MADRID 2014 ESMO congress

Management of Breast Cancer in Elderly

- Etienne Brain, MD PhD
- Medical Oncology
- Hôpital René Huguenin / Institut Curie, Saint-Cloud, France

UNICANCER

institutCurie
Together, let's beat cancer.

Disclosures

- Research funding: TEVA (Cephalon), QIAGEN (Ipsogen)
- Advisory role: Amgen, Roche, Pierre Fabre
- Honoraria: GSK, Cephalon, Roche, AstraZeneca

A frailty revealed…

- 2006: Mrs BON… IR… 84 yo
  - No previous medical history (high blood sugar?)
  - Husband: 86 yo w/ severe advanced Parkinson, 2 children
  - Breast self exam → T1c N0 M0 left breast; 54 kg, 167 cm
- Conservative surgery + axillary lymph node dissection
  - Invasive ductal carcinoma, 17 mm, SBR II
  - 8 N-
  - ER- PgR-, Ki 67 40%, HER2-
- Adjuvant strategy
  - Chemotherapy with anthracylines (GERICO 06)? + XRT
- Scoring
  - Oncologist: PS 0 → **"Easy! Go for it"**
  - Geriatrician
    - Functional status, cognition, nutrition, GDS → OK
    - **<u>However</u>!** 3 falls < 1 year

… treatment decision process

- LVEF by MUGA scan normal
- Not in GERICO 06 trial, but OK for the oncology staff!
- The lady **“accepted”….**

… treatment decision process & respect

- LVEF by MUGA scan normal
- Not in GERICO 06 trial, but OK for the oncology staff!
- The lady **“accepted”…. but DID she?**

- Central venous access + 1 cycle of chemo → febrile neutropenia + severe stroke (cardiac arythmia?)
  - Chemotherapy stopped
  - Husband placed in nursing home
  - Delayed XRT
  - Recovered with neurological sequelae
  - Seniors residence
  - No relapse so far (last visit early 2014)

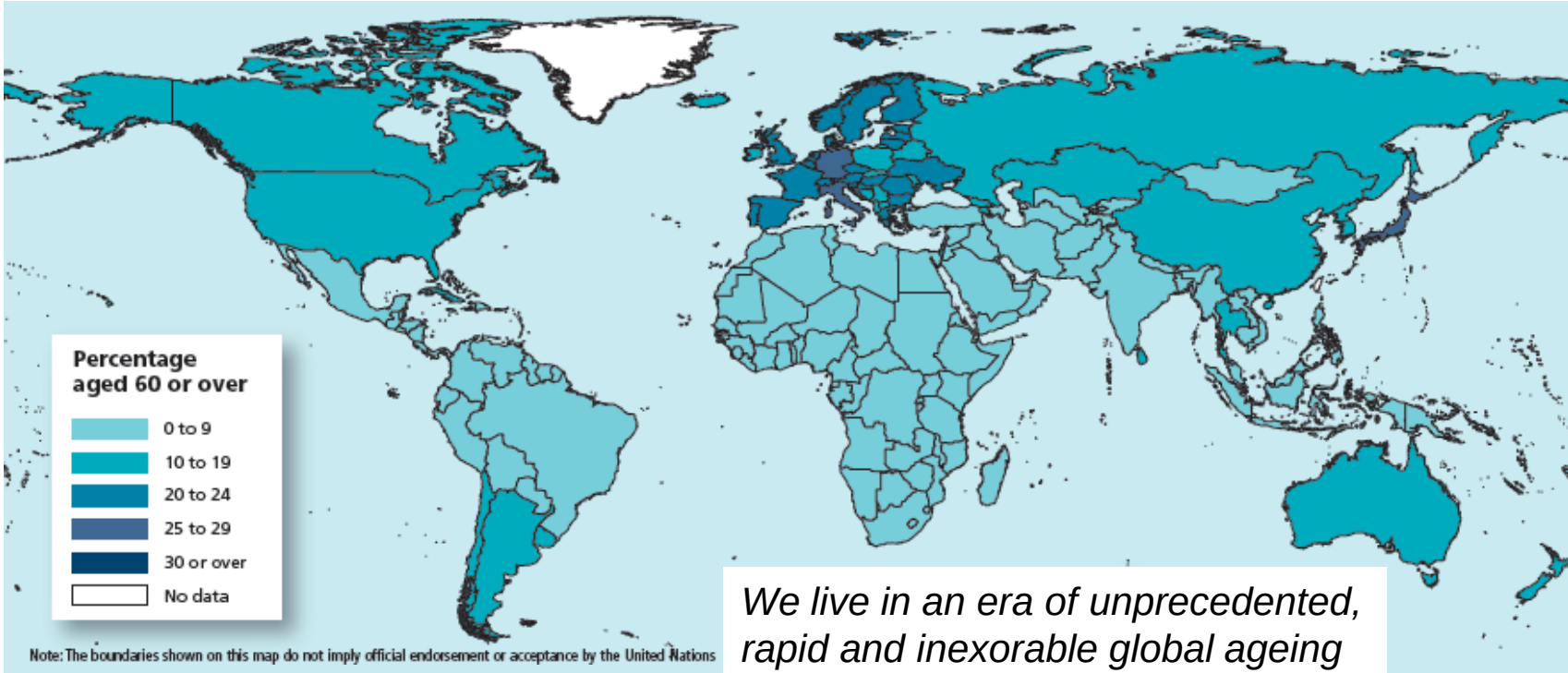
Pelike from Attica
480–470 BC
Musée du Louvre

Current dilemna and extreme positions

1. Therapeutic **nihilism**
   - Elderly patients **do not receive** any treatment
2. The **intermediate** position?
   - Elderly patients **may** benefit from treatments
3. Blind therapeutic **enthusiasm**
   - Elderly patients receive **futile/non beneficial** treatments

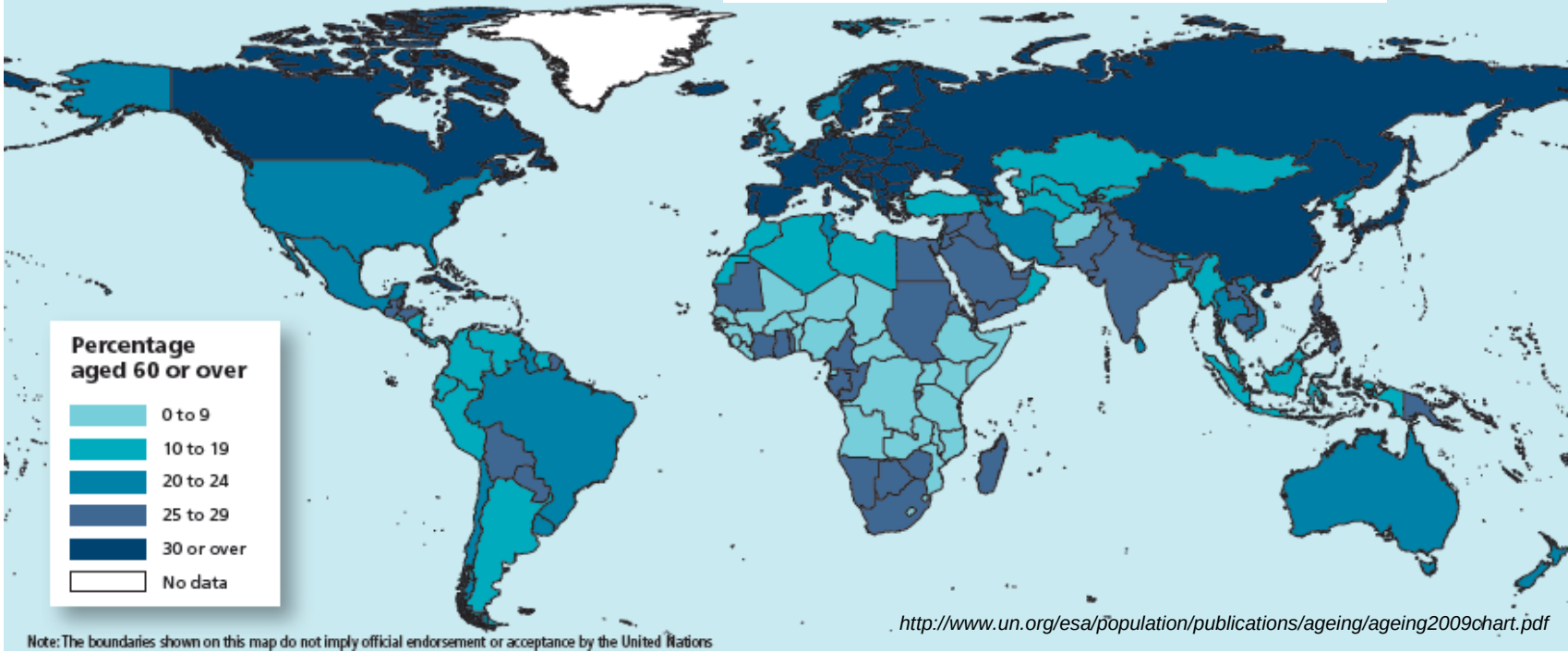
→ Place and role of **geriatrician** and **oncologist**

2009



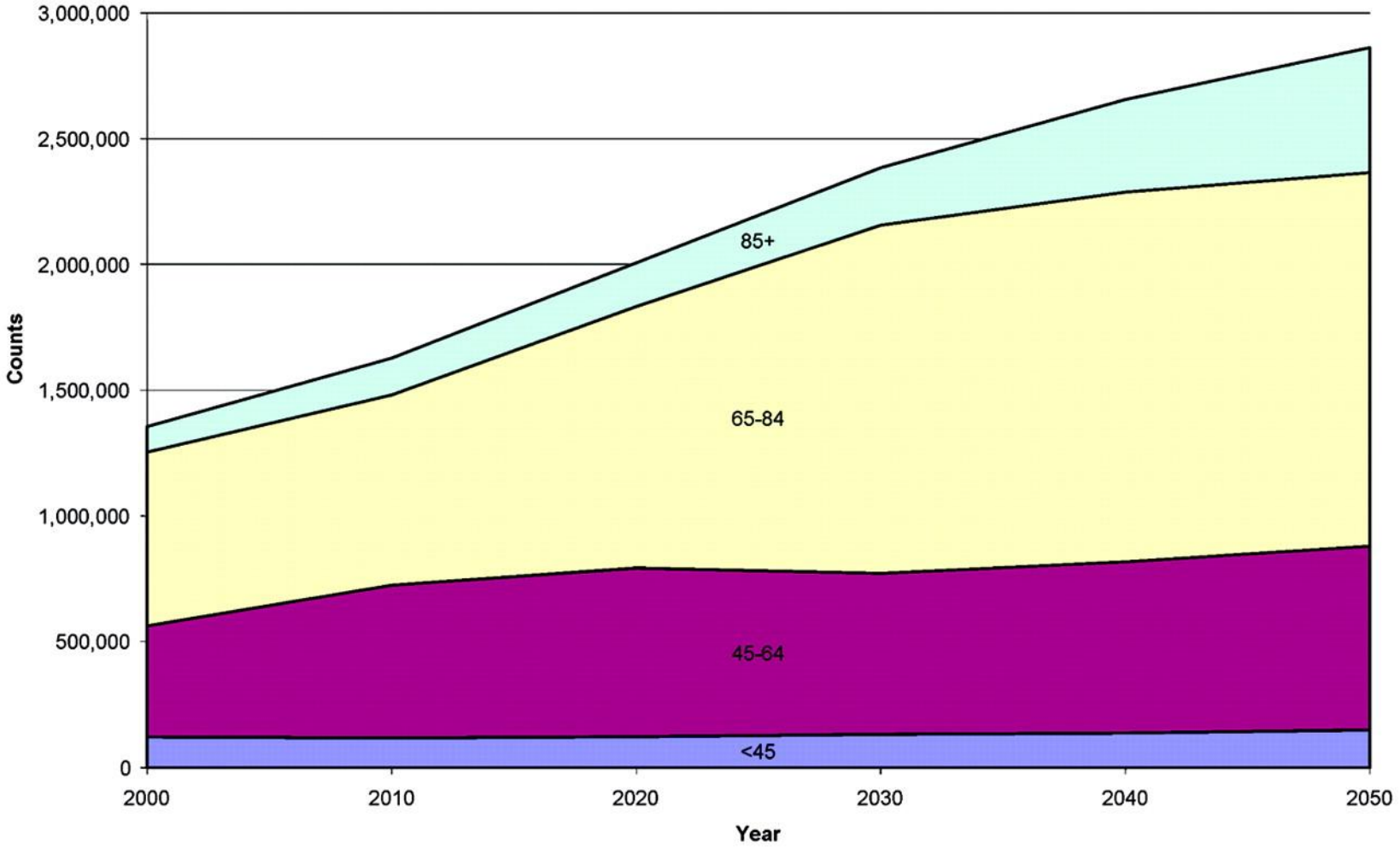
We live in an era of unprecedented, rapid and inexorable global ageing

2050



http://www.un.org/esa/population/publications/ageing/ageing2009chart.pdf

Projected number of cancer cases for 2000–2050 by age group (<45, 45–64, 65–84, 85+) based on projected census population estimates and delay-adjusted SEER-17 cancer incidence rates



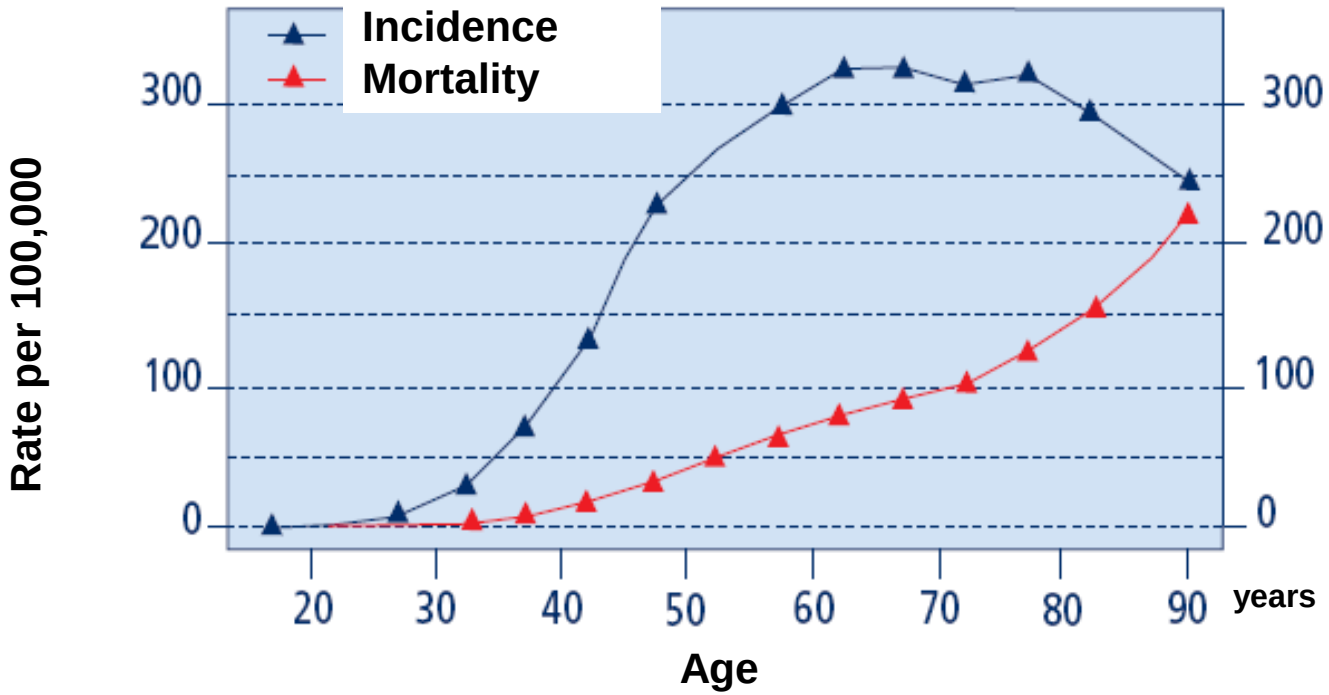
Incidence of cancer from 2010 to 2030 (Smith JCO 2009)

- *+11% < 65 yo*
- *+67% > 65 yo*

Hayat. The Oncologist 2007;12:20-37

The Oncologist

Breast cancer incidence



40% or 25% x 1.5 in 2030 ?

Age	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75+	Total
	63.3	119.7	187.3	177.3	182.8	211.3	220	231.1	220.4	89.2

de Vathaire. FRANCIM/INSERM 1996, IVS 2003

Cancer survival in Europe 1999–2007 by country and age: results of EUROCARE-5—a population-based study

*Roberta De Angelis, Milena Sant, Michel P Coleman, Silvia Francisci, Paolo Baili, Daniela Pierannunzio, Annalisa Trama, Otto Visser, Hermann Brenner, Eva Ardanaz, Magdalena Bielska-Lasota, Gerda Engholm, Alice Nennecke, Sabine Siesling, Franco Berrino, Riccardo Capocaccia, and the EUROCARE-5 Working Group**

Summary

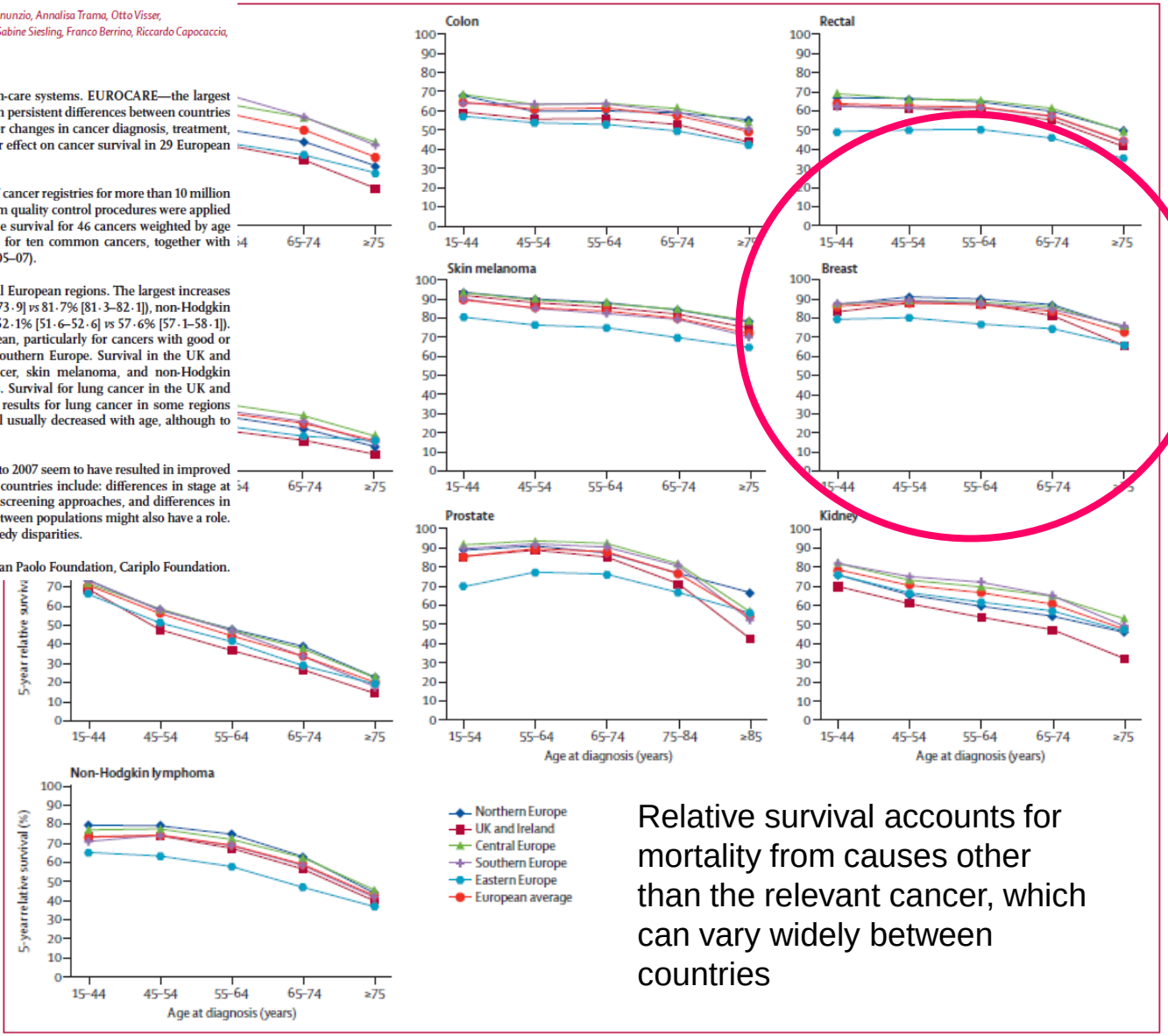
Background Cancer survival is a key measure of the effectiveness of health-care systems. EUROCARE—the largest cooperative study of population-based cancer survival in Europe—has shown persistent differences between countries for cancer survival, although in general, cancer survival is improving. Major changes in cancer diagnosis, treatment, and rehabilitation occurred in the early 2000s. EUROCARE-5 assesses their effect on cancer survival in 29 European countries.

Methods In this retrospective observational study, we analysed data from 107 cancer registries for more than 10 million patients with cancer diagnosed up to 2007 and followed up to 2008. Uniform quality control procedures were applied to all datasets. For patients diagnosed 2000–07, we calculated 5-year relative survival for 46 cancers weighted by age and country. We also calculated country-specific and age-specific survival for ten common cancers, together with survival differences between time periods (for 1999–2001, 2002–04, and 2005–07).

Findings 5-year relative survival generally increased steadily over time for all European regions. The largest increases from 1999–2001 to 2005–07 were for prostate cancer (73·4% [95% CI 72·9–73·9] *vs* 81·7% [81·3–82·1]), non-Hodgkin lymphoma (53·8% [53·3–54·4] *vs* 60·4% [60·0–60·9]), and rectal cancer (52·1% [51·6–52·6] *vs* 57·6% [57·1–58·1]). Survival in eastern Europe was generally low and below the European mean, particularly for cancers with good or intermediate prognosis. Survival was highest for northern, central, and southern Europe. Survival in the UK and Ireland was intermediate for rectal cancer, breast cancer, prostate cancer, skin melanoma, and non-Hodgkin lymphoma, but low for kidney, stomach, ovarian, colon, and lung cancers. Survival for lung cancer in the UK and Ireland was much lower than for other regions for all periods, although results for lung cancer in some regions (central and eastern Europe) might be affected by overestimation. Survival usually decreased with age, although to different degrees depending on region and cancer type.

Interpretation The major advances in cancer management that occurred up to 2007 seem to have resulted in improved survival in Europe. Likely explanations of differences in survival between countries include: differences in stage at diagnosis and accessibility to good care, different diagnostic intensity and screening approaches, and differences in cancer biology. Variations in socioeconomic, lifestyle, and general health between populations might also have a role. Further studies are needed to fully interpret these findings and how to remedy disparities.

Funding Italian Ministry of Health, European Commission, Compagnia di San Paolo Foundation, Cariplo Foundation.



Relative survival accounts for mortality from causes other than the relevant cancer, which can vary widely between countries

Figure 2: **Age-specific 5-year relative survival for adults with cancer diagnosed in 2000–07**
The European mean is the (population) weighted mean of country-specific relative survival estimates.

De Angelis. Lancet Oncol 2013

- Most common shortcut in statistics

"1 in 8 women will develop BC in their lifetime"

instead of

"If everyone lived beyond the age of 70, 1 in 8 of those women would get or have had BC"

- Since BC risk increases w/ age, lifetime risk changes depending on age
  - Age 20-29 1 in 2,000
  - Age 30-39 1 in 229
  - Age 40-49 1 in 68
  - Age 50-59 1 in 37
  - Age 60-69 1 in 26
  - Ever 1 in 8

not correct

more correct

Worldwidebreastcancer.com/breast-cancer-statistics-worldwide

Screening and diagnosis

Breast-cancer screening > 70?

Research

Original Investigation

Cancer Screening Rates in Individuals With Different Life Expectancies

Trevor J. Royce, MD, MS; Laura H. Hendrix, MS; William A. Stokes, MD; Ian M. Allen, MD, MPH; Ronald C. Chen, MD, MPH

IMPORTANCE Routine cancer screening has unproven net benefit for patients with limited life expectancy.

OBJECTIVE To examine the patterns of prostate, breast, cervical, and colorectal cancer screening in the United States in individuals with different life expectancies.

DESIGN, SETTING, AND PARTICIPANTS Data from the population-based National Health Interview Survey (NHIS) from 2000 through 2010 were used and included 27 404 participants aged 65 years or older. Using a validated mortality index specific for NHIS, participants were grouped into those with low (<25%), intermediate (25%-49%), high (50%-74%), and very high (≥75%) risks of 9-year mortality.

MAIN OUTCOMES AND MEASURES Rates of prostate, breast, cervical, and colorectal cancer screening.

RESULTS In participants with very high mortality risk, 31% to 55% received recent cancer screening, with prostate cancer screening being most common (55%). For women who had a hysterectomy for benign reasons, 34% to 56% had a Papanicolaou test within the past 3 years. On multivariate analysis, very high vs low mortality risk was associated with less screening for prostate (odds ratio [OR], 0.65 [95% CI, 0.50-0.85]), breast (OR, 0.43 [95% CI, 0.35-0.53]), and cervical (OR, 0.50 [95% CI, 0.36-0.70]) cancers. There was less screening for prostate and cervical cancers in more recent years compared with 2000, and there was no significant interaction between calendar year and mortality risk for any cancer screening ($P > .05$ for all cancers). Our sensitivity analysis showed that screening was also common in individuals with less than 5-year life expectancy.

CONCLUSIONS AND RELEVANCE A substantial proportion of the US population with limited life expectancy received prostate, breast, cervical, and colorectal cancer screening that is unlikely to provide net benefit. These results suggest that overscreening is common in both men and women, which not only increases health care expenditure but can lead to net patient harm.

JAMA Intern Med. doi:10.1001/jamainternmed.2014.3895
Published online August 18, 2014.

Invited Commentary
Related article
Supplemental content at jamainternalmedicine.com

Author Affiliations: Department of Radiation Oncology, University of North Carolina at Chapel Hill, Chapel Hill (Royce, Hendrix, Stokes, Allen, Chen); School of Medicine, University of North Carolina at Chapel Hill, Chapel Hill (Royce, Stokes, Allen); Cecil G. Sheps Center for Health Services Research, University of North Carolina at Chapel Hill, Chapel Hill (Chen); Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill, Chapel Hill (Chen).
Corresponding Author: Ronald C. Chen, MD, MPH, Department of Radiation Oncology, University of North Carolina Hospitals, CB No. 7512, Chapel Hill, NC 27599 (ronald_chen@med.unc.edu).

Age (yr)	Nb of trial(s)	Relative risk of death (95%CI)
60-69	Malmö & Ostergöland	0.68 (0.54-0.87)
70-79	Ostergöland	1.12 (0.73- 1.72)

Invited Commentary

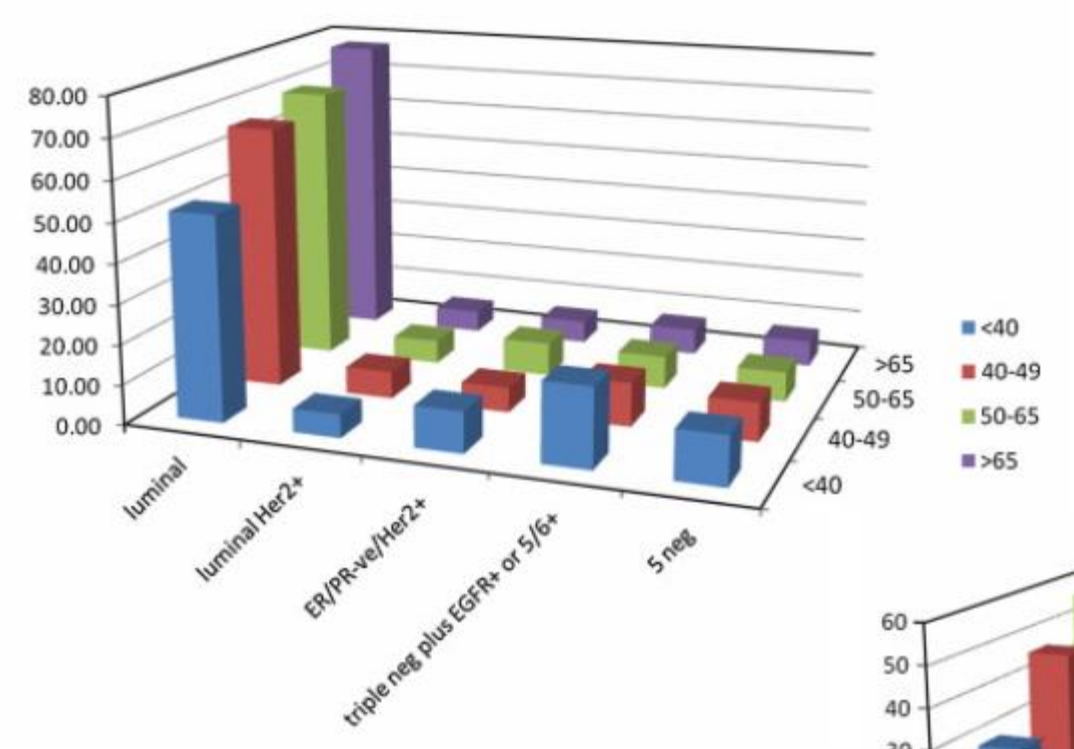
Cancer Screening in Older Persons
A New Age of Wonder

Cary P. Gross, MD

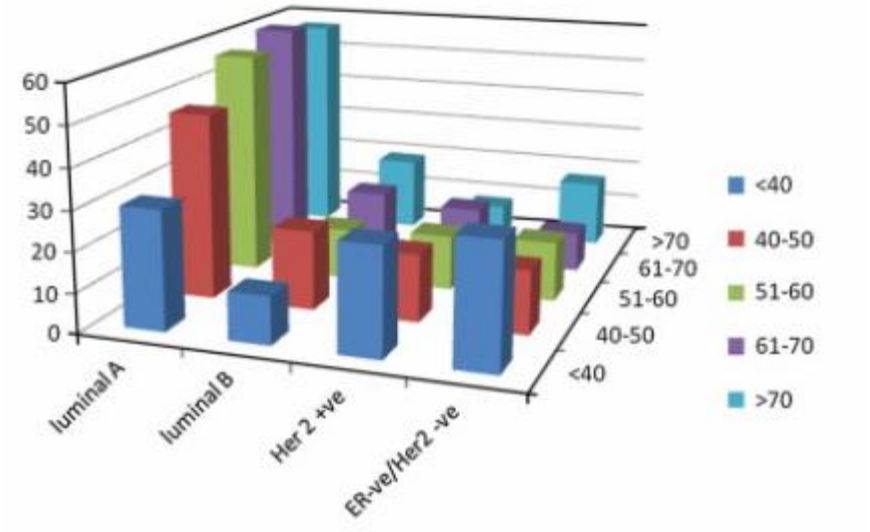
75+: YES YOU CAN, but

- No mass screening
- Depends on **life expectancy**

Warner. NEJM 2011; Royce. JAMA 2014; Gross. JAMA 2014



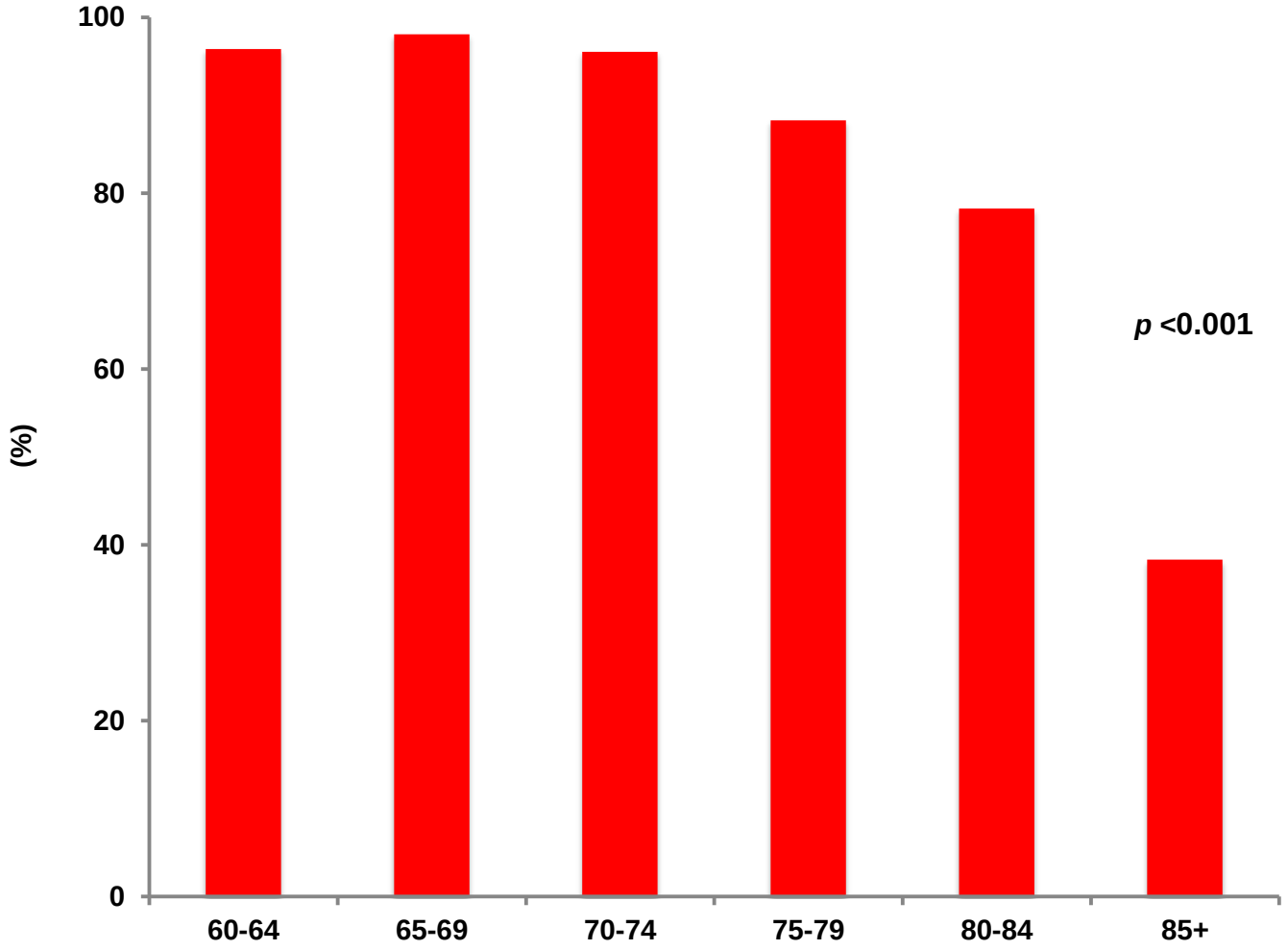
- British Columbia Cancer Agency
- 1986-1992
- 4,046 patients



- Jules Bordet
- 2,723 patients

Cheang. Clin Cancer Res 2008; Durbecq. CROH 2008

Local treatment

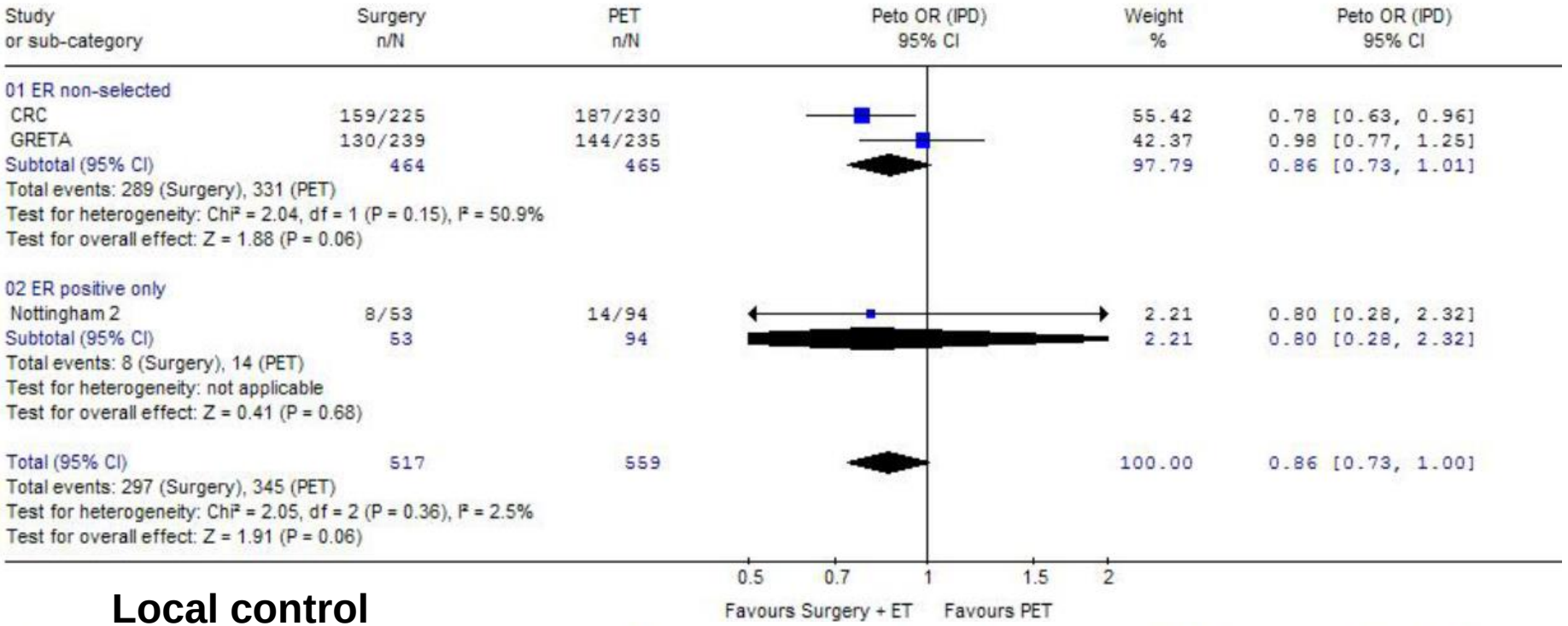


Percentage of women with stage 1 or 2 disease and a Charlson score of 0 who underwent surgery (n=850)

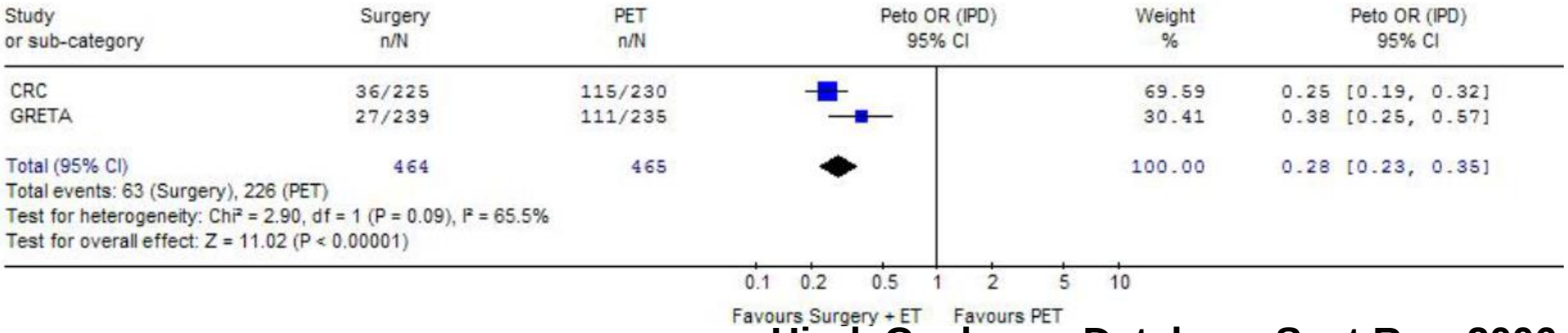
Moran. EBCC-9, abstract 415, 2014

Surgery + endocrine TTT vs ET only

OS



Local control

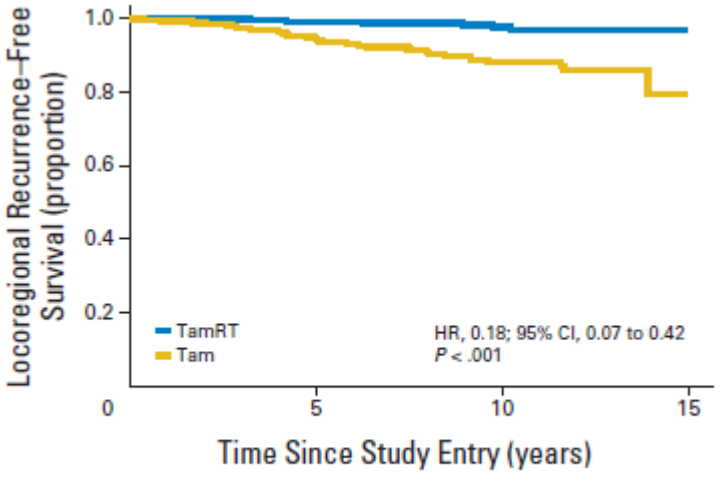


Hind. Cochrane Database Syst Rev. 2006

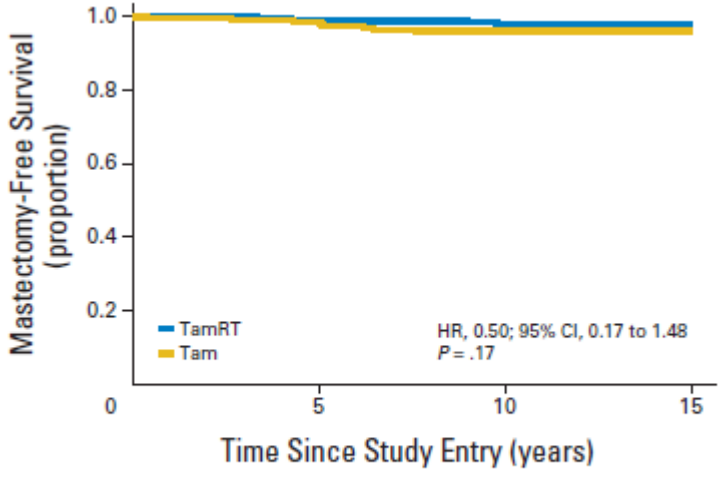
Primary endocrine treatment

1. Converting mastectomy into BCS
2. Allowing pre-habilitation
3. Non-operable patients

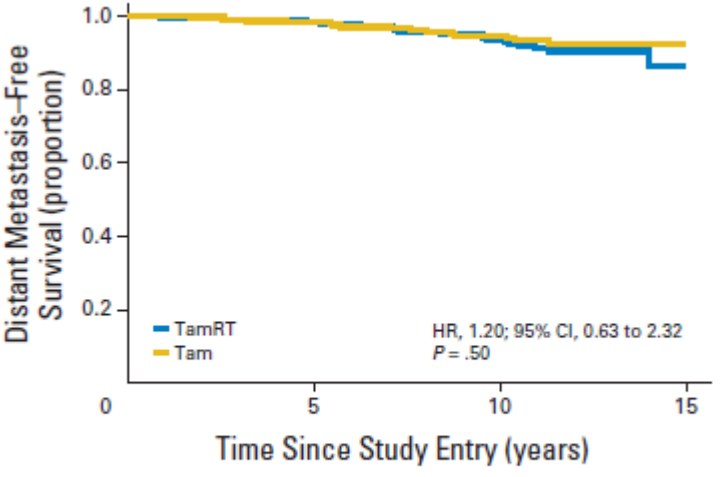
After BCS: TAM vs XRT + TAM (CALGB 9343)



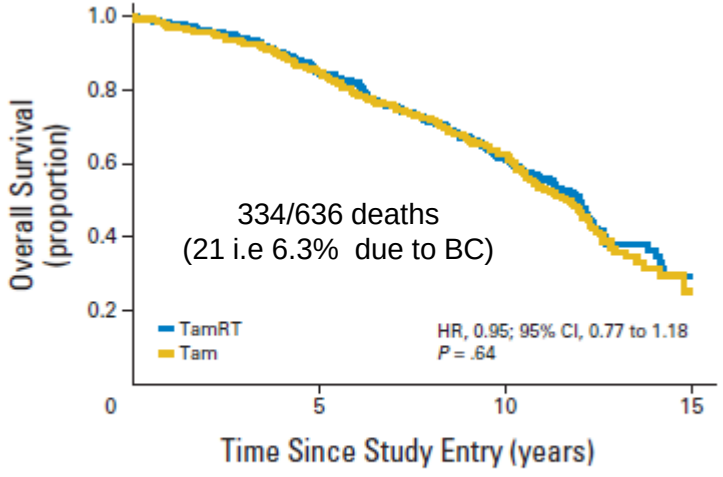
No. at risk				
TamRT	317	261	162	7
Tam	319	243	144	2



No. at risk				
TamRT	317	261	162	7
Tam	319	252	153	2



No. at risk				
TamRT	317	260	165	7
Tam	319	254	157	2



No. at risk				
TamRT	317	264	168	7
Tam	319	262	167	4

Hughes. J Clin Oncol 2013

XRT

- **Omission if pT1 ER+? (NCCN)**
  - According to **life expectancy**
  - > 80 yo, multi-morbidities, good compliance to endocrine treatment?
- **Low risk patients**
  - Once-per-week fraction schedule (Whelan regimen)
  - Accelerated partial breast irradiation (APBI)
    - Larger radiation doses given to the localized tumour bed (instead of to the entire breast)

  → Spare extensive travel
- **Don’t neglect the psychological burden of recurrence!**

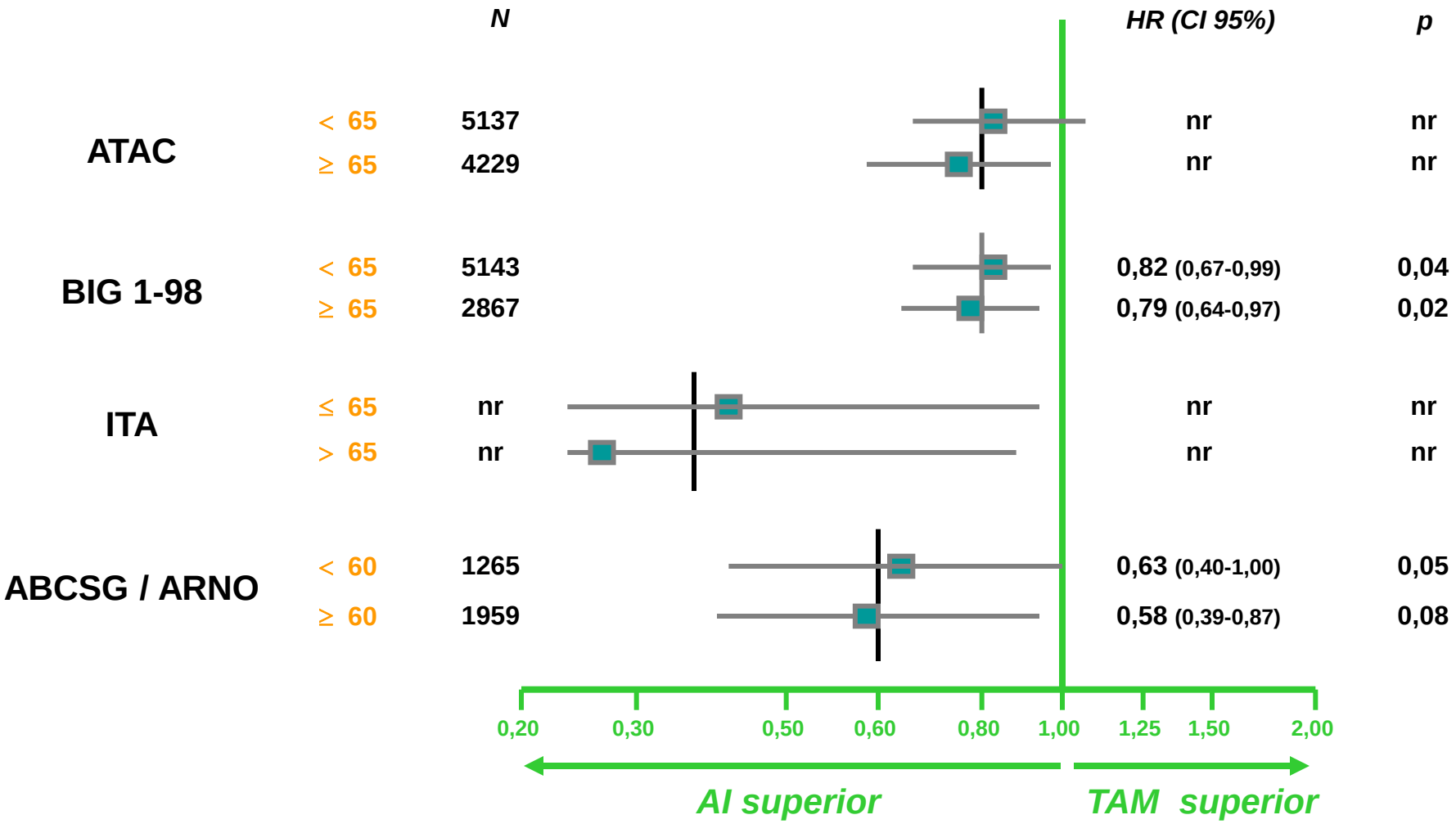
Khan. Semin Radiat Oncol 2012

Systemic treatment

Endocrine treatment

Relatively easy!

Benefit of AI according to age



Hot flushes
Thrombosis & embolism
Uterus cancer
Gynecological tractus
Vaginal discharge
Cataract

TAM

?

Neurocognition
Sexuality

Arthralgias & myalgias
Osteoporosis
Fractures
Dryness
Cardiovascular
Lipid profile

AI

COMPLIANCE is the issue!!!

Chemotherapy

Less easy…

Doxorubicin, CHF and age

- SEER 1992-2002: 43,338 women 66-80 years, no CHF history
  - stage I to III BC, chemotherapy vs no
  - AC: younger, fewer comorbidities, advanced (*p*=.001)
  - $CHF_{10\ years}$ (%)

AC	Other chemo	No chemo
N = 4,712	N = 3,921	N = 34,705
38.4	32.5	29

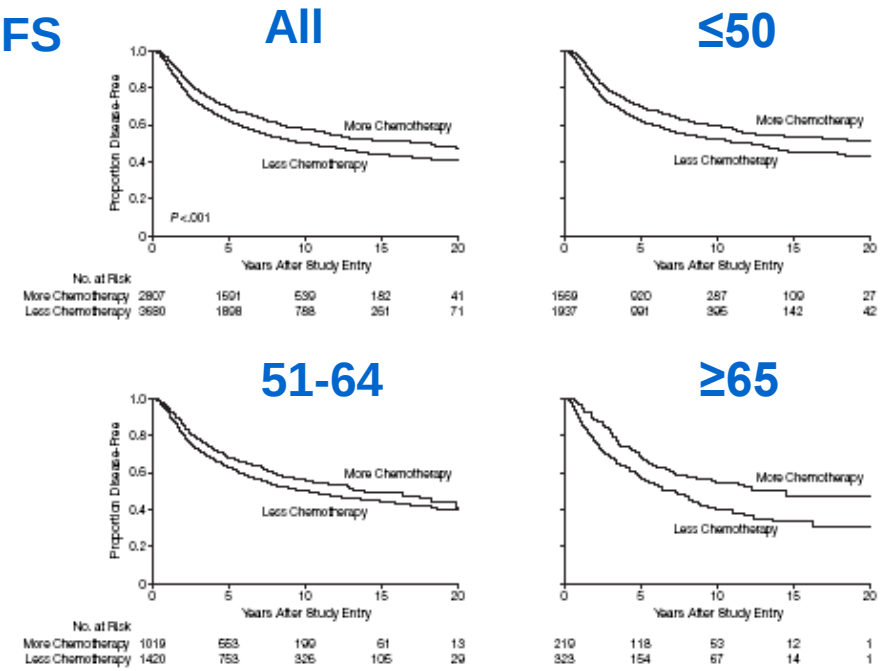
  - 66-70 years HR 1.26 (95% CI, 1.12-1.42) if AC
  - 71-80 years no impact of CT type

Baseline	HR	(95%CI)
Age (decade)	1.79	(1.66-1.93)
Black	1.40	(1.30-1.50)
Trastuzumab	1.46	(1.21-1.77)
Hypertension	1.45	(1.39-1.52)
Diabetes	1.74	(1.66-1.83)
Coronary	1.58	(1.39-1.79)
Left XRT	1.04	(0.98-1.11)

Pinder. J Clin Oncol 2007

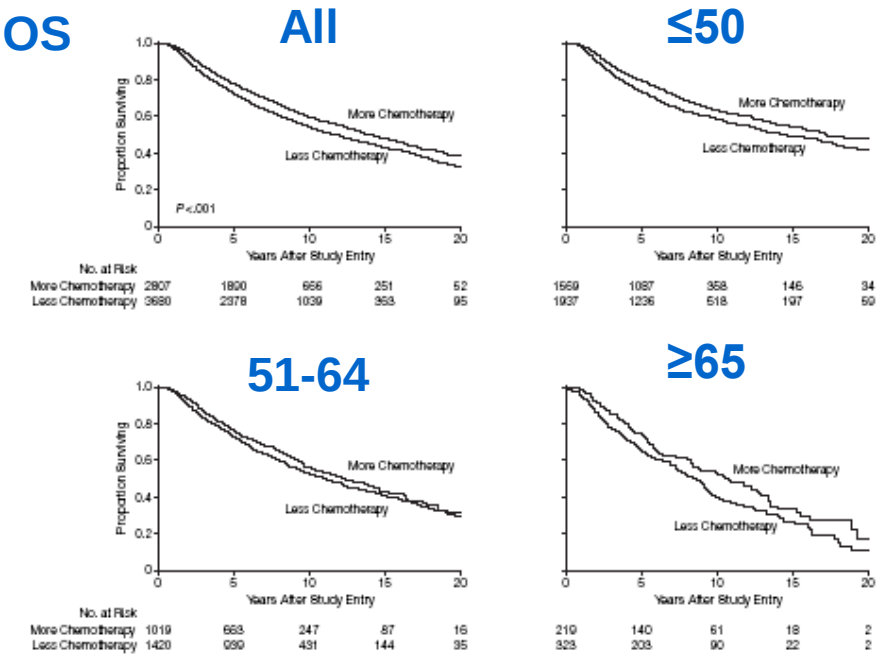
Adjuvant chemo for breast cancer

DFS



- CALGB (1975-1999)
- 4 randomized trials
- 6487 pts
  - > 65 yo 542 (8%)
  - > 70 yo 159 (2%)

OS



- Results
  - Benefit **identical**
  - Toxicity **careful!!**
    - **Toxic deaths 1.5%**

Muss. JAMA 2005

2012 Oxford

Comparisons between different polychemotherapy regimens for early breast cancer: meta-analyses of long-term outcome among 100 000 women in 123 randomised trials

Early Breast Cancer Trialists' Collaborative Group (EBCTCG)

Lancet 2012; 379: 432–44
Published Online December 6, 2011
DOI:10.1016/S0140-6736(11)61625-5
See Comment page 390

Correspondence to: Early Breast Cancer Trialists' Collaborative Group (EBCTCG) Secretariat, Clinical Trial Service Unit (CTSU), Richard Doll Building, Old Road Campus, Oxford OX3 7LF, UK
bc.overview@ctsu.ox.ac.uk

Summary

Background Moderate differences in efficacy between adjuvant chemotherapy regimens for breast cancer are plausible, and could affect treatment choices. We sought any such differences.

Methods We undertook individual-patient-data meta-analyses of the randomised trials comparing: any taxane-plus-anthracycline-based regimen versus the same, or more, non-taxane chemotherapy (n=44 000); one anthracycline-based regimen versus another (n=7000) or versus cyclophosphamide, methotrexate, and fluorouracil (CMF; n=18 000); and polychemotherapy versus no chemotherapy (n=32 000). The scheduled dosages of these three drugs and of the anthracyclines doxorubicin (A) and epirubicin (E) were used to define standard CMF, standard 4AC, and CAF and CEF. Log-rank breast cancer mortality rate ratios (RRs) are reported.

Findings In trials adding four separate cycles of a taxane to a fixed anthracycline-based control regimen, extending treatment duration, breast cancer mortality was reduced (RR 0·86, SE 0·04, two-sided significance $2p=0·0005$). In trials with four such extra cycles of a taxane counterbalanced in controls by extra cycles of other cytotoxic drugs, roughly doubling non-taxane dosage, there was no significant difference (RR 0·94, SE 0·06, $2p=0·33$). Trials with CMF-treated controls showed that standard 4AC and standard CMF were equivalent (RR 0·98, SE 0·05, $2p=0·67$), but that anthracycline-based regimens with substantially higher cumulative dosage than standard 4AC (eg, CAF or CEF) were superior to standard CMF (RR 0·78, SE 0·06, $2p=0·0004$). Trials versus no chemotherapy also suggested greater mortality reductions with CAF (RR 0·64, SE 0·09, $2p<0·0001$) than with standard 4AC (RR 0·78, SE 0·09, $2p=0·01$) or standard CMF (RR 0·76, SE 0·05, $2p<0·0001$). In all meta-analyses involving taxane-based or anthracycline-based regimens, proportional risk reductions were little affected by age, nodal status, tumour diameter or differentiation (moderate or poor; few were well differentiated), oestrogen receptor status, or tamoxifen use. Hence, largely independently of age (up to at least 70 years) or the tumour characteristics currently available to us for the patients selected to be in these trials, some taxane-plus-anthracycline-based or higher-cumulative-dosage anthracycline-based regimens (not requiring stem cells) reduced breast cancer mortality by, on average, about one-third. 10-year overall mortality differences paralleled breast cancer mortality differences, despite taxane, anthracycline, and other toxicities.

Interpretation 10-year gains from a one-third breast cancer mortality reduction depend on absolute risks without chemotherapy (which, for oestrogen-receptor-positive disease, are the risks remaining with appropriate endocrine therapy). Low absolute risk implies low absolute benefit, but information was lacking about tumour gene expression markers or quantitative immunohistochemistry that might help to predict risk, chemosensitivity, or both.

Funding Cancer Research UK; British Heart Foundation; UK Medical Research Council.

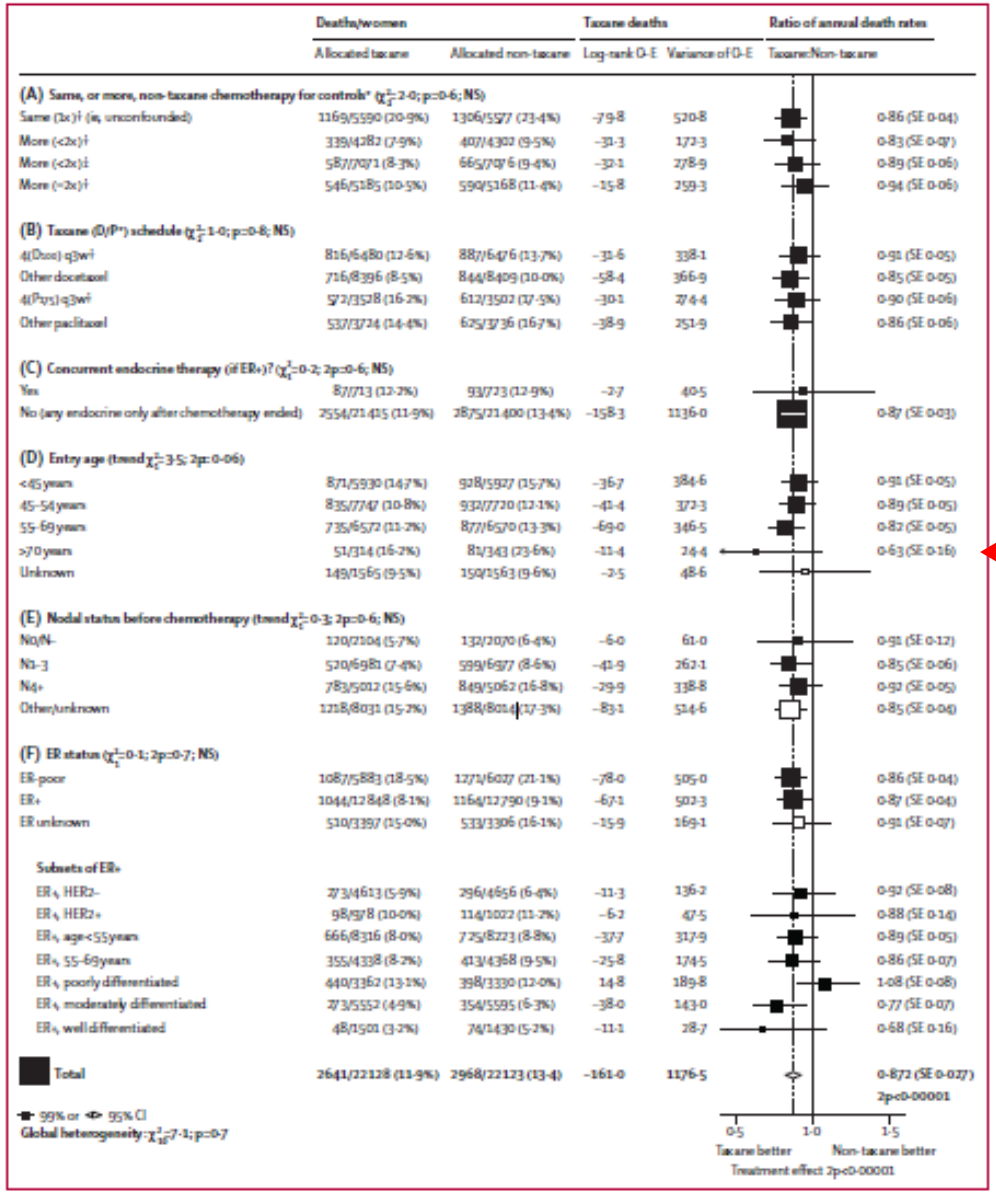


Figure 2: Subgroup analyses of breast cancer mortality (mortality with recurrence, by log-rank subtraction) for taxane-plus-anthracycline-based regimens versus the same, or more (less than doubled or roughly doubled), non-taxane cytotoxic chemotherapy

D=docetaxel. P=paclitaxel. 4(D100) q3w=four doses of docetaxel 100 mg/m² at intervals of 3 weeks. 4(P175) q3w=four doses of paclitaxel 175 mg/m² at intervals of 3 weeks. ER=oestrogen receptor. NS=not significant. *First four subgroups are as in the forest plots (webappendix pp 21–26) that give details of each trial's cytotoxic regimens. †Taxane courses do not overlap other chemotherapy courses. ‡Taxane given concurrently with anthracycline.

Low influence of age (< 70 yo), pN, pT, differentiation, ER or TAM

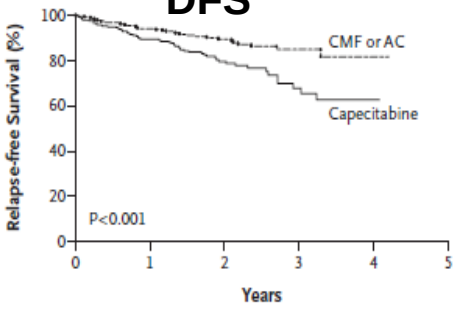
ECBCTG. Lancet 2012

… mostly if ER-!

CALGB / CTSU 49907 (AC or CMF vs X)

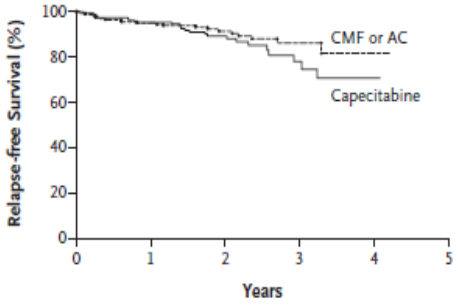
DFS

All



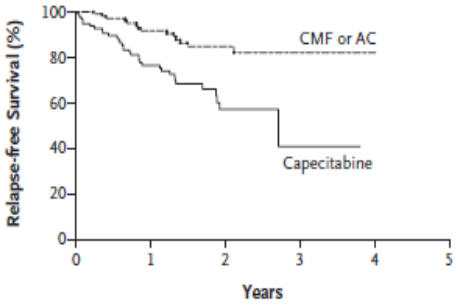
No. at Risk						
CMF or AC	326	254	124	46	2	0
Capecitabine	307	237	96	29	1	0

ER+



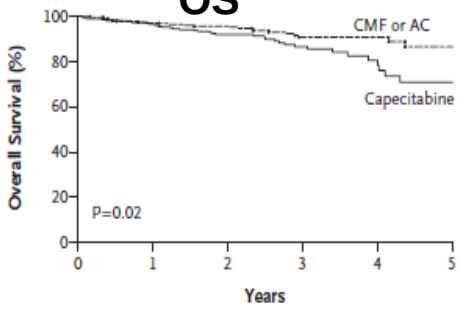
No. of Patients at Risk		No. of Events
CMF or AC	218	21
Capecitabine	209	26

ER-

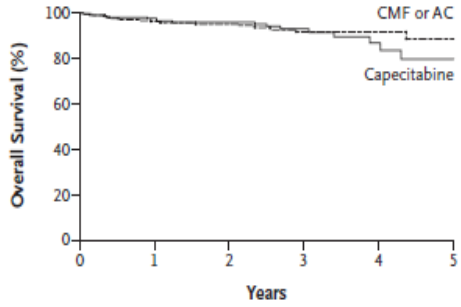


No. of Patients at Risk		No. of Events
CMF or AC	106	14
Capecitabine	97	34

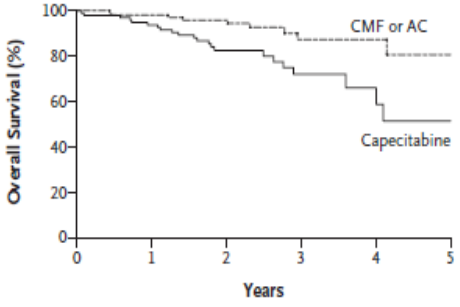
OS



No. at Risk						
CMF or AC	326	297	216	117	58	7
Capecitabine	307	279	180	90	36	8



No. of Patients at Risk		No. of Events
CMF or AC	218	15
Capecitabine	209	16



No. of Patients at Risk		No. of Events
CMF or AC	106	9
Capecitabine	97	22

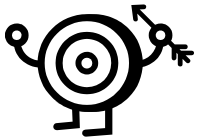
Muss. NEJM 2009

General recommendations for adjuvant chemo in elderly

- **Focus** on ER-
- **Regimen**
  - **Validated** **4 AC, 6 CMF**
  - Option 4 TC
  - ! Capecitabine no
  - Sequential regimen **no data**
  - Liposomal doxorubicin?
- **Primary prophylaxis** of febrile neutropenia w/ G-CSF

- *No restriction on trastuzumab if chemo indicated*

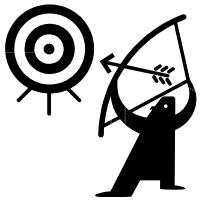
Targeted treatments



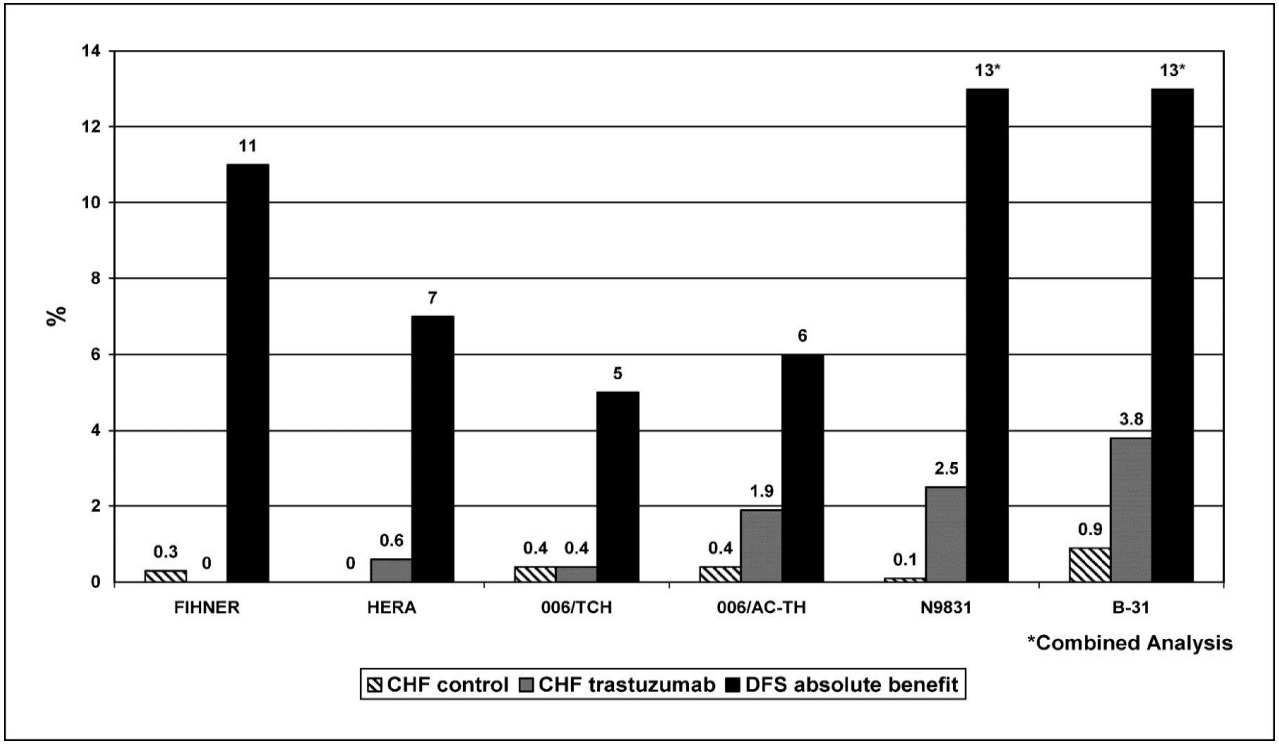
Lack of specific data

(for ex, in HERA: > 60 yo less than 16%)

but evidence of clinical benefit!



The incidence of CHF from the Finnish Herceptin Study (FINHER), Herceptin Adjuvant trial (HERA), Breast Cancer International Collaborative Group trial 006 (006) with TCH and AC-TH analyzed separately, the North Central Cancer Treatment Group trial 9831 (N9831), and NSABP B-31 (B-31).



Bird B R H , Swain S M Clin Cancer Res 2008;14:14-24

- NSABP B31
  - **Age**
    - **2% < 50 yo vs 5.4% > 60 yo**
  - LVEF > 4 AC
    - 12% if LVEF < 55%)
  - Concomitant > sequential
  - **Hypertension comedications**
- B31/N9831
  - 6.7% pts who had completed AC had a lower LVEF or developed cardiac symptoms preventing the initiation of TZT
  - 1/3 pts who started TZT discontinued it: 4.7% with symptomatic CHF, 14.2% with confirmed asymptomatic decline in LVEF, and the rest for noncardiac reasons

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

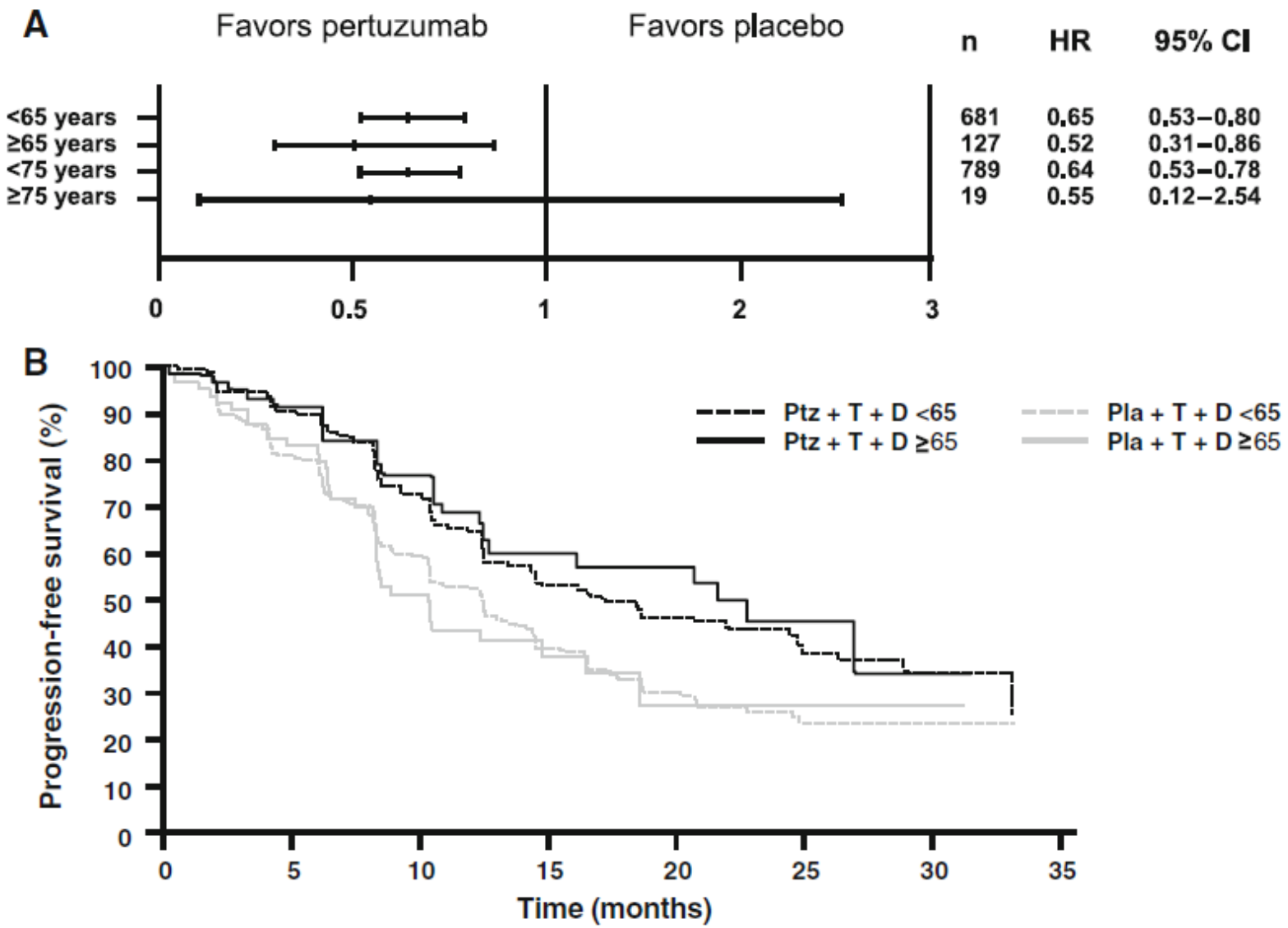
Duration and Toxicity of Adjuvant Trastuzumab in Older Patients With Early-Stage Breast Cancer: A Population-Based Study

Ines Vaz-Luis, Nancy L. Keating, Nancy U. Lin, Huichuan Lii, Eric P. Winer, and Rachel A. Freedman

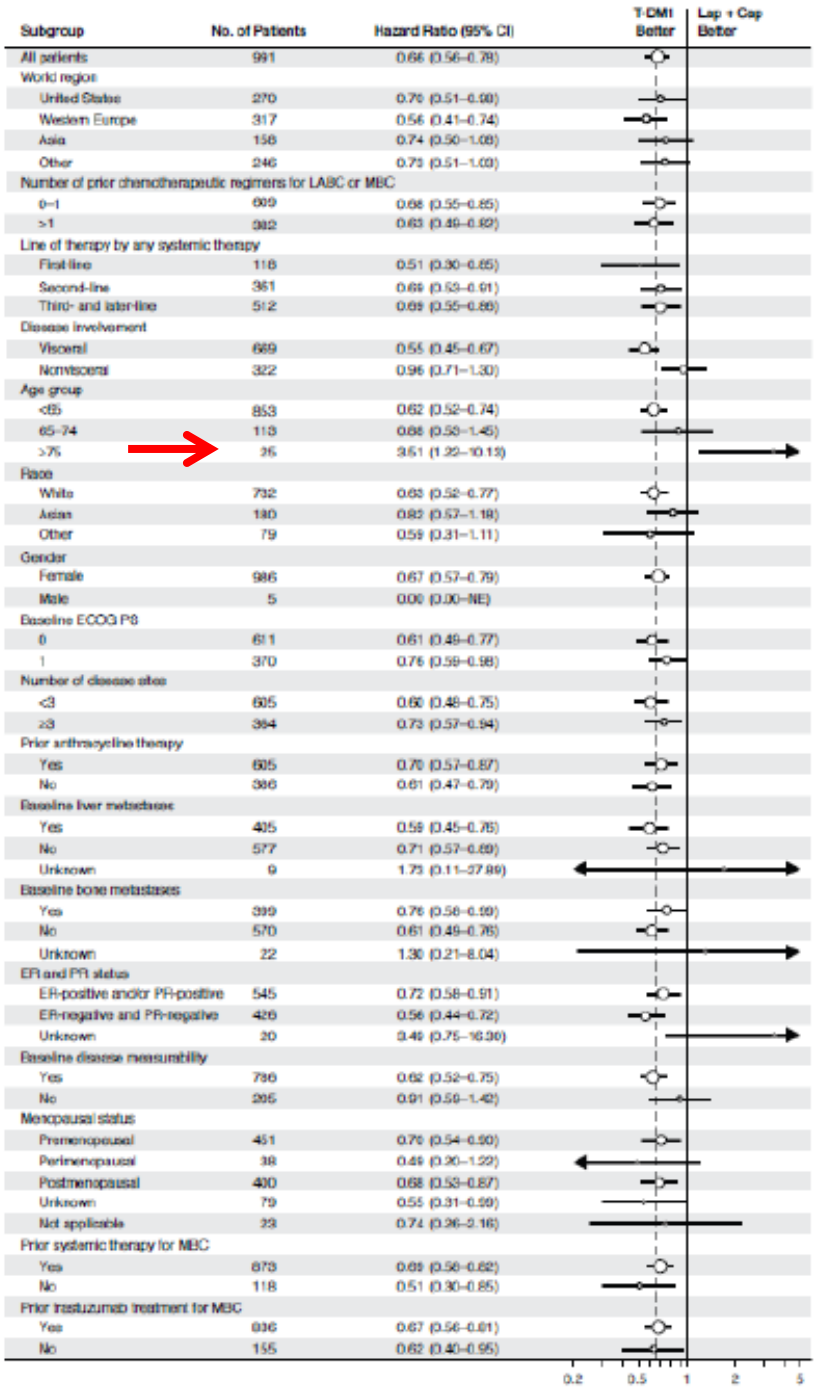
- SEER database
- 2,028 patients ≥ 66, stage I-III, 2005-2009, trastuzumab
  - 71.2% < 76
  - 66.8% wo/ comorbidities (Charlson)
  - 85.2% w/ chemotherapy
  - 81.7% w/ complete trastuzumab treatment (> 9 months)
  - Factors correlated w/ incomplete treatment
    - Age 80+ vs 66-70 OR 0.40 (0.30-0.55)
    - Comorbidities 2 vs 0 OR 0.65 (0.49-0.88)

Vaz-Luiz. J Clin Oncol 2014

Pertuzumab



Miles, Breast Cancer Res Treat 2013



T-DM1

Table 4. Incidence of Grade ≥ 3 AEs by Patient Subgroup in T-DM1–Exposed Patients

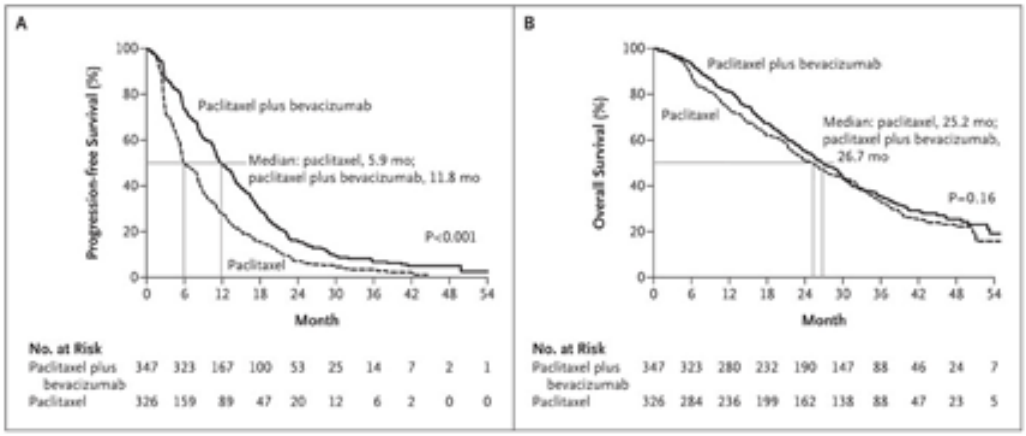
Subgroup	Total No. of Patients (N = 884)	Grade ≥ 3 AE: No. of Patients	Grade ≥ 3 AE: %
Age, years			
< 65	762	335	44.0
≥ 65	122	63	51.6
≥ 65 to < 75	93	49	52.7
≥ 75	29	14	48.3
Race			
White	692	288	41.6
Asian	99	63	63.6
Other	93	47	50.5
Previous systemic therapy for MBC			
Yes	722	336	46.5
No	162	62	38.3
Previous anthracycline use			
Yes	586	267	45.6
No	298	131	44.0

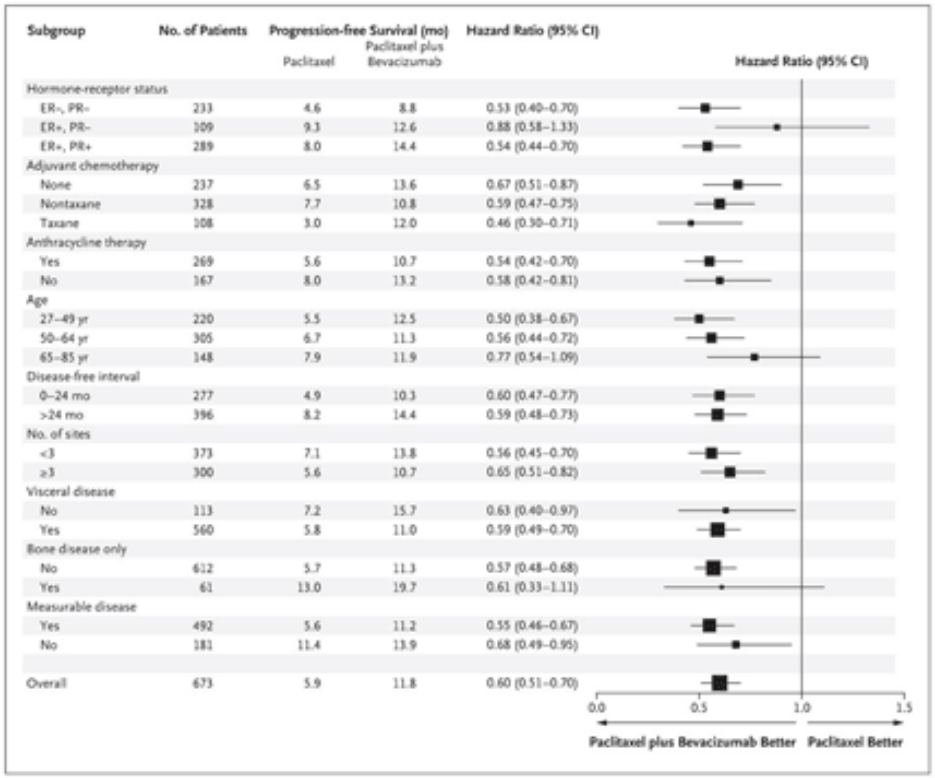
Abbreviations: AE, adverse event; MBC, metastatic breast cancer; T-DM1, trastuzumab emtansine.

Diéras. JCO 2014
Verma. N Engl J Med 2013

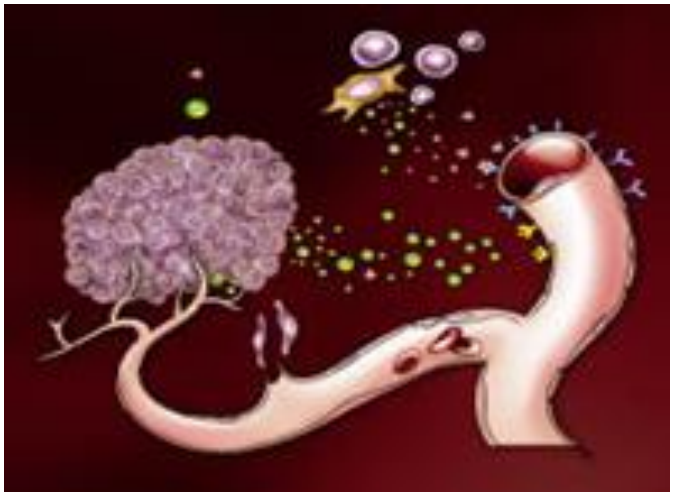
Bevacizumab

MBC L1





> 65 yo ≤ 20%



Miller. N Engl J Med 2007

ATHENA: CT wo/anthracyclines + beva

%	< 70 N = 2,018	70+ N = 233*
Hypertension grade ≥ 3	**4.2**	**6.9**
Proteinuria grade ≥ 3	**1.5**	**4.0**
ATE (A or V)	3.3	2.9
Stop for toxicity	**15**	**23**
ATE	1.8	2.9
CHF	0.3	0.6
HTN	1.8	2.9

*175 (7.8%) 70+, 51 (2.3%) 75+, 7 (0.3%) 80+

Biganzoli. Annals Oncol 2011

VOLUME 31 · NUMBER 28 · OCTOBER 1 2013

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Contraindicated Use of Bevacizumab and Toxicity in Elderly Patients With Cancer

Dawn L. Hershman, Jason D. Wright, Emerson Lim, Donna L. Buono, Wei Yann Tsai, and Alfred I. Neugut

- SEER database
- 3,039 patients ≥ 66, stage IV breast, lung, colon cancer, 2004-2007, bevacizumab
  - Contra-indication defined as 2 claims for thrombosis, cardiac disease, stroke, hemorrhage, hemoptysis, or GI perforation
  - Toxicity defined as 1st development of 1 condition > beva
  - Beva use associated w/ white race, later year of diagnosis, tumor type, and decreased comorbid conditions
  - 35.5% had contra-indication
    - Black race, increased age, comorbidity, later year of diagnosis, lower socioeconomic status, lung and CRC
  - If no contra-indication → 30% complication (black race)

Hershman. J Clin Oncol 2013

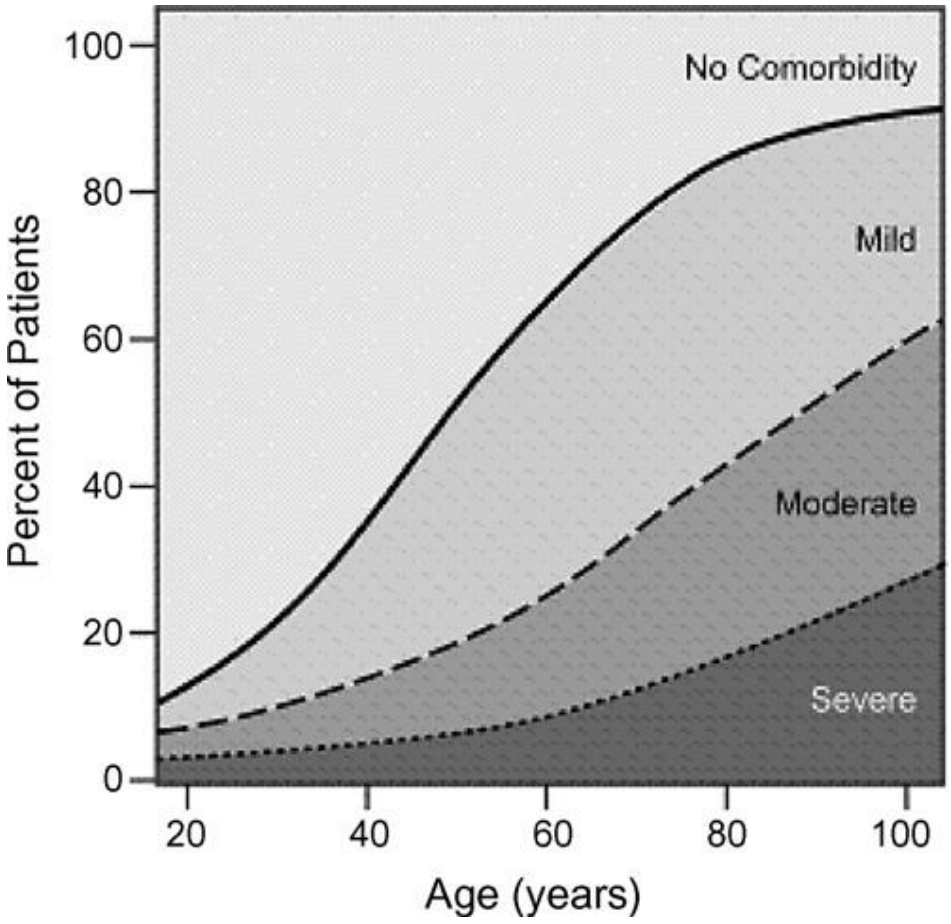
Definition of “old” x ageing heterogeneity

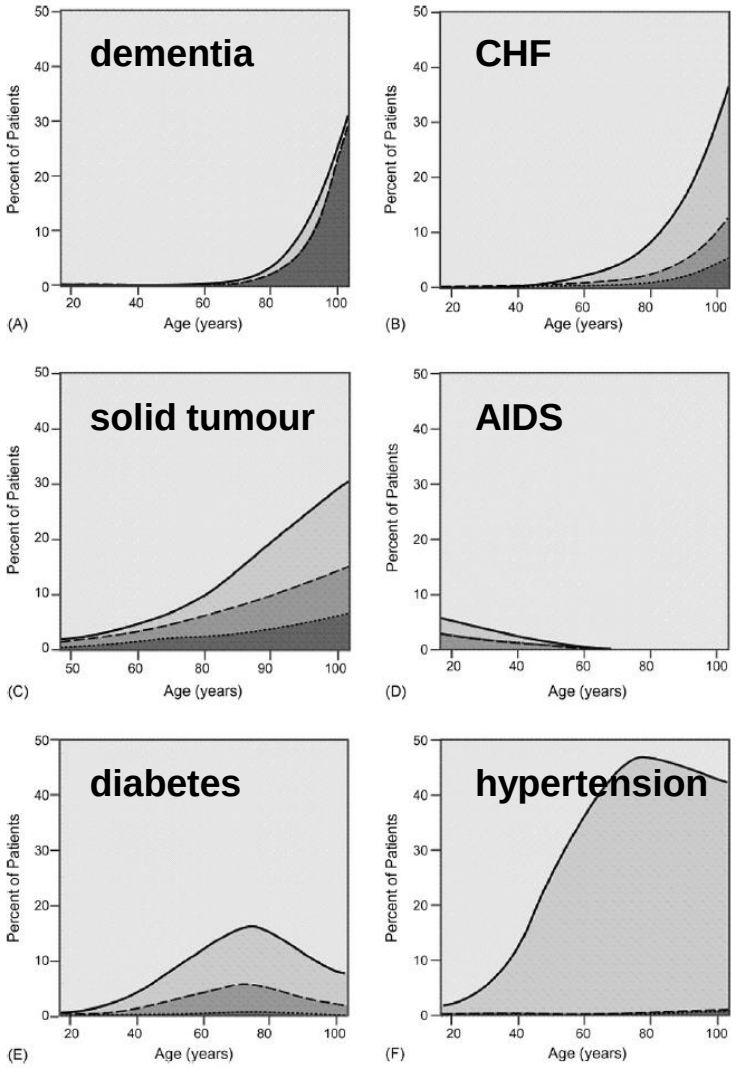
Women life expectancy

Age	Top 25th% Fit	50th% Intermediate	Lowest 25th% Sick
50	40	33	24.5
70	21.3	15.7	9.5
75	17	11.9	6.8
80	13	8.6	4.6
85	9.6	5.9	2.9
90	6.8	3.9	1.8
95	4.8	2.7	1.1

Walter JAMA 2001

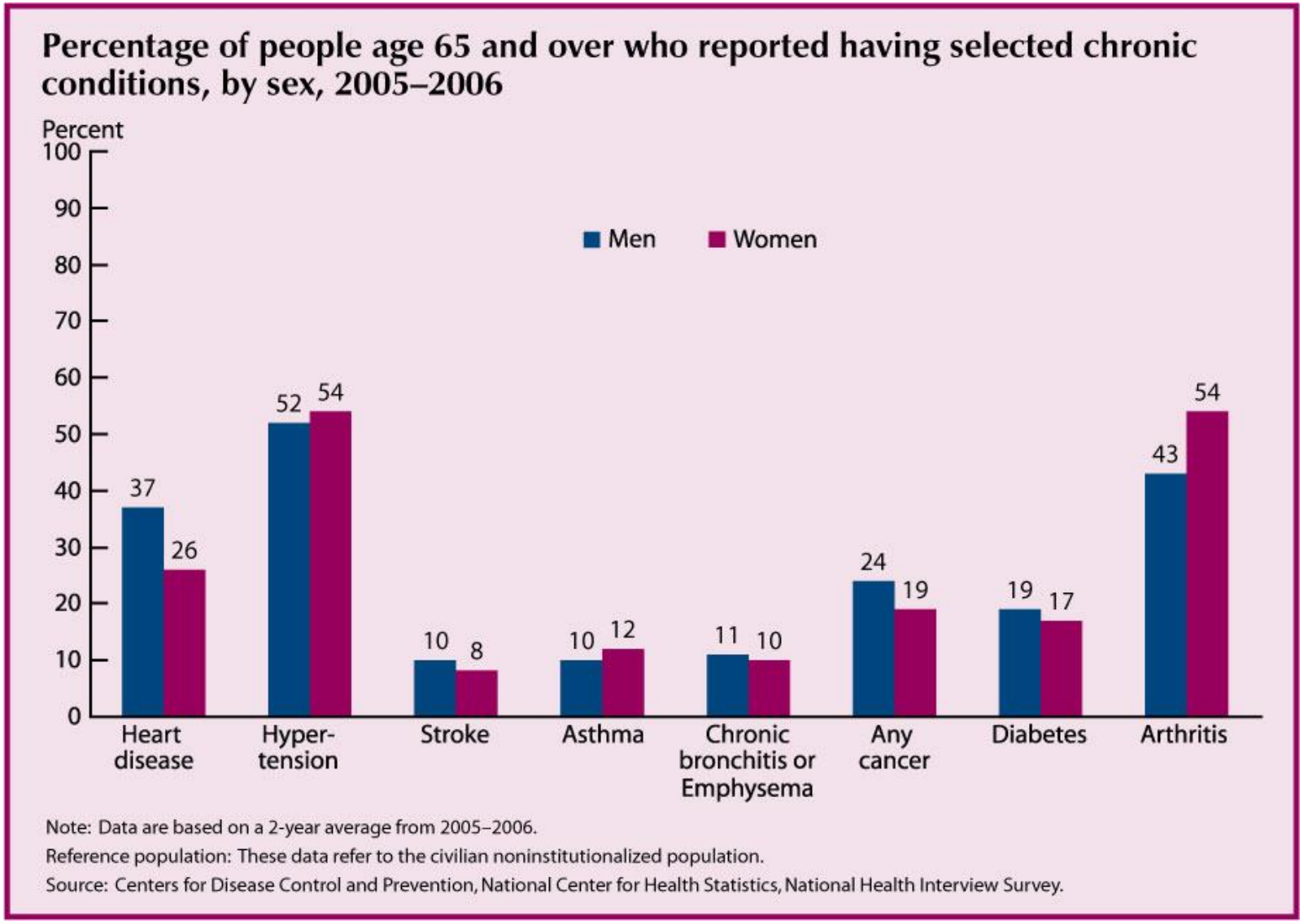
Multimorbidities across age





Piccirillo, Critical Rev Oncol Haematol 2008

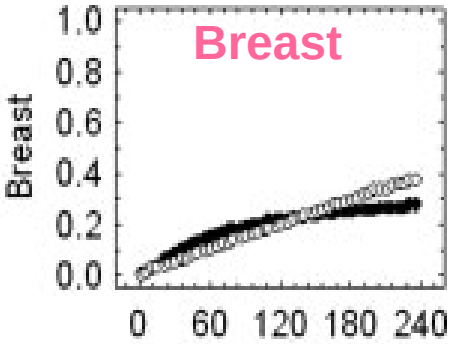
Co-morbidity @ AgeingStats.Gov

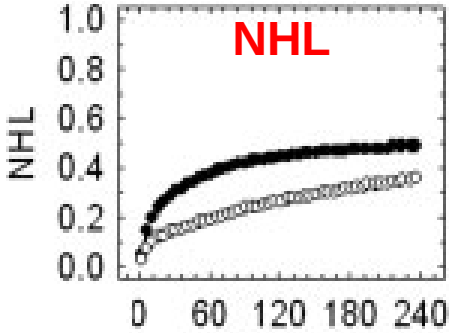


http://www.agingstats.gov/Agingstatsdotnet/Main_Site/Data/2008_Documents/Health_Status.aspx

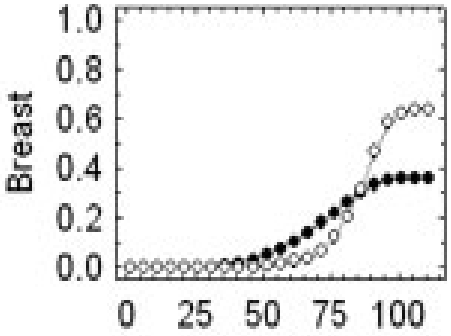
Competing causes of mortality

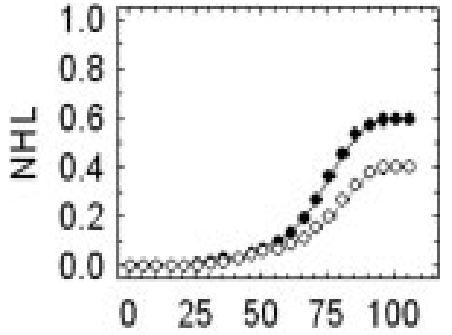
Cumulative probability of death vs time from diagnosis



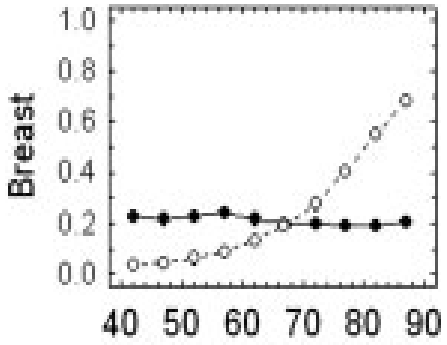


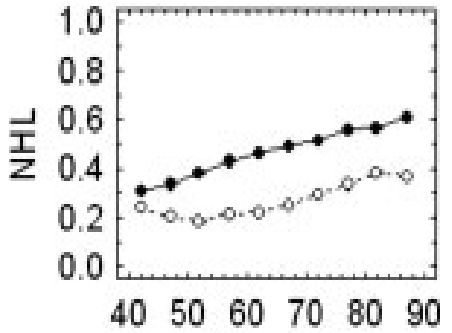
Cumulative probability of death vs attained age





Competing HR of death vs age at diagnosis



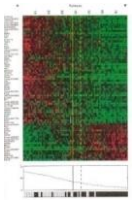


Deaths attributed to the primary cancer (solid dots) and those attributed to comorbidity (open circles)

Kendal. Cancer 2008

Balance of goals according to age

- **Young patient**
  - Social and family obligations (children)
  - Quantity of life +++
- **Oncology**
  - Therapies and innovation
  - Toxicity, response, survival
    - RECIST
    - NCI CTC v4.0
    - Survival
      - DFS, PFS, DDFS, OS
  - Fast-moving world
  - "Molecular portrait" of tumour & GEP



- **Elderly patient**
  - QoL+++
  - Independence
  - Staying at home
- **Geriatrics**
  - Symptoms, diagnosis
  - Quality of survival, i.e. amount of life with good QoL
    - Cognition
    - Functional status
    - QoL
    - Nutrition, etc.
  - Requiring time
  - "Global portrait" of patient & CGA

CGA

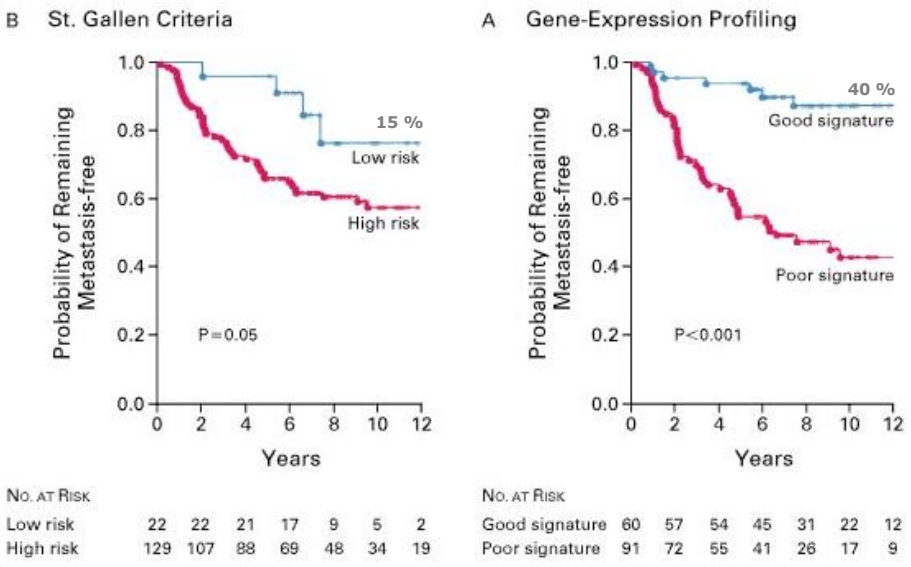
Mammaprint®

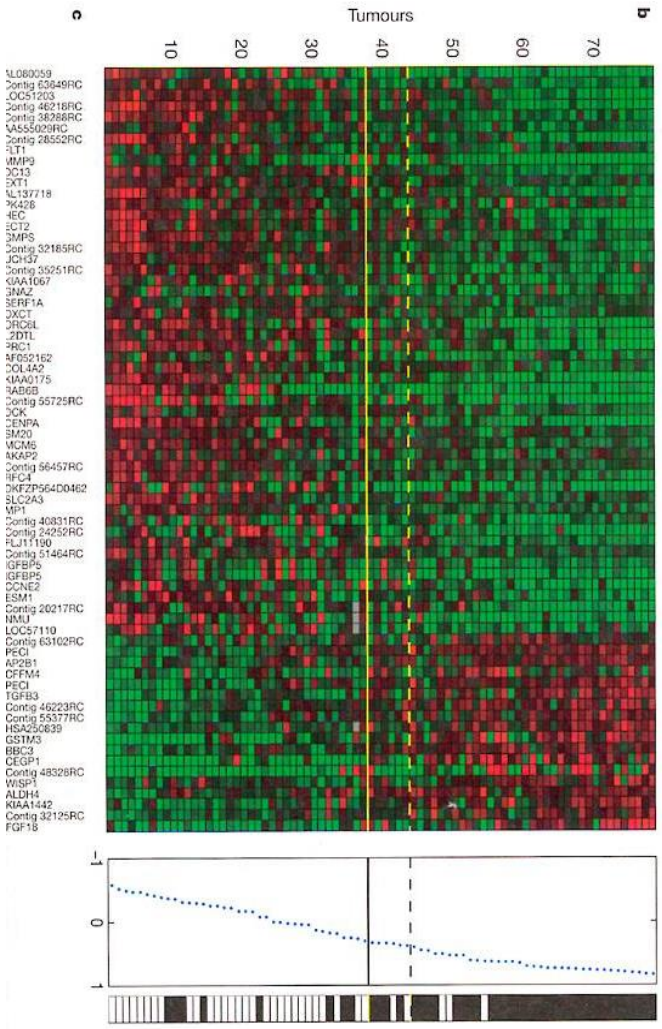
The New England
Journal of Medicine

VOLUME 347 DECEMBER 19, 2002 NUMBER 25

A GENE-EXPRESSION SIGNATURE AS A PREDICTOR OF SURVIVAL IN BREAST CANCER

295 pts < 53 yo





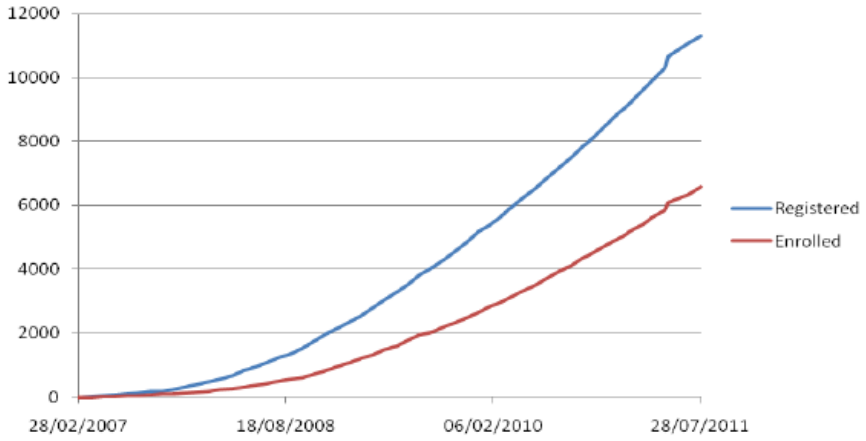
25,000 genes, 78 tumours, 70 genes, 17 pN0, all < 55 yo

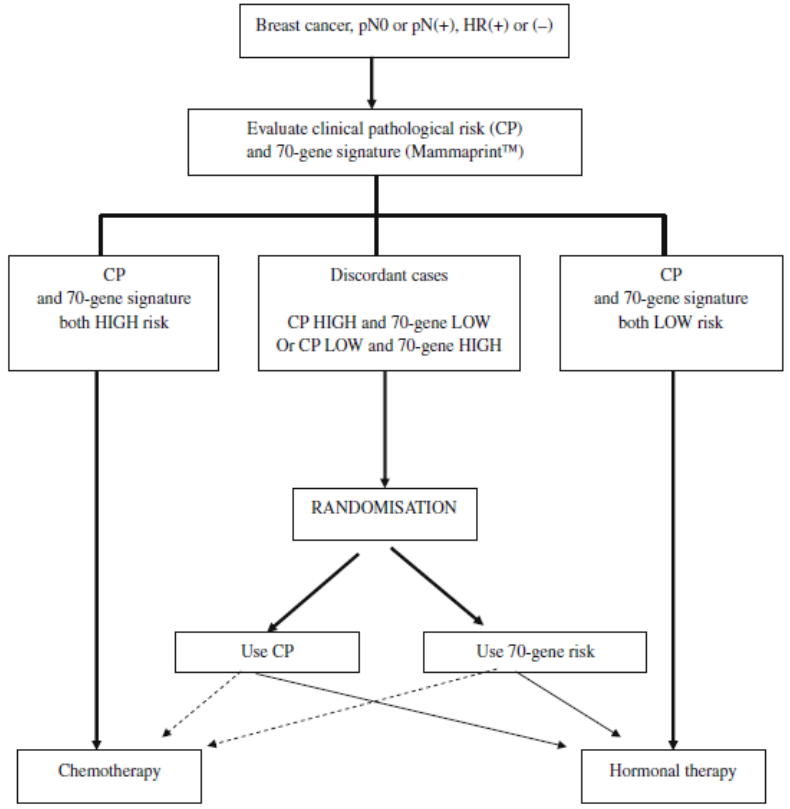
van't Veer, Nature 2002; van de Vijver, NEJM 2002

MINDACT

MINDACT
Microarray In Node-negative and 1 to 3 positive lymph node Disease may Avoid ChemoTherapy
EORTC 10041 / BIG 3-04
TRANSBIG

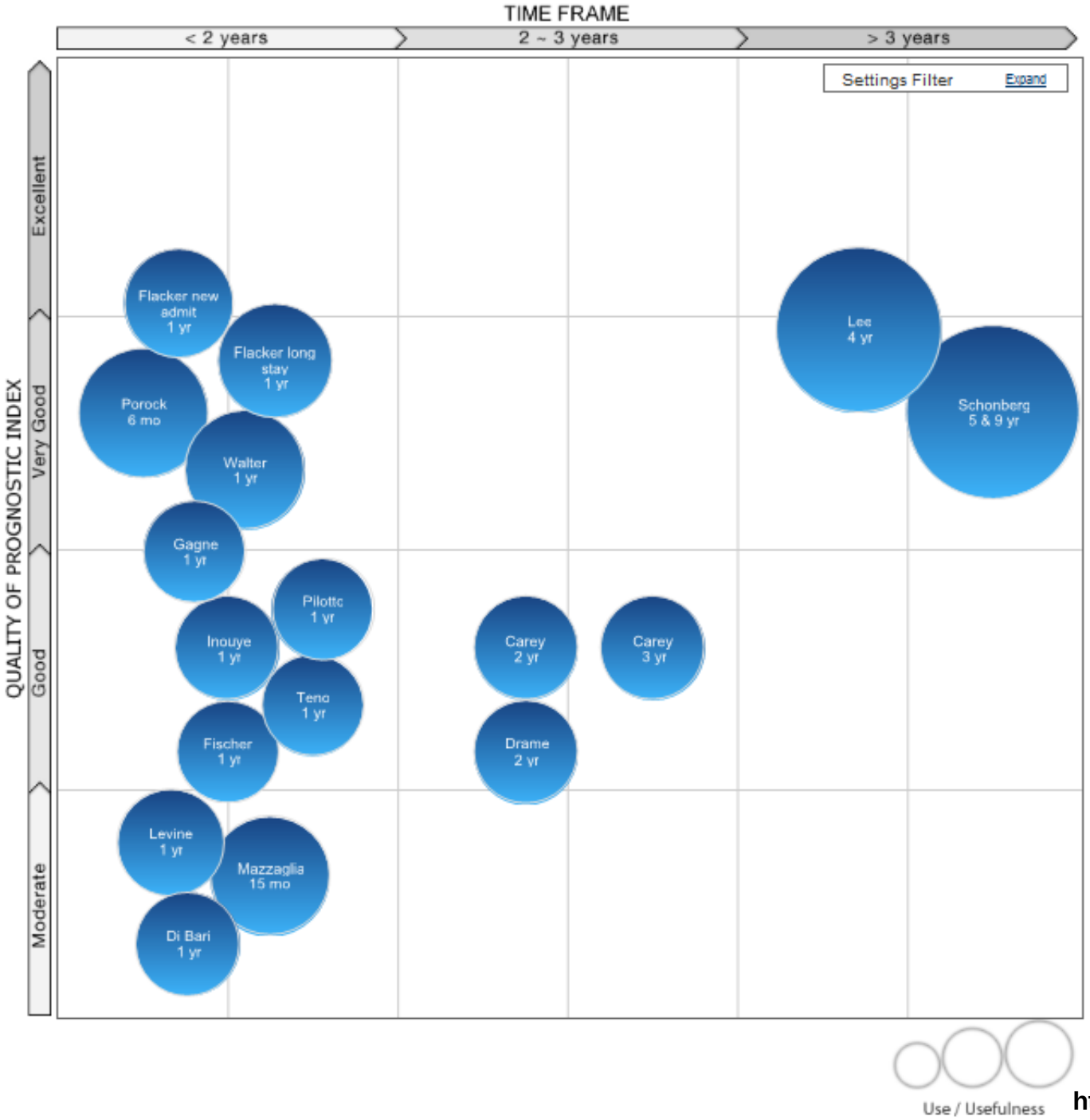
- 6,600 pts **< 70**
  - FEB 2007-AUG 2011
  - 11,291 registered pts
  - 6,673 enrolled (59.1%)





Abbreviations and legends
pN0: no axillary node involved at pathological examination ; pN(+): 1 to 3 axillary nodes involved;
HR (+) or (–): hormone-receptor-positive or negative; CP: clinicopathological risk
HIGH risk LOW risk

Fig. 2 – MINDACT design.



http://www.eprognosis.org/

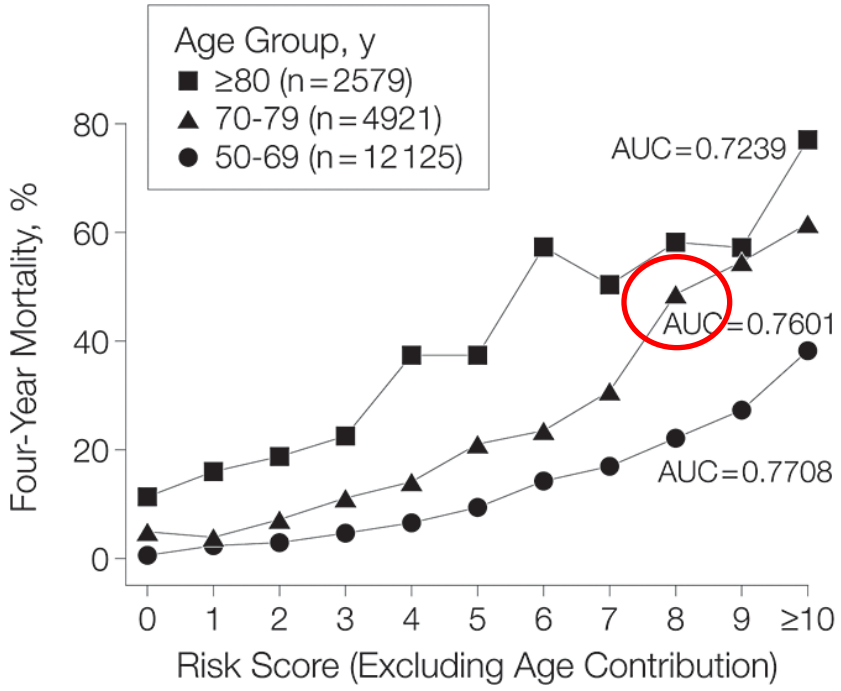
4-year mortality score in general elderly population

Box. Four-Year Mortality Index for Older Adults

1. Age _____	60-64: 1 point 65-69: 2 points 70-74: 3 points 75-79: 4 points 80-84: 5 points ≥85: 7 points
2. Sex (Male/Female)	Male: 2 points
3. a. Weight: _____ b. Height: _____ 703 × (weight in pounds/ height in inches^2) BMI = _____	BMI <25: 1 point
4. Has a doctor ever toldyou that you have diabetes or high blood sugar? (Y/N)	Diabetes: 1 point
5. Has a doctor told you that you have cancer or a malignant tumor, excluding minor skin cancers? (Y/N)	Cancer: 2 points
6. Do you have a chronic lung disease that limits your usual activities or makes you need oxygen at home? (Y/N)	Lung Disease: 2 points
7. Has a doctor told you that you have congestive heart failure? (Y/N)	Heart Failure: 2 points
8. Have you smoked cigarettes in the past week? (Y/N)	Smoke: 2 points
9. Because of a health or memory problem do you have any difficulty with bathing or showering? (Y/N)	Bathing: 2 points
10. Because of a health or memory problem, do you have any difficulty with managing your money—such as paying your bills and keeping track of expenses? (Y/N)	Finances: 2 points
11. Because of a health problem do you have any difficulty with walking several blocks? (Y/N)	Walking: 2 points
12. Because of a health problem do you have any difficulty with pulling or pushing large objects like a living room chair? (Y/N)	Push or Pull: 1 point
Total Points: _____	

Health retirement study

- > 50 yo (40% > 70 yo)
  - Construction 11,701 subjects
  - Validation 8,009 subjects



Score ≥ 8 = 25% of 70+
Score ≥ 8 = 50% of 75+

Lee. JAMA 2006

5 key messages for elderly BC patients

1. **Under and over-treament** are frequent
2. **Access to innovation** is unbalanced
3. **Geriatric problems** are far more frequent than usually believed
   - 2/3 impaired G8, > 50% functional dependence, >10% cognitive dysfunctions, 20% depression, > 40% significant comorbidities, > 50% risk of malnutrition, polypharmacy, etc.
4. **→ Comprehensive Geriatric Assessment CGA**
   - Brings to clinicians new information in > 2/3 cases
   - Modifies clinical decision in 20-25% cases (function & nutrition)
5. **Competing risks for mortality**
   → call for a certain degree of assessment of life expectancy to balance treatment decision

Caillet. J Clin Oncol 2011; Kenis. Ann Oncol 2013
Bode. EBCC9 2014, abstract 414

EUSOMA
European Society of Breast Cancer Specialists
Improving Breast Cancer Care in Europe
EJC The official journal of EUSOMA

Management of elderly patients with breast cancer: updated recommendations of the International Society of Geriatric Oncology (SIOG) and European Society of Breast Cancer Specialists (EUSOMA)

Laura Biganzoli, Hans Wildiers, Catherine Oakman, Lorenza Marotti, Sibylle Loibl, Ian Kunkler, Malcolm Reed, Stefano Ciatto, Adri C Voogd, Etienne Brain, Bruno Cutuli, Catherine Terret, Margot Gosney, Matti Aapro, Riccardo Audisio

As the mean age of the global population increases, breast cancer in older individuals will be increasingly encountered in clinical practice. Management decisions should not be based on age alone. Establishing recommendations for management of older individuals with breast cancer is challenging because of very limited level 1 evidence in this heterogeneous population. In 2007, the International Society of Geriatric Oncology (SIOG) created a task force to provide evidence-based recommendations for the management of breast cancer in elderly individuals. In 2010, a multidisciplinary SIOG and European Society of Breast Cancer Specialists (EUSOMA) task force gathered to expand and update the 2007 recommendations. The recommendations were expanded to include geriatric assessment, competing causes of mortality, ductal carcinoma in situ, drug safety and compliance, patient preferences, barriers to treatment, and male breast cancer. Recommendations were updated for screening, primary endocrine therapy, surgery, radiotherapy, neoadjuvant and adjuvant systemic therapy, and metastatic breast cancer.

Lancet Oncol 2012; 13: e148–60

Sandro Pitigliani Medical Oncology Unit, Istituto Toscano Tumori, Hospital of Prato, Prato, Italy (L Biganzoli MD, C Oakman MD); **Department of General Medical Oncology, University Hospitals, Leuven, Belgium** (H Wildiers MD); **EUSOMA, Florence, Italy** (L Marotti BSc); **German Breast Group, University of Frankfurt,**

SIOG
INTERNATIONAL SOCIETY OF GERIATRIC ONCOLOGY

Biganzoli. Lancet Oncol 2012

SIOG

INTERNATIONAL SOCIETY OF GERIATRIC ONCOLOGY

2014

LISBON
PORTUGAL
23 - 25 OCT.

14th SIOG Meeting, Lisbon - Portugal




SAVE THE DATE - 23 to 25 October 2014