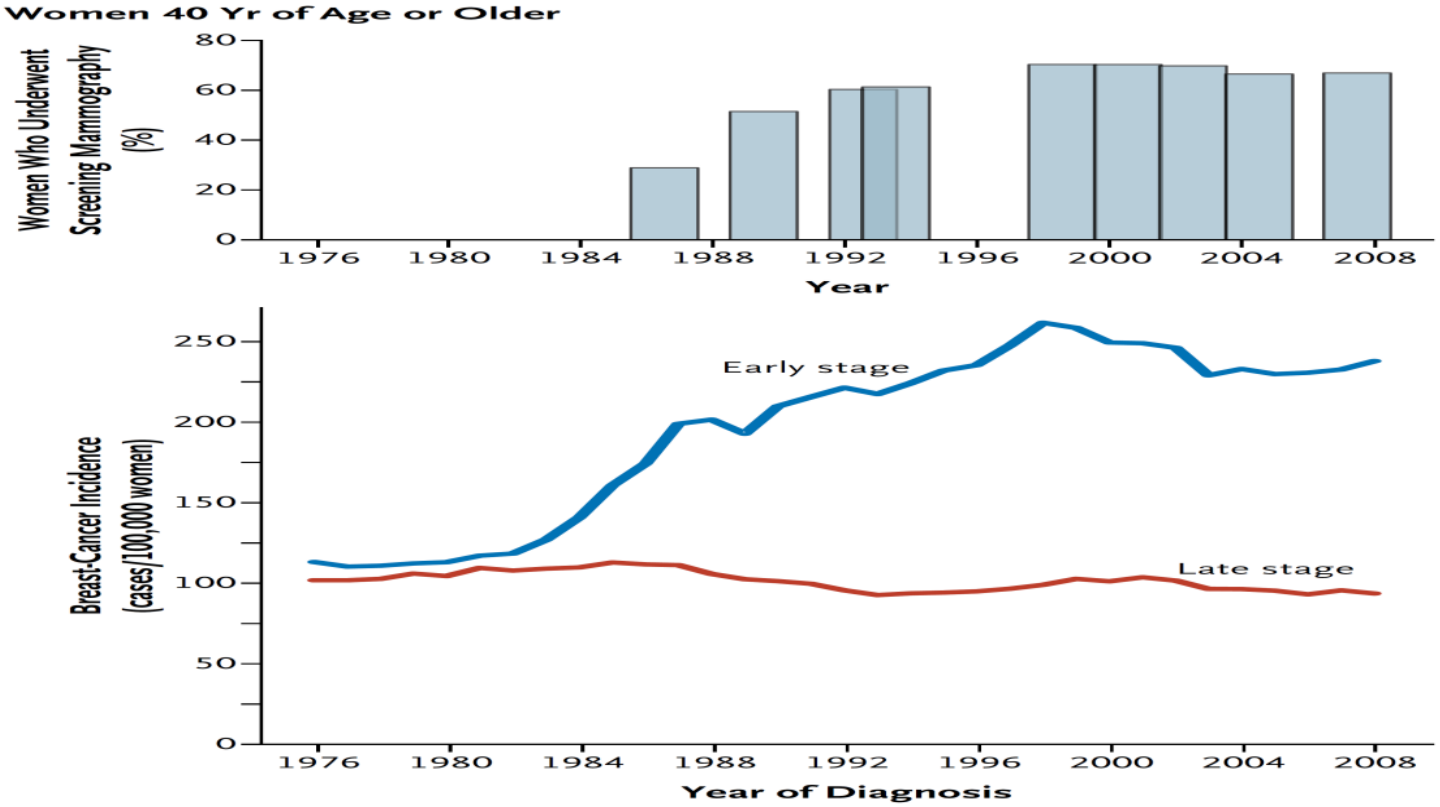

Diversity of Breast Tumor Subtypes
Normal Breast
HER2+
Basal-like
Luminal-B
Luminal-A
HER2 cluster
Basal cluster
Kenlins
Luminal cluster
Proliferation cluster

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effect of Three Decades of Screening Mammography on Breast-Cancer Incidence

Archie Bleyer, M.D., and H. Gilbert Welch, M.D., M.P.H.



GÜÇLÜ KANITLARA RAĞMEN…

Prevalence of tamoxifen use for breast cancer chemoprevention among U.S. women

Erika A. Waters[1], **Kathleen A. Cronin**[2], **Barry I. Graubard**[3], **Paul K. Han**[2], and **Andrew N. Freedman**[2]

Prevalence estimates for use of tamoxifen in two nationally-representative U.S. data sources (NHIS 2000, NHIS 2005)

NHIS 2000[1]		NHIS 2005[2]	
Number using tamoxifen (95% CI)	**Percentage**	**Number using tamoxifen (95% CI)**	**Percentage**
120,737 (95% CI 75,416-183,219)	0.20 (95% CI 0.13-0.31)	51,575 (95% CI 19,596-109,936)	0.08 (95% CI 0.03-0.17)

[1] Weighted estimate from a sample of 27 women who report using tamoxifen out of a total sample size of 10,601

[2] Weighted estimate from a sample of 8 women who report using tamoxifen out of a total sample size of 10,690

TEMEL VARSAYIM

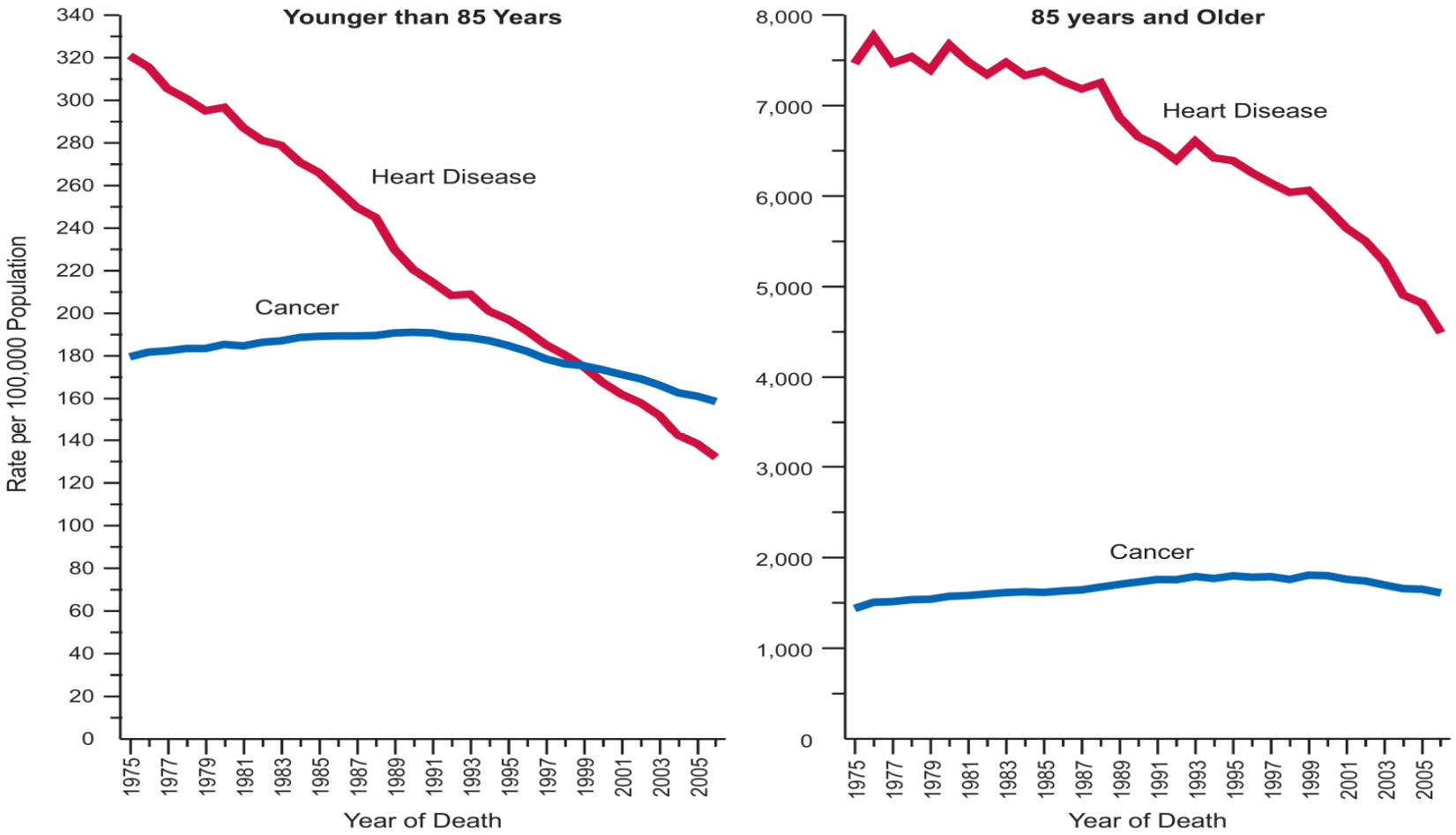
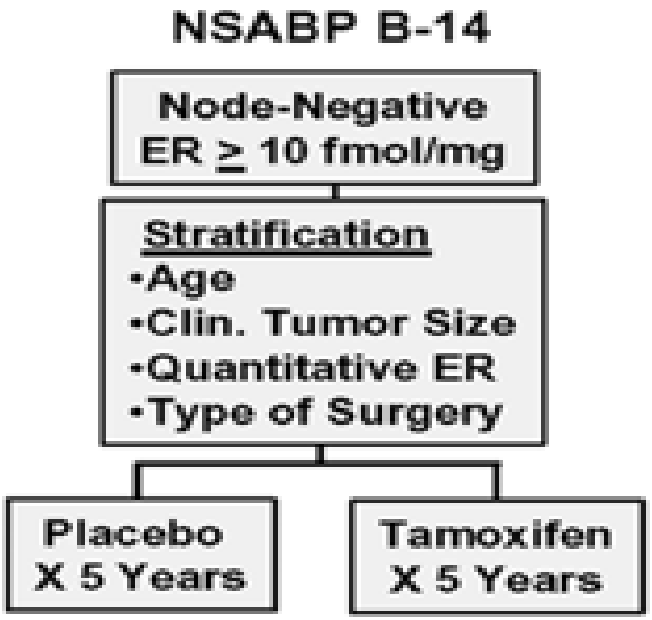
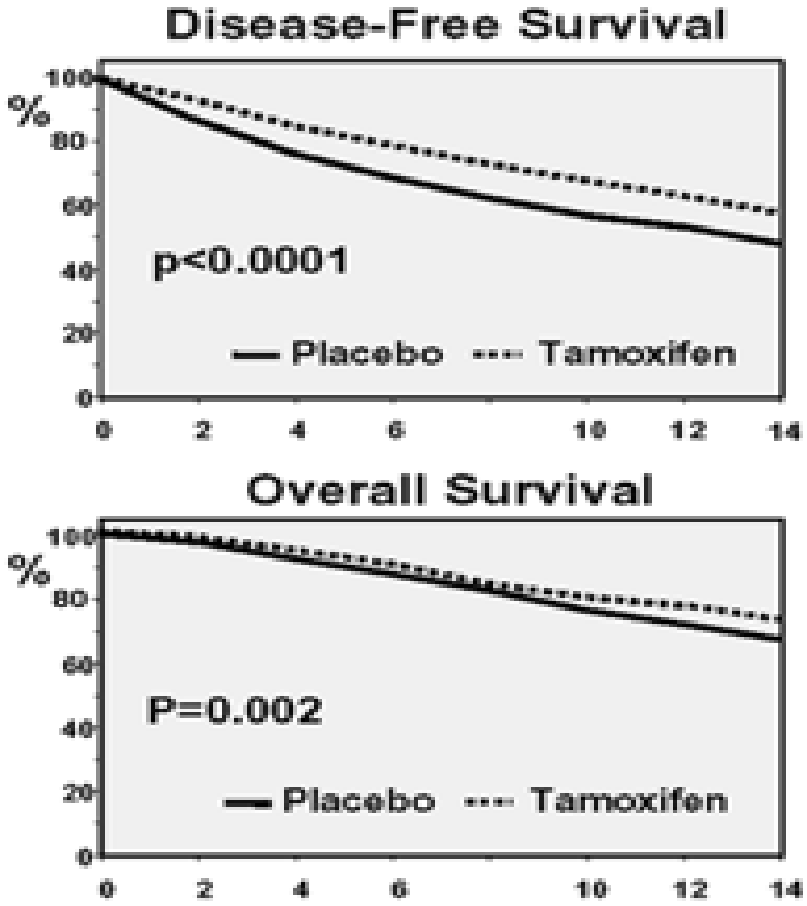


FIGURE 6. Death Rates* For Cancer and Heart Disease for Ages Younger Than 85 Years and 85 Years and Older, 1975 to 2006.

KANIT!!!

NSABP B-14 ÇALIŞMASI

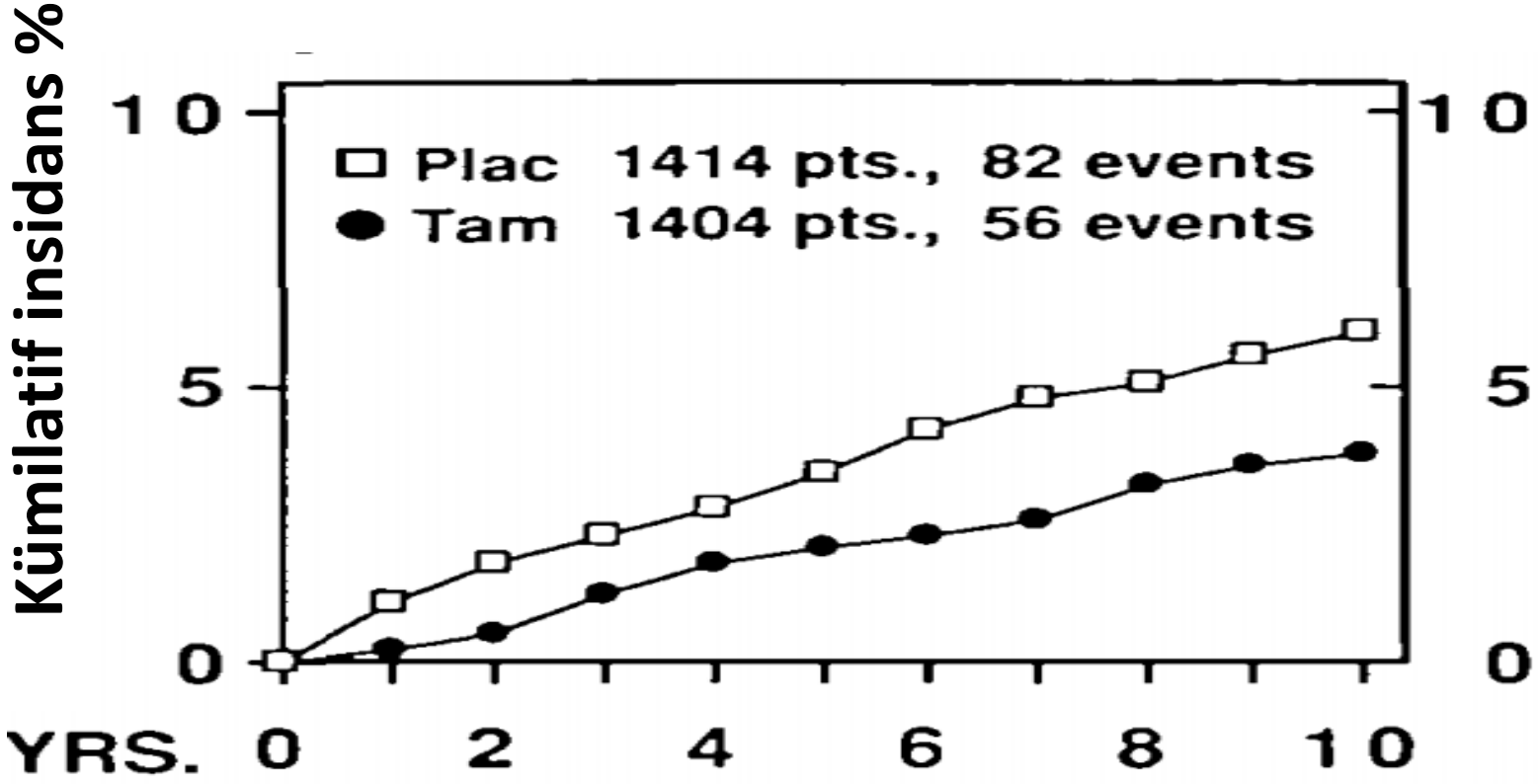




KANIT!!!

NSABP B-14 ÇALIŞMASI

Kontralateral meme kanseri insidansı



Tamoxifen for Prevention of Breast Cancer: Report of the National Surgical Adjuvant Breast and Bowel Project P-1 Study

Bernard Fisher, Joseph P. Costantino, D. Lawrence Wickerham, Carol K. Redmond, Maureen Kavanah, Walter M. Cronin, Victor Vogel, André Robidoux, Nikolay Dimitrov, James Atkins, Mary Daly, Samuel Wieand, Elizabeth Tan-Chiu, Leslie Ford, Norman Wolmark, and other National Surgical Adjuvant Breast and Bowel Project Investigators

Meme kanseri için yüksek riskli kadınlar (n=13.388)

Tamoksifen 20 mg/gün, 5 yıl (n=6597)

Plasebo, 5 yıl (n=6610)

Birincil Sonlanım Noktası
- İnvaziv Meme Kanseri

1. >60 veya 35-59 yaş arası 5 yıllık meme kanseri gelişme olasılığı ≥ %1.66 (Gail Risk Skorlaması)
2. LCIS hikayesi
3. Pre-Postmenapozal kadınlar

Median 54.6 aylık takip sonrası
RR= 0.51, 95% CI =0.39-0.66

İkincil sonlanım noktası
- Non-invaziv meme kanseri
- Meme kanseri dışı invaziv kanserler
- Osteoporotik kırıklar
- Vasküler olaylar
- İskemik kalp hastalığı
- Yaşam kalitesi

Tamoxifen for Prevention of Breast Cancer: Report of the National Surgical Adjuvant Breast and Bowel Project P-1 Study

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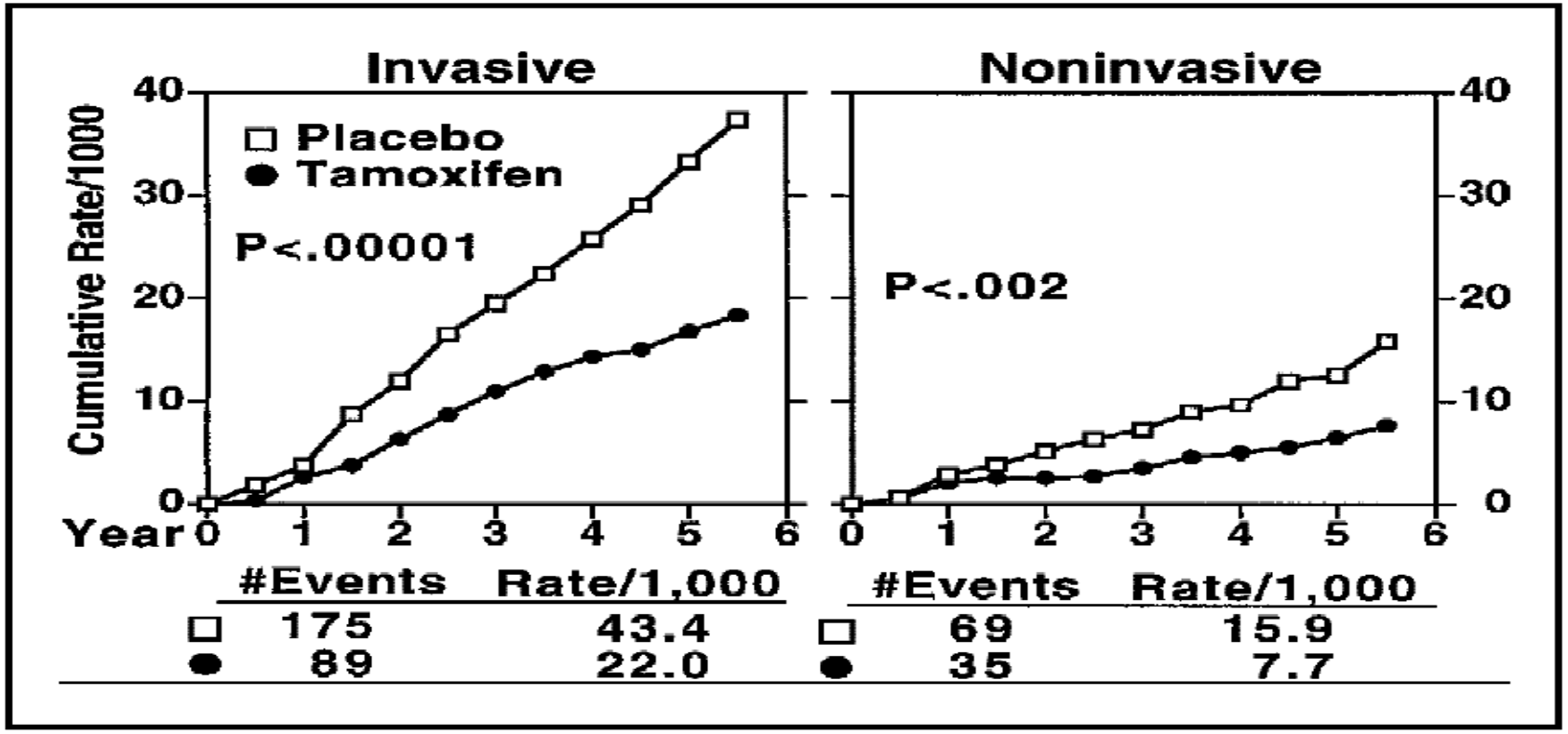

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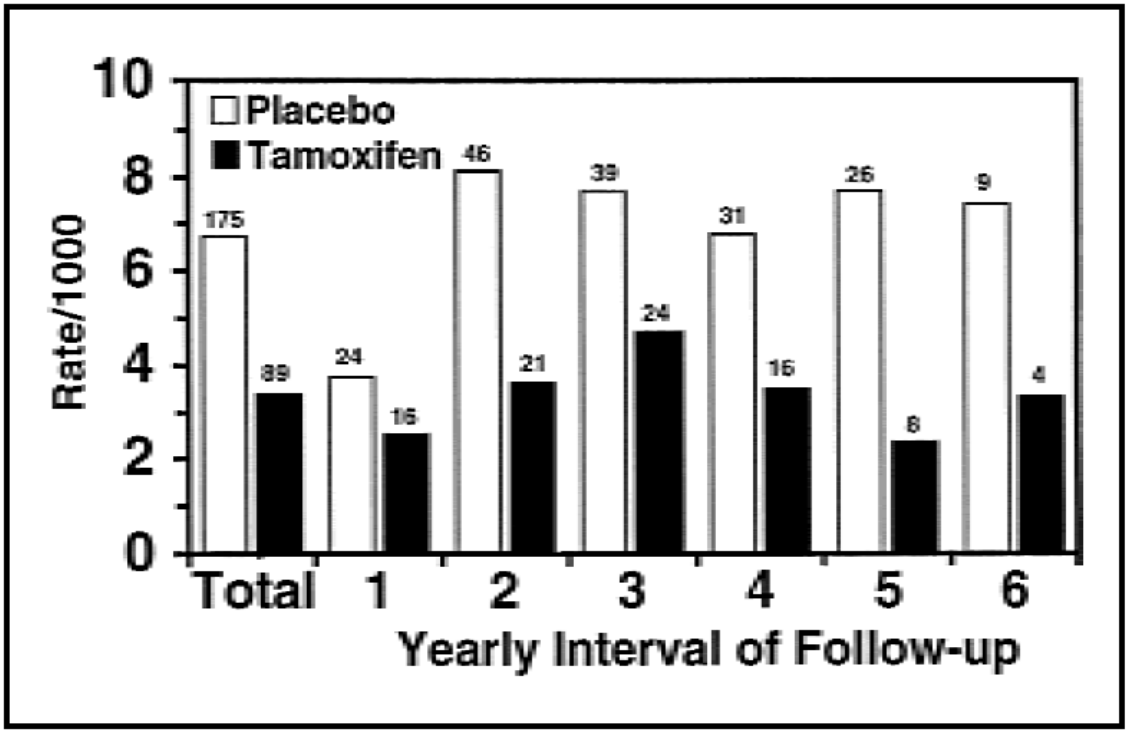

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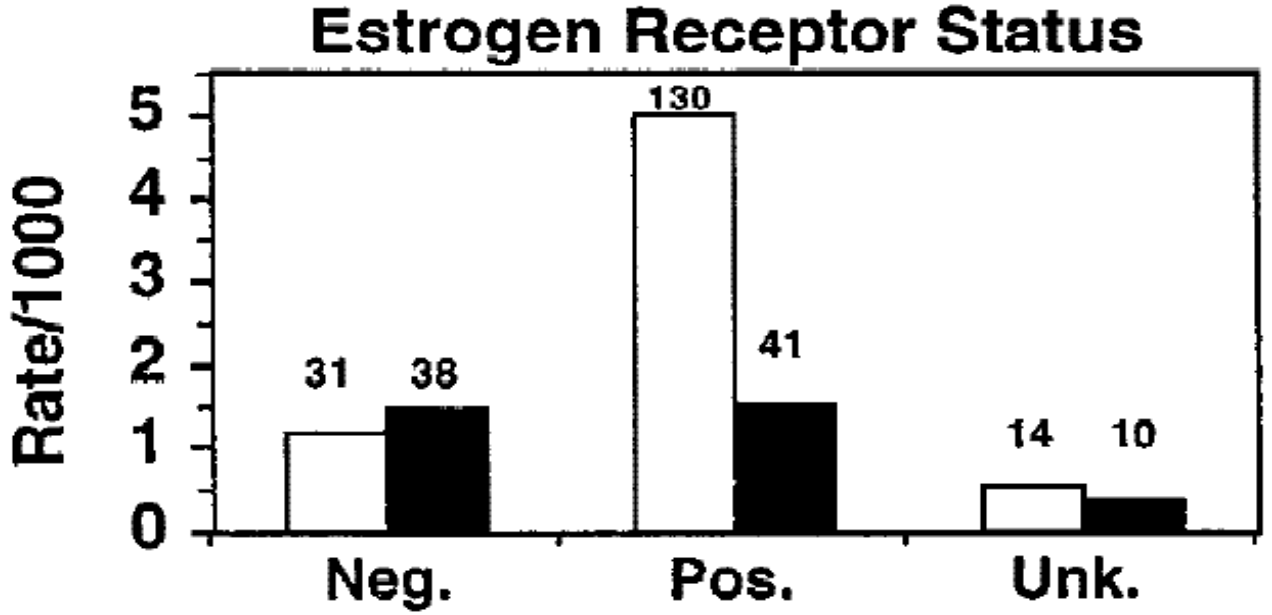

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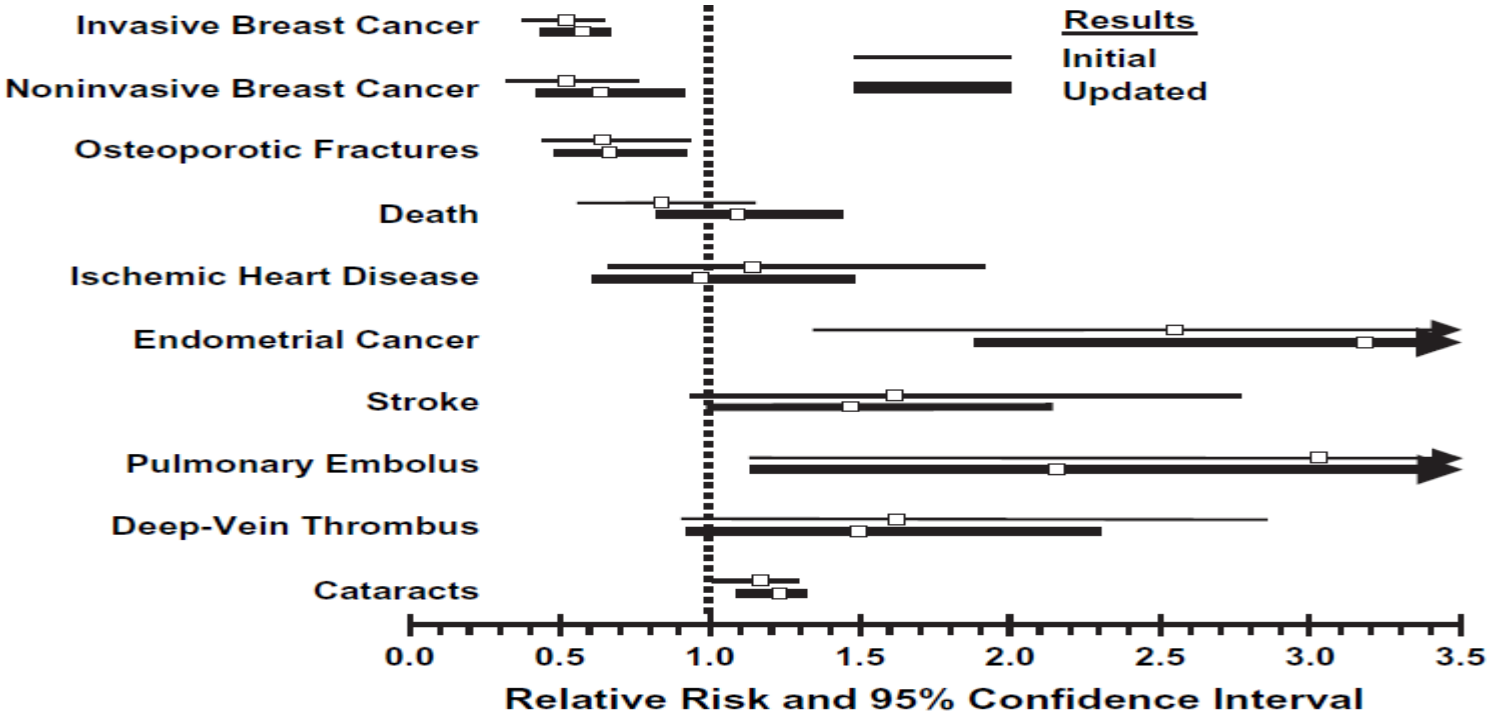
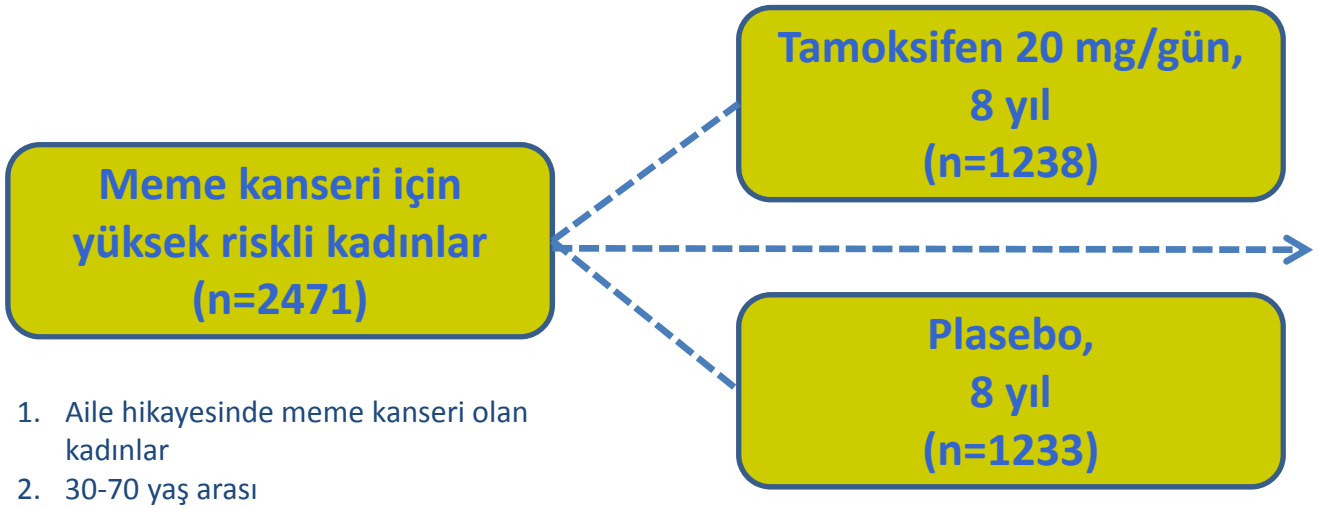


Fig. 1. Comparison of relative risks (with 95% confidence intervals) of benefits and undesirable effects of tamoxifen from the initial and updated results of NSABP P-1.

Twenty-Year Follow-up of the Royal Marsden Randomized, Double-Blinded Tamoxifen Breast Cancer Prevention Trial

Trevor J. Powles, Sue Ashley, Alwynne Tidy, Ian E. Smith, Mitch Dowsett



1. Aile hikayesinde meme kanseri olan kadınlar
2. 30-70 yaş arası

Birincil Sonlanım Noktası
•İnvaziv Meme Kanseri

ER + meme kanseri için
Median 13 yıllık takip sonrası
HR = 0.48, 95% CI = 0.29-0.79; (P = .005)

İkincil sonlanım noktası
•ER pozitif invaziv meme kanseri

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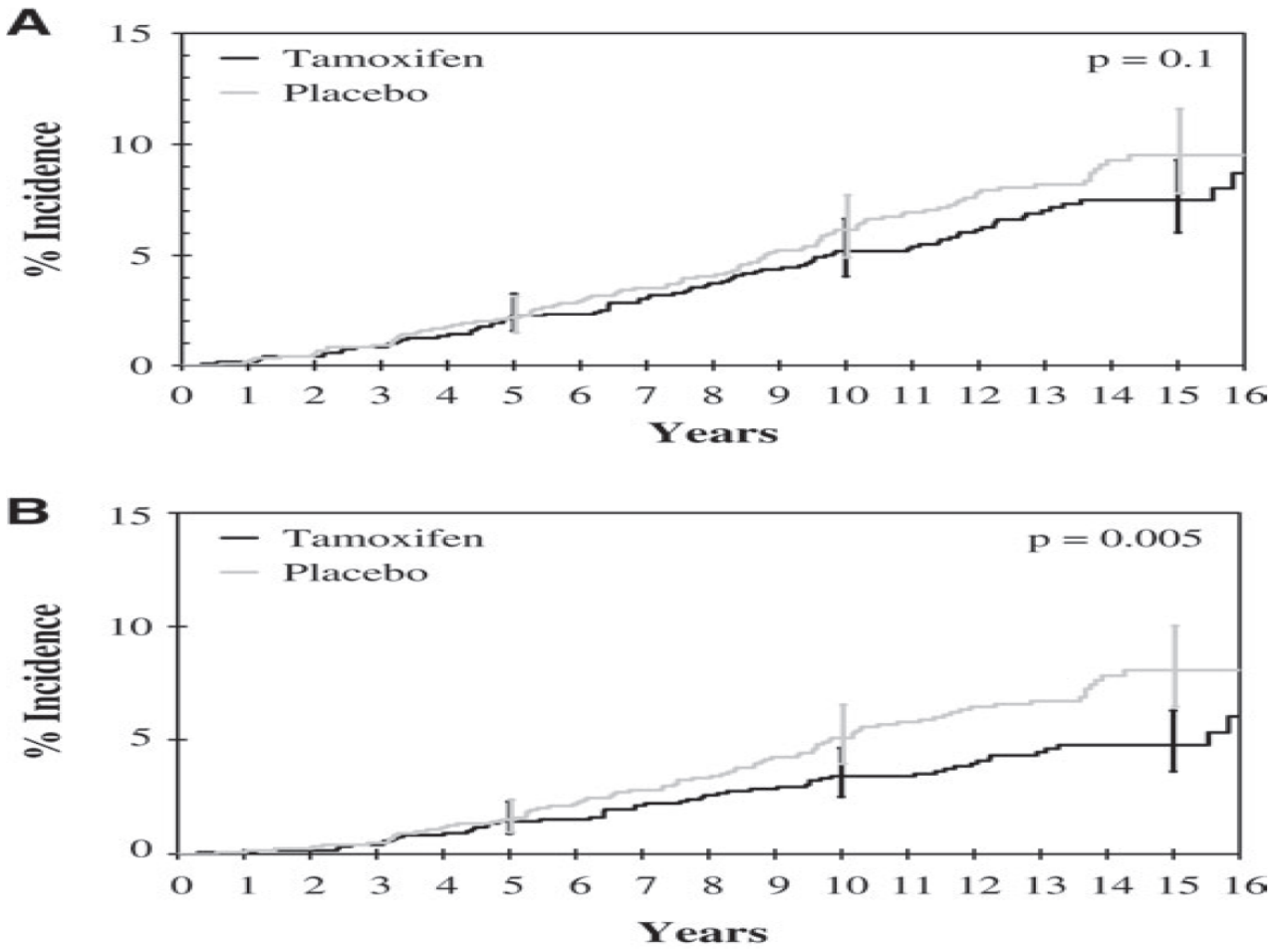
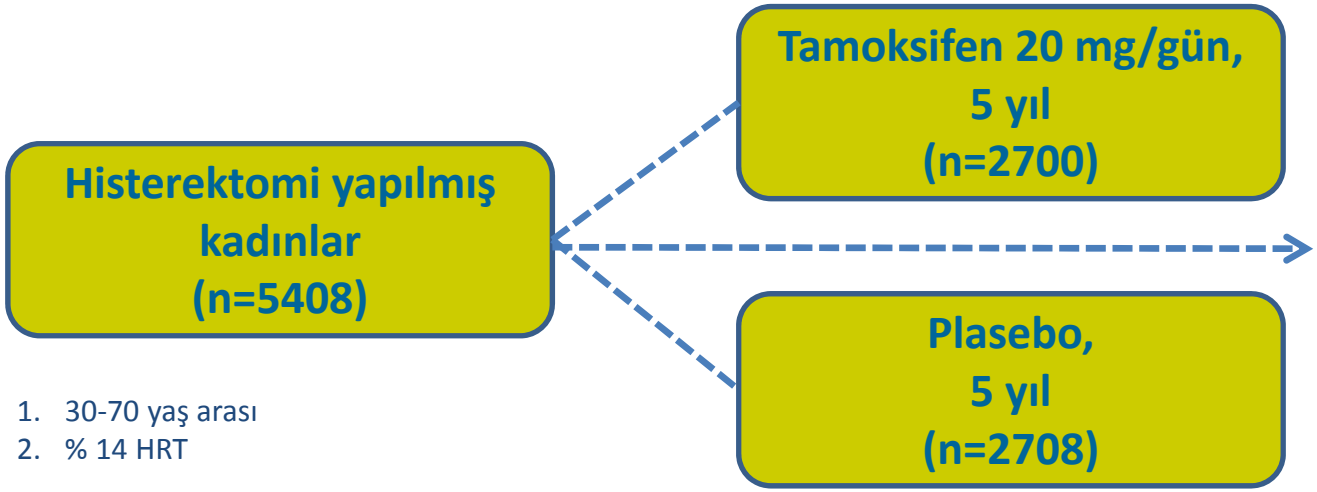


Tamoxifen for the Prevention of Breast Cancer: Late Results of the Italian Randomized Tamoxifen Prevention Trial Among Women With Hysterectomy

Umberto Veronesi, Patrick Maisonneuve, Nicole Rotmensz, Bernardo Bonanni, Peter Boyle, Giuseppe Viale, Alberto Costa, Virgilio Sacchini, Roberto Travaglini, Giuseppe D'Aiuto, Pasquale Oliviero, Francesco Lovison, Giacomo Gucciardo, Marco Rosselli del Turco, Maria Grazia Muraca, Maria Antonietta Pizzichetta, Serafino Conforti, Andrea Decensi

For the Italian Tamoxifen Study Group



1. 30-70 yaş arası
2. % 14 HRT

Birincil Sonlanım Noktası
- İnvaziv Meme Kanseri İnsidansı

ER + meme kanseri (>160 cm, 24 yaşından önce doğum yapmamış, 14 yaşından önce menarş ve en az fonksiyonel bir over)
Median 11 yıllık takip sonrası
HR = 0.24, 95% CI = 0.10-0.59

İkincil sonlanım noktası
- ER pozitif invaziv meme kanseri

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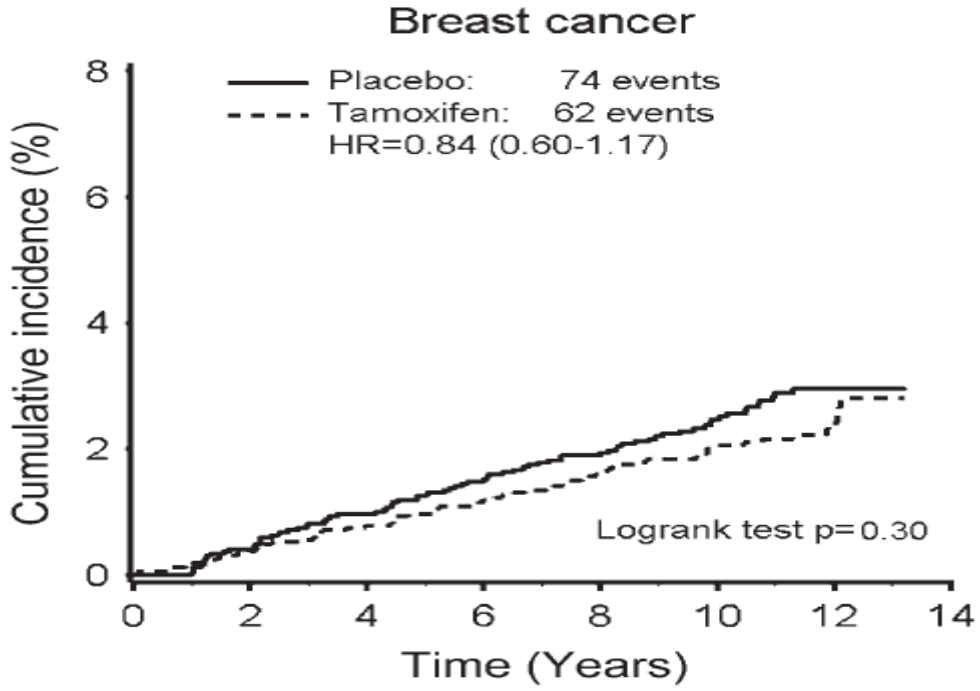

Women at risk

P	**2708**	**2696**	**2670**	**2649**	**2625**	**2064**	**903**
T	**2700**	**2686**	**2672**	**2657**	**2636**	**2094**	**901**

Tamoxifen for the Prevention of Breast Cancer: Late Results of the Italian Randomized Tamoxifen Prevention Trial Among Women With Hysterectomy

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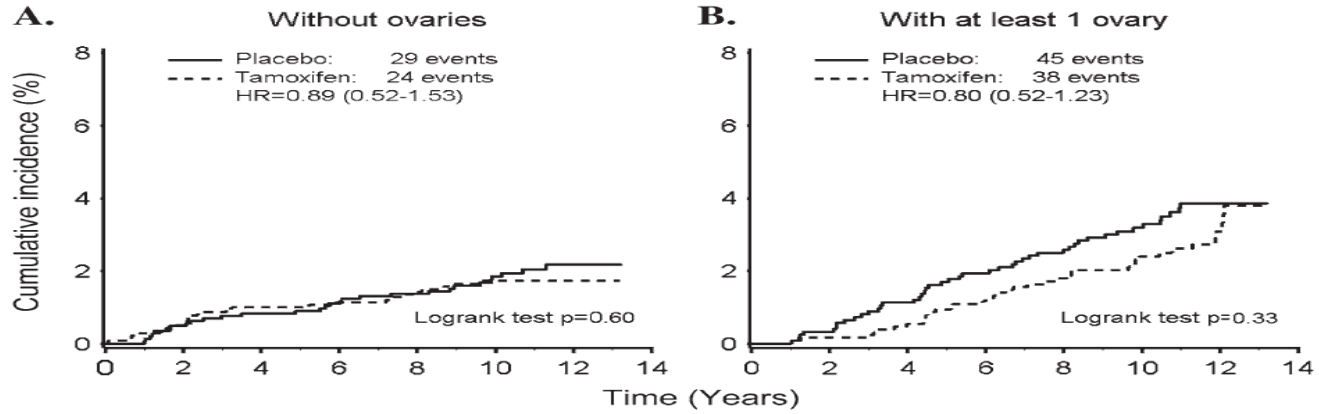
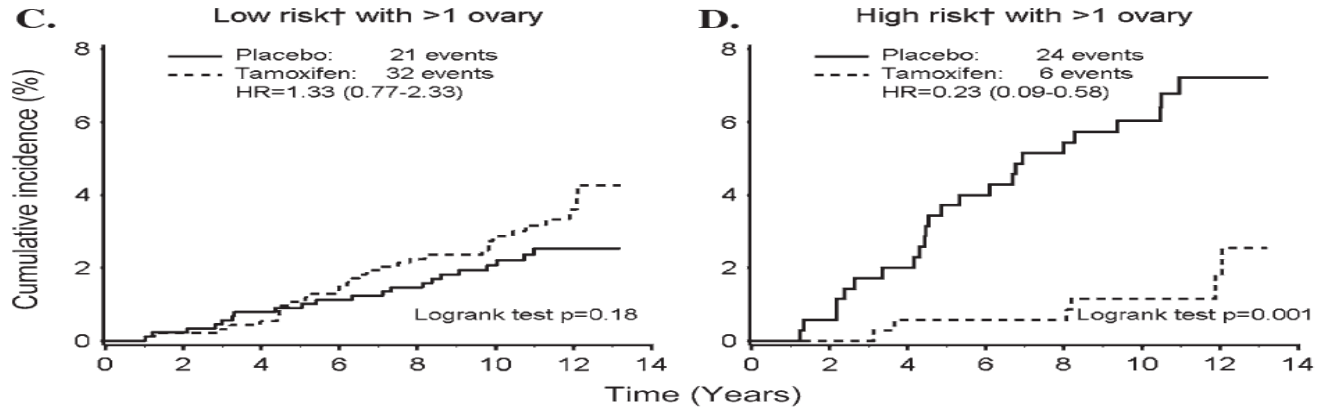


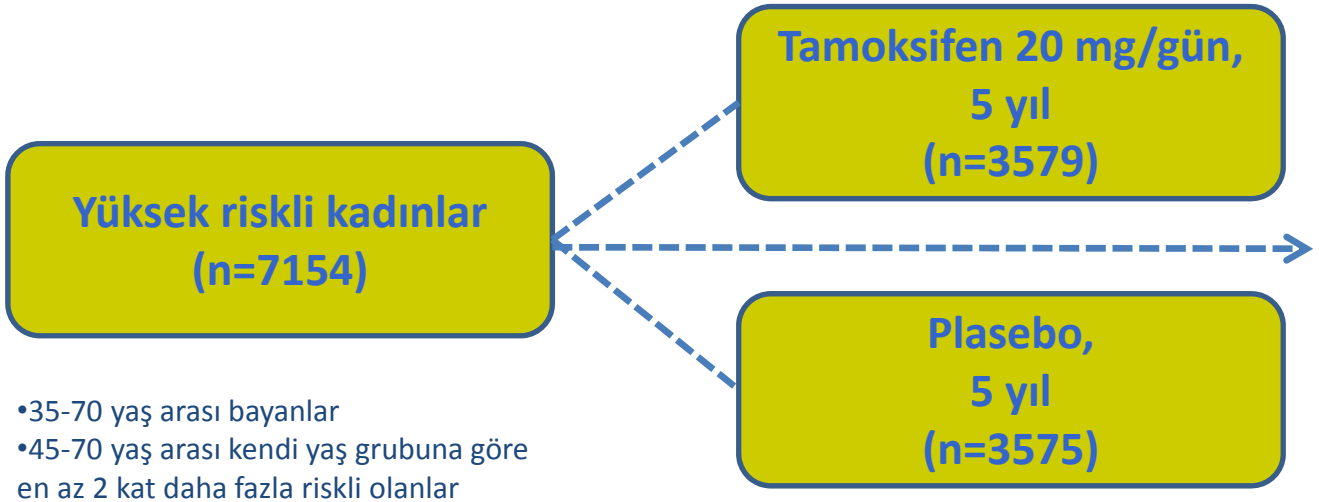
Women at risk

P	1465	1457	1446	1436	1428	1094	448	1243	1239	1224	1213	1197	970	455
T	1411	1400	1392	1389	1378	1072	424	1289	1286	1280	1268	1258	1022	477



Tamoxifen for prevention of breast cancer: extended long-term follow-up of the IBIS-I breast cancer prevention trial

Jack Cuzick, Ivana Sestak, Simon Cawthorn, Hisham Hamed, Kaija Holli, Anthony Howell, John F Forbes, on behalf of the IBIS-I Investigators*



•35-70 yaş arası bayanlar
•45-70 yaş arası kendi yaş grubuna göre en az 2 kat daha fazla riskli olanlar
•<45 yaş için 2 kattan fazla riski olanlar

Birincil Sonlanım Noktası
•İnvaziv Meme Kanseri
•Duktal karsinoma in-situ

Meme kanseri
Median 16 yıllık takip sonrası
[HR] 0·71 [95% CI 0·60–0·83], p<0·0001)

İkincil sonlanım noktası
•ER pozitif invaziv meme kanseri
•Tüm nedenlere bağlı ölüm
•Yan etkiler

Tamoxifen for prevention of breast cancer: extended long-term follow-up of the IBIS-I breast cancer prevention trial

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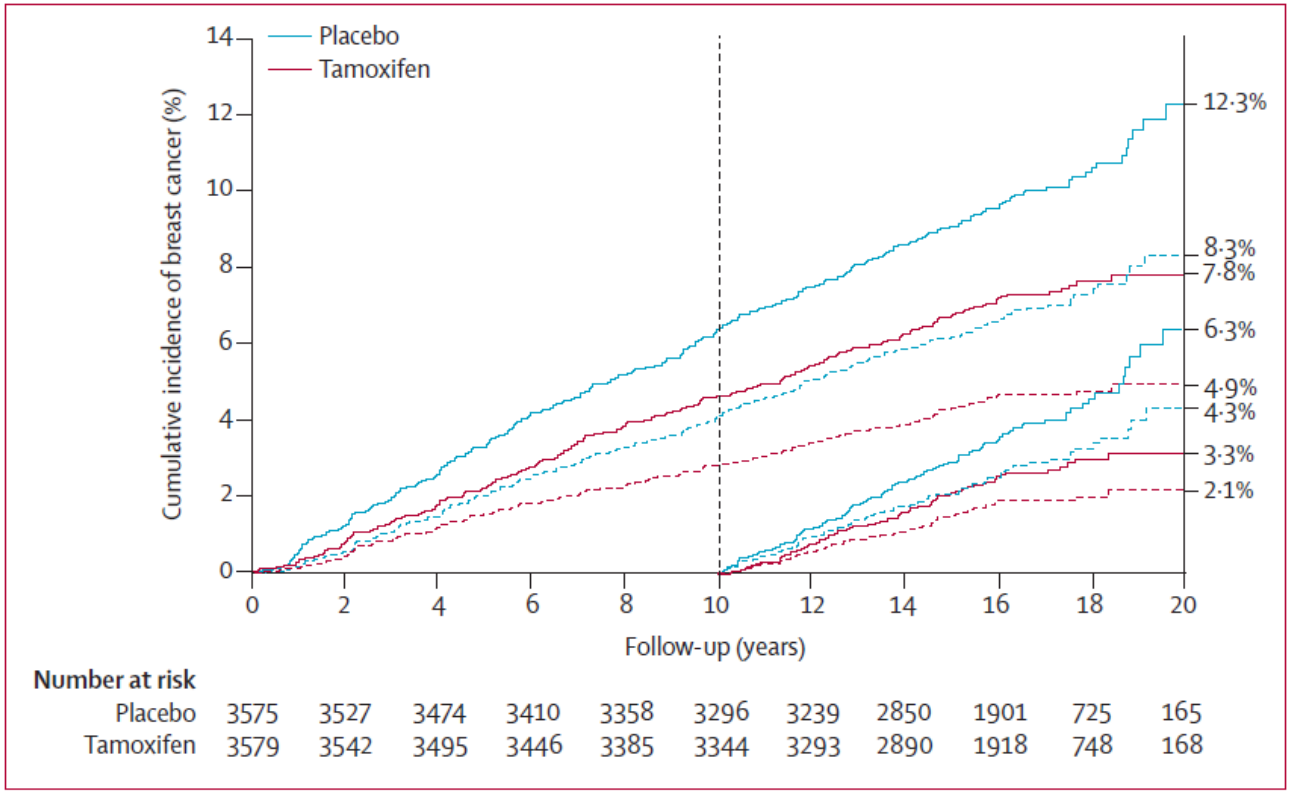

Figure 1: **Cumulative incidence of breast cancers over time**
All breast cancers (solid lines) and invasive oestrogen receptor-positive breast cancers (dashed lines), according to treatment group and duration of follow-up.

Tamoxifen for prevention of breast cancer: extended long-term follow-up of the IBIS-I breast cancer prevention trial

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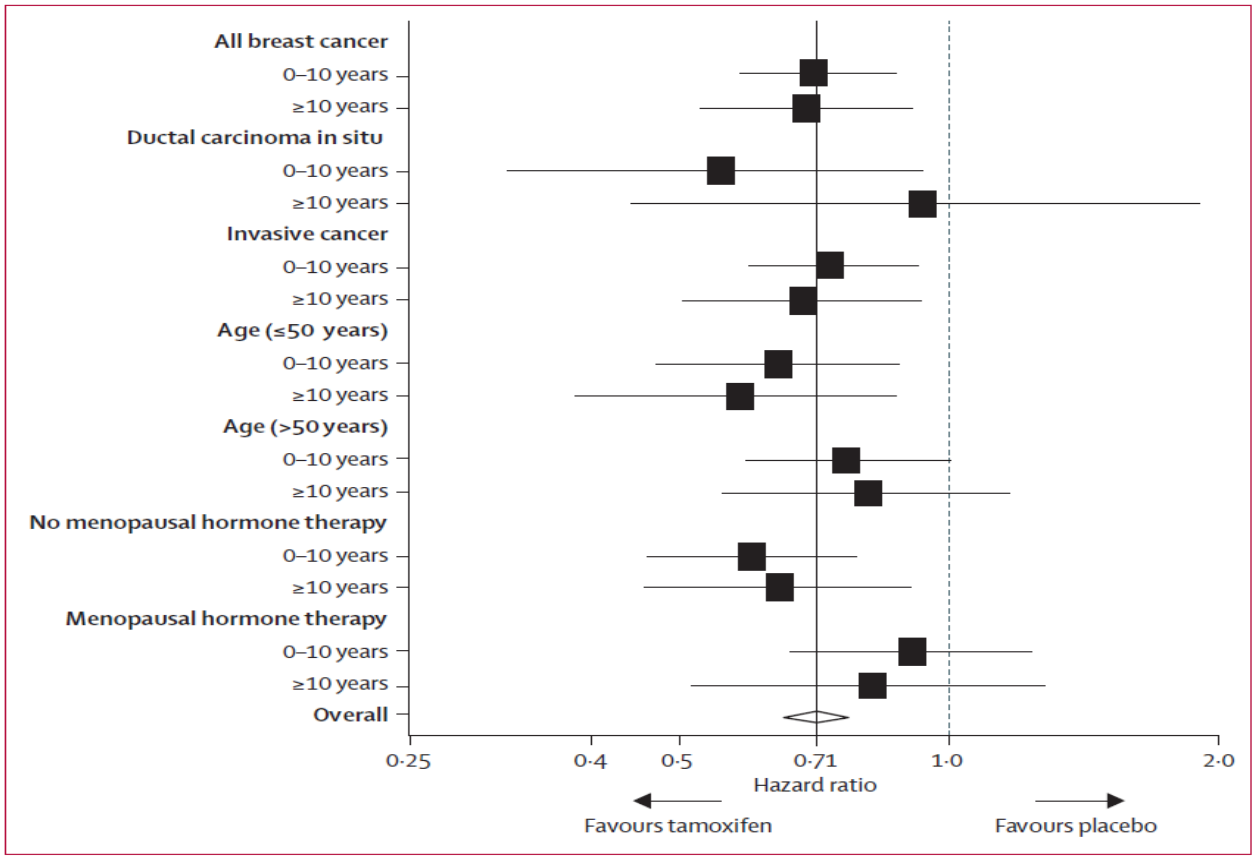
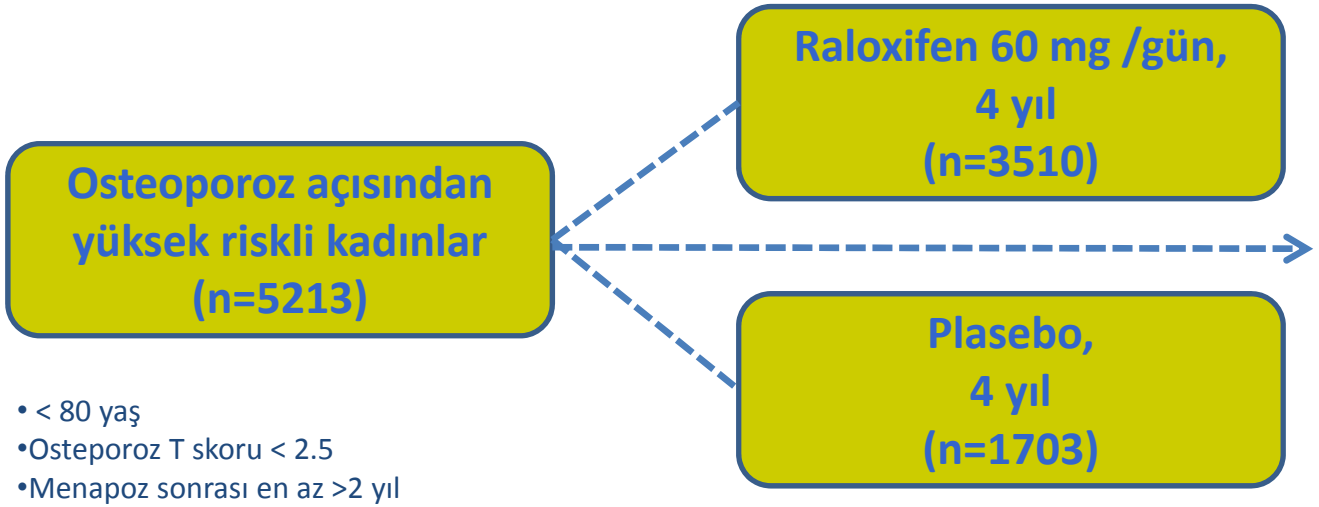


Figure 3: **Forest plot for subgroup analyses according to follow-up periods (0–10 years *vs* ≥10 years)**
Horizontal lines are 95% CIs.

Continuing Outcomes Relevant to Evista: Breast Cancer Incidence in Postmenopausal Osteoporotic Women in a Randomized Trial of Raloxifene

Silvana Martino, Jane A. Cauley, Elizabeth Barrett-Connor, Trevor J. Powles, John Mershon, Damon Disch, Roberta J. Secrest, Steven R. Cummings

For the CORE Investigators



- < 80 yaş
- Osteoporoz T skoru < 2.5
- Menapoz sonrası en az >2 yıl

Birincil Sonlanım Noktası
- İnvaziv Meme Kanseri
- Duktal karsinoma in-situ

Meme kanseri
Median 7,9 yıllık takip sonrası
HR 0.41; 95%CI 0.24-0.71

İkincil sonlanım noktası
- ER pozitif invaziv meme kanseri
- Tüm nedenlere bağlı ölüm
- Yan etkiler

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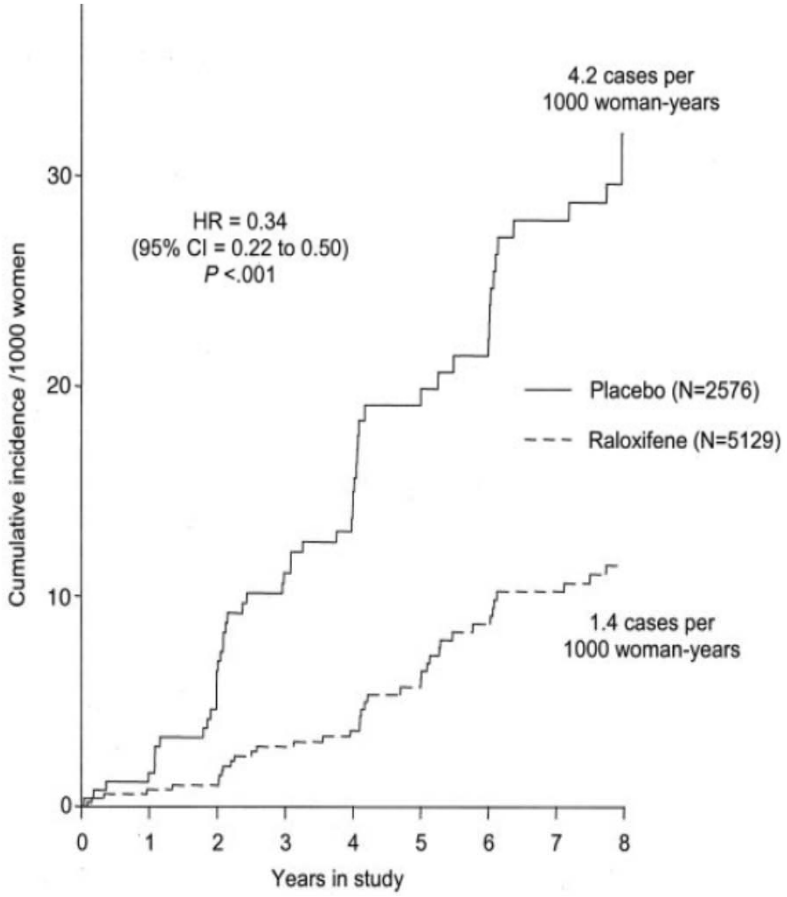


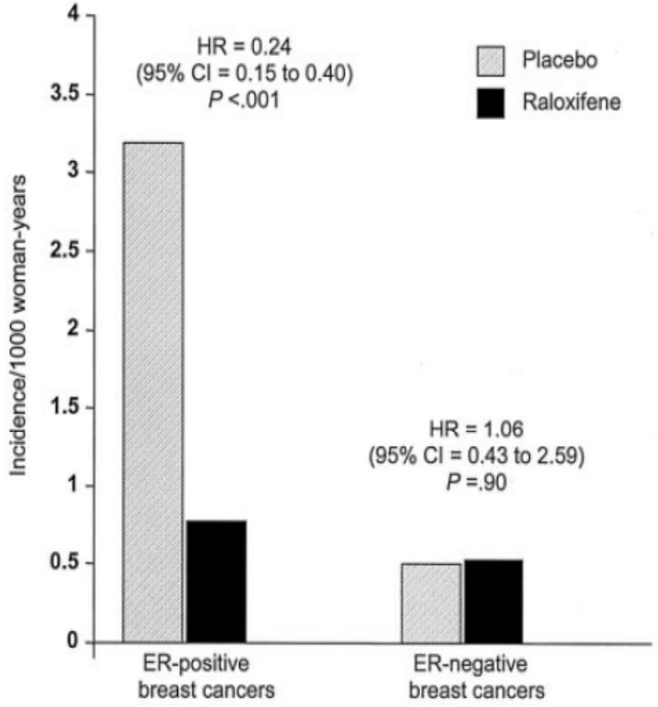
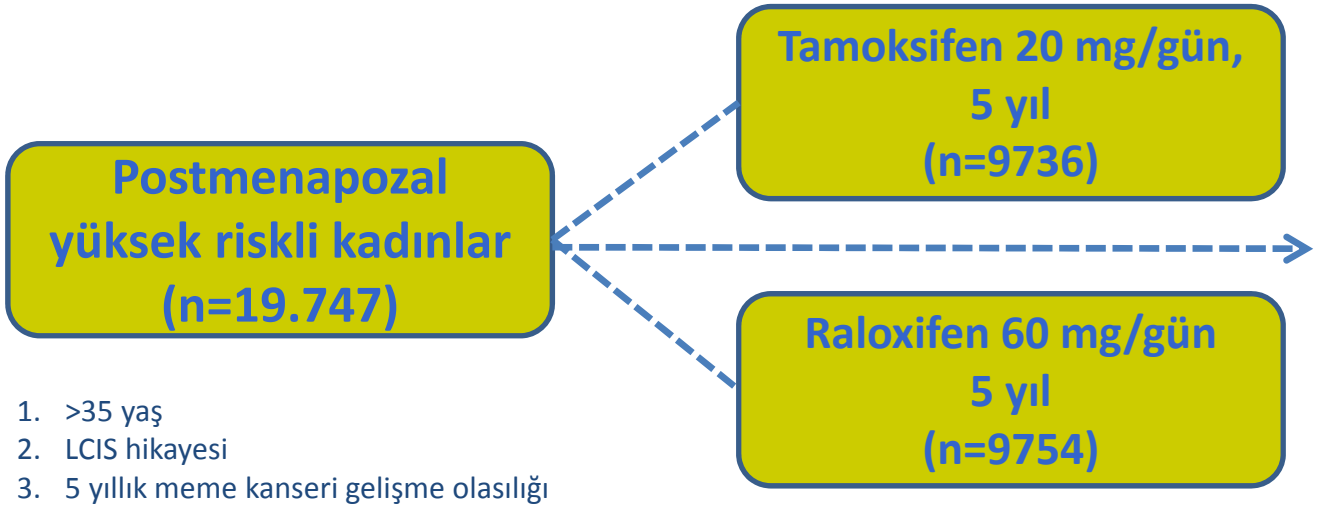


Fig. 4. Annual incidence rate per 1000 woman-years of follow-up for adjudicate invasive breast cancers over the 8 years from the time of randomization in th MORE trial to the end of the CORE trial for the 7705 MORE participants. Th numbers of ER-positive invasive breast cancers in the placebo and raloxifene group were 44 and 22, respectively; the numbers of ER-negative invasive breast cancers i

Effects of Tamoxifen vs Raloxifene on the Risk of Developing Invasive Breast Cancer and Other Disease Outcomes

The NSABP Study of Tamoxifen and Raloxifene (STAR) P-2 Trial



1. >35 yaş
2. LCIS hikayesi
3. 5 yıllık meme kanseri gelişme olasılığı ≥ %1.66 (GAİL)

Median 6.7 yıllık takip sonrası
RR=0.2, 95% CI =0.82-1.28

Birincil Sonlanım Noktası
- Meme Kanseri İnsidansı

İkincil sonlanım noktası
- Non-invaziv meme kanseri
- Uterus kanseri
- Osteoporotik kırıklar
- Stroke
- Pulmoner emboli
- DVT
- Katarakt
- Herhangi nedenli ölüm

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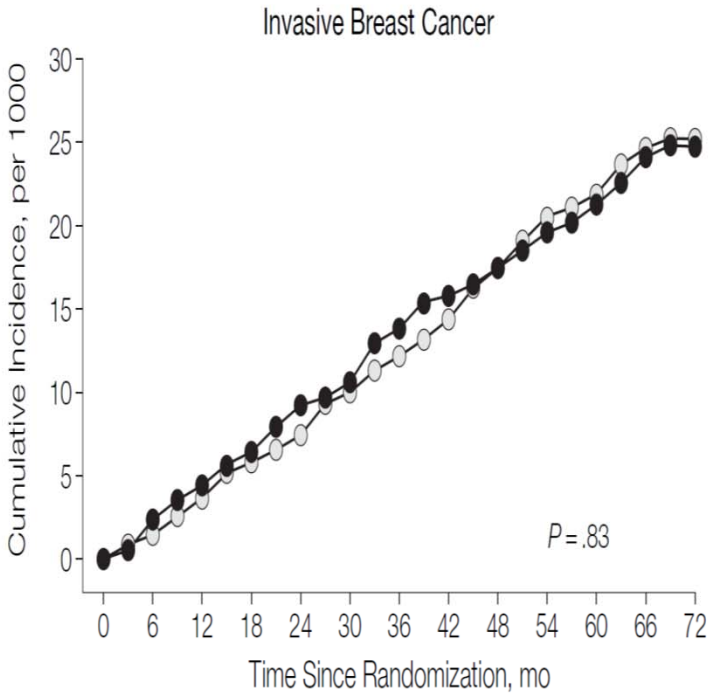

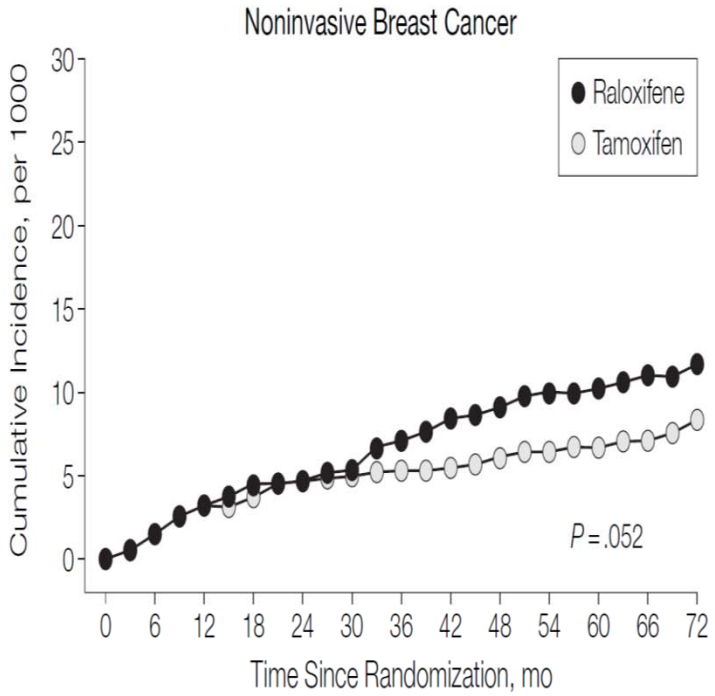

No. at Risk

Raloxifene	9745	8916	6701	4323	833	9745	8885	6667	4291	828
Tamoxifen	9726	8931	6653	4254	809	9726	8909	6633	4243	805

Effects of Tamoxifen vs Raloxifene on the Risk of Developing Invasive Breast Cancer and Other Disease Outcomes

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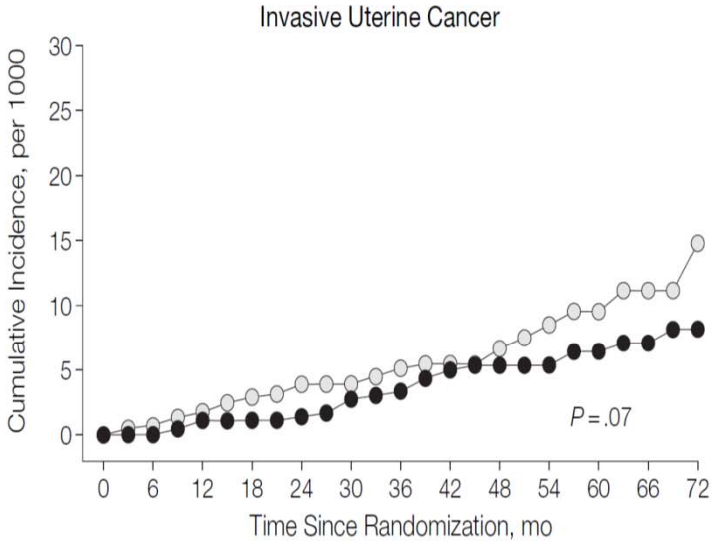

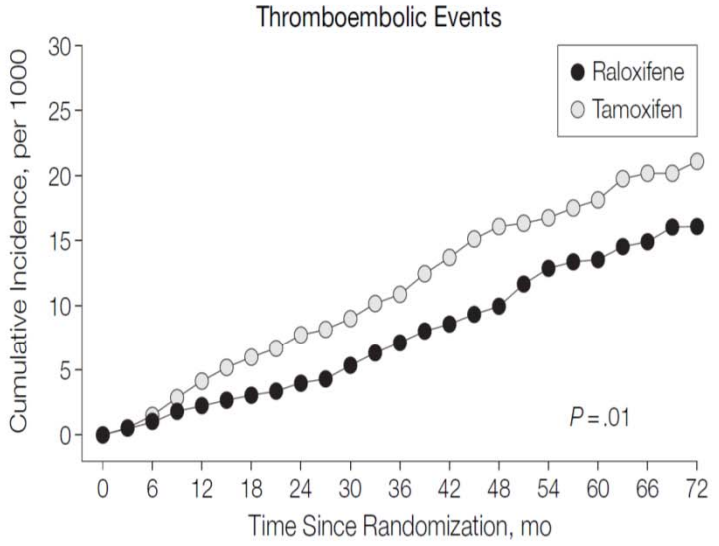

No. at Risk					
Raloxifene	4712	4304	3219	2094	408
Tamoxifen	4732	4291	3106	1971	367

9745	8962	6764	4362	836
9726	8948	6682	4286	813

Selective oestrogen receptor modulators in prevention of breast cancer: an updated meta-analysis of individual participant data

*Jack Cuzick, Ivana Sestak, Bernardo Bonanni, Joseph P Costantino, Steve Cummings, Andrea DeCensi, Mitch Dowsett, John F Forbes, Leslie Ford, Andrea Z LaCroix, John Mershon, Bruce H Mitlak, Trevor Powles, Umberto Veronesi, Victor Vogel, D Lawrence Wickerham, for the SERM Chemoprevention of Breast Cancer Overview Group**

	N	Recruitment period	Treatment groups and daily dose	Treatment duration (years)	Entry criteria	Present status	Median follow-up (months)
Marsden[5,6]	2471	1986–96	Placebo (1233) Tamoxifen 20 mg (1238)	5–8	High risk, family history	Blinded, further follow-up	171·6 (153·9–184·0)
IBIS-I[7,8]	7109	1992–2001	Placebo (3566) Tamoxifen 20 mg (3573)	5	Greater than two times relative risk	Blinded, further follow-up	96 (80·1–117·1)
NSABP-P-1[9,10]	13 205	1992–97	Placebo (6707) Tamoxifen 20 mg (6681)	5	>1·6% 5 year risk	Unblinded, no follow-up	57·6 (35·4–64·9)
Italian[11,12]	5408	1992–97	Placebo (2708) Tamoxifen 20 mg (2700)	5	Normal risk, women with hysterectomy	Unblinded, further follow-up	139·6 (122·0–146·1)
MORE[13]/CORE[14]*	7705/6511	1994–98/ 1998–2002	Placebo (2576) Raloxifene 60 mg (2557)/ Placebo (2576) Raloxifene 120 mg (2572)	4/8	Normal risk, postmenopausal women with osteoporosis	Unblinded, no follow-up	71·3 (47·1–95·4)
RUTH[15]	10 101	1998–2000	Placebo (5057) Raloxifene 60 mg (5044)	5	Normal risk, postmenopausal women with established or risk of CHD	Unblinded, no follow-up	66·7 (60·1–72·3)
STAR[16,17]	19 490	1999–2004	Raloxifene 60 mg (9875) Tamoxifen 20 mg (9872)	5	>1·6% 5 year risk, postmenopausal women	Unblinded, no follow-up	81 (60·8–96.6)
PEARL[18,19]	8856	2001–07	Placebo (2852) Lasofoxifene 0·50 mg (2852) Lasofoxifene 0·25 mg (2852)	5	Normal risk, postmenopausal women with osteoporosis	Blinded, no follow-up	59·6 (58·8–60·1)
GENERATIONS[20,21]	9354	2004–09	Placebo (4678) Arzoxifene 20 mg (4676)	4	Normal risk, postmenopausal with low BMD or osteoporosis	Unblinded, no follow-up	54·3 (28·3–56·1)

Data in parenthesis are number of randomised participants. CHD=coronary heart disease. BMD=bone mineral density. *The CORE trial was done in a subset of women originally enrolled in the MORE trial.

Table 1: Details of breast cancer prevention trials

Selective oestrogen receptor modulators in prevention of breast cancer: an updated meta-analysis of individual participant data

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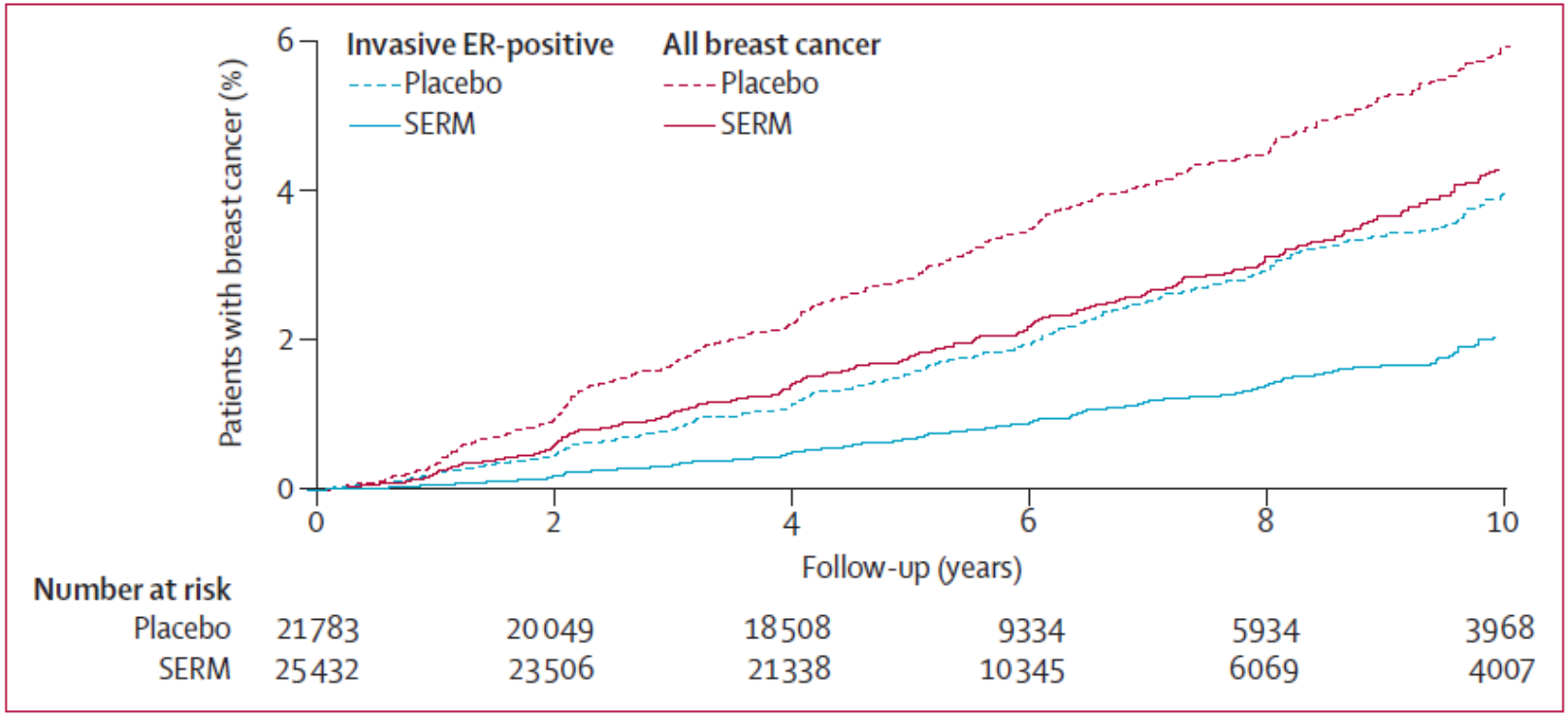

Figure 1: Cumulative incidence for all breast cancer (including ductal carcinoma in situ) and all ER-positive invasive cancers in years 0–10 according to treatment allocation
SERM=selective oestrogen receptor modulator. ER=oestrogen receptor.

Selective oestrogen receptor modulators in prevention of breast cancer: an updated meta-analysis of individual participant data

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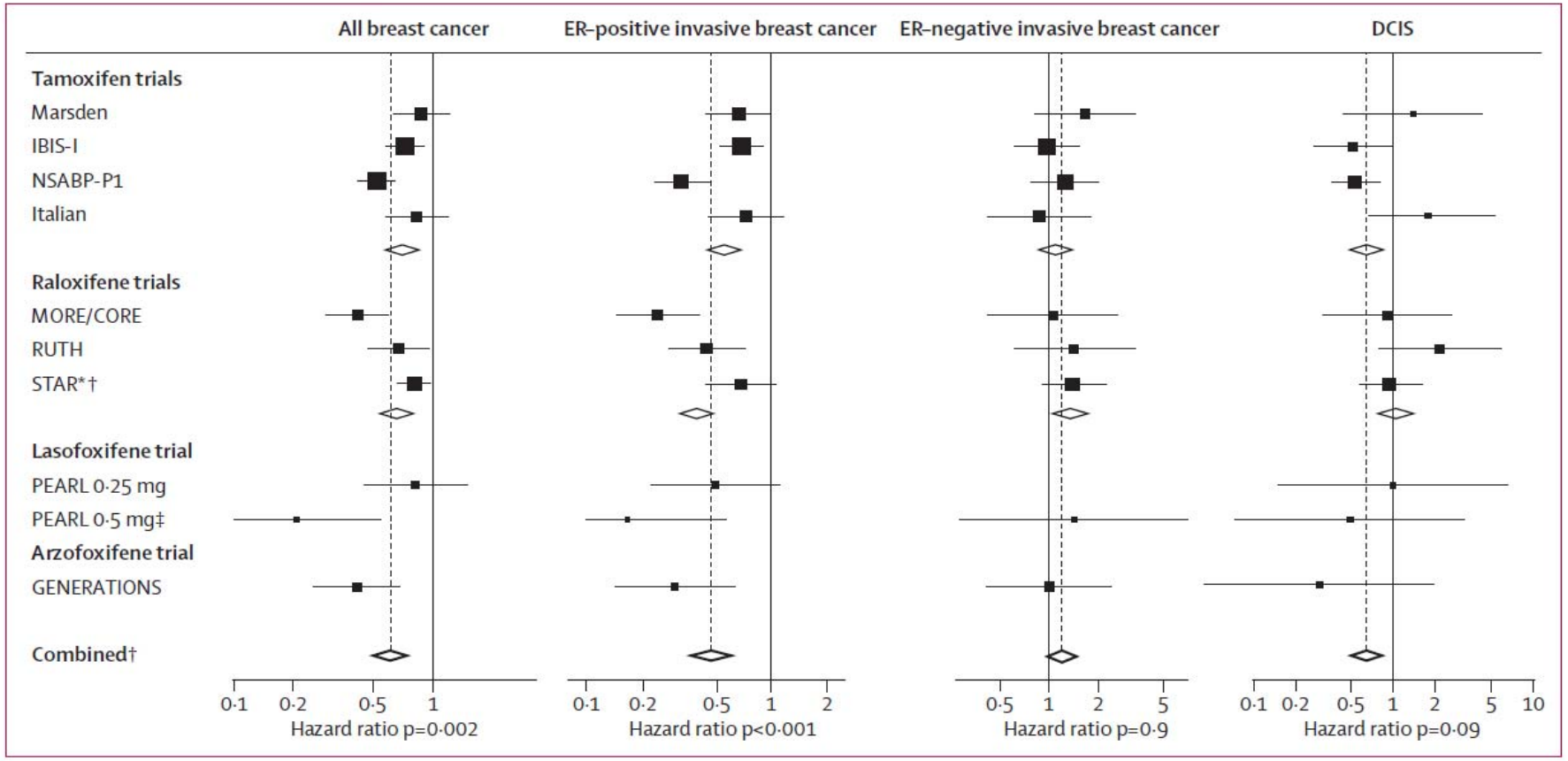


Figure 3: **All breast cancers, invasive breast cancer, and DCIS in years 0–10**
ER=oestrogen receptor. DCIS=ductal carcinoma in situ. *Adjusted by overall tamoxifen effect to give raloxifene versus placebo comparisons. †STAR data not included in comparisons. ‡Data for ER-invasive cancer are pooled.

Annals of Internal Medicine | CLINICAL GUIDELINE

Medications for Risk Reduction of Primary Breast Cancer in Women: U.S. Preventive Services Task Force Recommendation Statement

Virginia A. Moyer, MD, MPH, on behalf of the U.S. Preventive Services Task Force*

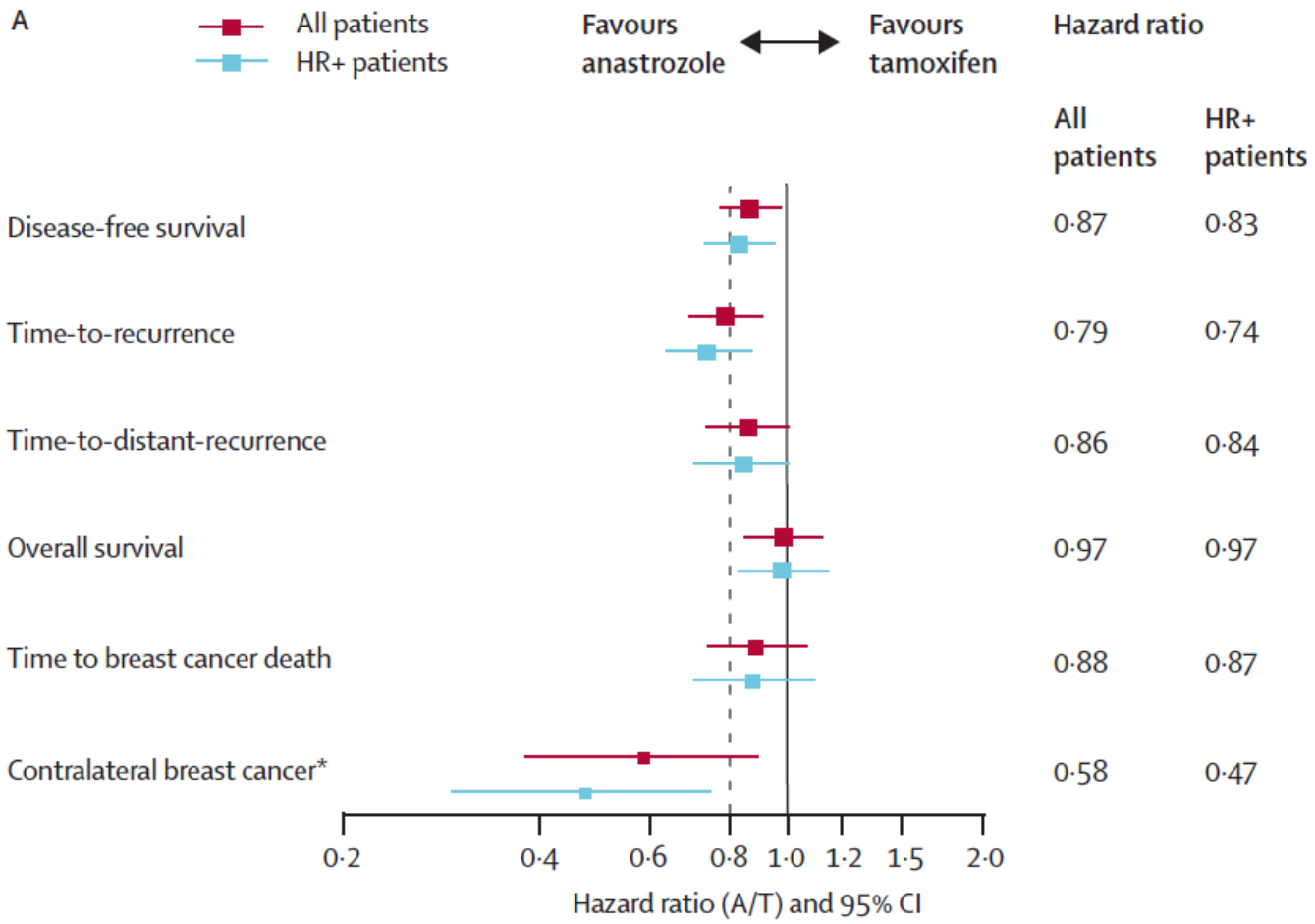
Table. Summary of Primary Prevention Trials*

Major Clinical Outcome	Raloxifene vs. Tamoxifen	Tamoxifen vs. Placebo	Raloxifene vs. Placebo
Events reduced (benefits)			
Invasive breast cancer	5 (1–9) fewer events per 1000 women with tamoxifen	7 (4–12) fewer events per 1000 women with tamoxifen	9 (4–14) fewer events per 1000 women with raloxifene
ER-positive breast cancer	No difference	8 (3–13) fewer events per 1000 women with tamoxifen	8 (4–12) fewer events per 1000 women with raloxifene
ER-negative breast cancer	No difference	No difference	No difference
Noninvasive cancer	No difference	No difference	No difference
All-cause mortality	No difference	No difference	No difference
Vertebral fracture	No difference	No difference	7 (5–9) fewer events per 1000 women with raloxifene
Nonvertebral fracture	Not reported	3 (0.2–5) fewer events per 1000 women with tamoxifen	No difference
Events increased (harms)			
Thromboembolic events	4 (1–7) more events per 1000 women with tamoxifen	4 (2–9) more events per 1000 women with tamoxifen	7 (2–15) more events per 1000 women with raloxifene
Coronary heart disease	No difference	No difference	No difference
Stroke	No difference	No difference	No difference
Endometrial cancer	5 (2–9) more events per 1000 women with tamoxifen	4 (1–10) more events per 1000 women with tamoxifen	No difference
Cataracts	15 (8–22) more events per 1000 women with tamoxifen	No difference	No difference

ER = estrogen receptor.
* Numbers in parentheses are 95% CIs.

Results of the ATAC (Arimidex, Tamoxifen, Alone or in Combination) trial after completion of 5 years' adjuvant treatment for breast cancer

Lancet 2005; 365: 60–62 *ATAC Trialists' Group**



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 23, 2011 VOL. 364 NO. 25

Exemestane for Breast-Cancer Prevention in Postmenopausal Women

Meme kanseri için yüksek riskli postmenapozal kadınlar (n=4560)

Exemestan 25 mg /gün, 5 yıl (n=2285)

Plasebo, 5 yıl (n=2275)

Birincil Sonlanım Noktası
- İnvaziv Meme Kanseri

1. >60 veya
2. 5 yıllık meme kanseri gelişme olasılığı ≥ %1.66 (Gail Risk Skorlaması)
3. LCIS . Atipik duktal veya lobuler hiperplazi hikayesi
4. Mastektomi yapılmış DCIS

Meme kanseri
Median 35 aylık takip sonrası
HR 0.35; 95%CI 0.18 to 0.70)

İkincil sonlanım noktası
İnvaziv ve noninvaziv meme Kanseri
ER negatif invaziv meme kanseri
LCİS, atipik duktal / lobüler hiperplazi
Kırık
Kardiyovasküler olay
Tüm diğer kanserler
Yaşam kalitesi
- Tüm nedenlere bağlı ölüm
- Yan etkiler

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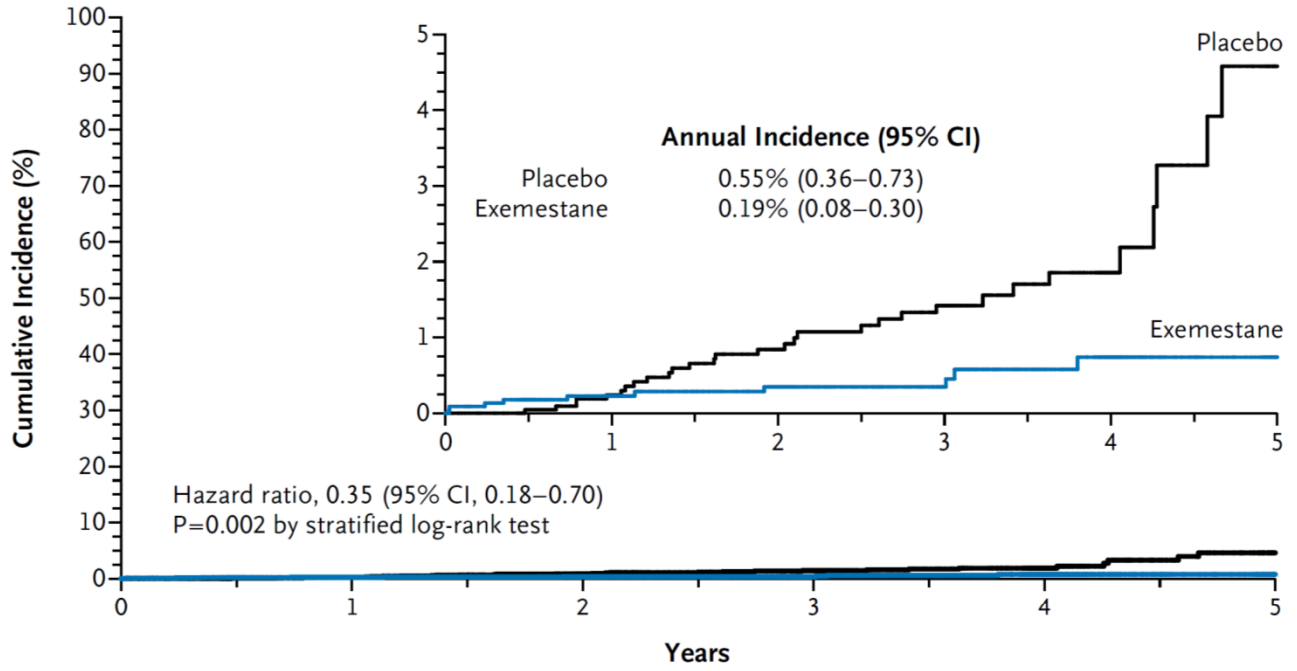

No. at Risk

Placebo	2275	1905	1468	986	477	82
Exemestane	2285	1902	1468	980	464	77

Figure 1. Cumulative Incidence of Invasive Breast Cancer.

CI denotes confidence interval.

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Exemestane for Breast-Cancer Prevention in Postmenopausal Women

Table 2. Incidence of Invasive and Preinvasive Breast Events by Treatment Group.*

Type of Event	Exemestane (N=2285)		Placebo (N=2275)		Hazard Ratio (95% CI)†	P Value‡
	No. of Cases	Annual Incidence (%)	No. of Cases	Annual Incidence (%)		
Invasive breast cancer						
All cases	11	0.19	32	0.55	0.35 (0.18–0.70)	0.002
ER-positive	7	0.12	27	0.46	0.27 (0.12–0.60)	<0.001
ER-negative	4	0.07	5	0.09	0.80 (0.21–2.98)	0.74

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ESTABLISHED IN 1812 JUNE 23, 2011 VOL. 364 NO. 25

Exemestane for Breast-Cancer Prevention in Postmenopausal Women

Table 3. Side Effects during Treatment, According to Severity.*

Side Effect	Exemestane (N = 2240)					Placebo (N = 2248)					P Value
	Grade 1	Grade 2	Grade 3	Grade 4	Total	Grade 1	Grade 2	Grade 3	Grade 4	Total	
	no.				no. (%)	no.				no. (%)	
Any	464	931	536	32	1963 (88)	557	877	437	30	1901 (85)	0.003
Cardiac: hypertension	119	109	112	1	341 (15)	124	118	109	3	354 (16)	0.65
Endocrine											
Hot flashes	489	344	67		900 (40)	450	225	43		718 (32)	<0.001
Fatigue	342	150	31	2	525 (23)	305	135	25		465 (21)	0.03
Sweating	284	201	1		486 (22)	263	169	1		433 (19)	0.046
Insomnia	117	98	15		230 (10)	127	55	7		189 (8)	0.04
Constitutional and gastrointestinal											
Diarrhea	77	32	9		118 (5)	58	16	1		75 (3)	0.002
Heartburn	223	92	17		332 (15)	200	79	10		289 (13)	0.06
Nausea	137	15	3		155 (7)	102	18	2		122 (5)	0.04
Musculoskeletal: arthritis	102	113	30	2	247 (11)	96	83	17		196 (9)	0.01
Neurologic											
Dizziness	145	35	9		189 (8)	152	48	9		209 (9)	0.32
Mood alteration or depression	123	90	19	4	236 (11)	128	98	8	1	235 (10)	0.96
Pain											
Back	106	77	21	2	306 (9)	119	80	23		222 (10)	0.45
Extremity	67	68	17	1	153 (7)	60	54	8		122 (5)	0.054
Joint	294	293	75	3	665 (30)	308	264	33	1	606 (27)	0.04
Muscle	69	62	16		147 (7)	111	67	14		192 (9)	0.01
Upper respiratory: cough	196	28	10		234 (10)	224	31	11		266 (12)	0.14
Sexual function: vaginal dryness	209	142	1		352 (16)	219	124			343 (15)	0.68
Secondary-end-point toxic effects											
Clinical skeletal fracture					149 (6.7)					143 (6.4)	0.72
New osteoporosis					37 (1.7)					30 (1.3)	0.39
Cardiovascular events					106 (4.7)					111 (4.9)	0.78
Other solid tumors or hematologic malignant lesions					43 (1.9)					38 (1.7)	0.58

Anastrozole for prevention of breast cancer in high-risk postmenopausal women (IBIS-II): an international, double-blind, randomised placebo-controlled trial

*Jack Cuzick, Ivana Sestak, John F Forbes, Mitch Dowsett, Jill Knox, Simon Cawthorn, Christobel Saunders, Nicola Roche, Robert E Mansel, Gunter von Minckwitz, Bernardo Bonanni, Tiina Palva, Anthony Howell, on behalf of the IBIS-II investigators**

Meme kanseri için yüksek riskli postmenapozal kadınlar (n=3864)

Anastrazol 1 mg /gün, 5 yıl (n=1920)

Plasebo, 5 yıl (n=1944)

Birincil Sonlanım Noktası
- İnvaziv Meme Kanseri
- DCİS

1. Aile hikayesi
2. Atipik hiperplazi veya LCİS
3. Nulliparite
4. > 30 yaşında ilk doğum
5. Memenin > % 50 sini kaplayan opasite

Meme kanseri
Median 5 yıllık takip sonrası
HR 0.47; 95%CI 0.32 to 0.68)

İkincil sonlanım noktası
ER pozitif invaziv meme kanseri
LCİS, atipik duktal / lobüler hiperplazi
Kırık
Kardiyovasküler olay
Tüm diğer kanserler
Yaşam kalitesi
- Tüm nedenlere bağlı ölüm
- Yan etkiler

Anastrozole for prevention of breast cancer in high-risk postmenopausal women (IBIS-II): an international, double-blind, randomised placebo-controlled trial

*Jack Cuzick, Ivana Sestak, John F Forbes, Mitch Dowsett, Jill Knox, Simon Cawthorn, Christobel Saunders, Nicola Roche, Robert E Mansel, Gunter von Minckwitz, Bernardo Bonanni, Tiina Palva, Anthony Howell, on behalf of the IBIS-II investigators**

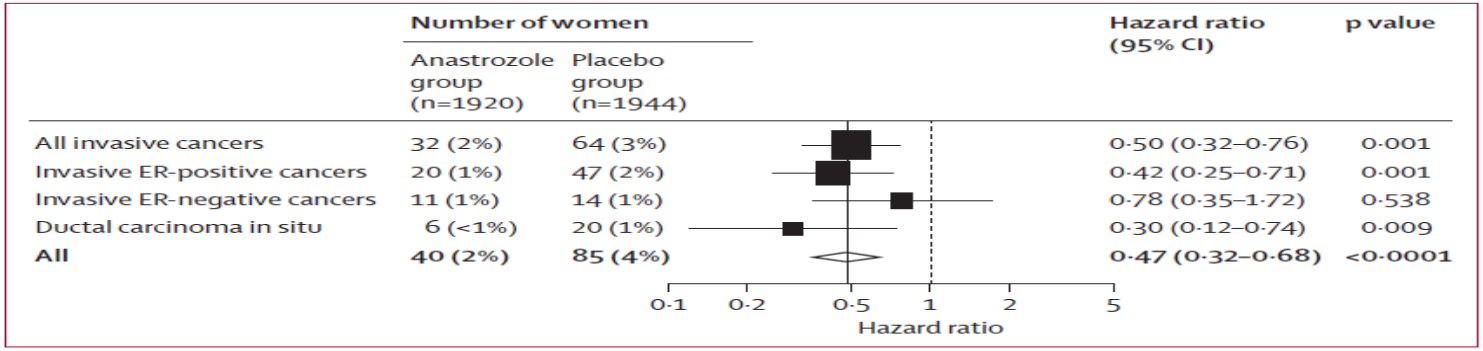


Figure 2: **Analyses by type of breast cancer**
Numbers in subgroups do not match totals because of missing data. ER=oestrogen receptor.

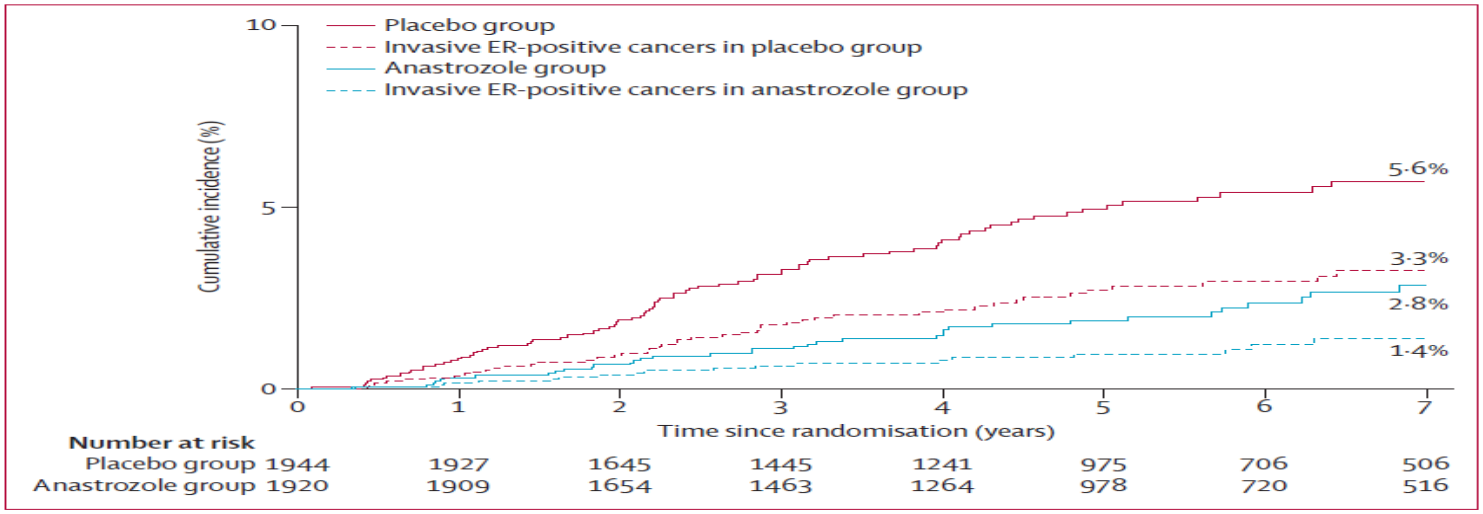


Figure 3: **Cumulative incidence of all breast cancers and of invasive ER-positive breast cancers**
ER=oestrogen receptor.

Anastrozole for prevention of breast cancer in high-risk postmenopausal women (IBIS-II): an international, double-blind, randomised placebo-controlled trial

*Jack Cuzick, Ivana Sestak, John F Forbes, Mitch Dowsett, Jill Knox, Simon Cawthorn, Christobel Saunders, Nicola Roche, Robert E Mansel, Gunter von Minckwitz, Bernardo Bonanni, Tiina Palva, Anthony Howell, on behalf of the IBIS-II investigators**

	Anastrozole group (n=1920)	Placebo group (n=1944)
Breast cancer	2 (<1%)	0
Other cancer	7 (<1%)	10 (1%)
Cerebrovascular accident or stroke	2 (<1%)	2 (<1%)
Cardiac arrest	3 (<1%)	1 (<1%)
Other	4 (<1%)	4 (<1%)
Total	18 (1%)	17 (1%)

Data are n (%).

Table 2: Causes of death

TÜM BU BİLGİLER IŞIĞINDA…

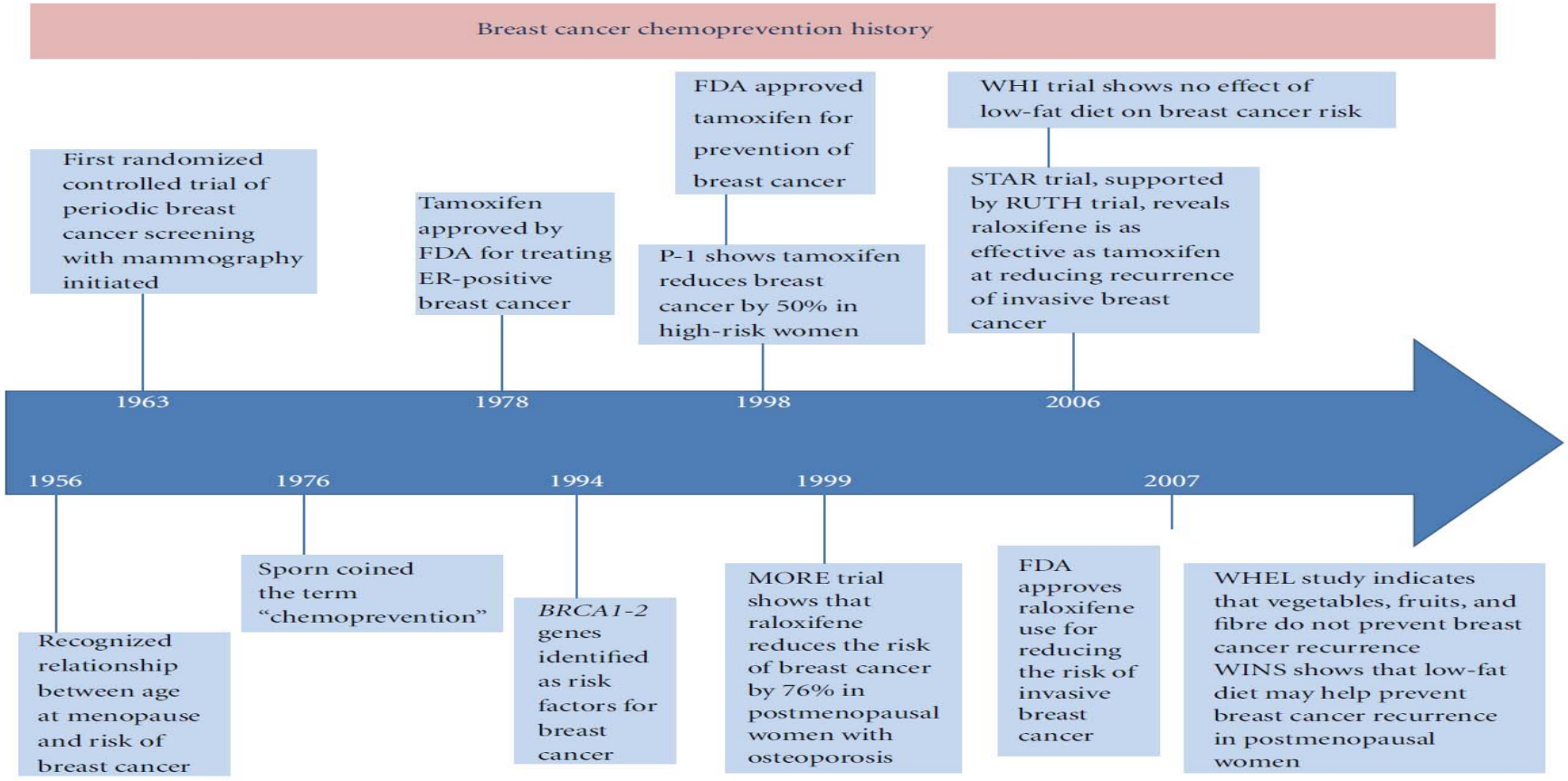


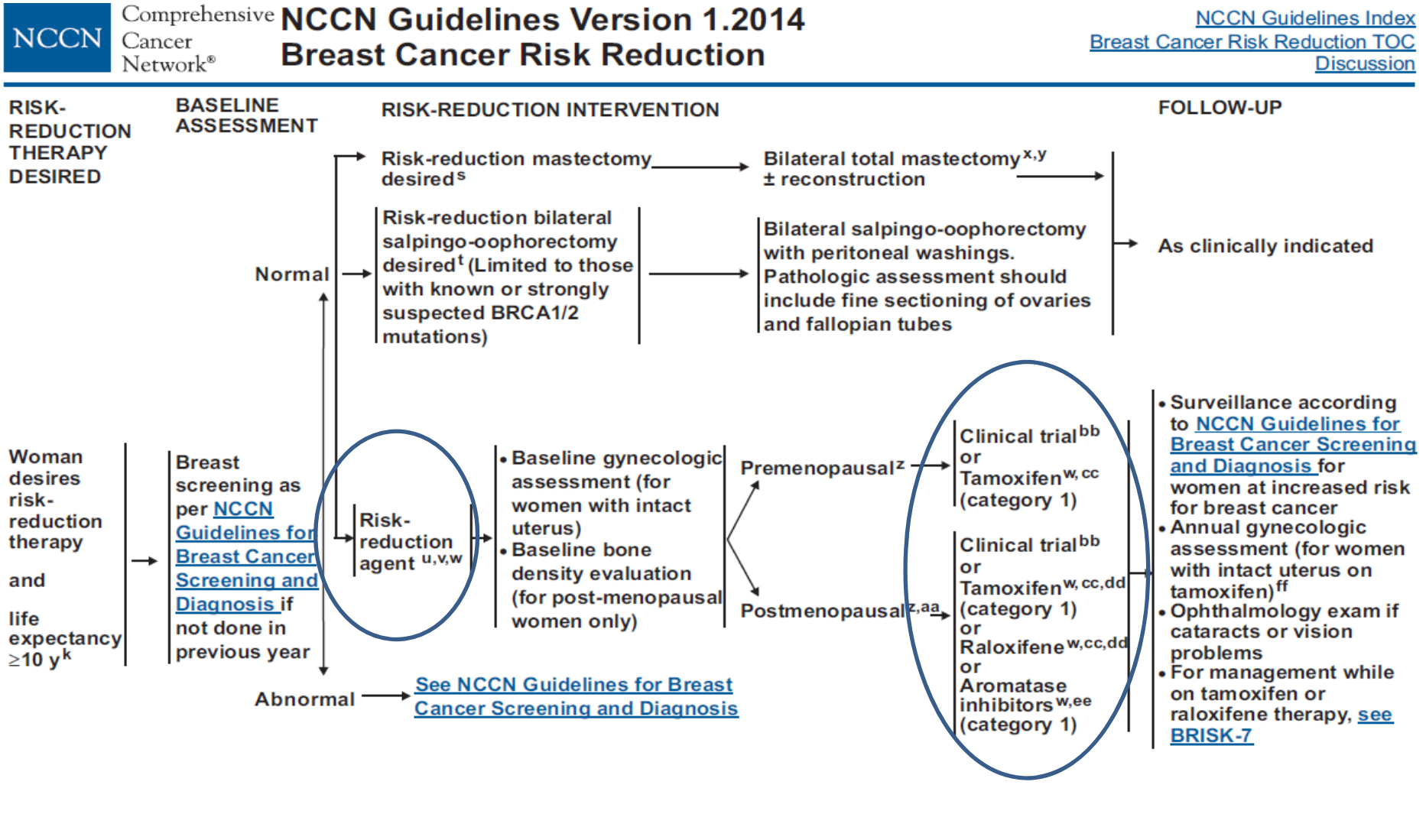
FIGURE 1: Breast cancer chemoprevention history.

KANITLAR GÜÇLÜ !!!!

- NSABP P-1 NNT 48
- MORE RUTH STAR NNT 112
- MAP 3 NNT 26
- IBIS 2 NNT 36

- PRIMER KARDIYOVASKULER OLAY ÖNLENMESİ (STATİN) NNT 60

KEMOPREVANSİYON MÜMKÜN!!!



GÜÇLÜ KANITLARA RAĞMEN…

Prevalence of tamoxifen use for breast cancer chemoprevention among U.S. women

Erika A. Waters[1], **Kathleen A. Cronin**[2], **Barry I. Graubard**[3], **Paul K. Han**[2], and **Andrew N. Freedman**[2]

Prevalence estimates for use of tamoxifen in two nationally-representative U.S. data sources (NHIS 2000, NHIS 2005)

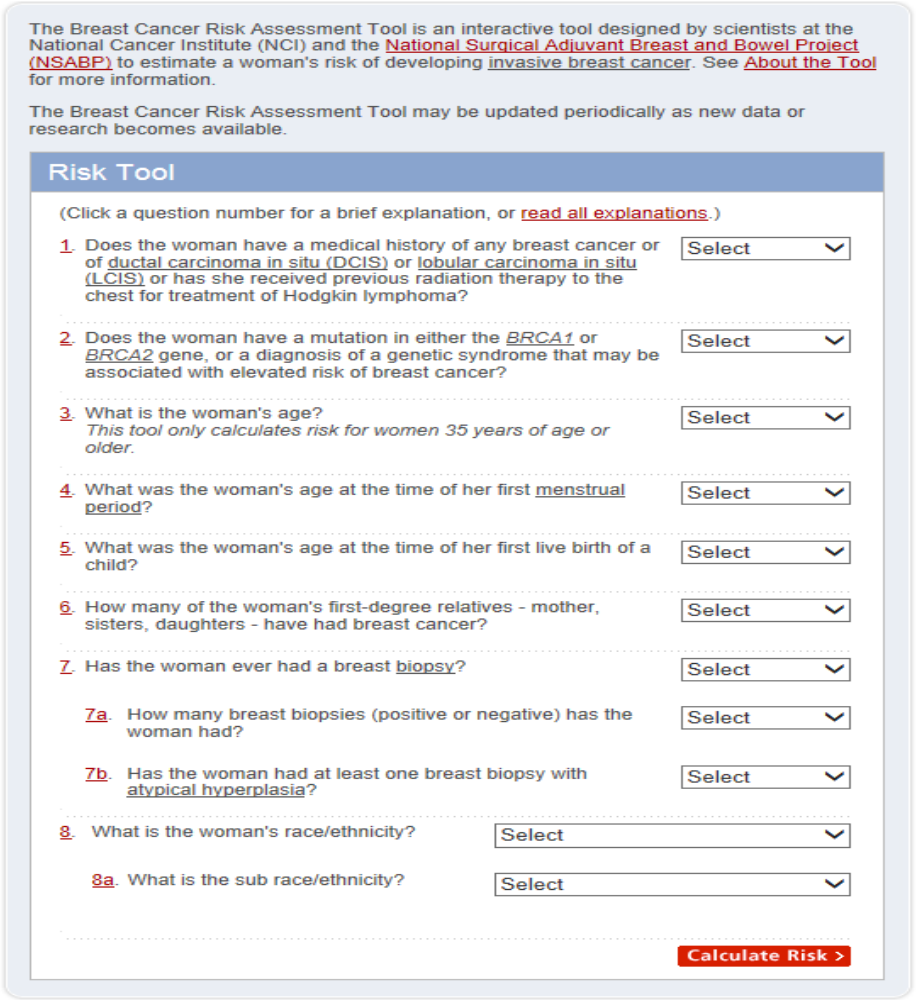
NHIS 2000[1]		NHIS 2005[2]	
Number using tamoxifen (95% CI)	**Percentage**	**Number using tamoxifen (95% CI)**	**Percentage**
120,737 (95% CI 75,416-183,219)	0.20 (95% CI 0.13-0.31)	51,575 (95% CI 19,596-109,936)	0.08 (95% CI 0.03-0.17)

[1] Weighted estimate from a sample of 27 women who report using tamoxifen out of a total sample size of 10,601

[2] Weighted estimate from a sample of 8 women who report using tamoxifen out of a total sample size of 10,690

SORUNLAR ve ÇÖZÜM ÖNERİLERİ

SORUNLAR ve ÇÖZÜM ÖNERİLERİ



The Breast Cancer Risk Assessment Tool is an interactive tool designed by scientists at the National Cancer Institute (NCI) and the National Surgical Adjuvant Breast and Bowel Project (NSABP) to estimate a woman's risk of developing invasive breast cancer. See About the Tool for more information.

The Breast Cancer Risk Assessment Tool may be updated periodically as new data or research becomes available.

Risk Tool

(Click a question number for a brief explanation, or read all explanations.)

1. Does the woman have a medical history of any breast cancer or of ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS) or has she received previous radiation therapy to the chest for treatment of Hodgkin lymphoma? — Select
2. Does the woman have a mutation in either the *BRCA1* or *BRCA2* gene, or a diagnosis of a genetic syndrome that may be associated with elevated risk of breast cancer? — Select
3. What is the woman's age? *This tool only calculates risk for women 35 years of age or older.* — Select
4. What was the woman's age at the time of her first menstrual period? — Select
5. What was the woman's age at the time of her first live birth of a child? — Select
6. How many of the woman's first-degree relatives - mother, sisters, daughters - have had breast cancer? — Select
7. Has the woman ever had a breast biopsy? — Select
   - 7a. How many breast biopsies (positive or negative) has the woman had? — Select
   - 7b. Has the woman had at least one breast biopsy with atypical hyperplasia? — Select
8. What is the woman's race/ethnicity? — Select
   - 8a. What is the sub race/ethnicity? — Select

Calculate Risk >

SORUNLAR ve ÇÖZÜM ÖNERİLERİ

Kalibrasyon

Diskriminasyon

SORUNLAR ve ÇÖZÜM ÖNERİLERİ

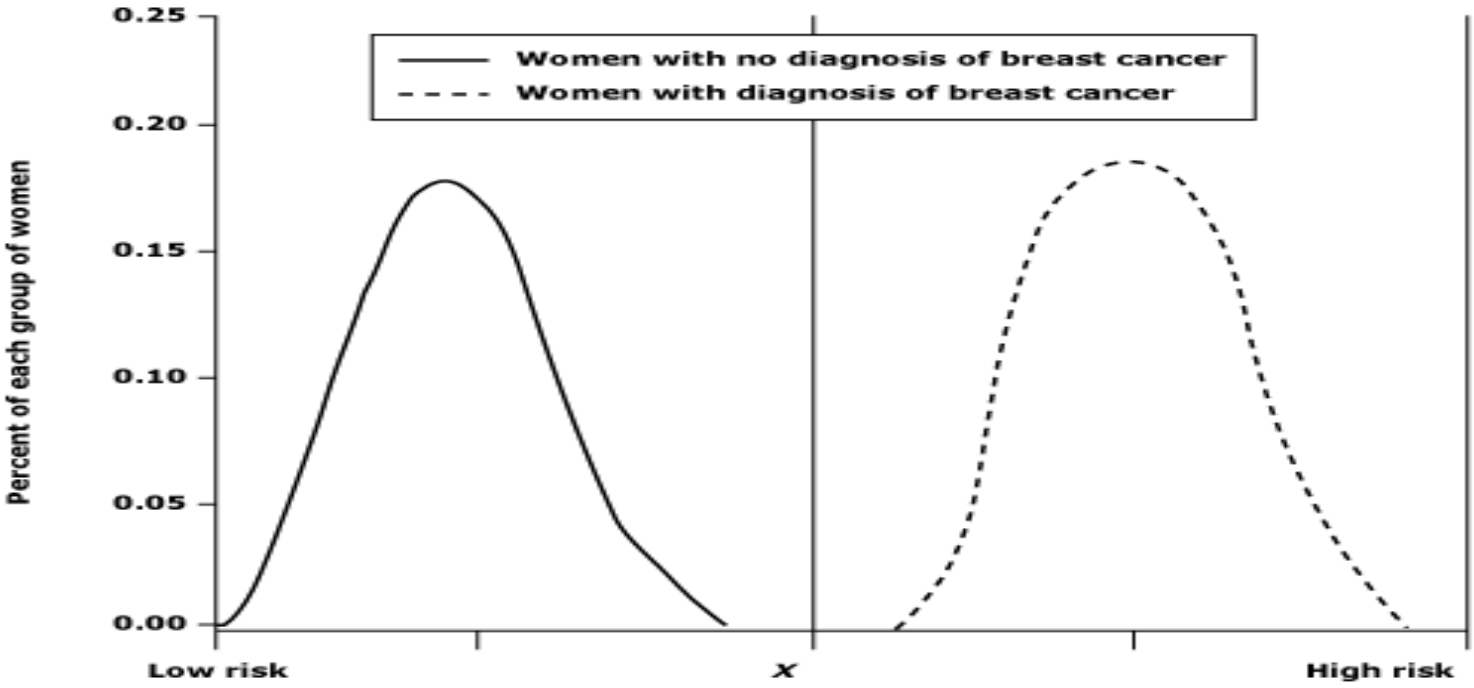
Kalibrasyon

Calibration of BCRAT in the Breast Cancer Prevention Trial (Costantino et al, JNCI 1999)

Age Group	# women	O	E	E/O
<=49	2332	60	55.9	0.9
50-59	1807	43	48.4	1.1
>=60	1830	52	54.7	1.1
All ages	5969	155	159.0	1.0

SORUNLAR ve ÇÖZÜM ÖNERİLERİ

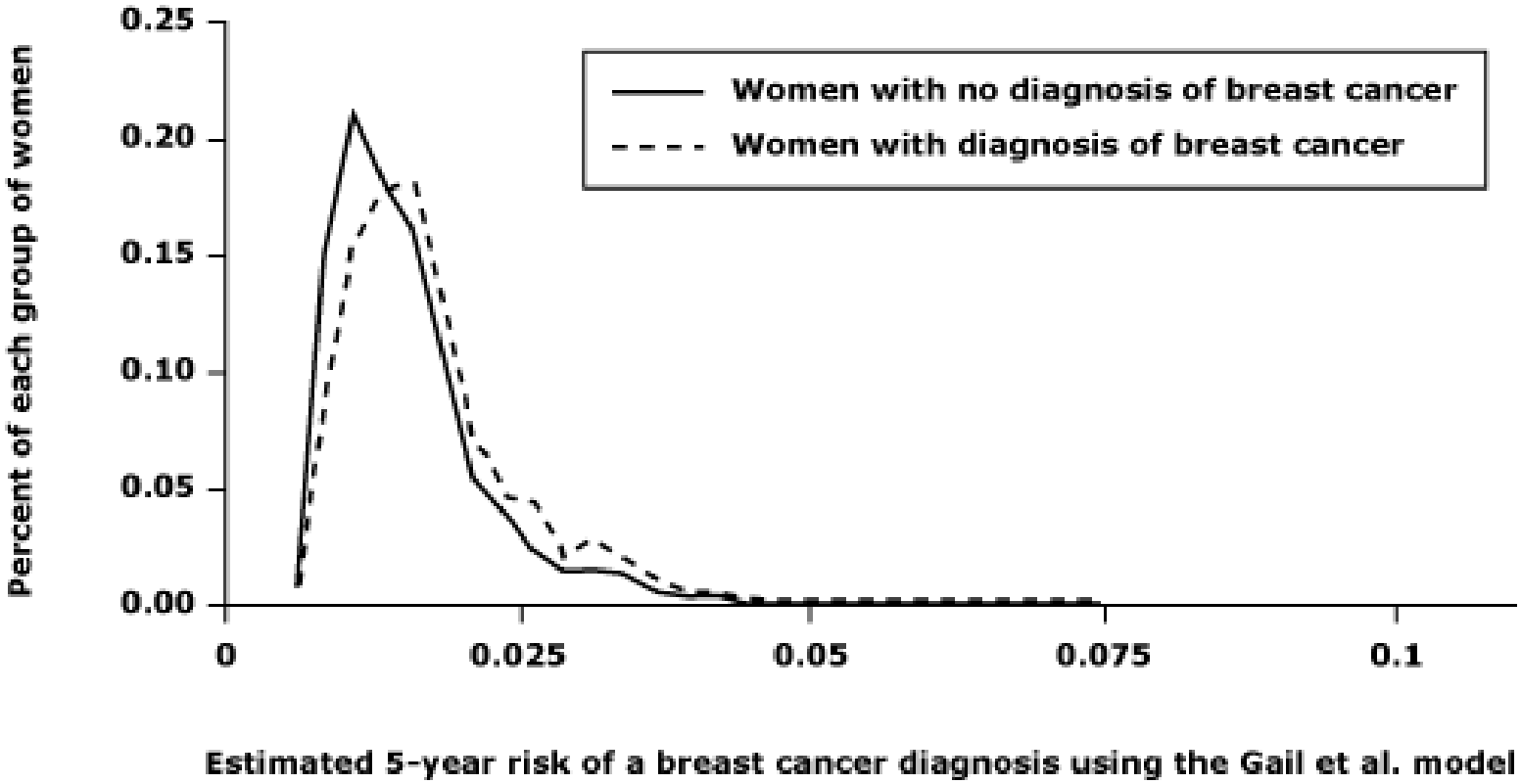
Diskriminasyon



Estimated 5-year risk of a breast cancer diagnosis using the Gail et al. model

SORUNLAR ve ÇÖZÜM ÖNERİLERİ

Diskriminasyon



SORUNLAR ve ÇÖZÜM ÖNERİLERİ

Model	Data collection and calculation*	Relatives with breast or ovarian cancer	Additional risk factors in model	Accuracy studies						
				Study, year (reference)	Population	Reference standard	Sensitivity (percent)	Specificity (percent)	PPV	NPV
FHAT	Clinical scoring tool; referral threshold of 10 is equivalent to a 2-fold increase in risk for breast or ovarian cancer.	First-, second-, and third-degree	Age at diagnosis, bilateral breast cancer, breast and ovarian cancer in the same person, breast cancer in men, colon and prostate cancer	Gilpin et al, 2000[1]	35 carriers and 149 noncarriers	10 percent threshold	94	51	0.31	0.97
				Parmigiani et al, 2007[2]	33 carriers and 559 noncarriers	10 percent threshold	94	32	•	Δ
				Panchal et al, 2008[3]	200 carriers and 100 noncarriers	10 percent threshold	70	63	–	–
Manchester scoring system	Clinical scoring tool; referral threshold of 10 for *BRCA1*- or *BRCA2*-specific scores or 15 combined. Not intended for Ashkenazi Jewish persons.	First-, second-, and third-degree	Type of cancer (breast, ovarian, pancreatic, or prostate), affected family members, age at diagnosis	Evans et al, 2004[4]	23 carriers and 235 noncarriers	10 precent threshold	87	66	0.20	0.98
				Barcenas et al, 2006[5]	69 carriers and 306 noncarriers	10 percent threshold	93	41	0.28	0.96
				Panchal et al, 2008[3]	200 carriers and 100 noncarriers	15 percent threshold	58	71	–	–
				Antoniou et al, 2008[6]	365 carriers and 1569 noncarriers	15 percent threshold	92	33	0.24	0.95
RST	Clinical checklist of 13 items; referral threshold of 2 positive responses.	First- and second-degree	Breast cancer in women ≤50 y (self or relatives), ovarian cancer at any age (self or relatives), ≥2 cases of breast cancer in women aged >50 y on the same side of the family; breast cancer in men; Jewish ancestry	Bellcross et al, 2009[7]	296 women randomly selected from 2462 tested while having screening mammography	Correctly assigns to high mutation probability compared with BOADICEA, BRCAPRO, and Myriad II models at 10 percent thresholds	BOADICEA: 89	BOADICEA: 77	BOADICEA: 0.28	BOADICEA: 0.99
							BRCAPRO: 91	BRCAPRO: 76	BRCAPRO: 0.24	BRCAPRO: 0.98
							Myriad II: 91	Myriad II: 78	Myriad II: 0.34	Myriad II: 0.99
							Overall: 81◇	Overall: 92◇	Overall: 0.80◇§	Overall: 0.92◇¥
PAT	Clinical scoring tool; optimum referral threshold of 8.	First-, second-, and third-degree	Breast cancer in women aged ≤50 y or >50 y, ovarian cancer at any age, breast cancer in men, Ashkenazi Jewish ancestry	Hoskins et al, 2006[8]	737 women identified at potentially increased risk from 3906 tested while having screening mammography‡	Correctly assigns to high mutation probability compared with the Myriad II model at the 10 percent threshold	100	93	0.63	1.00
FHS-7	Clinical checklist of 7 items; referral threshold of 1 positive response.	First-degree	Any relatives with breast cancer at age ≤50 y, bilateral breast cancer, breast and ovarian cancer in the same person, breast cancer in men, ≥2 relatives with breast and/or ovarian cancer, ≥2 relatives with breast and/or colon cancer	Ashton-Prolla et al, 2009[9]	885 women with ≥1 positive response and 910 with no positive responses from 9218 women tested in primary care clinics	Correctly assigns to high mutation probability compared with genetic evaluation†	88	56	0.63	1.00

SORUNLAR ve ÇÖZÜM ÖNERİLERİ

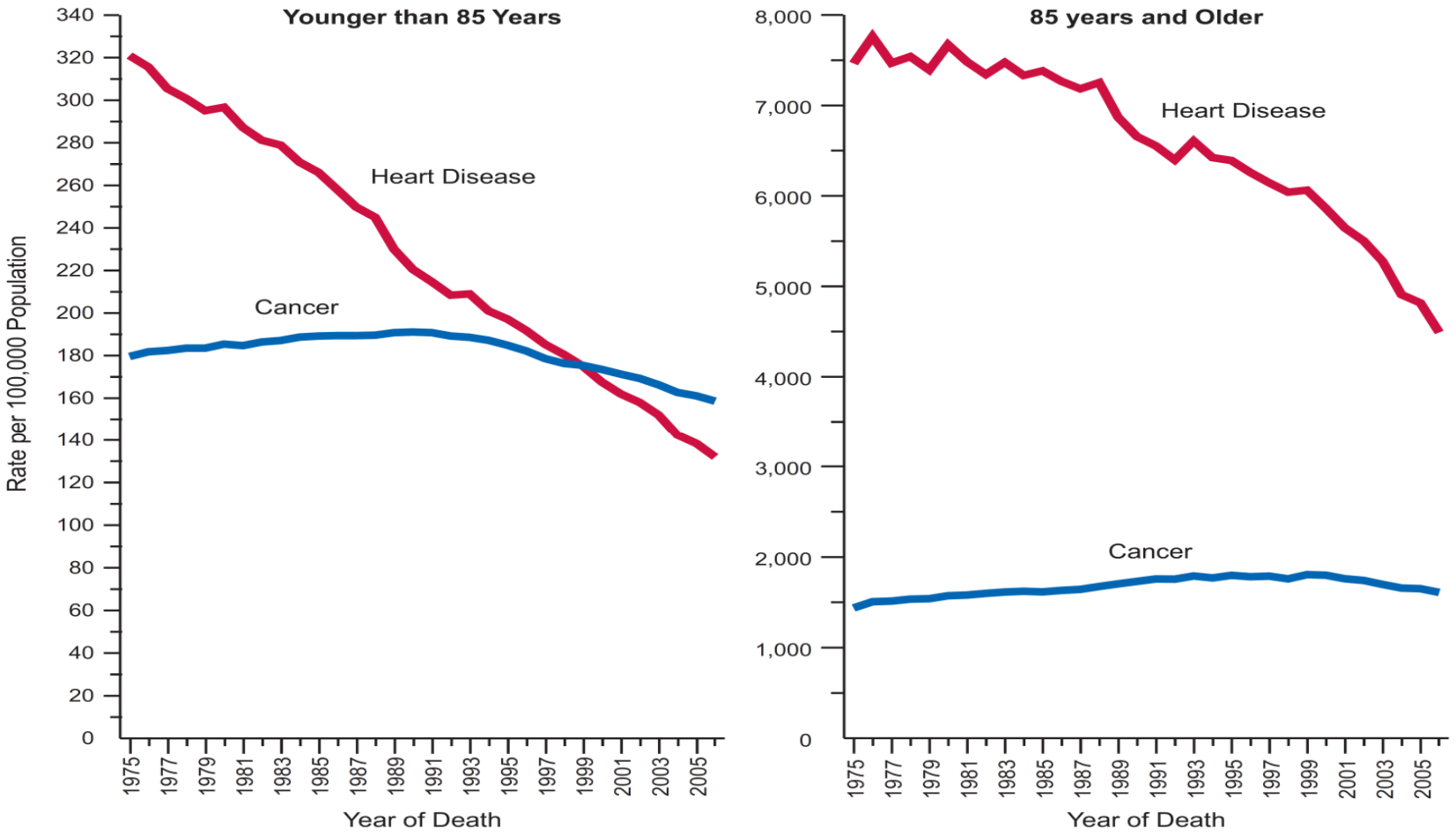
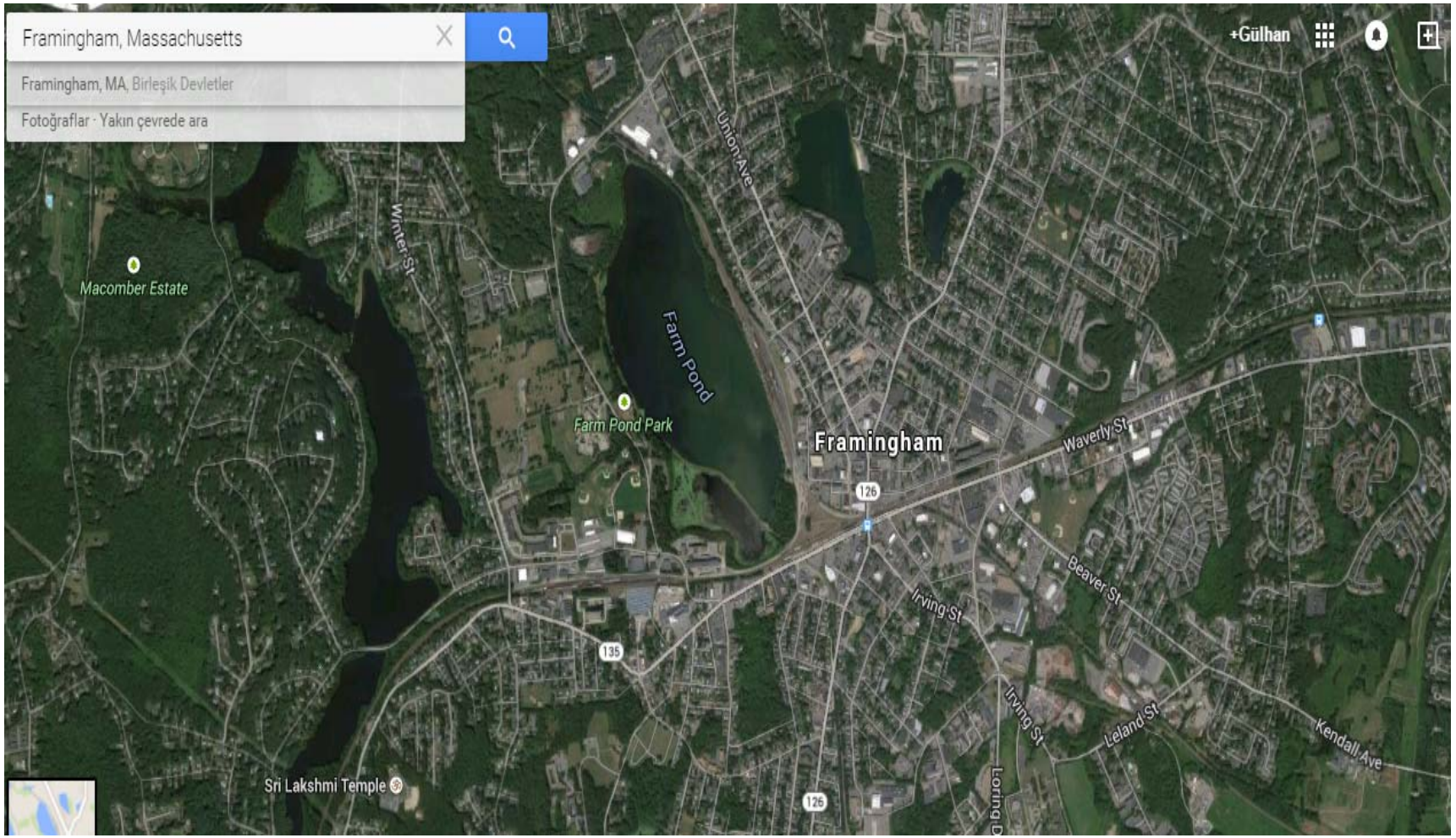


FIGURE 6. Death Rates* For Cancer and Heart Disease for Ages Younger Than 85 Years and 85 Years and Older, 1975 to 2006.

SORUNLAR ve ÇÖZÜM ÖNERİLERİ



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Annals of Internal Medicine | CLINICAL GUIDELINE

Medications for Risk Reduction of Primary Breast Cancer in Women: U.S. Preventive Services Task Force Recommendation Statement

Virginia A. Moyer, MD, MPH, on behalf of the U.S. Preventive Services Task Force*

Plasebo	SERM
İnvaziv meme kanseri	İnvaziv meme kanseri
Kalça kırığı	Kalça kırığı
Stroke	Stroke
Pulmoner tromboemboli	Pulmoner tromboemboli
Endometrial kanser	Endometrial kanser
İnsitu meme kanseri	İnsitu meme kanseri
Derin ven trombozu	Derin ven trombozu

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Figure 2. Benefit–risk indices for tamoxifen and raloxifene chemoprevention in white non-Hispanic women with uterus, by a group and level of 5-y projected risk for invasive breast cancer.

	Tamoxifen vs. Placebo (with uterus)			Raloxifene vs. Placebo (with uterus)		
5-year projected risk of IBC (%)	50–59	60–69	70–79	50–59	60–69	70–79
1.5	–133	–310	–325	21	–11	-15
2.0	–105	–283	–298	43	11	7
2.5	–78	–255	–271	65	33	29
3.0	–51	–228	–244	86	55	51
3.5	–25	–202	–217	108	76	71
4.0	3	–175	–190	128	97	93
4.5	29	–148	–164	150	119	115
5.0	56	–121	–137	172	140	136
5.5	83	–95	–111	193	161	157
6.0	109	–69	–84	214	183	179
6.5	135	–42	–58	236	204	199
7.0	162	–15	–32	256	225	221

5-year projected risk of IBC is ≥1.67%

Using BCPT data and WHI baseline rates

Combining RR from BCPT and STAR using WHI baseline rates

Strong evidence of benefits outweighing risks
Moderate evidence of benefits outweighing risks
Benefits do not outweigh risks

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Figure 3. Benefit–risk indices for tamoxifen and raloxifene chemoprevention in white non-Hispanic women without uterus, by age group and level of 5-y projected risk for invasive breast cancer.

	Tamoxifen vs. Placebo (without uterus)			Raloxifene vs. Placebo (without uterus)		
5-year projected risk of IBC (%)	50–59	60–69	70–79	50–59	60–69	70–79
1.5	3	–53	–93	27	2	–4
2.0	31	–26	–66	49	23	18
2.5	57	2	–39	71	45	40
3.0	84	29	–12	92	67	62
3.5	111	56	15	114	88	82
4.0	138	83	42	134	109	104
4.5	164	109	69	156	131	126
5.0	191	136	96	178	152	147
5.5	218	163	121	199	173	168
6.0	244	189	148	220	195	190
6.5	270	215	175	242	216	210
7.0	297	242	201	262	237	232

5-year projected risk of IBC is ≥1.67%

Using BCPT data and WHI baseline rates

Combining RR from BCPT and STAR using WHI baseline rates

Strong evidence of benefits outweighing risks
Moderate evidence of benefits outweighing risks
Benefits do not outweigh risks

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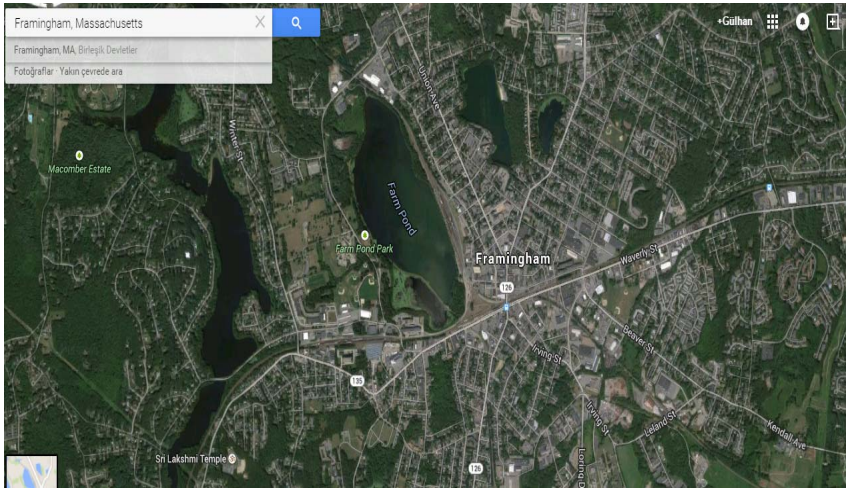
Framingham, Massachusetts
Framingham, MA, Birleşik Devletler
Fotoğraflar · Yakın çevrede ara
+Gülhan
Macomber Estate
Farm Pond
Farm Pond Park
Framingham
Waverly St
Beaver St
Irving St
Leland St
Kendall Ave
Sri Lakshmi Temple


Pfizer
LIPITOR
20 mg
atorvastatin calcium
30 Tablets