SEVERANCE

Panel Discussion 1: Apr. 20. Lotus Hall

Elderly Breast Cancer

Local Therapy

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Born in 1931 (86 year-old)
Carmen Dell'Orefice
(the world's oldest working model)

Definition of the ‘older’ or ‘elderly’ person

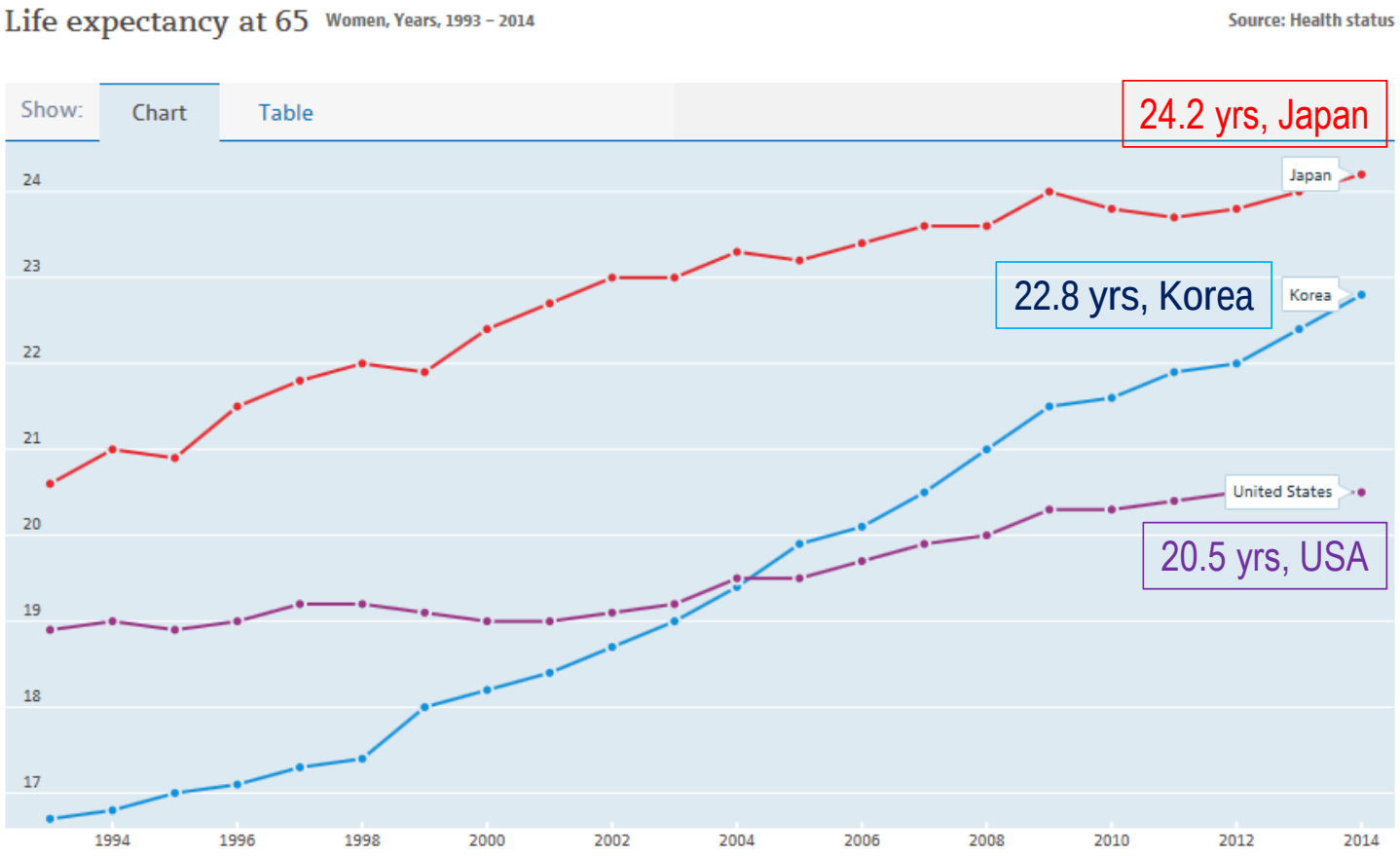
✓ **WHO website** (http://www.who.int/healthinfo/survey/ageingdefnolder/en/)

- Most developed world countries: chronological age of **65 years** as a definition of 'elderly' or ‘older’ person.
- The United Nations: cutoff is **60+ years** to refer to the older population.

✓ **NCCN Task Force Report** (JNCCN 2008;6[suppl 4]:S1-S25)

- Some members: ‘**≥ 70 years**’ be used to define “older” patients.
- **Little or no data** exist to make evidence-based decisions because this population is dramatically under-represented in breast cancer clinical trials.
- Therefore, **expert-driven consensus** is recommended for this population.

Life Expectancy at age 65 years old



- The average number of years : a person at certain age can be expected to live, assuming that age-specific mortality levels remain constant.
- The actual age-specific death rate of any particular birth cohort cannot be known in advance.
- If death rates are falling, actual life spans will be higher than life expectancy calculated using current death rates.
- The methodology used to calculate life expectancy can vary slightly between countries.

OECD (2017), Life expectancy at 65 (indicator). doi: 10.1787/0e9a3f00-en (Accessed on April 2017).

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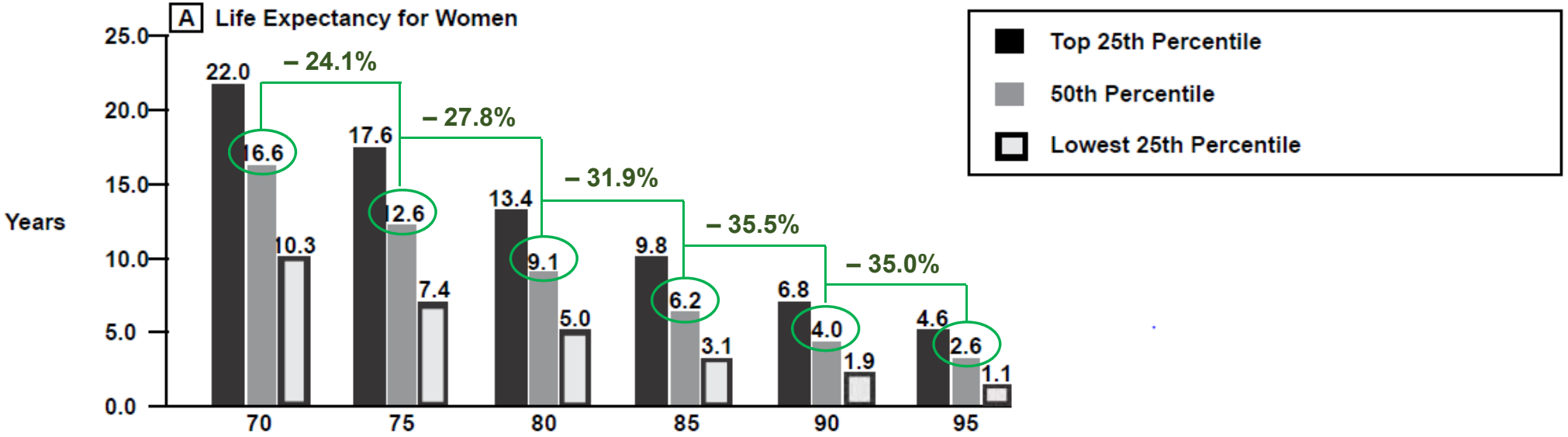
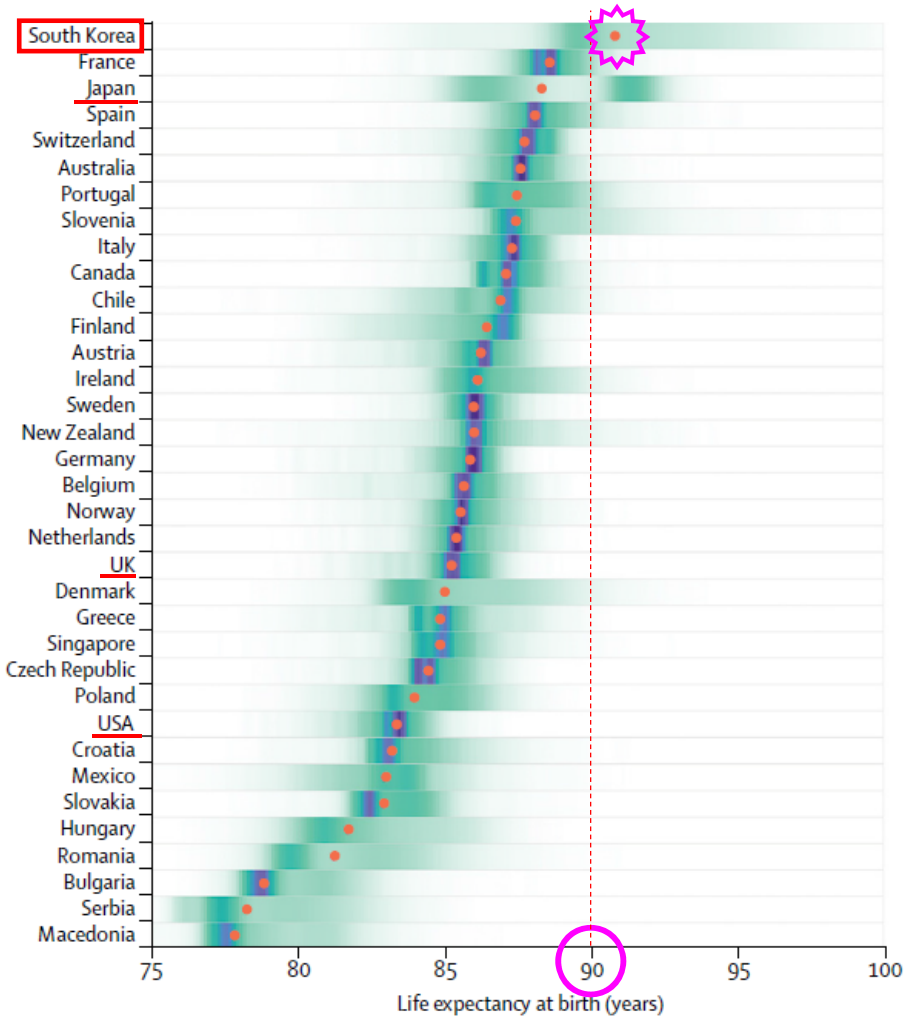
UPPER, MIDDLE, AND LOWER QUARTILES OF LIFE EXPECTANCY FOR WOMEN AND MEN AT SELECTED AGES[a]



[a]Data from the Life Tables of the United States 2008. See the life expectancy tables in the National Vital Statistics Reports at http://www.cdc.gov/nchs/data/nvsr/nvsr61/nvsr61_03.pdf

Future Life Expectancy :
projections with a Bayesian model ensemble



Women at birth in 2030.

Kontis et al. Lancet 2017;389:1323-35.

Clinical Questions of Geriatric Oncology

- **Basic questions** are…

✓ Is the patient going to **die with cancer** or **of cancer**?

✓ Is the patient going to **experience the consequence of cancer** during his or her lifetime?

✓ Is the patient able to **tolerate cancer treatment**?

✓ What are the **long-term consequences of cancer** and **cancer treatment** in older aged persons?

- **Chronologic age** is a weak surrogate for patient function and comorbidities.
- In addition, **the social consequences** include the health of the home caregiver and the economic implications of caring for an aging patient.

Comprehensive Geriatric Assessment and Clinical Implications

Assessment	Clinical Implications
FUNCTIONAL STATUS	
Activities of daily living and instrumental activities	Relation to life expectancy, functional dependence, and tolerance of stress
COMORBIDITY	
No. of comorbid conditions and comorbidity indices	Relation to life expectancy and tolerance of stress
MENTAL STATUS	
Folstein Mini-Mental Status Examination	Relation to life expectancy and functional dependence
EMOTIONAL CONDITION	
Geriatric Depression Scale	Relation to life expectancy may indicate motivation to receive treatment
NUTRITIONAL STATUS	
Mini Nutritional Assessment Polypharmacy	Reversible condition; possible relationship to survival Risk of drug interactions
GERIATRIC SYNDROMES	
Delirium, dementia, depression, falls, incontinence, spontaneous bone fractures, neglect and abuse, failure to thrive, vertigo	Relation to survival and functional dependence

Balducci L. Cancer in the Elderly: Biology, Prevention, and Treatment

Physiologic Decline with Aging

Organ System	Major Physiologic Changes
Cardiovascular	- **Decreased** number of myocytes, ventricular and arterial compliance, and β-adrenergic responsiveness - Fibrosis of conducting pathways with increased arrhythmias - Increased dependence on preload (including atrial kick), diastolic dysfunction, and silent ischemia
Respiratory	- **Decreased** chest wall compliance, maximum inspiratory and expiratory force, lung elasticity (small airway collapse), PaO2 but no change in PaCO2, FVC and FEV1, ventilator responses to hypoxemia and hypercapnia, and normal airway protective mechanisms (increased risk for aspiration) - Ventilation-perfusion mismatch
Renal	- **Decrease** in number of functional nephrons and tubular cells, renal blood flow, GFR, CrCl despite normal serum Cr level, tubular function (loss of concentrating ability), clearance of certain drugs - Increased susceptibility to dehydration, and lower urinary tract dysfunction and infection
Hepatobiliary	- **Decreased** liver volume, number of hepatocyte mitochondria, hepatic blood flow - Increased hepatocyte size and ploidy, sensitivity to and decreased clearance of certain drugs, and incidence of gallstones and gallstone-related diseases - Synthetic capacity unchanged
Immune	- **Involution** of thymus gland - **Decreased** production and differentiation of naïve T cells, and T cell mitogenic activity - Increase in inflammatory cytokines and autoantibodies

Yeo H, et al. Sabiston Textbook of Surgery

The American College of Surgeons (ACS) and The American Geriatric Society (AGS)

Best Practice Guidelines for the Geriatric Surgical Patient

Preoperative Assessment

In addition to conducting a complete and thorough history and physical examination of the patient, the following assessments are strongly recommended:

- ☐ Assess the patient's **cognitive ability** and **capacity** to understand the anticipated surgery (see Section I.A, Section I.B, and Appendix I).
- ☐ Screen the patient for **depression** (see Section I.C).
- ☐ Identify the patient's risk factors for developing postoperative **delirium** (see Section I.D).
- ☐ Screen for **alcohol** and other **substance abuse/dependence** (see Section I. E).
- ☐ Perform a preoperative **cardiac** evaluation according to the American College of Cardiology/American Heart Association (ACC/AHA) algorithm for patients undergoing noncardiac surgery (see Section II and Appendix II).
- ☐ Identify the patient's risk factors for postoperative **pulmonary** complications and implement appropriate strategies for prevention (see Section III).
- ☐ Document **functional status** and history of **falls** (see Section IV).
- ☐ Determine baseline **frailty** score (see Section V and Appendix III).
- ☐ Assess patient's **nutritional status** and consider preoperative interventions if the patient is at severe nutritional risk (see Section VI and Appendix IV).
- ☐ Take an accurate and detailed **medication history** and consider appropriate perioperative adjustments. Monitor for **polypharmacy** (see Section VII, Appendix V, Appendix VI, and Appendix VII).
- ☐ Determine the patient's **treatment goals** and **expectations** in the context of the possible treatment outcomes (see Section VIII).
- ☐ Determine patient's **family** and **social support system** (see Section VIII).
- ☐ Order appropriate preoperative **diagnostic tests** focused on elderly patients (see Section IX).

ACS NSQIP®/AGS BEST PRACTICE GUIDELINES:
Optimal Preoperative Assessment of the Geriatric Surgical Patient

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APPROACH TO DECISION MAKING IN THE OLDER ADULT

Life expectancy

↓

Patient's decision-making capacity

↓

Patient's goals & values

Is the patient at moderate or high risk of dying or suffering from cancer considering his or her overall life expectancy?[a,b]

- **No** → **Symptom management/supportive care** See NCCN Guidelines for Palliative Care
- **Yes** ↓

Does this patient have decision-making capacity?[c,d]

Patients must have the ability to:

- Understand the relevant information about proposed diagnostic tests or treatments
- Appreciate their situation (including their underlying values and current medical situation)
- Use reason to make a decision
- Communicate a consistent choice

- **No** →
  - Obtain information from:
    - Patient's proxy
    - Advance directive
    - Living will
    - Health care power of attorney
    - Clinician's documentation
  - Consider consult from ethics committee or social worker or consider palliative care (See NCCN Guidelines for Palliative Care)
- **Yes** ↓

- Assess the patient's goals and values regarding the management of his or her cancer
- Are the patient's goals and values consistent with wanting anti-cancer therapy?[e]

- **No** → **Symptom management/supportive care** (See NCCN Guidelines for Palliative Care)
- **Yes** → **Assessment of Risk Factors** (See OAO-2)

Assessment of Risk Factors

Comorbidities
- cardiovascular, renal, neuropathy, anemia, osteoporosis, liver, diabetes, lung, hearing/vision loss, prior cancer Dx & Tx, chronic infection, decubitus/pressure ulcers

Geriatric Syndromes
- ADL, IADL, mobility problems, falls, dementia, delirium, depression, nutritional deficiency, polypharmacy

Socioeconomic Issues
- poor living conditions, no caregiver or limited social support, low income, transportation barriers/access problems, under-insurance/high out-of-pocket costs for medications

Special considerations for patients able to tolerate treatment

Surgery
- **In general, age is not the primary consideration for surgical risk.**
- Emergency surgery carries increased risk of complications.
- Assess physiologic status and the ACS/AGS guidelines for older patients.
- Increased need for functional assistance pre-surgery predicts postop. complications, extended hospital stay, and 6-month mortality.
- Impaired cognitive status is a risk factor for postop. complications, prolonged length of stay, and 6-month overall postop. mortality.
- Older age is a risk factor for postoperative delirium.
- Delirium is a risk factor for functional and cognitive decline.
- Preventive measures exist for delirium (Yale Delirium Prevention Trial and Hospital Elder Life Program (HELP); NICE Guideline for Prevention of Delirium)

Radiation Therapy
- Use caution with concurrent chemoradiation therapy; dose modification of chemotherapy may be necessary.
- **Nutritional support** and **pain control** for radiation therapy-induced mucositis.

NCCN Guidelines – Older Adult Oncology (2016)

DISEASE-SPECIFIC ISSUES RELATED TO AGE

Breast Cancer*

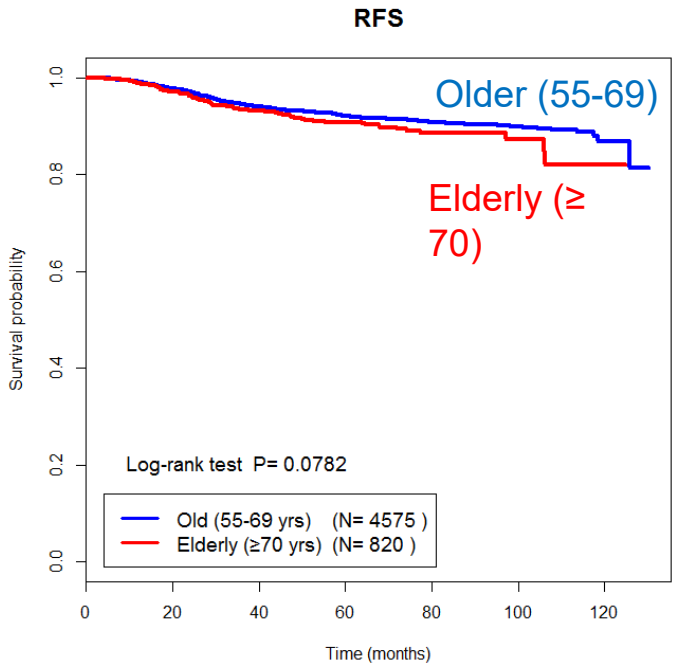
See NCCN Guidelines for Breast Cancer

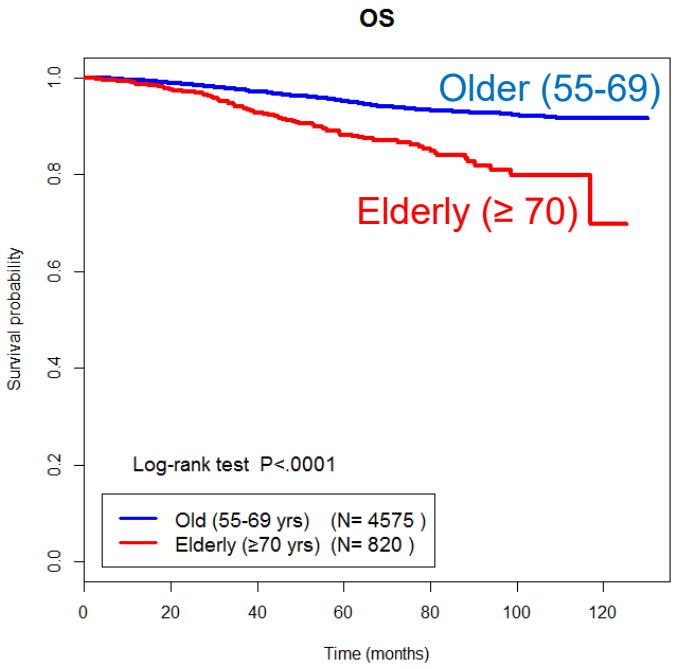
- Multiple studies have shown that older women often do not receive "standard of care" treatment, and do not do as well as younger women with the same stage of breast cancer.
- Women older than 75 years receive less aggressive treatment and have higher mortality from early-stage breast cancer than younger women.[1-3] Biologic as well as chronologic age should be considered in selecting treatments for older women with breast cancer.

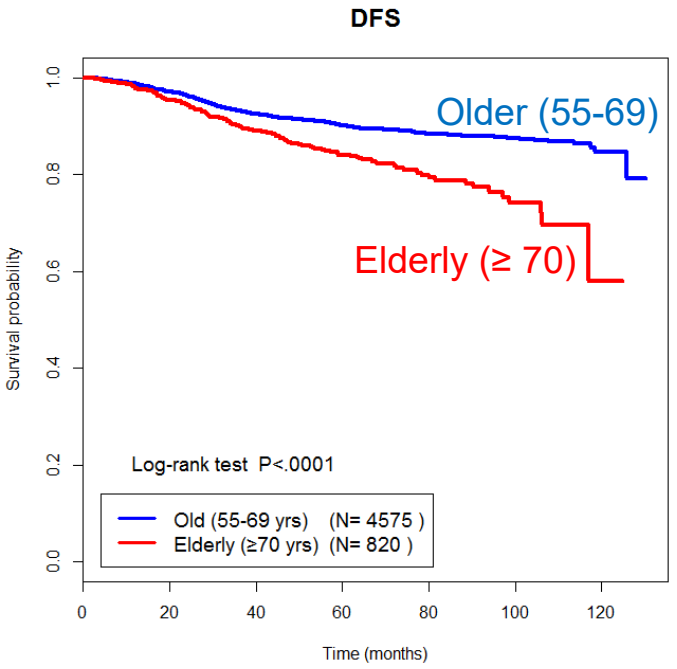
A preliminary retrospective study of Korea Big 5 Hospitals

N = 5,395 underwent surgery from 2005 to 2010;
Median FU periods = 73.0 months

Asan, NCC, Samsung, Seoul, and Yonsei







Unpublished data.

Tumor Biology between older and young women with breast cancer

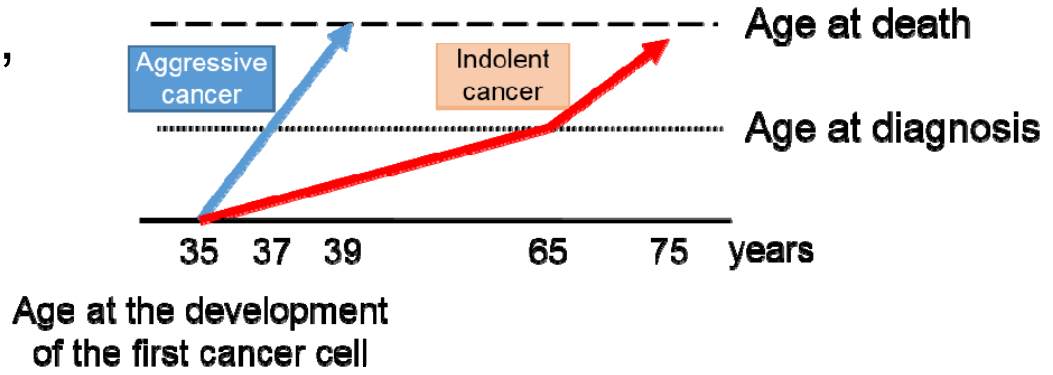
- **Older** women tend to have **fewer adverse prognostic features**.

✓ Increased ER/PR-positive tumors

✓ Lower HER2-positive tumors

✓ Lower aggressive other markers; tumor grade, proliferative marker, p53 mutation, S-phase fraction, lymphovascular invasion..

- By a process of **natural selection**, it is reasonable to expect a concentration of more indolent tumors among older persons.



Balducci L. Cancer in the Elderly: Biology, Prevention, and Treatment

Management of elderly patients with breast cancer
: Updated recommendations of the SIOG and EUSOMA

Therapy	2012 Recommendations of the *International Society of Geriatric Oncology* (SIOG) / *European Society of Breast Cancer Specialists* (EUSOMA)
Surgery	**- Patients 70 years or older should be offered the same surgery as younger patients.** - Standard of care is BCS plus WBRT, or mastectomy with or without postoperative radiotherapy. - Mastectomy is indicated for large or multifocal tumours not amenable to conservative excision, patients who are not fit for WBRT, and patients who prefer mastectomy to BCS plus WBRT. - ALND is indicated for clinically positive or highly suspected nodes. - In clinically node negative disease, axillary staging by SLNB with completion ALND for tumour-positive SLNB remains the standard of care. - Omission of SLNB and completion ALND might be reasonable in some older patients.
Radiotherapy	**- WBRT after BCS, with a boost to the tumour bed, should be considered in all elderly patients since it decreases risk of local relapse.** - There is no subgroup of fit older patients in whom post-BCS WBRT can be systematically omitted. - Post-mastectomy chest-wall radiation should be considered for elderly patients with at least four nodes (N2-3) or a pT3/4 tumour (>5cm). - Hypofractionated radiation schedules offer similar local-regional control and adverse effects as standard WBRT. - The evidence for PBI in older patients is not sufficiently robust to recommend it as standard therapy.

Biganzoli et al. Lancet Oncol 2012;13:e148-60.

Surgery of the primary lesion in the elderly patients

- **Older women should be offered** the option of **breast conservation**, because body image and the loss of breast are important issues regardless of age.
- Operative mortality rate for breast surgery : very low (< 1%)
- BCS is a much less morbid procedure and preferable to mastectomy.

- **Main factor influencing surgical mortality** is not age but the presence of significant comorbidity.
- There may be at least a short-term **decrease in cognitive function after general anesthesia**.
- Attention should be paid to **functional status** and **comorbid illness** in making decisions about surgical management.

Omitting Primary Surgery

* No significant, † Significant, ‡ Not reported

Ref	Patients, n	Follow-up, months	Treatment	Overall Survival	Local Recurrence
Fentiman et al. Eur J Cancer 2003	164	120	Tamoxifen **Surgery**	39.0% 27.0%*	57.0% **9.0%†**
van Dalsen et al. J Surg Oncol 1995	171	41	Tamoxifen **Surgery**	68.0% 72.0%*	27.0% **6.0%†**
Robertson et al. BMJ 1988	135	24	Tamoxifen Surgery	85.0% 74.6%*	44.0% 24.6%‡
Gazet et al. Eur J Surg Oncol 1994	200	72	Tamoxifen Surgery	67.0% 72.0%*	56.0% 44.0%*
Mustacchi et al. Ann Oncol 2003	474	80	Tamoxifen **Surgery and Tamoxifen**	38.7% 45.6%*	47.2% **11.0%†**
Fennessy et al. Br J Surg 2004	455	151	Tamoxifen **Surgery and Tamoxifen**	28.8% **37.7%†**	50.0% **16.0%†**

Wildiers et al. Lancet Oncol 2007;8:1101-15.

Cochrane review (Surgery ± TAM vs. TAM alone)

- **Surgery ± TAM** showed no significant difference in OS but superior local disease control than TAM alone.
- Short estimated life expectancy of < 2–3 years, since it is the median duration of response to TAM.
- Still no data of aromatase inhibitors but may be another option.

Surgery vs TAM alone

Trial	Median follow-up	Surgery *n/N*	Primary endocrine therapy *n/N*	HR (95% CI)
Surgery primary endocrine therapy				
Mortality ('OS')				
EORTC 10851	10 years	60/82	50/82	1.11 (0.75–1.65)
Nottingham 1	5 years	28/65	28/66	1.06 (0.59–1.92)
St Georges	6 years	28/100	33/100	0.75 (0.44–1.26)
Mortality, recurrence or progression ('PFS')				
EORTC 10851	10 years	63/82	69/82	0.55 (0.39–0.77)
Nottingham 1	12 years	56/65	57/66	Not estimable
St Georges	6 years	60/100[a]	70/100[a]	Not estimable
Local recurrence or local progression as first event				
EORTC 10851	10 years	7/82	47/82	Not calculated[b]
Nottingham 1	9 years	16/65[a]	45/66[a]	Not calculated[b]
St Georges	6 years	36/100	53/100	Not calculated[b]
Distant metastases as first or simultaneous event				
EORTC 10851	10 years	15/82	7/82	Not calculated[b]
Nottingham 1	12 years	NR	NR	Not calculated[b]
St Georges	6 years	14/100	8/100	Not calculated[b]

Surgery + TAM vs TAM alone

Trial	Median Follow up	Surgery *n/N*	Primary endocrine therapy *n/N*	HR (95% CI)
Surgery plus endocrine therapy *vs* primary endocrine therapy				
Mortality ('OS')				
CRC	13 years	159/225	187/230	0.78 (0.63–0.96)
GRETA	7 years	130/239	144/235	0.98 (0.77–1.25)
Nottingham 2	5 years	8/53	14/94	0.80 (0.73–2.32)
Mortality or progression ('PFS')				
CRC	13 Years	NR	NR	NR
GRETA	7 years	140/239	188/235	0.65 (0.53–0.81)
Nottingham 2	5 years	NR	NR	NR
Local recurrence or local progression as first event				
CRC	13 years	36/225	115/230	0.25 (0.19–0.32)
GRETA	7 years	27/239	95/235	0.38 (0.25–0.57)
Nottingham 2	3 years	2/53	30/94	Not estimable
Distant metastases as first or simultaneous event				
CRC	13 years	20/225	14/235	Not estimable
GRETA	7 years	0/225	10/235	Not estimable
Nottingham 2	3 years	NR	NR	Not estimable

Hind et al. British J Cancer 2007;96:1025-9.

Breast Reconstruction

- The oldest aged woman underwent immediate breast reconstruction at my hospital : Implant; 78 yrs, LD flap; 68 yrs, and TRAM flap; 64 yrs.

- In USA (n = 127,501; TM+IBR),
  : 10.3%; age ≥ 65 yrs (1.5%; ≥ 75 yrs)
- 27.4% of age ≥ 65 yrs and TM+IBR
  : Contralateral prophylactic mastectomy
- 30-day unplanned re-admission
  : 3.7% (≥65 yrs) vs 2.9% (<65yrs), p<0.001

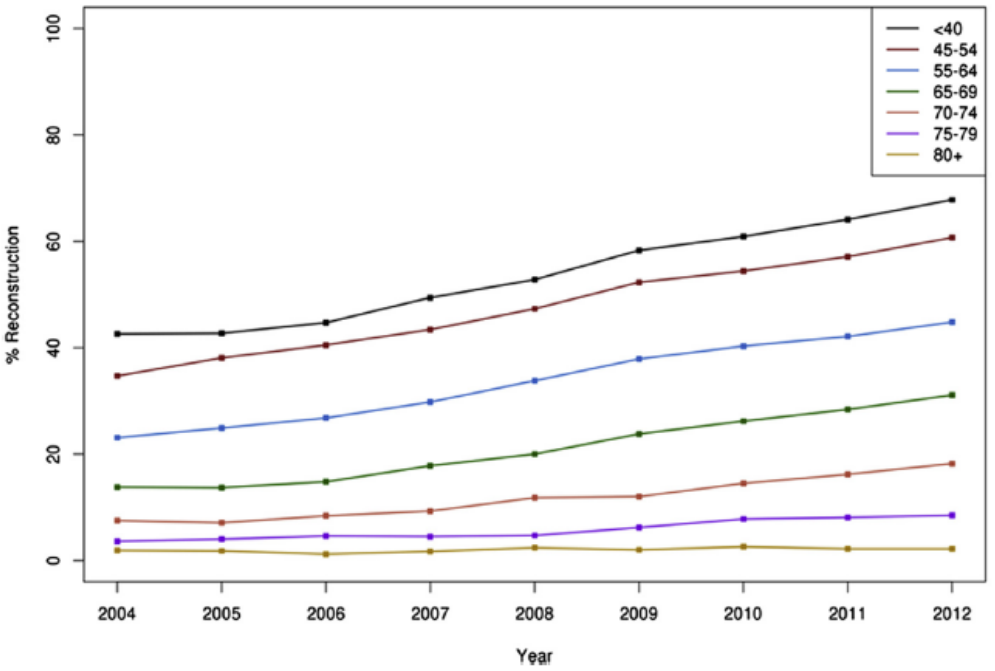


Figure 1. Trends in mastectomy with immediate breast reconstruction across age groups over time, 2004 to 2012. The increase for each age strata shown was statistically significant, $p < 0.001$.

Gibreel et al. J Am Coll Surg 2017 Feb. E-pub

Systematic review of breast reconstruction

- 42 articles (31-USA; 3-UK; 2-Itay, Canada; 1-Australia, France, Netherlands, Spain)
- Breast reconstruction rate of **6.1%** among mastectomy patients aged ≥ 60 years from 1987 to 2002.
- The majority of studies favored **implant-based** breast reconstruction for those aged ≥ 60.

- Mostly, **complication rates** were not higher in older women, and **QoL outcomes** were similar to younger women.
- Age alone should not be an exclusion criterion.

Oh et al. EJSO 2016;42:604-15.

Management of the Axilla

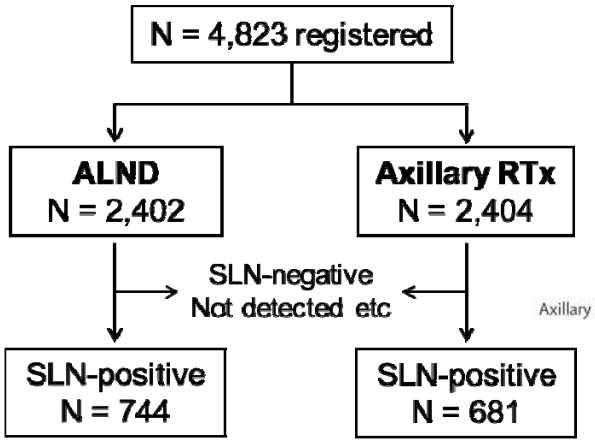
- **SLNB** is preferred in clinically node-negative disease.
- For elderly women with clinically positive ALNs who can tolerate surgery and do not meet the Z0011 criteria, **axillary dissection** represents the best treatment because no long-term difference in arm movement or pain between axillary clearance and not.

- **ALND may be omitted** in older patients had BCS and positive node based on the eligibility criteria for the Z0011 trial.

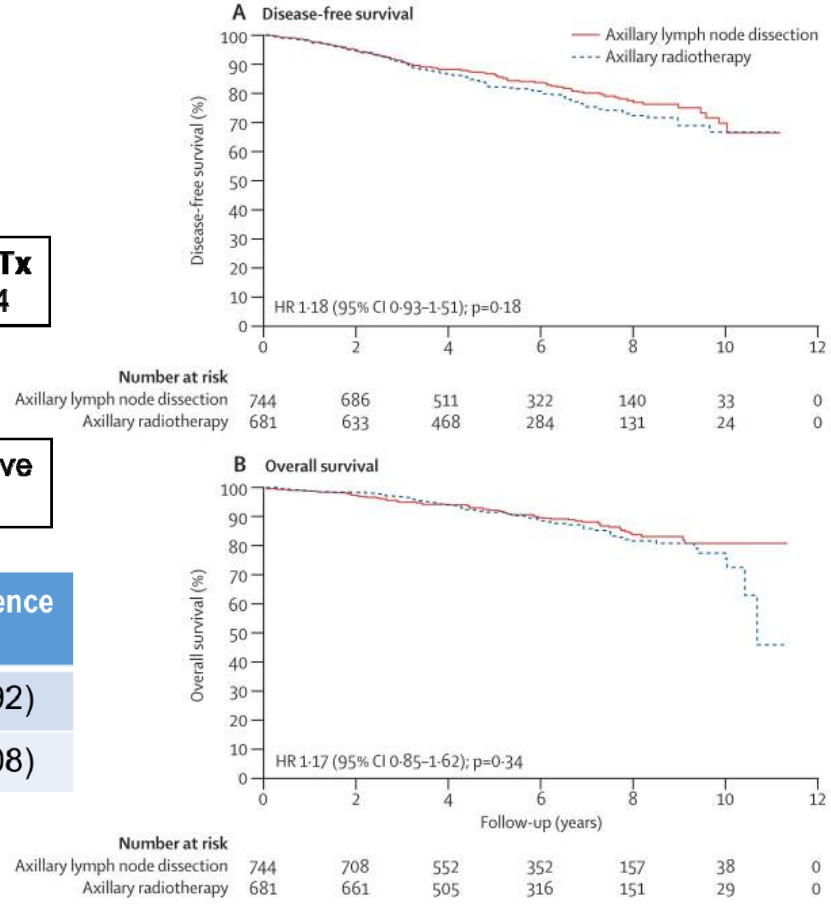
(negative margins, T1 or T2 tumor, SLN ≤ 2 involved, not matted LN, no extranodal extension, no preoperative therapy)

ALND vs Axillary RTx for SLN-positive Disease

- Alternative to completion ALND for SLN-positive disease is **axillary irradiation** (EORTC 10981-22023 AMAROS trial).



	5-yr axillary recurrence (95% CI)
ALND	0.43% (0.00-0.92)
Axillary RTx	1.19% (0.31-2.08)



Lymphoedema

	Axillary lymph node dissection	Axillary radiotherapy	p value
Clinical sign of lymphoedema in the ipsilateral arm			
Baseline	3/655 (<1%)	0/586 (0%)	0.25
1 year	114/410 (28%)	62/410 (15%)	<0.0001
3 years	84/373 (23%)	47/341 (14%)	0.003
5 years	76/328 (23%)	31/286 (11%)	<0.0001
Arm circumference increase >10% of the ipsilateral upper or lower arm, or both			
Baseline	33/655 (5%)	24/586 (4%)	0.497
1 year	32/410 (8%)	24/410 (6%)	0.332
3 years	38/373 (10%)	22/341 (6%)	0.080
5 years	43/328 (13%)	16/286 (5%)	0.0009

Data are n/N (%), unless otherwise specified.

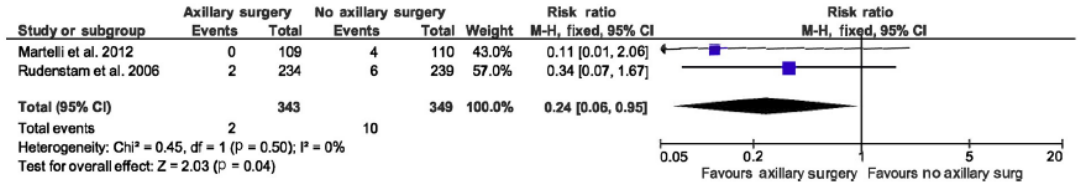
Donker et al. Lancet Oncol 2014;15:1303-10.

Omission of Axillary Staging
: Systematic review and meta-analysis

Study	Accrual period	Population	Follow-up (range)	Axillary surgery / No axillary surgery	Primary outcome	Secondary outcome	Adjuvant treatment
Martelli et al. (Single center)	1996–2000	Age 65–80 (median 70), cT1N0	50 (125–175)	109 / 110	OS and BCSS	Ipsilateral and contralateral breast cancer, distant metastasis. Overt axillary disease for no Axillary Dissection	WBRT, TAM 5 yrs
Rudenstam et al. (multicenter)	1993–2002	Age > 60 (median 74), node-negative	79	234 / 237	Quality of life	OS, DFS, and breast cancer Mortality	RTx for BCS, TAM 5 yrs

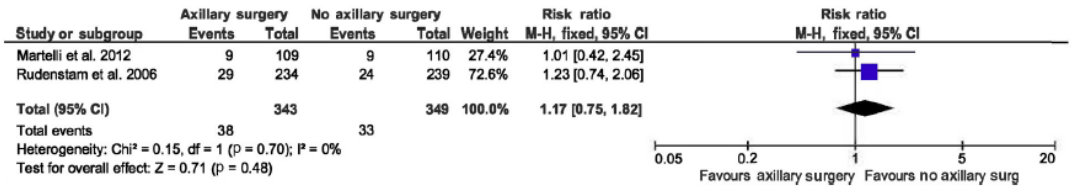
Axilla recur (surgery); RR = 0.24, **p=0.04**

Table 3A
Forest plot of pooled effect of axillary dissection versus no axillary dissection on recurrence in the axilla.



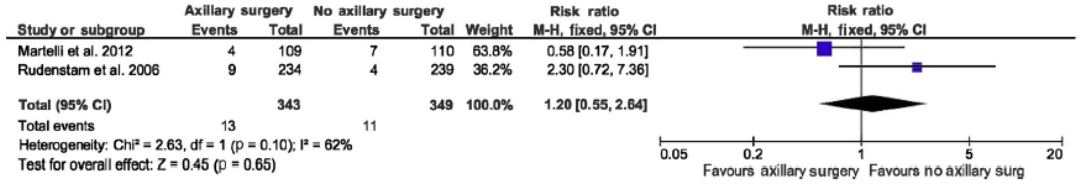
Distant recur (surgery); RR = 1.17, p=0.48

Table 3C
Forest plot of pooled effect of axillary dissection versus no axillary dissection on distant recurrence.



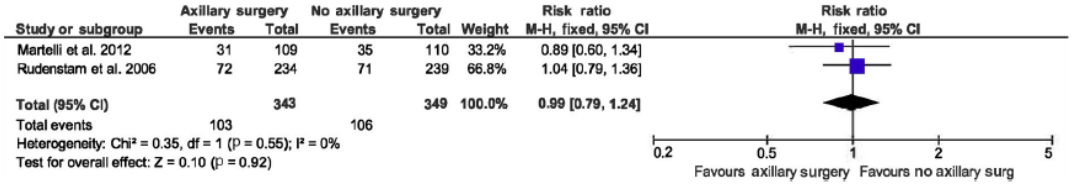
In-Breast recur (surgery); RR = 1.20, p=0.65

Table 3B
Forest plot of pooled effect of axillary dissection versus no axillary dissection on recurrence in the breast.



Overall survival (surgery); RR = 0.99, p=0.92

Table 4A
Forest plot of pooled effect of axillary dissection versus no axillary dissection on overall mortality.



Liang et al. J Geriatr Oncol 2017;8:140-7.

Omission of Axillary Staging

- Axillary evaluation may not always be necessary in the elderly women with clinically benign preoperative nodal exam.
- T ≤ 2cm, ER-positive or PR-positive, and BCS

-> axillary evaluation, even with SLNB, has little utility.

-> Omission of SLNB might be possible in some elderly patients.

- T > 2cm, ER-negative and PR-negative

-> SLNB to determine who might best benefit from adjuvant chemotherapy or axillary treatment.

Radiation Therapy

- Older women **tolerate breast irradiation** with good to excellent cosmesis.
- Chronologic age alone should not be a limiting factor in its inclusion.

- EBCTCG meta-analysis confirm radiotherapy after BCS reduces the risk of local failure as well as death rate.
- But local recurrence was inversely associated with patients' age therefore, the benefit might be less significant as increasing age.
- In **elderly** with **advanced disease (T3-4 or N2-3)**, **PMRT** improves the survival but still remains debatable in patients with N1 status or individual risk factors of local recurrence.

Booster after BCS

- EORTC 22881-10882 Trial (16 Gy booster vs no; median 10.8 yrs)

: **Higher dose** improved local control but severe fibrosis increased.

: No difference in survival.

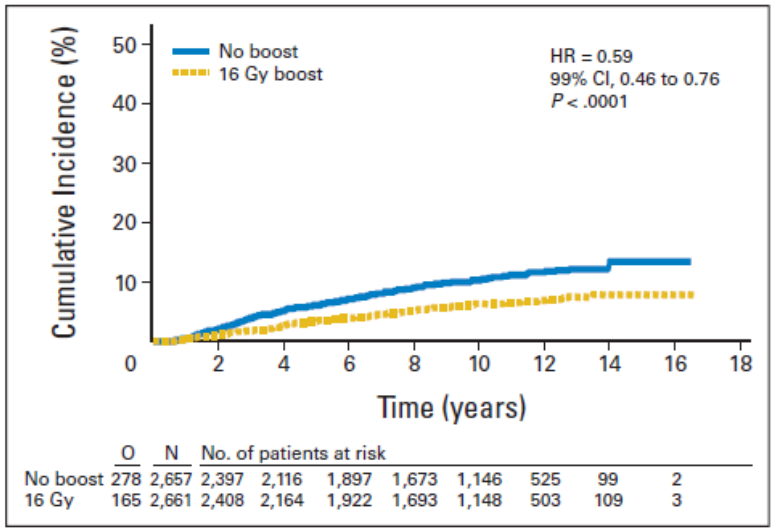
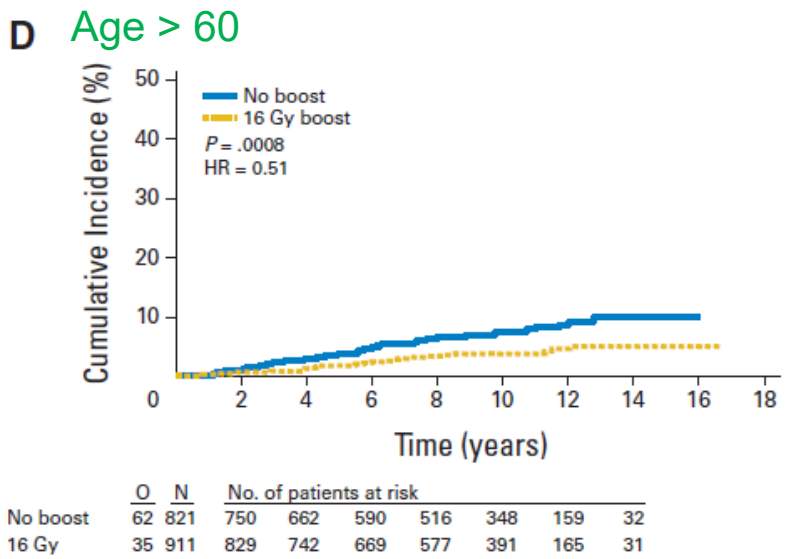


Fig 2. Cumulative incidence of recurrence of tumor as first event in the ipsilateral breast after 50 Gy whole-breast irradiation or 50 Gy whole-breast irradiation and a boost of 16 Gy. HR, hazard ratio; O, occurrences; N, number of patients at risk.



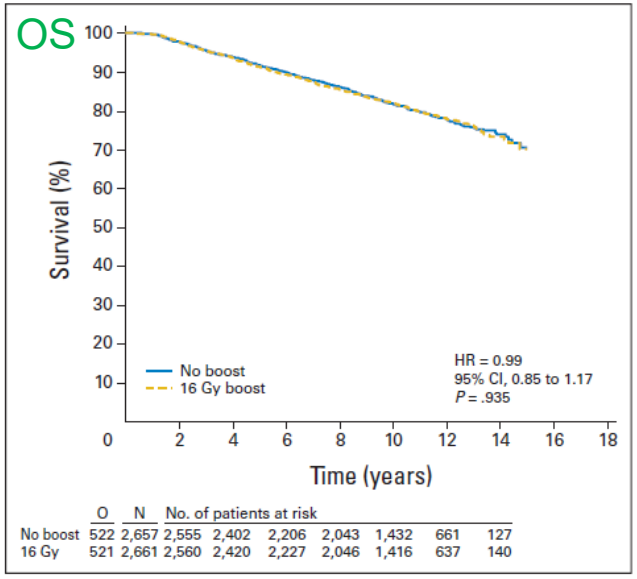


Fig 5. Survival after 50 Gy irradiation of the breast or 50 Gy irradiation and a boost. HR, hazard ratio; O, occurrences; N, number of patients at risk.

Bartelink et al. J Clin Oncol 2007;25:3259-65.

Omitting Radiation Therapy
A systematic review & meta-analysis

Ref (year)	N (total)	N (70+)	Study period	Age	Inclusion criteria					Intervention	Control	Primary outcome
					Tumor	Hormone receptor	Surgery (BCS)	Axillary staging	Adju. EndoTx			
PRIME II (2015)	1,326	1,326	03-09	≥65	≤3cm, N0	ER/PR+	(-) margin (≥1mm)	SLNB or ALND	TAM 5yr; other ET allowed	WBRT (40–50 Gy); boost 10–15 Gy permitted	No RT	IBTR
CALGB 9343 (2004)	636	636	94-99	≥70	≤2cm, N0	ER+	(-) inked margin	Clinical ALND allowed, but discouraged	TAM 5yr	WBRT (45 Gy); boost up to 14 Gy	No RT	Local or regional recurrence
Fyles (2004)	769	325	92-00	≥50	≤5cm, N0	Any (81% ER+)	(-) inked margin	ALND or Clinical	TAM 5yr	WBRT (40 Gy); boost 12.5 Gy	No RT	DFS
Fisher (2002)	673	100	89-94, 96-98	Any	<1cm, N0	Any	(-) margin	ALND	TAM (BID) 5yr	WBRT (50 Gy); no boost	No RT	IBTR

Chesney et al. Radiat and Oncol 2017;123:1-9.

Outcomes	Relative effect (95% CI)	Illustrative comparative risks, per 1000 patients (95% CI)		Risk difference, per 1000 patients (95% CI)
		Assumed risk TAM alone	Corresponding risk TAM and RTx	
IBTR at 5 yrs (n=2387)	**0.18 (0.10–0.34)**	60	10 (6–20)	50 fewer (40 fewer to 54 fewer)
IBTR at 10 yrs (n=891)	**0.27 (0.13–0.54)**	80	20 (10–40)	60 fewer (40 fewer to 70 fewer)
Axillary Recurrence at 5 yrs (n=2287)	**0.28 (0.10–0.81)**	12	3 (1–10)	9 fewer (2 fewer to 11 fewer)
Distant Recurrence at 5 yrs (n=2287)	1.49 (0.87–2.54); N-S	22	30 (20–50)	8 more (28 more to 2 fewer)
Overall Survival at 5 yrs (n=2287)	0.98 (0.79–1.22); N-S	165	160 (130–200)	5 fewer (35 more to 35 fewer)

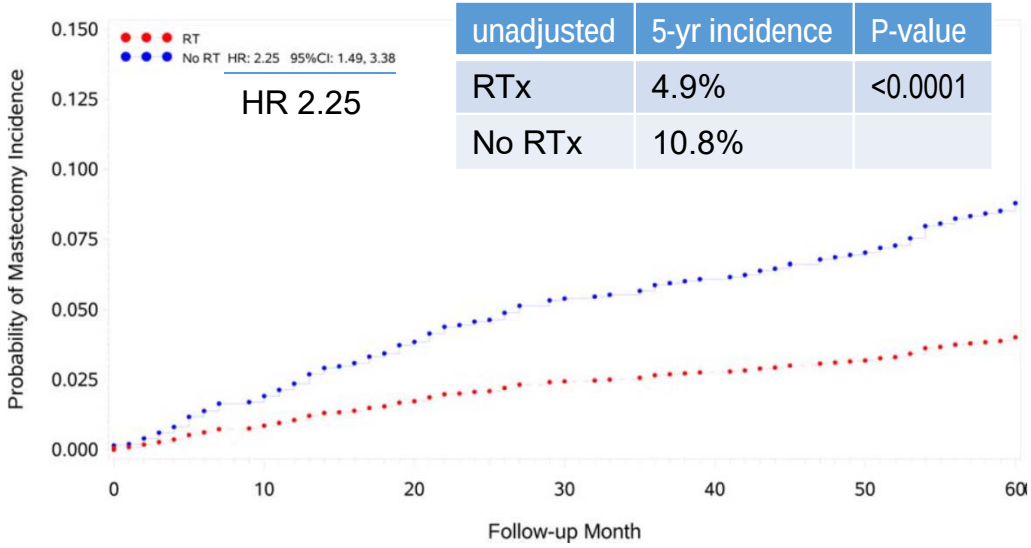
- For elderly women (≥ 70 yrs), **radiotherapy reduces the risk of breast and axillary recurrence**, but does not impact DRFS, BCCS, or OS in EBC treated with BCS and TAM.
- The value of this risk reduction must be weighed by women and their physicians when considering the omission of adjuvant radiotherapy.

Chesney et al. Radiat and Oncol 2017;123:1-9.

BCT among elderly women (≥ 70 yrs) with T1-2 N0 ER-Negative breast cancer

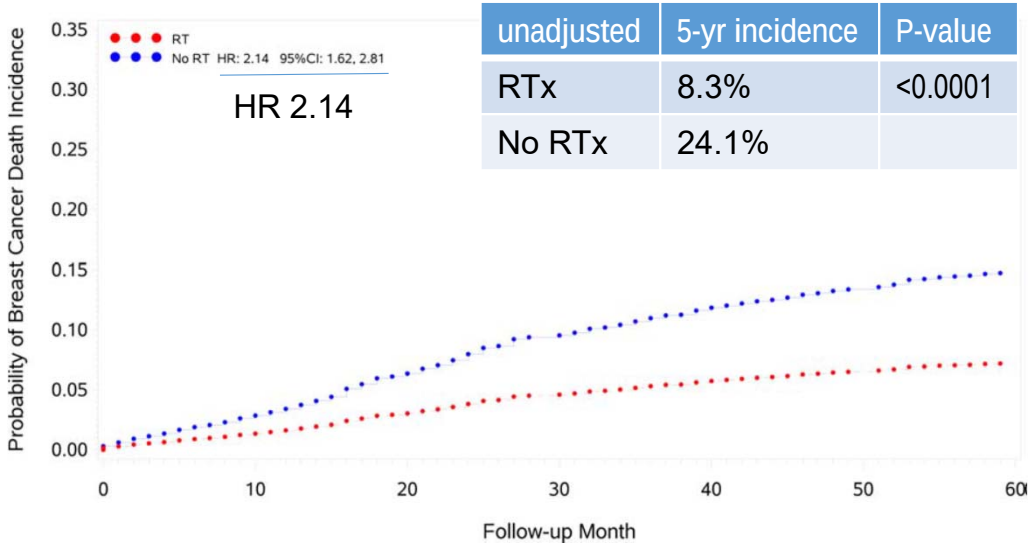
- SEER-Medicare-linked data, N = 3,432
- **Radiotherapy** after BCS in elderly with T1-2N0 ER(-) is associated with a reduced incidence of future mastectomy and breast cancer death.
- Probably smaller benefit in women aged ≥ 80 years or T1 tumors.

Adjusted Cumulative Incidence of Mastectomy Curves Comparing the Effect of Radition



unadjusted	5-yr incidence	P-value
RTx	4.9%	<0.0001
No RTx	10.8%	

Adjusted Cumulative Incidence of Breast Cancer Death Curves Comparing the Effect of Radition



unadjusted	5-yr incidence	P-value
RTx	8.3%	<0.0001
No RTx	24.1%	

Eaton et al. Cancer 2016;122:3059-68.

Schedule of Radiation Therapy

✓The schedule and duration of RTx may be obstacles in the elderly.

- **Hypofraction** radiation schedule (13-16 vs standard 25 fractions)

: Comparable locoregional relapse and less common toxicity.

	Inclusion criteria	Treatment: hypofractionation versus WBRT	Local recurrence rate	Comment
Bentzen et al; START A (2008)[37]	BCS or mastectomy	39 Gy in 13 fractions over 5 weeks versus 41·6 Gy in 13 fractions over 5 weeks versus 50 Gy in 25 fractions over 5 weeks	5·2% (5 year) 3·5% (5 year) 3·6% (5 year)	..
Bentzen et al; START B (2008)[38]	BCS or mastectomy	40 Gy in 15 fractions over 3 weeks versus 50 Gy in 25 fractions over 5 weeks	2·2% (5 year) 3·3% (5 year)	Better breast cosmesis with hypofractionation
Whelan et al; Canadian trial (2010)[39]	BCS, TI–2N0M0, clear resection margins	42·5 Gy in 16 fractions over 3 weeks versus 50 Gy in 25 fractions over 5 weeks	6·2% (10 year) 6·7% (10 year)	No significant difference in breast cosmesis and late cardiotoxicity between treatment groups

WBRT–whole-breast radiotherapy. BCS–breast-conserving surgery.

Table 3: Studies of hypofractionation versus standard fractionation WBRT

Biganzoli et al. Lancet Oncol 2012;13:e148-60.

PBI for the elderly

- **Accelerated partial breast irradiation (PBI)**

: Intra/postoperative brachytherapy (interstitial implants, MammoSite balloon catheter)

: targeted intraoperative radiotherapy (TARGIT), and

: electron intraoperative radiotherapy (ELIOT)

- A meta-analysis of RCT showed **PBI** was associated with higher risk of local & axillary failure but comparable OS & distant metastasis were demonstrated.

Valachis et al. Breast J 2010;16:245-51.

- This might be an option for low-risk elderly patients.

Conclusion (I)

- **Management of elderly** breast cancer is **complex** because this population is also heterogeneous.
- **Limited data** are available, mainly because the aging population is poorly represented, especially in randomized clinical trials.
- It is appropriate for patient to participate in decision-making process, since elderly preferences often favor quality of life and independence.

- **Local treatment of breast and axilla for elderly** women should be managed similarly to young women.
- **Chronologic age alone** does not provide adequate information.

Conclusion (II)

- Considering life expectancy, CGA, the risk/benefit of treatment, tumor biology and available data, optimal local therapy should be determined for elderly patients with breast cancer.
- Clinicians should inform their patients that **under-treatment** strongly increases the risk of loco-regional recurrence but not survival.

- **Multidisciplinary approach** between **oncology** and **geriatrics teams** can result in the facilitation of treatment and the coordination of care for elderly cancer patients.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