GERIATRIC ONCOLOGY

WHAT IS DIFFERENT IN THE TREATMENT OF CANCER ELDERLY ?

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Department of Medical Oncology
(Prof Jerusalem)
Breast and GI tumors
CHU ST LIEGE
BELGIUM

OLDER PATIENTS AND CANCER

The older population with cancer is increasing but there is still paucity of data because this population was during many year underrepresented in clinical trials and because of the heterogeneity. Older in clinical trials generally were the most fit that do not represent the all population in the real life

Chronological Age
≠
Functional Age

WHAT IS GERIATRIC ONCOLOGY

ONCOLOGISTS HAVE TO IMPLANT GERIATRIC PRINCIPLES TO MANAGE OLDER PATIENTS WITH CANCER

NEEDS FOR COLLABORATION
BETWEEN
GERIATRICIANS
AND CLINICAL ONCOLOGIST
AND OTHER SPECIALISTS

WHAT IS GERIATRIC ONCOLOGY

All Oncologists Are Geriatric Oncologists...They Just Don't Know It Yet

By Stuart Lichtman, MD, FACP, FASCO

August 25, 2019

DEFINITION

WHAT IS GERIATRIC ONCOLOGY ?

GO initiatives across the globe are revolutionizing the way older adults with cancer are being treated.

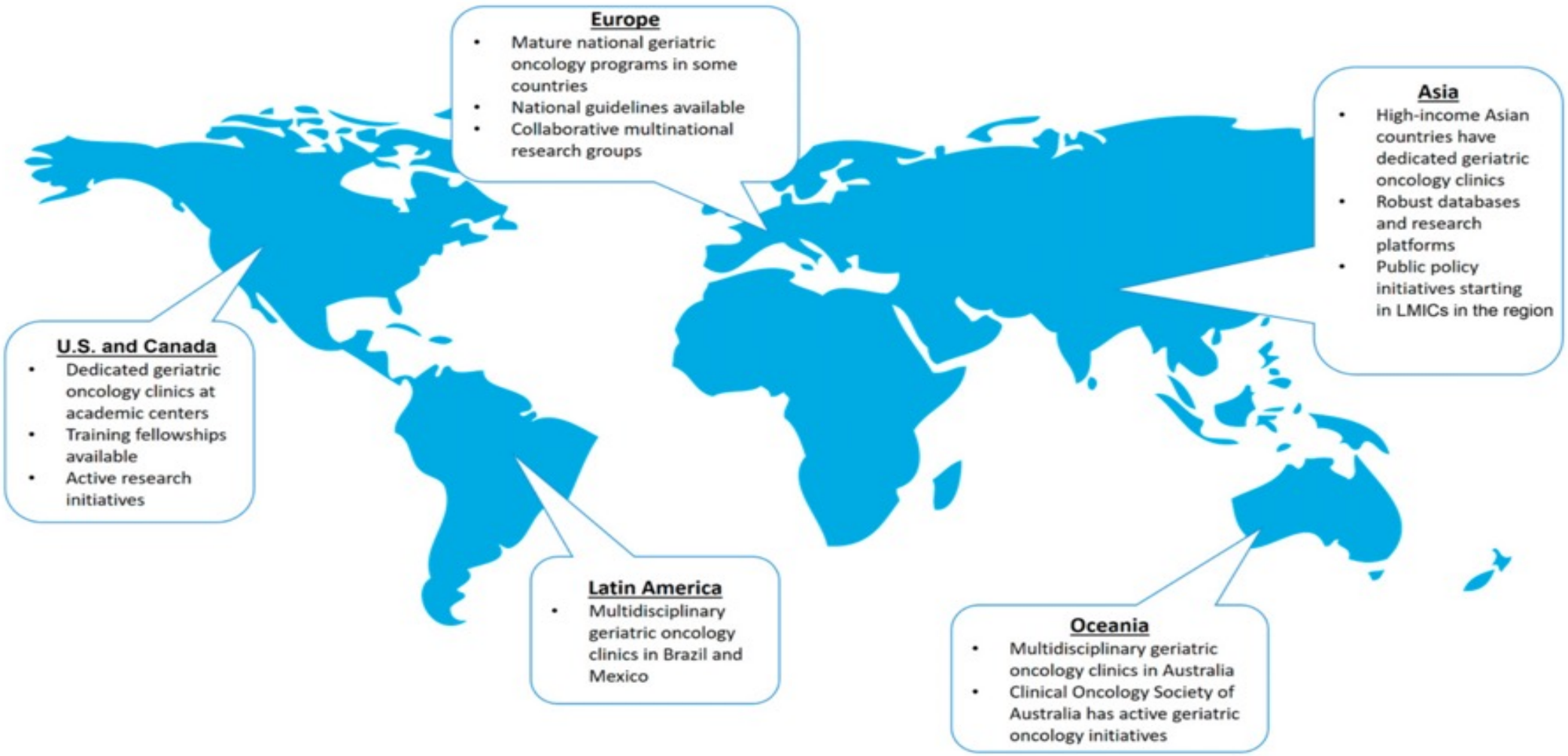


FIGURE 1. Global Geriatric Oncology Initiatives by Continent

Ravindran Kanesvaran, ; Supriya Mohile, ; Enrique Soto-Perez-de-Celis, ; and Harpreet Singh,
ASCO EDUCATIONAL BOOK 2020

WHAT IS GERIATRIC ONCOLOGY ?

SIOG

INTERNATIONAL SOCIETY
OF GERIATRIC ONCOLOGY

To improve the care of older patients with cancer around the world

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

European Society for Medical Oncology

ESMO HANDBOOK OF
CANCER IN THE SENIOR PATIENT

FROG

FRANCILIAN ONCOGERIATRIC GROUP

ASCO

American Society of Clinical Oncology

Making a world of difference in cancer care

Cancer in Older Adults

Cancer.Net

Doctor-Approved Patient Information from ASCO®

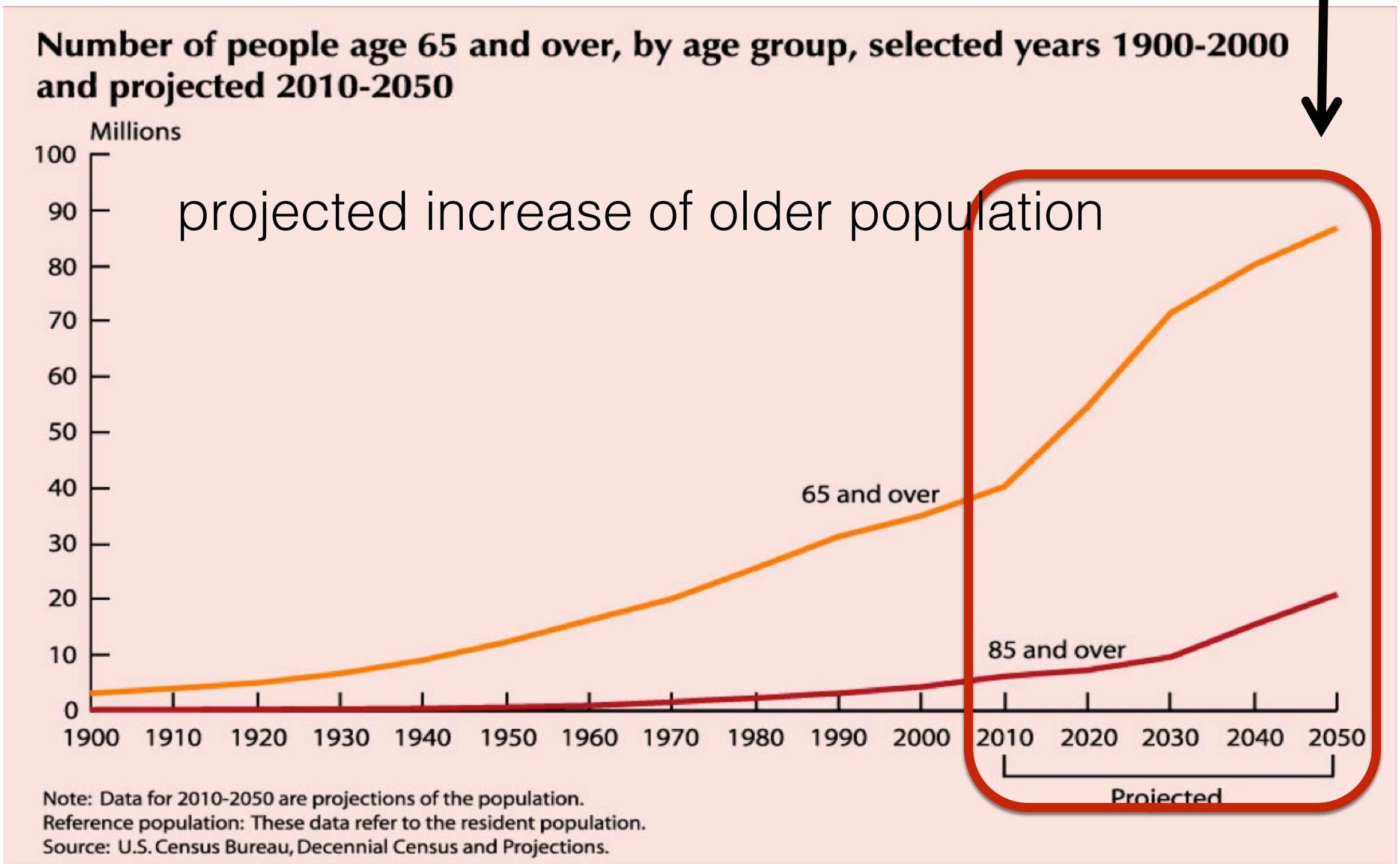
Different task forces around the world develop guidelines and recommendations for GO

EPIDEMIOLOGY

WHY GERIATRIC ONCOLOGY ??

1) AGEING POPULATION

ELDERLY POPULATION



projected increase of older population

Causes of mortality in Western European Countries

Principle causes of deaths

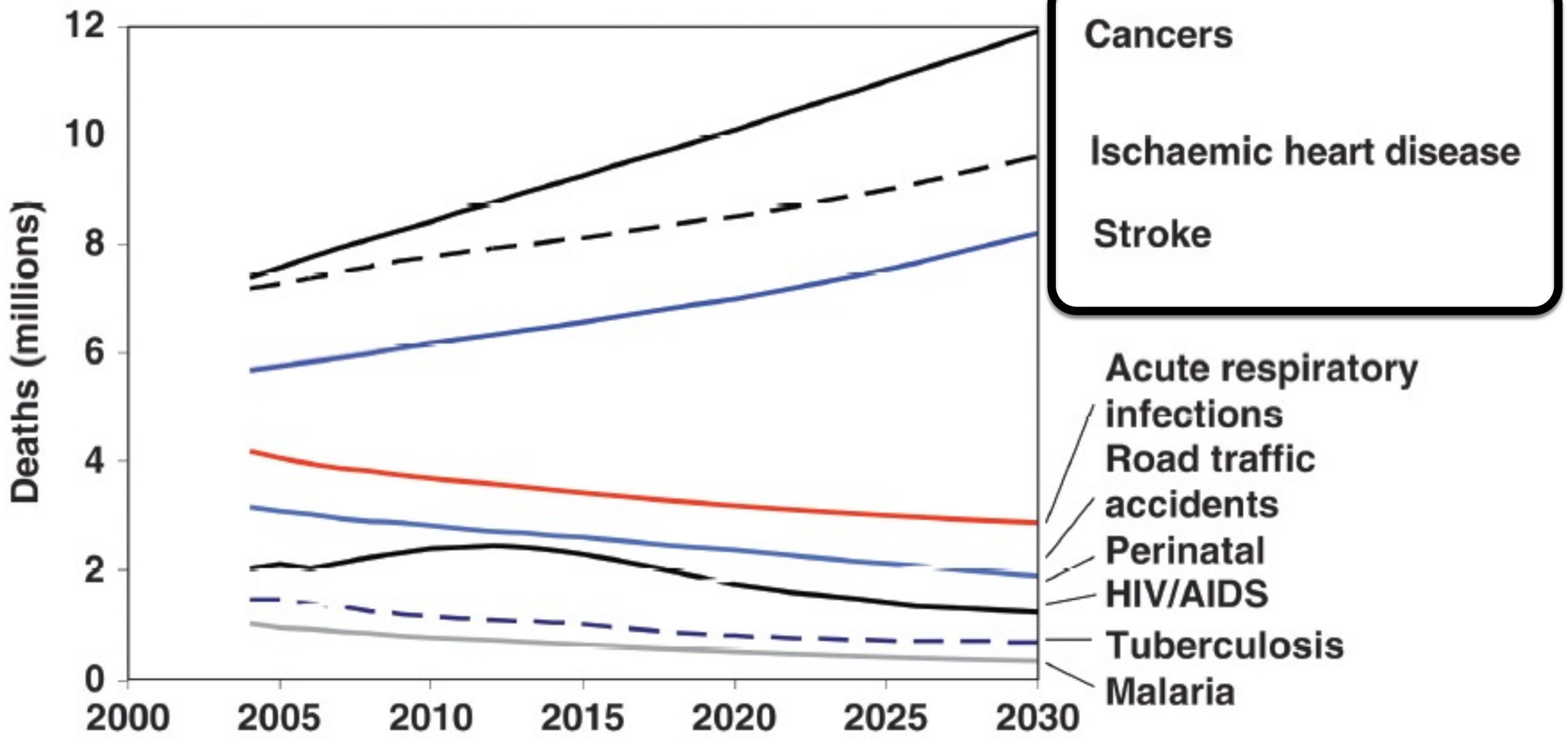
- **30,7% cardio-vascular diseases (CVD)**
- **27,6% cancers**

Men: 27,7% CVD, 32,4% cancers

Women: 33,3% CVD, 22,6% cancers

2) INCREASE OF CANCER INCIDENCE WITH AGE

CAUSES OF DEATH



INCREASING CAUSES OF DEATH:

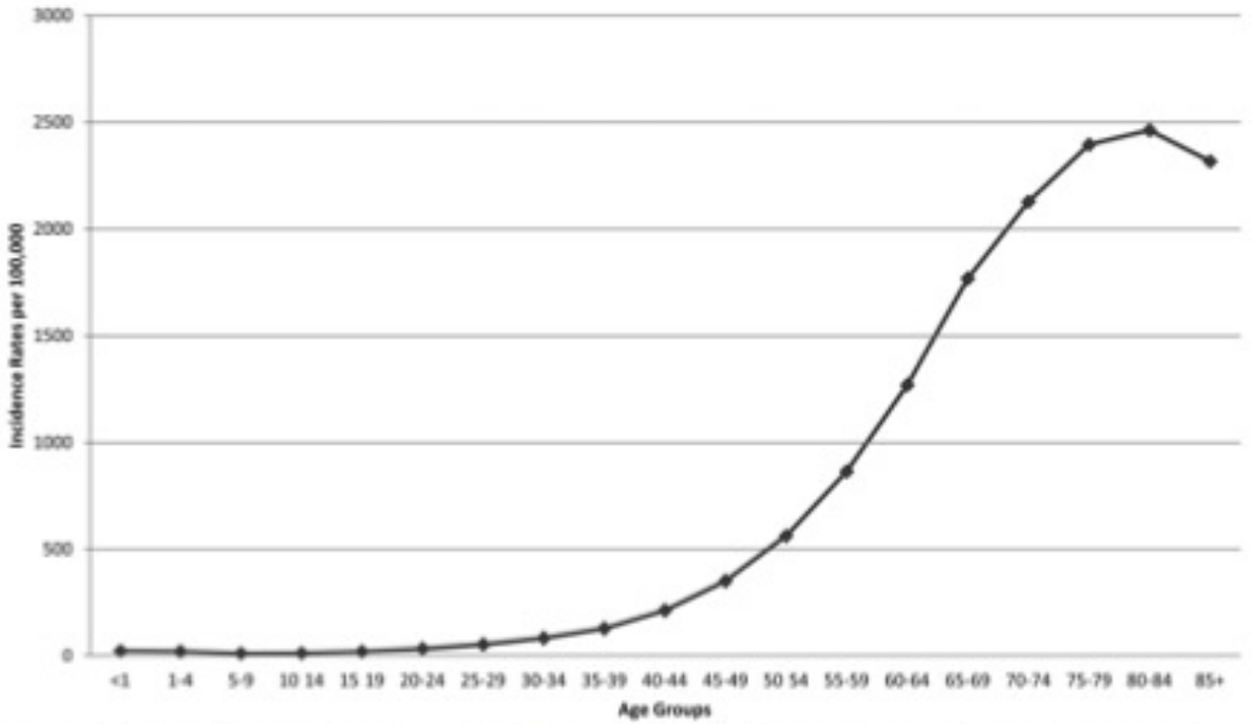
CANCERS, ISCHAEMIC HEART DISEASE, STROKE

CANCER ET AGE

- **ELDERLY POPULATION IS STEADILY INCREASING**
- **BY THE YEAR OF 2030, I FOR 5 WILL BE MORE THAN 65 YEAR OLD**
- **AGE=MOST IMPORTANT RISK FACTOR OF CANCER**
- **60 % OF CANCERS ARE DIAGNOSED AFTER 65 YEARS**
- **70 % OF MORTALITY BY CANCER OCCUR AFTER 65 YEARS**

CANCER ET AGE

Incidence increase with age but is falling after 80 years



Thakkar et Al, Am J Med Sci,2014

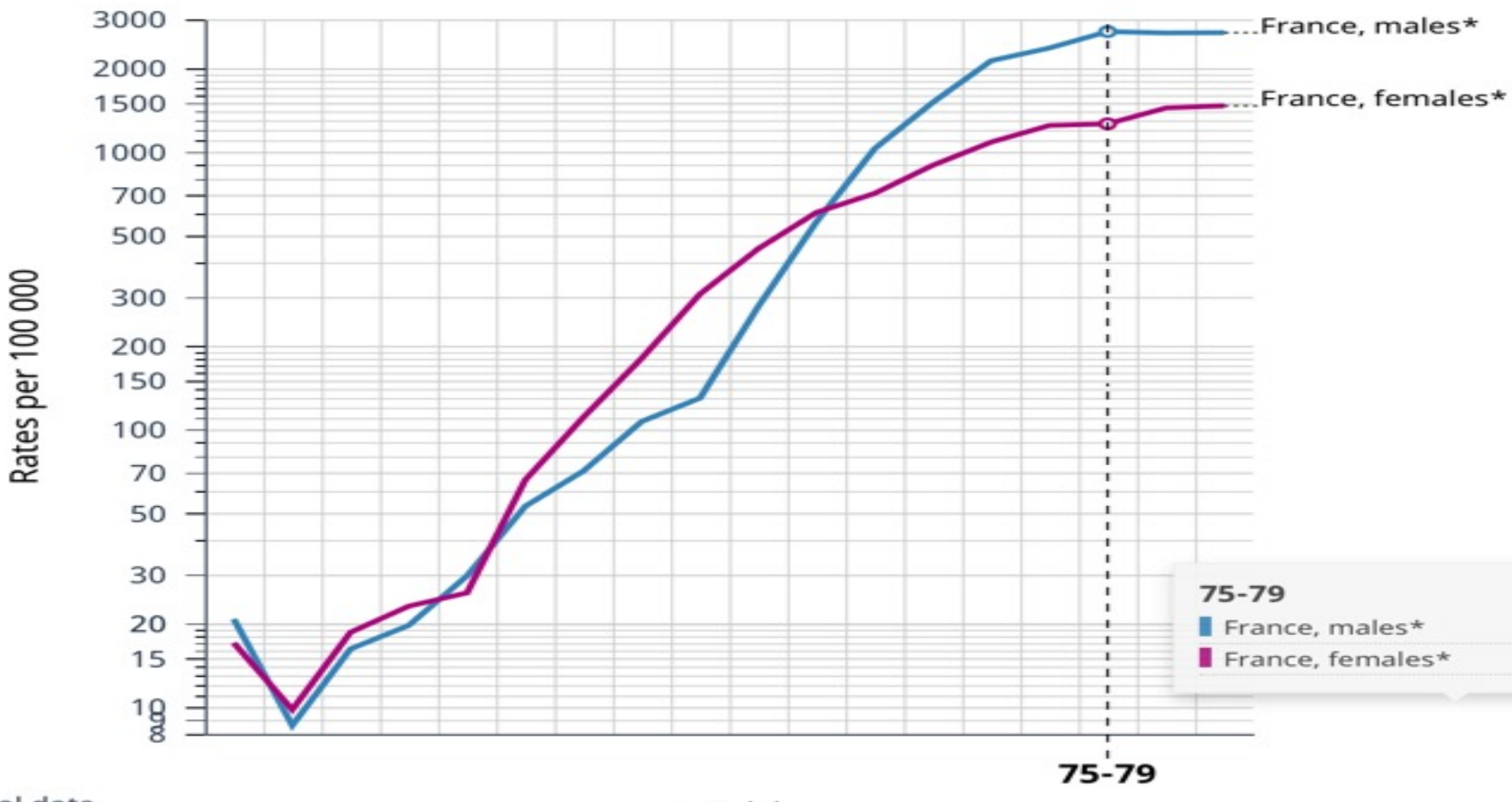
Year	Population in millions 2010	2050
World	6.909	9.150
Africa	1.033	1.998

	Age	2010	2050
World	Over 60	11	22
	Over 80	2	4
Africa	Over 60	5	11
	Over 80	0	1
Asia	Over 60	10	24
	Over 80	1	4
	Over 80	3	7

the elderly are 10 times more likely to get cancer and 15 times more likely to die from cancer than people under the age of 65 years.

CANCER ET AGE

Rates per 100 000, incidence, males and females, in 2012
All sites excl. non-melanoma skin cancer
*France**

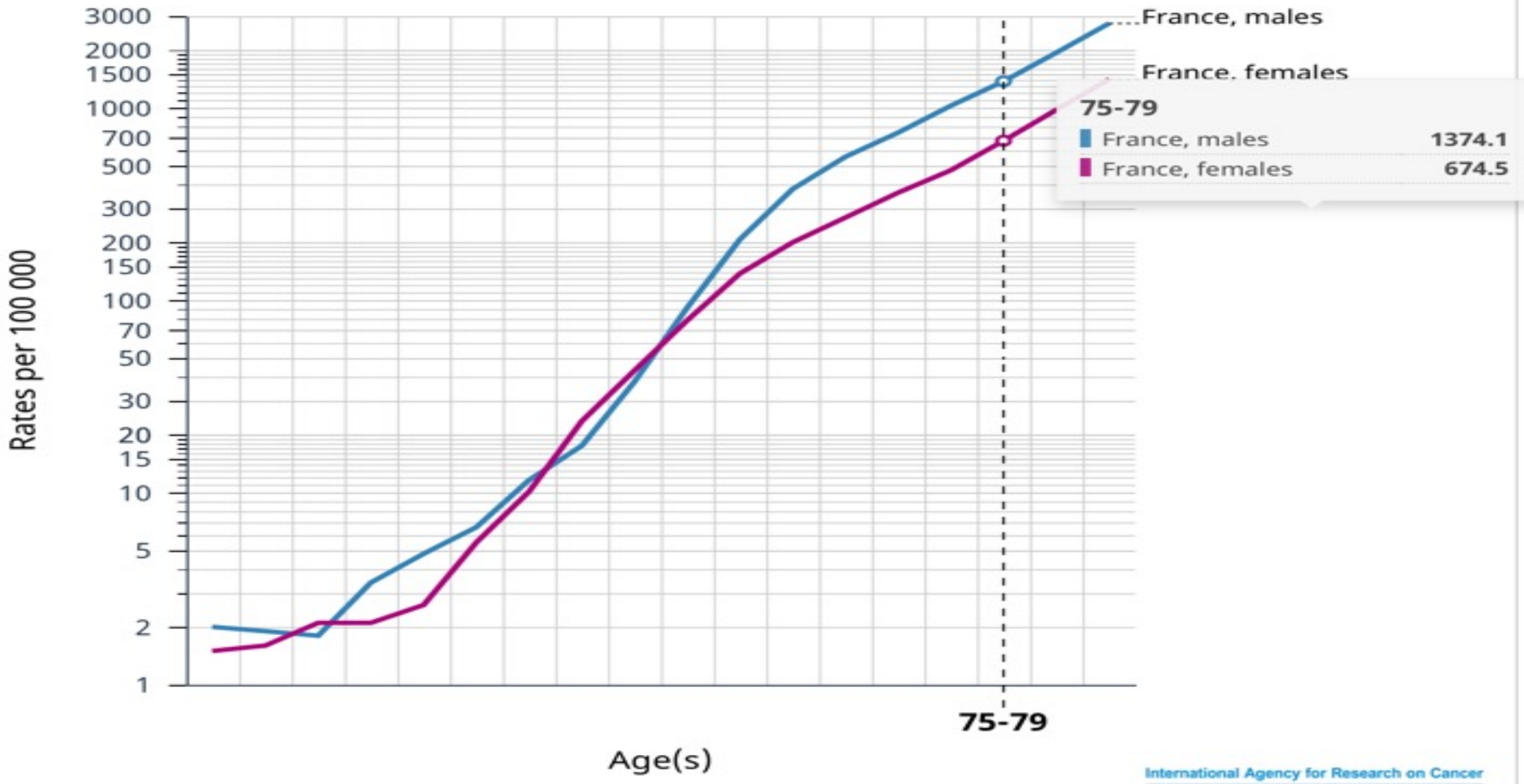


* Subnational data

International Agency for Research on Cancer
World Health Organization

CANCER ET AGE

Rates per 100 000, mortality, males and females, in 2012
All sites excl. non-melanoma skin cancer
France



International Agency for Research on Cancer
World Health Organization

CANCER ET AGE

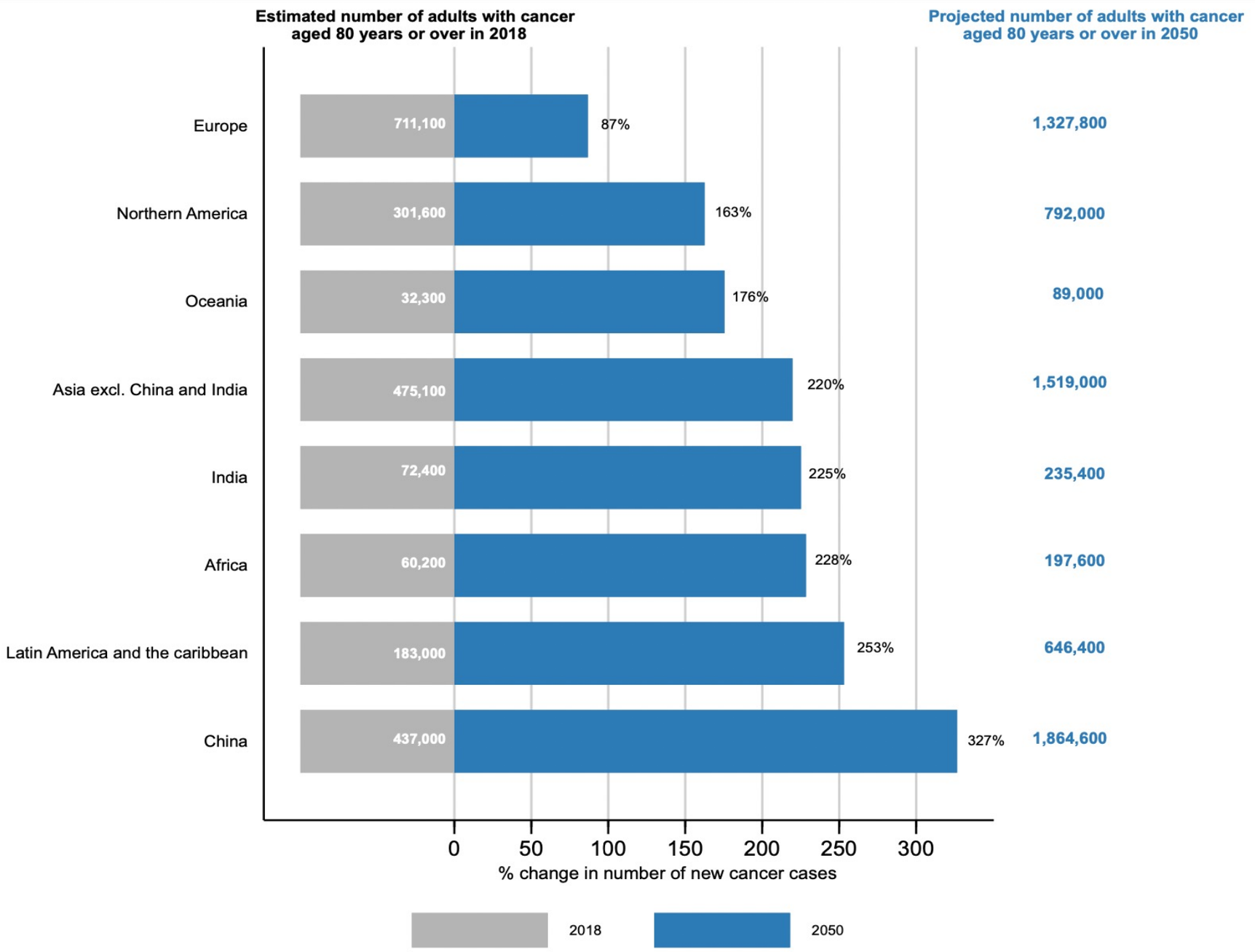


FIGURE 4 Percentage change in the number of new cancer cases among adults aged 80 years or older by 2050 by world region plus China [Color figure can be viewed at wileyonlinelibrary.com]

Int. J. Cancer. 2021;148:601–608

CANCER ET AGE

IN CONCLUSION,WHAT DO ALL THESE NUMBERS MEAN ?

1) CANCER IS A DISEASE ASSOCIATED WITH AGING:60 % of cancer ≥65 years
2) POPULATION OF CANCER SURVIVORS WILL GROW RAPIDLY IN THE NEXT FEW DECADES: by 2030 it is expected that about 19 % of the population will be age ≥ 65 years
3) AT THE SAME TIME, LENGH OF SURVIVAL FROM CANCER IS STEADILY INCREASING: earlier diagnosis and better treatment

CANCER IN ELDERLY: MANY CHALLENGES

- **Lack of data from clinical trials:**
- **Heterogeneity of the population**
- **Life expectancy**
- **Patient expectations and preferences**
- **Aging is an heteregeneous process (**not al young patient are healthy and functional ; not all older patient are sick and dependent)

Because of the significative cancer incidence and mortality in older patients, at present

Because of projected increase of older cancer patients in the next decades and the demographic effect

ONCOGERIATRIC=

MAIN challenge for healthcare
and also in bioethics
because all these older patients need to be treated in the optimal way for the cancer
but also concerning all age associated conditions

WHAT DO WE HAVE TO HELP US ?

WHAT DO WE HAVE TO HELP US ?

- **Extensive epidemiological data as shown above**
- **Data from many different studies on the results of treatment in most tumor types for elderly with guidelines and recommendations from task force groups and scientific societies**
- **special approach to evaluate older cancer patient (COMPREHENSIVE GERIATRIC ASSESSMENT)**
- **tools to predict treatment related toxicity**
- **specific methodology for clinical trials in older patients**

WHAT DO WE NEED TO HELP US ?

A BETTER INTEGRATED APPROACH BETWEEN ONCOLOGY AND GERIATRICS

- **Currently, GERIATRICIANS ARE ONLY INVOLVED IN THE DEVELOPPEMENT OF CGA**

BUT, WE NEED CHANGES

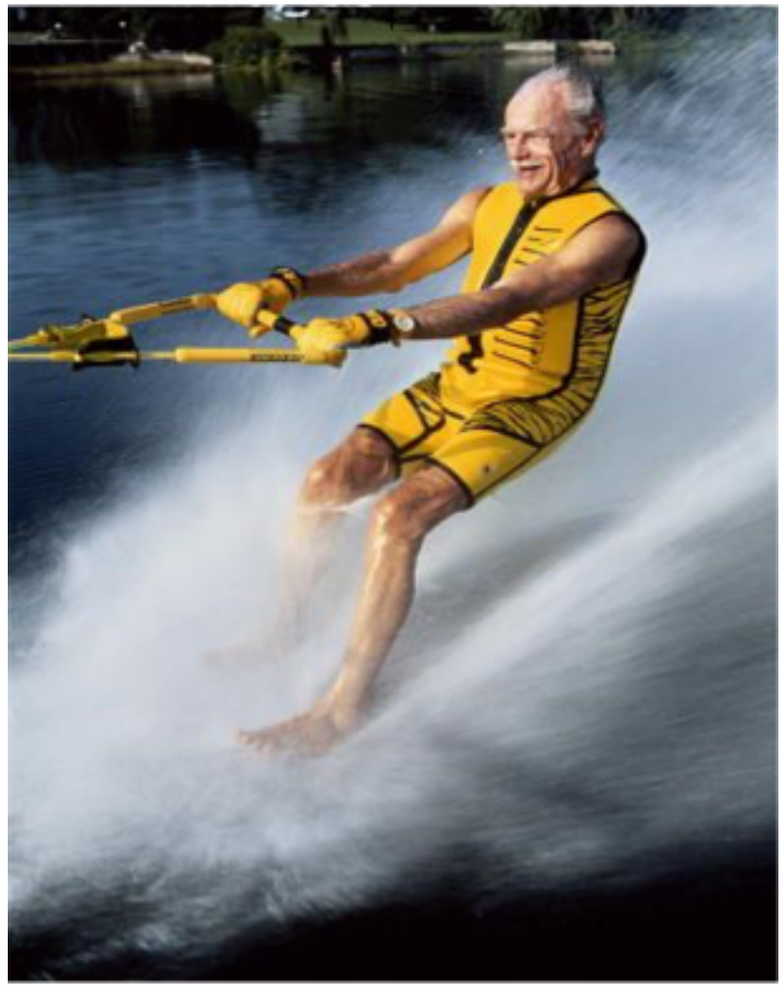
- **GERIATRICIANS HAVE A BETTER KNOWLEDGE OF THE DISEASES AFFECTING ELDERLY PATIENTS THAT MAY INTERFERE WITH THEIR CANCER TREATMENT**

- **THEY ARE ABLE TO DEAL WITH THE SOCIAL PROBLEMS IMPEDING THE MANAGEMENT OF THE NEOPLASTIC DISEASES**

- **THEY HAVE BETTER KNOWLEDGE OF AGE-RELATED OBSTACLES (VULNERABILITY PREVENTION,REHABILITY AND HOME CARE REFERRAL, STOPPING INAPPROPRIATE MEDICATIONS…)**

WHAT'S DIFFERENCE ABOUT OLDERS ?

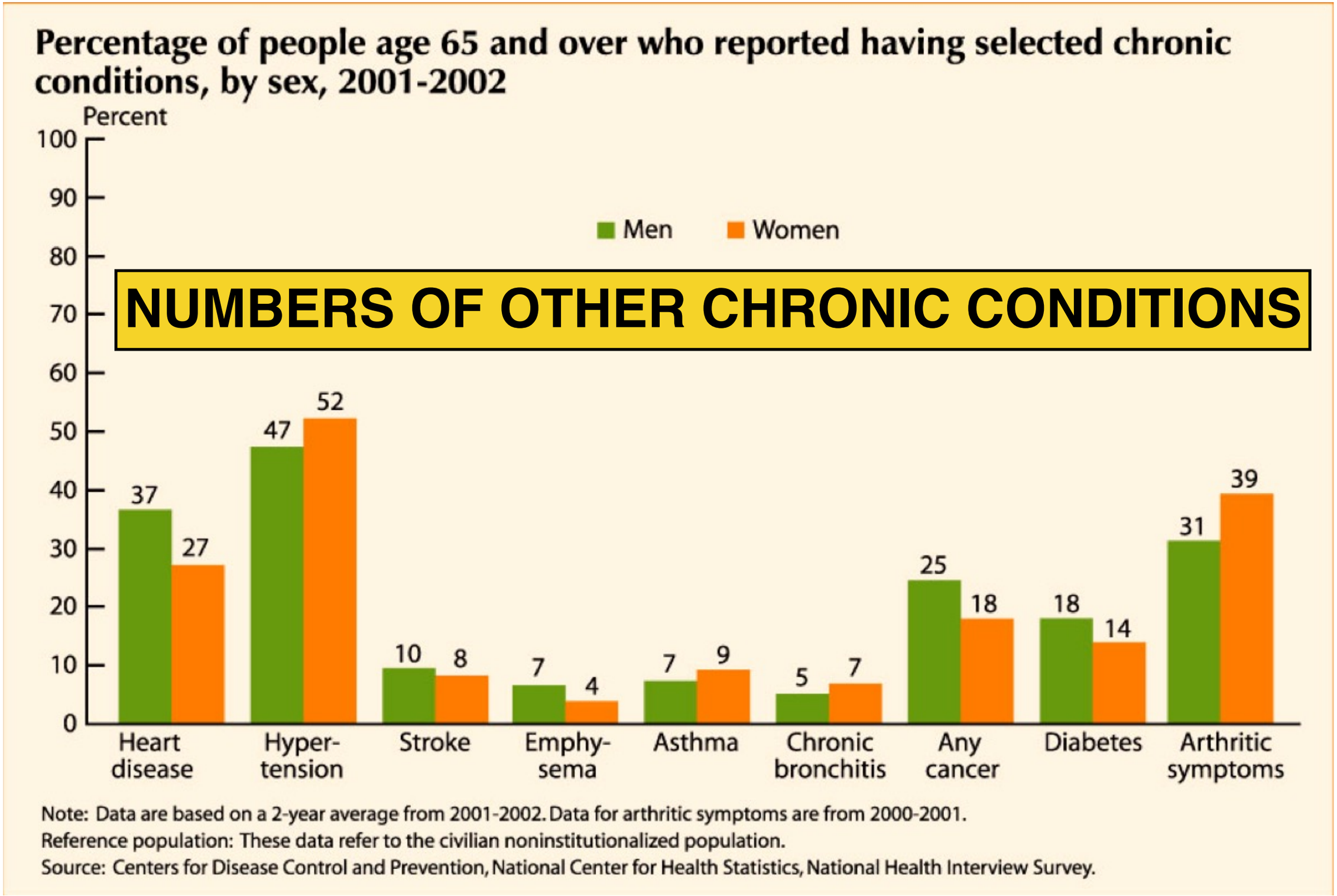
- Heterogeneity of health status
- Physiologic change
- Tendency to have multiple, often interacting disease
- some cancers progress slowly when elderly(breast cancer, prostate) but some others may be more agressive (leukemia,ovarian cancer, brain tumors)



ELDERLY

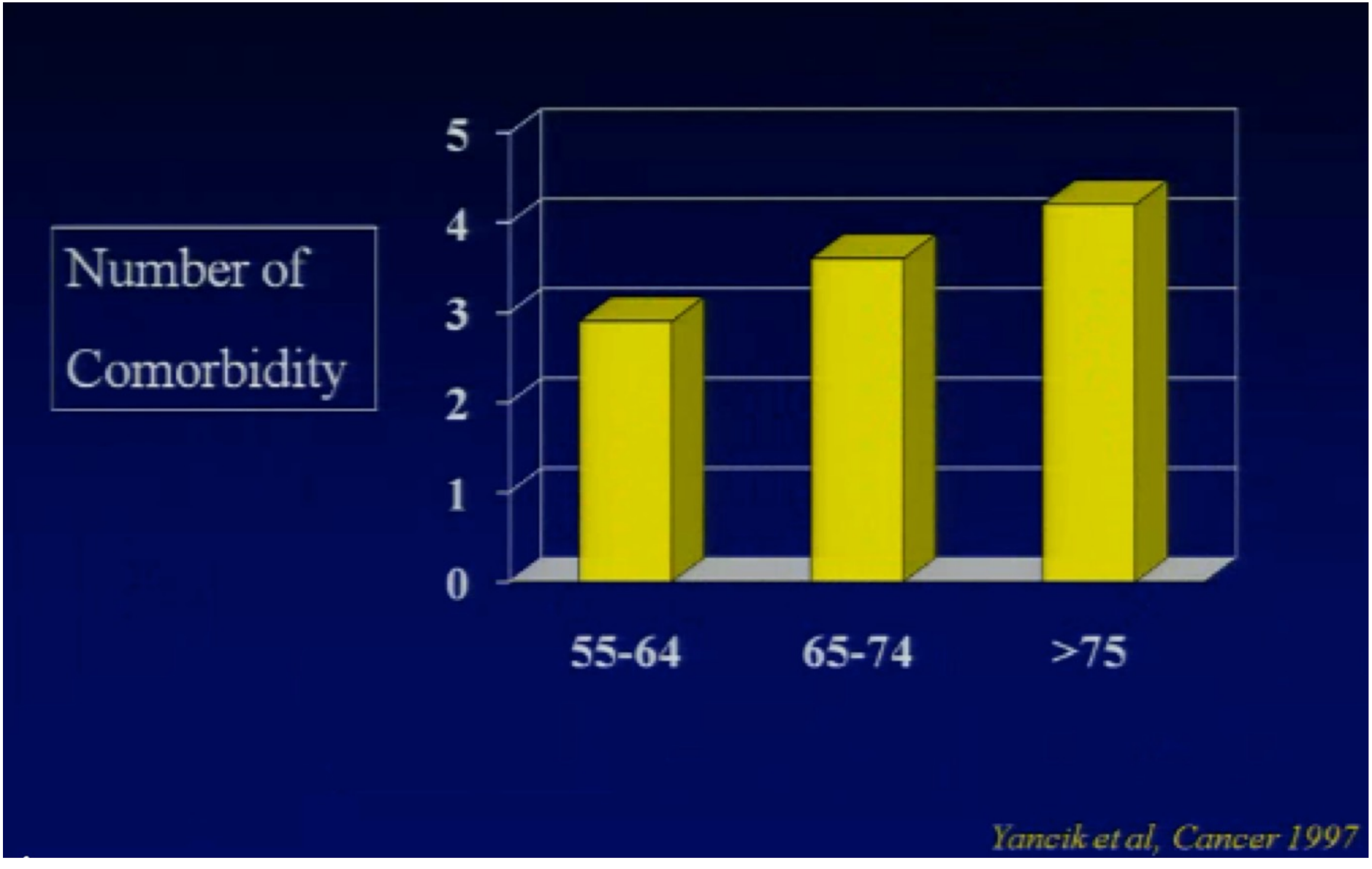
MANY DIFFERENCES IN OLDER PATIENTS ≥ 70 YEARS

WHAT'S DIFFERENCE ABOUT OLDERS ?



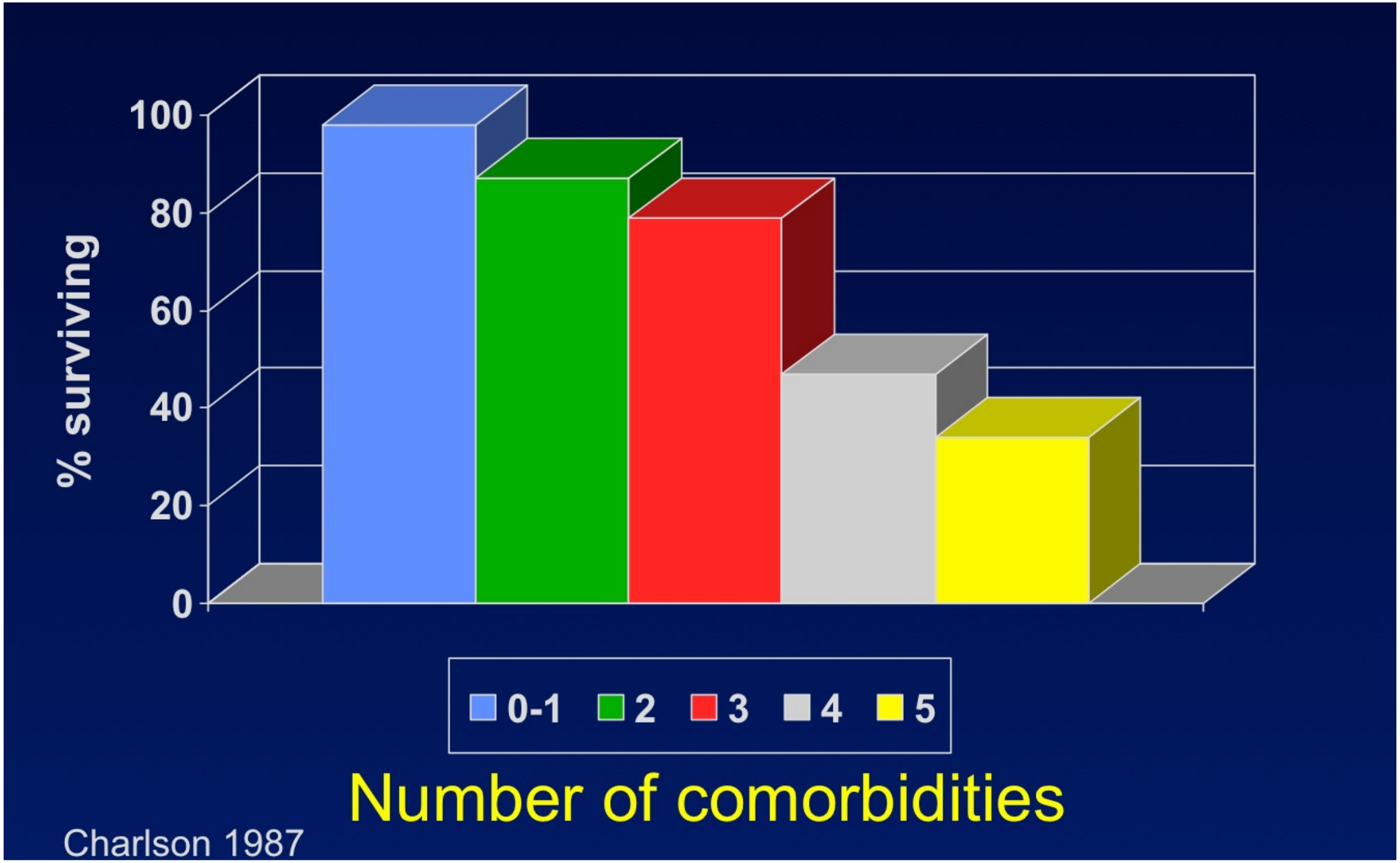
WHAT'S DIFFERENCE ABOUT OLDERS ?

Comorbidity increase with age



WHAT'S DIFFERENCE ABOUT OLDERS ?

NUMBER OF COMORBIDITIES LINK TO DECREASED 10 YEAR SURVIVAL



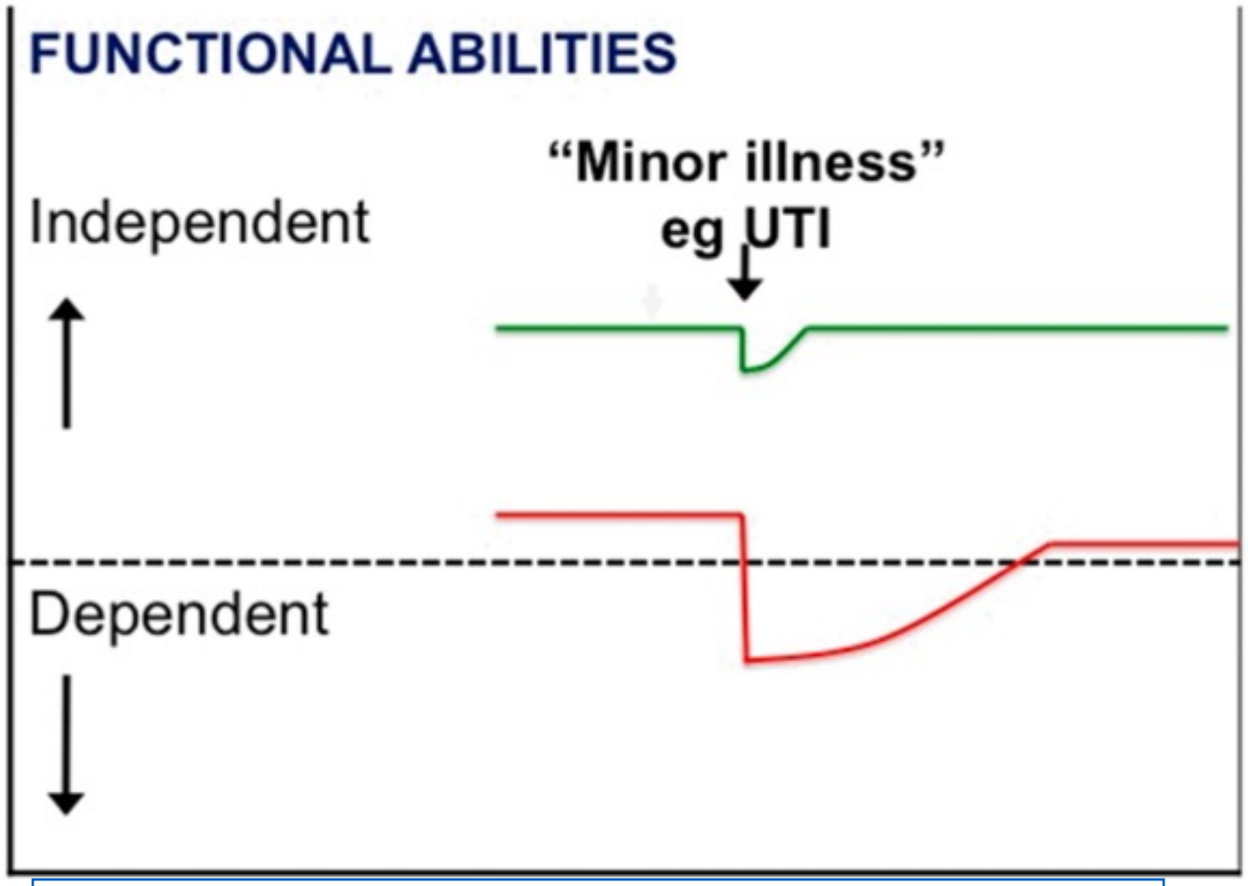
WHAT'S DIFFERENCE ABOUT OLDERS ?

- Unusual clinical presentation
- Underreporting symptoms
- Therapeutic decisions must deal with comorbidities, reduced tolerability,
- drug interaction because of high number of oral drugs (polypharmacy)

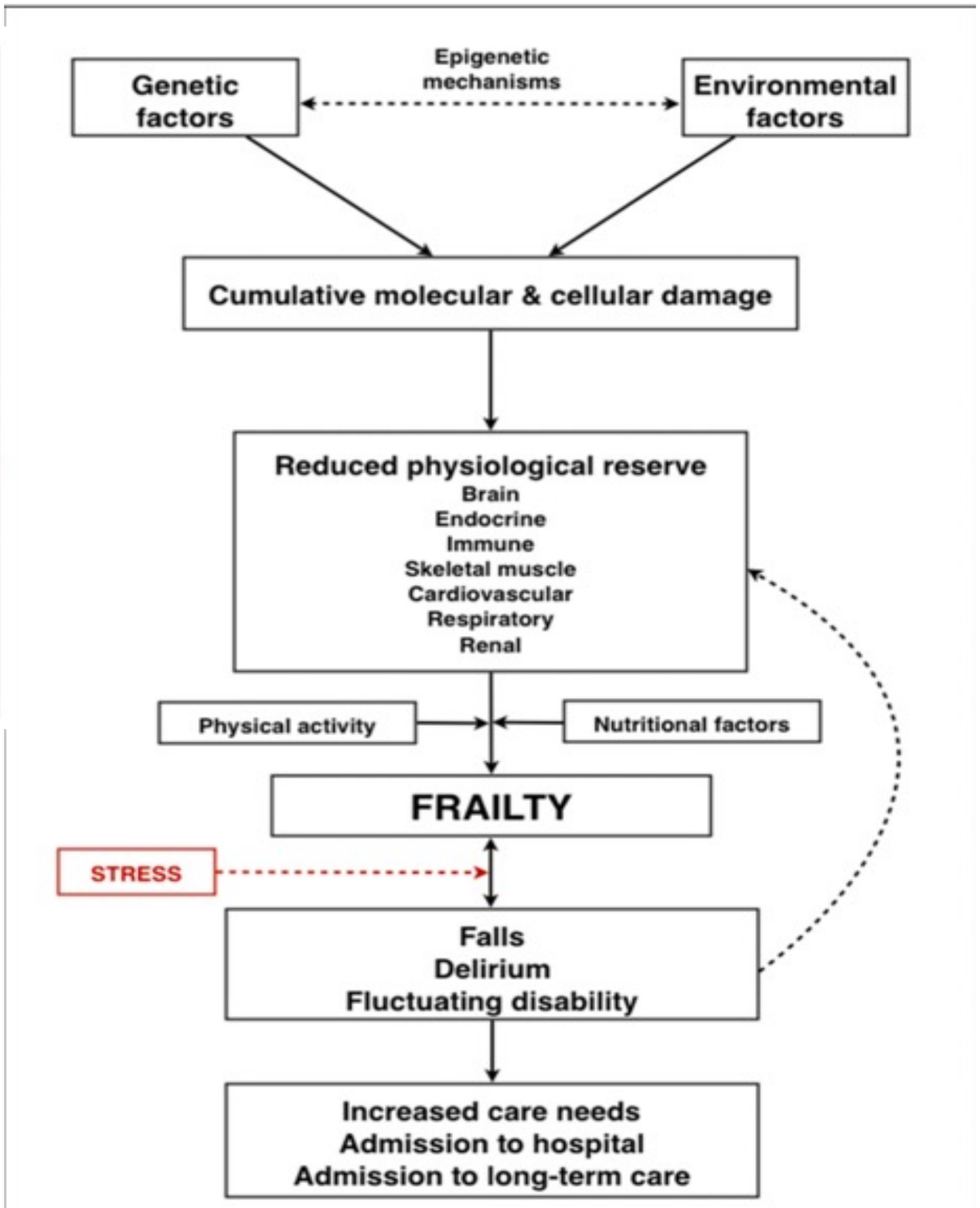
FOR ALL THESE REASONS, EVALUATION OF PS IS NOT ENOUGH TO SERVE IN BASE-LINE BEFORE TREATMENT

WE NEED MORE SPECIFIC TOOLS USED BY GERIATRICIANS

WHAT'S DIFFERENCE ABOUT OLDERS ?



FRAILTY means a state of increase vulnerability to stress like surgery,chemo,immuno,RT …increasing the risk of adverse outcome and dependance



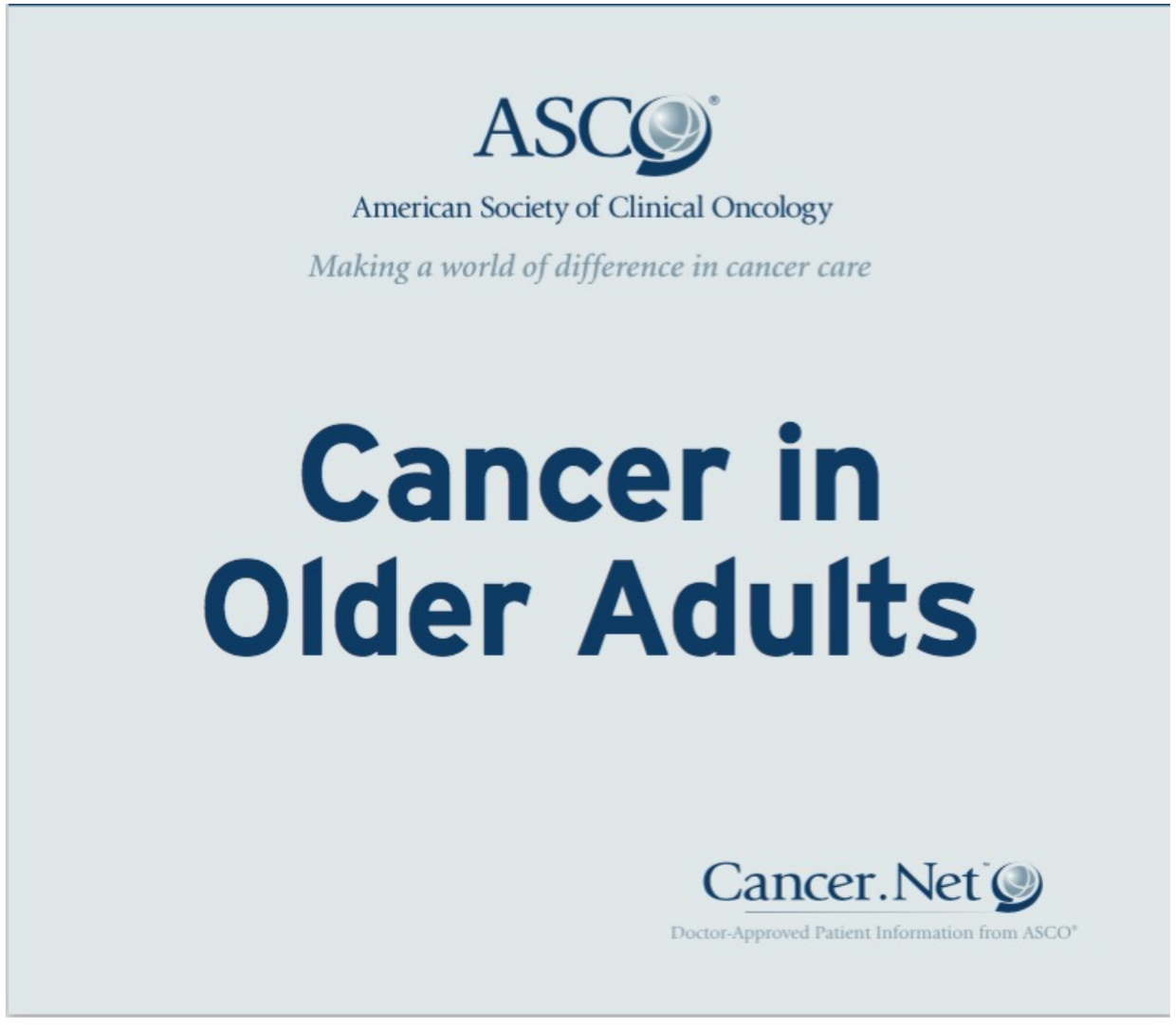
Clegg,Lancet,2013

GERIATRIC TOOLS FOR TREATING CANCER IN OLDER PATIENT

ESMO
GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE
European Society for Medical Oncology

ESMO HANDBOOK OF
CANCER IN THE SENIOR PATIENT

SIOG
INTERNATIONAL SOCIETY
OF GERIATRIC ONCOLOGY
To improve the care of older patients with cancer around the world



A LOT OF DIFFERENT TASK FORCE GROUPS
TRY TO DEVELOP AND EDIT DIFFERENT GUIDELINES AND RECOMMENDATIONS

FACTORS OTHER THAN CHRONOLOGICAL AGE THAT PREDICT MORBIDITY AND MORTALITY IN OLDER ADULT

- **Functional status**
- **comorbid medical conditions**
- **nutritional status**
- **cognition**
- **fatigue**
- **mental health status**
- **social support**
- **medications (polypharmacy)**
- **presence of Geriatric Syndromes**

(dementia,delirium,fall,incontinence,osteoporosis or spontaneous fracture,neglect or abuse,dizziness and syncopy,sleep disorders,constipation,…)

GERIATRIC ASSESSMENT

Wildiers,JCO,2014

2014 SIOG recommendations

Annals of Oncology 26: 288–300, 2015
doi:10.1093/annonc/mdu210
Published online 16 June 2014

Screening tools for multidimensional health problems warranting a geriatric assessment in older cancer patients: an update on SIOG recommendations†

L. Decoster[1]*, K. Van Puyvelde[2], S. Mohile[3], U. Wedding[4], U. Basso[5], G. Colloca[6], S. Rostoft[7],

44 studies on the use of 17 different screening tools

- 22 studies compared 14 screening tools with GA
- 12 studies reported relationship with outcome for 8 tools

Plan Cancer
Kankerplan

Tool	Developed for	Items	Abnormal	Time (min)
G8	Oncology pts	8	≤ 14	5
VES-13	General older pop	13	≥ 3	5
fTRST	Older pts at ED	5	≥ 2	2
GFI	General older pop	15	≥ 4	NR
SOF	General older pop	3	≥ 2	NR
Karnofsky PS	Oncology pts	1	≤ 80	1
ECOG PS	Oncology pts	1	≥ 1	1
Fried	General older population	5	≥ 3	NR
Barber	General older population	9	≥ 1	NR
ISAR	Older pts at ED	6	≥ 3	NR
OGS	Oncology pts	10	≥ 1	NR
aCGA	Oncology pts	15	≥ 1	5
Gerhematolim	Hematology pts	27	NR	NR
SAOP2	Oncology pts	15	≥ 1	NR
PPT	General older population	7	≤ 20	5
Handgrip	General older population	NA	NA	NA
Timed up and Go	General older population	NA	NA	NA

From Decoster, Plan Cancer

SIOG recommendations 2014

1. Sreening tools in older patients with cancer do not replace the CGA : if possible GA in all older patients with cancer is recommended
2. In a busy clinical practice the use of a screening tool is recommended to identify patients in need of further evaluation by GA and multidisciplinary approach
3. Clinicians should chose an extensively studied tool with a high sensitivity: which one ? G8 ? easy and quick…
4. depending of the context, an abnormal screening should be followed by:
    1. GA and directed intervention by a multidisciplinary team
    2. if no geriatric team available,close follow-up or supportive care team

SCREENING TOOL

normal

STOP

abnormal

GA

(! time: 60-90 min)

Geriatric intervention

Each institution has to chose a tool to evaluate older cancer patient and if abnormal, CGA is required

DEFINITION SCREENING TOOL

- BRIEF ASSESSMENT, CONDUCTED TO HELP THE CLINICIAN TO IDENTIFY THOSE OLDERS PATIENTS WITH CANCER IN NEED OF FURTHER EVALUATION BY GA
- MUST BE SHORT AND SIMPLE WITH HIGH SENSITIVITY (identify all patients at risk) and HIGH SPECIFICITY (limit the number of patients that undergo GA)

USE OF SCREENING TOOLS IN ONCOLOGY

- IDENTIFY PATIENTS WHO NEED A MULTIDISCIPLINARY APPROACH
- PROGNOSTIC/PREDICTIVE FOR OUTCOME MEASURES
- TREATMENT-RELATED TOXICITY, FUNCTIONAL DECLINE,SURVIVAL

G8 SCREENING TOOL

SCORE 14 OR LESS = abnormal

- **High sensitivity for functional decline in ADL (**Activities of Daily Living/Self-Care) **and IAD** (Instrumental Activities of Daily Living/Measures of Independence)
- **Predictive for chemotherapy toxicity**
- **Prognostic for survival**
- **Abnormal G8 prognostic for 6 months survival**

Baitar,journal of geriatric oncology,2013

The G8 questionnaire		
	Items	Possible answers/ Scores
A	Loss of appetite? Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?	0: severe anorexia 1: moderate anorexia 2: no anorexia
B	Loss of weight during the last months	0: weight loss >3 kg 1: does not know 2: weight loss between 1 and 3 kg 3: no weight loss
C	Mobility	0: bed or chair bound 1: able to get out bed/ chair but not to go out 2: goes out
E	Neuropsychological problems	0: severe dementia or depression 1: moderate dementia or depression 2: no psychological problem
F	Body Mass Index	0: BMI <18.5 1: BMI between 18.5 and <21 2: BMI 21 to <23 3: BMI ≥23
H	Takes >3 prescription drugs per day	0: yes 1: no
P	In comparison with other people of the same age, how do they consider their health status	0: not as good 0.5: does not know 1: as good 2: better
	Age	0: >85 1: 80–85 2: <80
	Total score	0–17

Comprehensive Geriatric Assessment (CGA)

- **Doing the CGA before offering a treatment**:
  1. can provide information on: hearing defect,visual deficit and cognitive impairments leading to the lack of understanding of the real meaning of information
  2. the knowledge of these elements can be clinically useful in order to obtain the patients consensus for treatment
- **some information captured through the CGA can be useful in order to identify obstacles to cancer treatment:**
  1. limited family and social support, lower education,
  2. difficulty in:
     1. having access to a mean of transport
     2. telephone calls
     3. self administration of drugs

GERIATRIC TOOLS FOR TREATING CANCER IN OLDER PATIENT

INTERVENTION TRIALS RESULTS:
Impact of GA on chemotoxicity

BELGIUM

Annals of Oncology 24: 1306–1312, 2013
doi:10.1093/annonc/mds619
Published online 4 January 2013

Relevance of a systematic geriatric screening and assessment in older patients with cancer: results of a prospective multicentric study

C. Kenis[1], D. Bron[2], Y. Libert[3], L. Decoster[4], K. Van Puyvelde[5], P. Scalliet[6], P. Cornette[7], T. Pepersack[8], S. Luce[9], C. Langenaeken[10], M. Rasschaert[11], S. Allepaerts[12], R. Van Rijswijk[13], K. Milisen[14,15], J. Flamaing[14,16], J.-P. Lobelle[17] & H. Wildiers[18,19*]

Report of feasibility and utility of Geriatric Assessment

- N=1967 patients≥ 70 years from 10 hospitals
- 70,7 % patients scored < 14 on G8 screening tool went onto CGA
- CGA detected unknown geriatric problem in 51,2% of patients
- interventions planned: 25,7 %
- treatment decisions changed: 25,3 %

EVIDENCE OF BENEFIT OF INTERVENTION IN GO

GAIN TRIAL

JAMA Oncology | Original Investigation

Geriatric Assessment–Driven Intervention (GAIN) on Chemotherapy-Related Toxic Effects in Older Adults With Cancer

A Randomized Clinical Trial

ELIGIBILITY

- AGE ≥ 65
- SOLID TUMOR
- ALL STAGES
- STARTING A NEW THERAPY
- ENGLISH,SPANISH OR CHINESE SPEAKERS

BASELINE

GA

Pre chemotherapy

R

N=600

GAIN ARM

USUAL CARE

+

GA DRIVEN INTERVENTIONS

N=398

SOC ARM

Standard of care

N=202

FU until end of chemo

Or

8 months post initiation of chemo

GA

PRIMARY ENDPOINTS

Incidence of grade 3-4 toxicitiy

SECONDARY ENDPOINTS

- Advance directive completion
- Unplanned hospitalizations
- Emergency room visits
- Average lengh of stay

JAMA Oncology November 2021 Volume 7, Number 11

EVIDENCE OF BENEFIT OF INTERVENTION IN GO

GAIN TRIAL

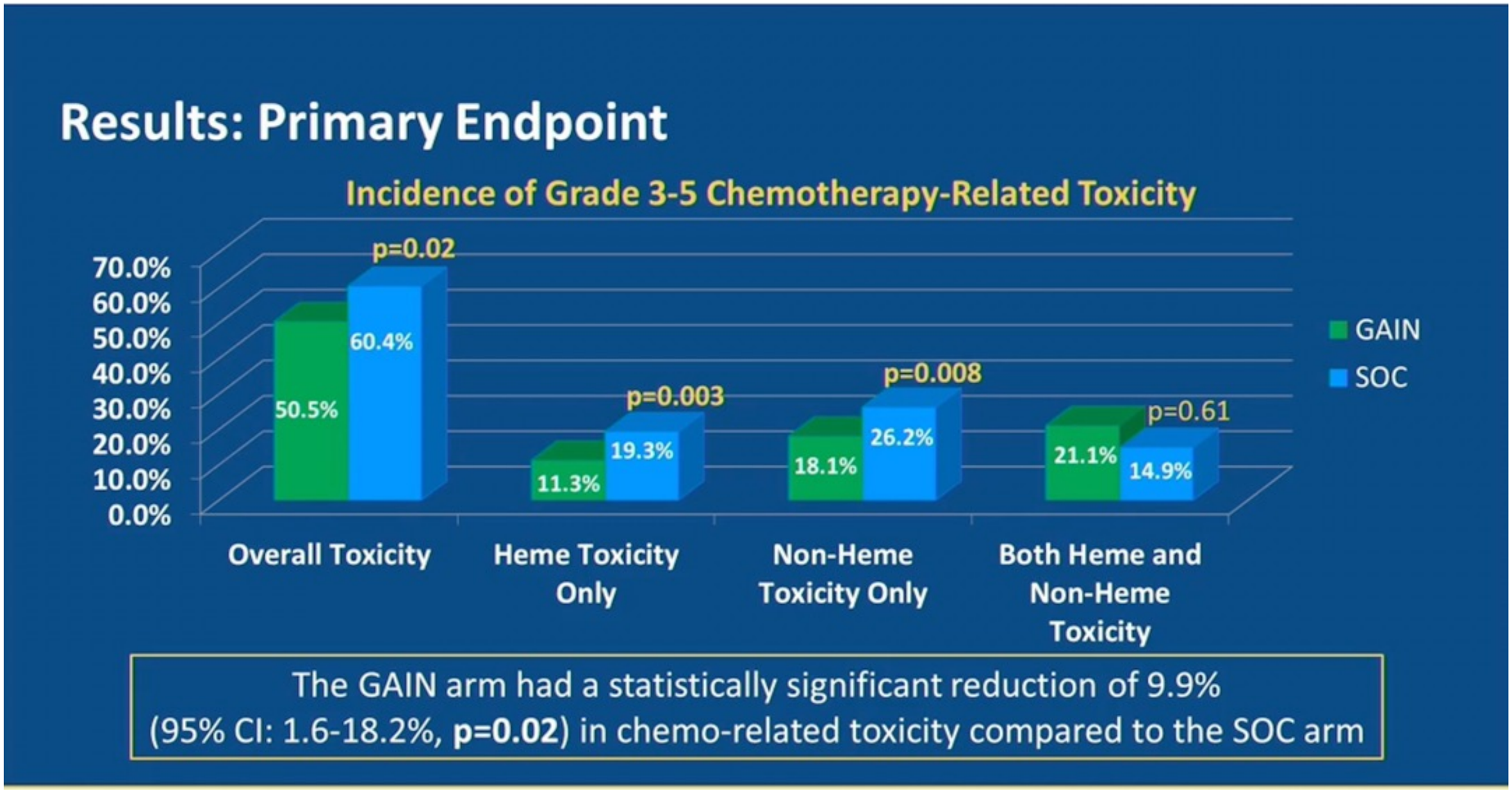
Figure 2. Geriatric Assessment–Driven Intervention (GAIN) Used in This Study

Domain	Deficit	Interventions
Functional status	• Limitations in activities of daily living and/or instrumental activities of daily living • History of falls • Timed Up and Go >13 s • Lack of energy	• Exercise prescription • Evaluate fall risk • Home safety evaluation • Gait strengthening • Reiki therapy
Comorbidities	• Presence of comorbid conditions • Hearing/visual impairments	• Management with treating physician or primary care • Referrals as appropriate • Pharmacy review of medications
Psychological status	• Feeling sad or depressed • Anxiety • Feeling nervous/worried	• Social work counseling • Psychiatry referral • Psychology referral • Chaplaincy referral • Support programs
Social activity	• Interference of physical or emotional problems on social activity	• Evaluation of physical/emotional concerns • Social work referral • Occupational therapy
Social support	• Lack of social support identified • Patient lives alone	• Counseling • Social work referral • Home safety evaluation • Support programs • Community resources
Nutrition	• Weight loss ≥5% • Body mass index ≤21 or ≥30 • Problems with eating or feeding	• Diet recommendations • Supplements • Oral care • Physical/occupational therapy for food intake problems
Cognition	• Abnormal cognitive screening • Confusion • Memory loss/impairment	• Assess decision-making capacity • Involve caregivers • Review of medications • Delirium prevention • Cognitive testing
Polypharmacy	• ≥5 Prescribed medications • ≥1 Over-the-counter medication • ≥1 Herb/vitamin supplement	• Recommendations regarding drug interactions, potentially inappropriate medications, duplicative medications
Spiritual well-being	• Anxiety in relation with religious belief/experience	• Chaplaincy referral and counseling • Encourage normal spiritual habits
Clinical symptoms	• Pain • Skin breakdown • Nausea • Incontinence • Adverse effects of treatment	• Supportive care/pain management referral • Manage symptoms with primary care team • Educational interventions

Geriatric Assessment–Driven Intervention (GAIN) Used in This Study Under the guidance of the multidisciplinary team and geriatric nurse practitioner, predefined geriatric assessment thresholds were established and interventions recommended..

EVIDENCE OF BENEFIT OF INTERVENTION IN GO

GAIN TRIAL



ASCO 2020 Daneng Li

EVIDENCE OF BENEFIT OF INTERVENTION IN GO

GAP70 +

Evaluation of geriatric assessment and management on the toxic effects of cancer treatment (GAP70+): a cluster-randomised study

Supriya G Mohile, Mostafa R Mohamed, Huiwen Xu, Eva Culakova, Kah Poh Loh, Allison Magnuson, Marie A Flannery, Spencer Obrecht,

Eligibility

Age ≥ 70

Incurable stage III-IV cancer

> 1GA domain impaired other than polypharmacy

Starting new chemotherapy or other agents with similar prevalence of toxicity

R
N=718

N=349

GA intervention arm

Oncology physicians provides with GA summary and GA-guided recommendations for each enrolled participant prior to starting a new chemo/agents with similar prevalence of toxicity

N=369

Standard of care

ENDPOINTS

- **Clinician-rated grade 3-5 toxicity**
- **Survival at 6 months**
- **Treatment decisions**
- **Functional and physical decline**
- **Patient reported toxicity**

Lancet 2021; 398: 1894–904

EVIDENCE OF BENEFIT OF INTERVENTION IN GO

GAP70 +

CANCER TYPE AND CHEMO

	All patients (n=718)	Geriatric assessment group (n=349)	Usual care group (n=369)
Lung cancer regimens			
Pemetrexed-carboplatin with or without pembrolizumab	66/180 (37%)	13/64 (20%)	53/116 (46%)
Paclitaxel-carboplatin with or without monoclonal antibody	36/180 (20%)	20/64 (31%)	16/116 (14%)
Carboplatin-etoposide	20/180 (11%)	5/64 (8%)	15/116 (13%)
Carboplatin-nab paclitaxel	17/180 (9%)	7/64 (11%)	10/116 (9%)
Gastro-intestinal cancer regimens			
FOLFOX (leucovorin, fluorouracil, and oxaliplatin) with or without bevacizumab	65/246 (26%)	25/132 (19%)	40/114 (35%)
Gemcitabine-nab paclitaxel	44/246 (18%)	24/132 (18%)	20/114 (18%)
Capecitabine	23/246 (9%)	21/132 (16%)	2/114 (2%)
FOLFIRI (leucovorin, fluorouracil, and irinotecan) with or without bevacizumab	18/246 (7%)	12/132 (9%)	6/114 (5%)
FOLFIRINOX (leucovorin, fluorouracil, irinotecan, and oxaliplatin) with or without bevacizumab	9/246 (4%)	3/132 (2%)	6/114 (5%)
Genito-urinary cancer regimens			
Abiraterone with or without prednisone	35/109 (32%)	22/56 (39%)	13/53 (25%)
Docetaxel with or without prednisone	32/109 (29%)	19/56 (34%)	13/53 (25%)
Enzalutamide with or without prednisone	13/109 (12%)	3/56 (5%)	10/53 (19%)
Gemcitabine-carboplatin	11/109 (10%)	3/56 (5%)	8/53 (15%)
Breast cancer regimens			
Palbociclib plus aromatase inhibitor	18/56 (32%)	6/19 (32%)	12/37 (32%)
Paclitaxel with or without trastuzumab	8/56 (14%)	1/19 (5%)	8/37 (22%)
Gemcitabine-carboplatin with or without trastuzumab	5/56 (9%)	2/19 (11%)	3/37 (8%)
Capecitabine	4/56 (7%)	0	4 (11%)
Lymphoma regimens			
Bendamustine-rituximab	18/46 (39%)	7/23 (30%)	11/23 (48%)
R-CHOP (rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone)	9/46 (20%)	5/23 (22%)	4/23 (17%)
Gynaecological cancer regimens			
Paclitaxel-carboplatin	19/43 (44%)	10/29 (34%)	9/14 (64%)

Data are n/N (%). Data are only reported for commonly received regimens at cycle one.

Table 2: **Treatment regimens received at cycle one**

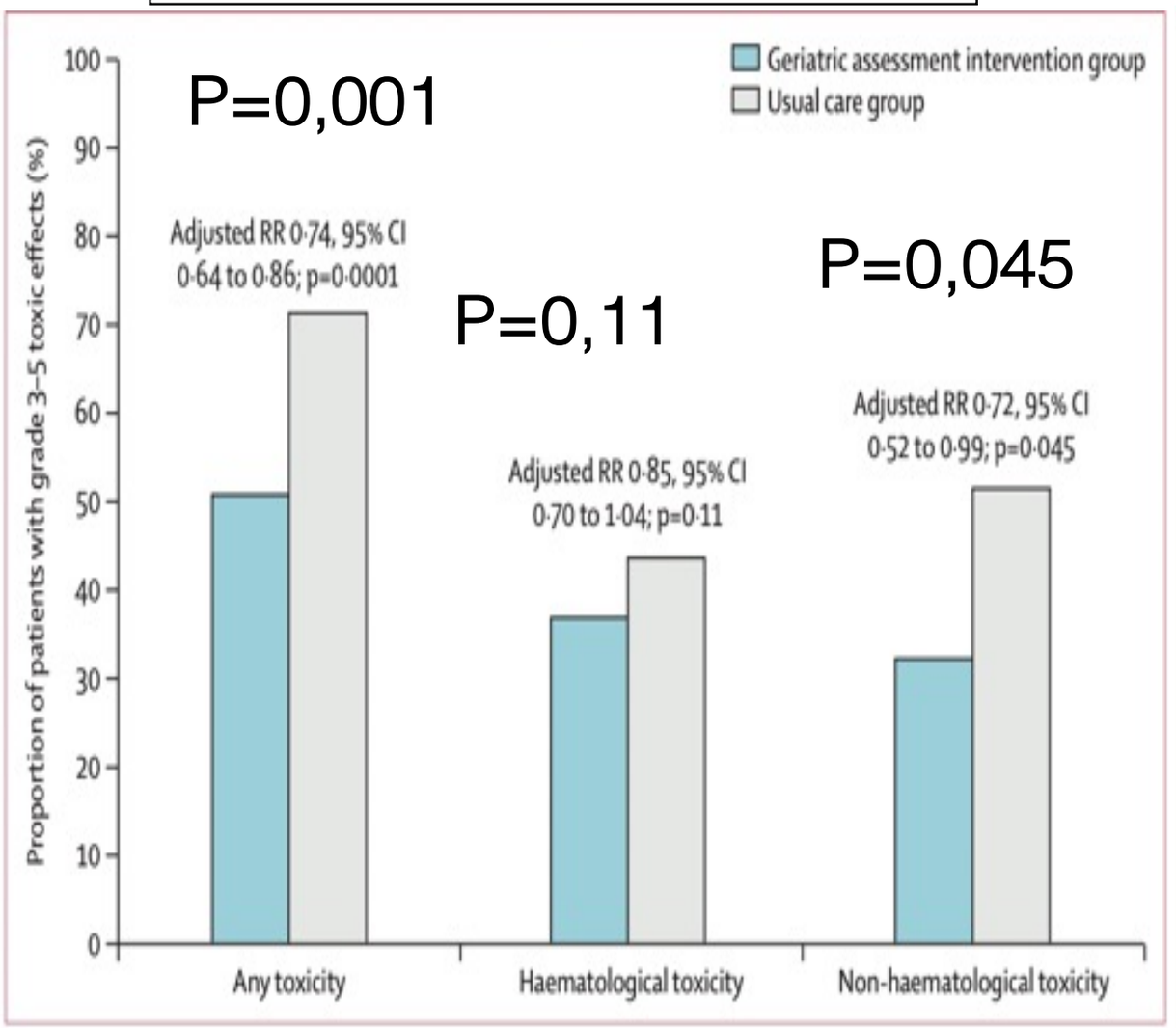
- **More patients in the intervention group had previous chemotherapy and had gastrointestinal cancers;**
- **lung cancer was more prevalent in the usual care group**
- **The mean number of geriatric assessment domain impairments was 4·5 and was not significantly different between the study groups.**
- **Patients in the intervention group had a lower prevalence of impaired physical performance, but a higher prevalence of impaired social support and cognitive impairment**

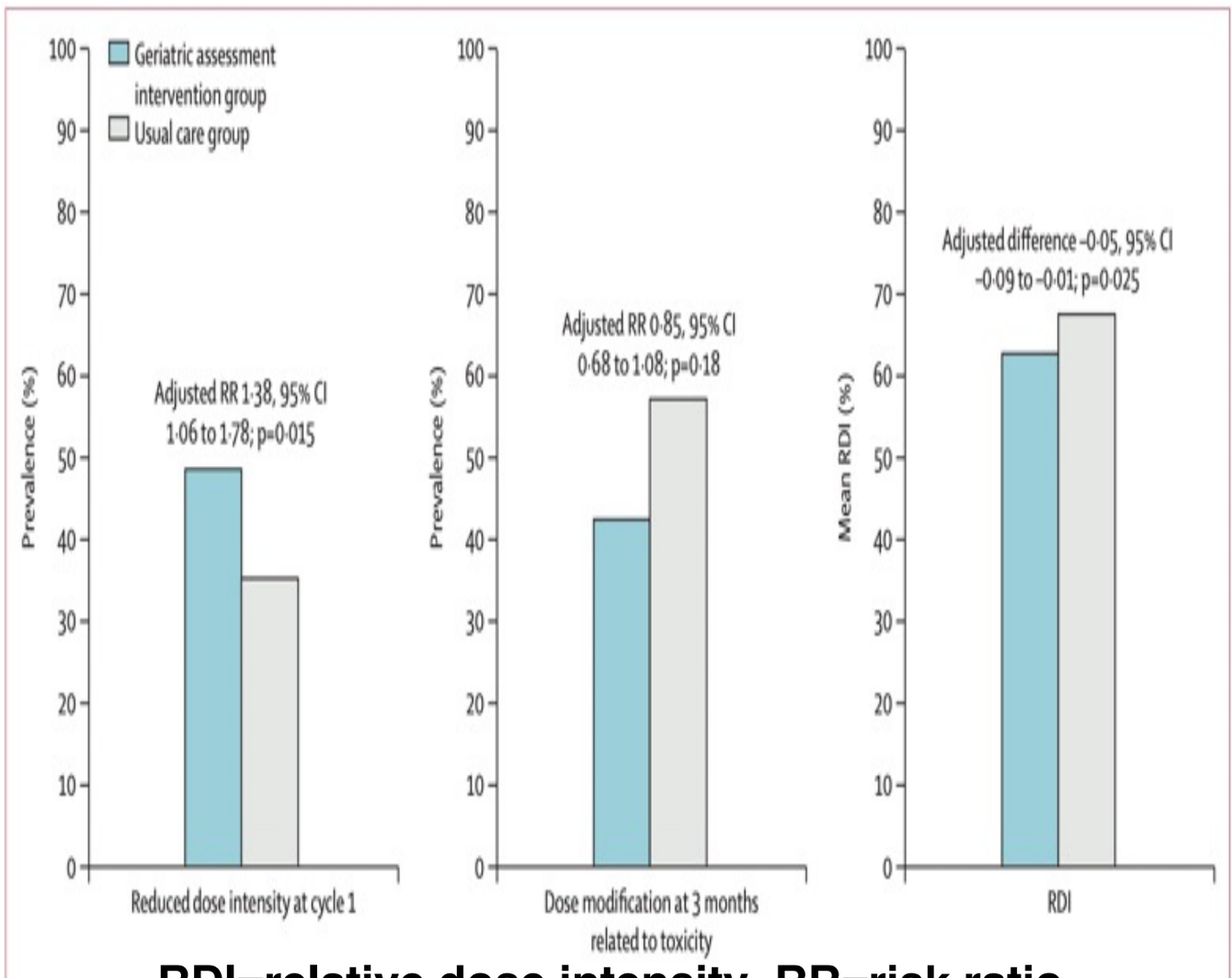
EVIDENCE OF BENEFIT OF INTERVENTION IN GO

GAP70 +

any grade 3–5 AEs over 3 months LESS IF GA

Dose intensity Higher reduced DI and lower RDI in GA





RDI=relative dose intensity. RR=risk ratio.

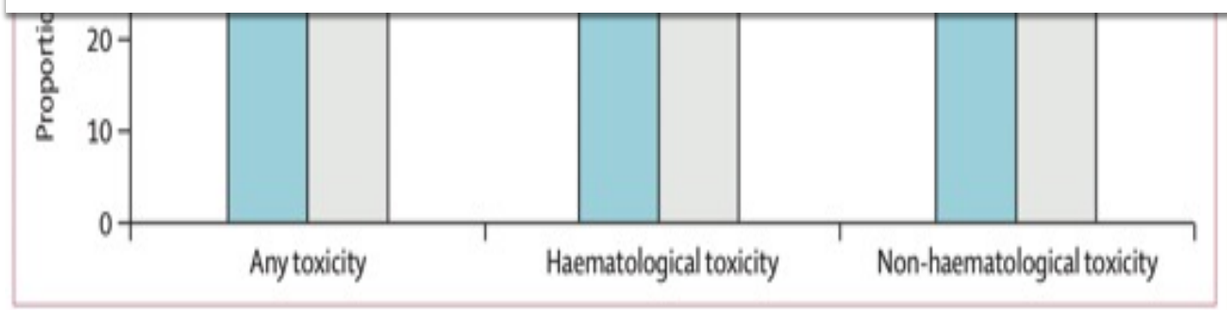
Lancet 2021; 398: 1894–904

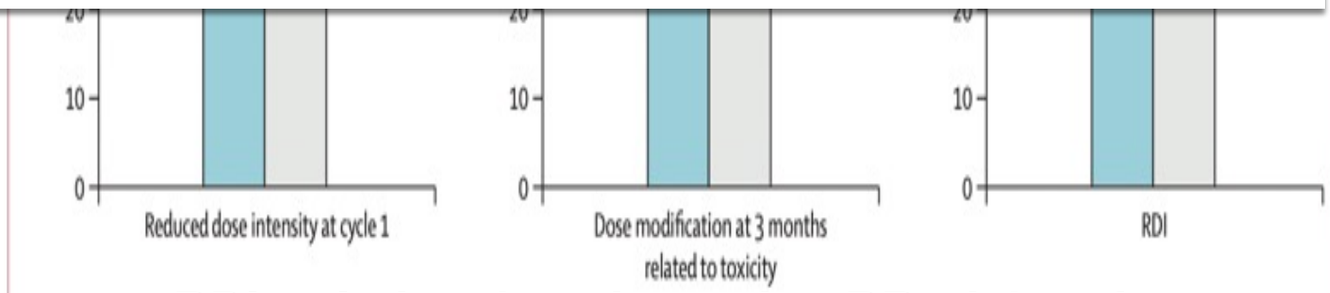
EVIDENCE OF BENEFIT OF INTERVENTION IN GO

GAP70 +

any grade 3–5 AEs over 3 months	Dose intensity Higher reduced DI and lower RDI in GA

The trial met its primary endpoint—the geriatric assessment intervention reduced the risk of serious toxic effects by over 20%.
Importantly, reduced dose intensity in the intervention group did not compromise survival, which was similar between the study groups at 6 months and 1 year





RDI=relative dose intensity. RR=risk ratio.

Lancet 2021; 398: 1894–904

EVIDENCE OF BENEFIT OF INTERVENTION IN GO IN PROGRESS

> J Geriatr Oncol. 2022 Jan;13(1):116-123. doi: 10.1016/j.jgo.2021.07.005. Epub 2021 Aug 4.

Predictive value of geriatric oncology screening and geriatric assessment of older patients with cancer: A randomized clinical trial protocol (PROGNOSIS-RCT)

> BMC Geriatr. 2021 Jan 30;21(1):88. doi: 10.1186/s12877-021-02045-9.

Geriatric assessment and intervention in older vulnerable patients undergoing surgery for colorectal cancer: a protocol for a randomised controlled trial (GEPOC trial)

FACTORS HELPING THE ONCOLOGIST

DIFFERENT PROGNOSTIC AND THERAPEUTIC IMPLICATIONS DIVIDING PATIENTS IN:

FIT:

FULL DOSE TREATMENT

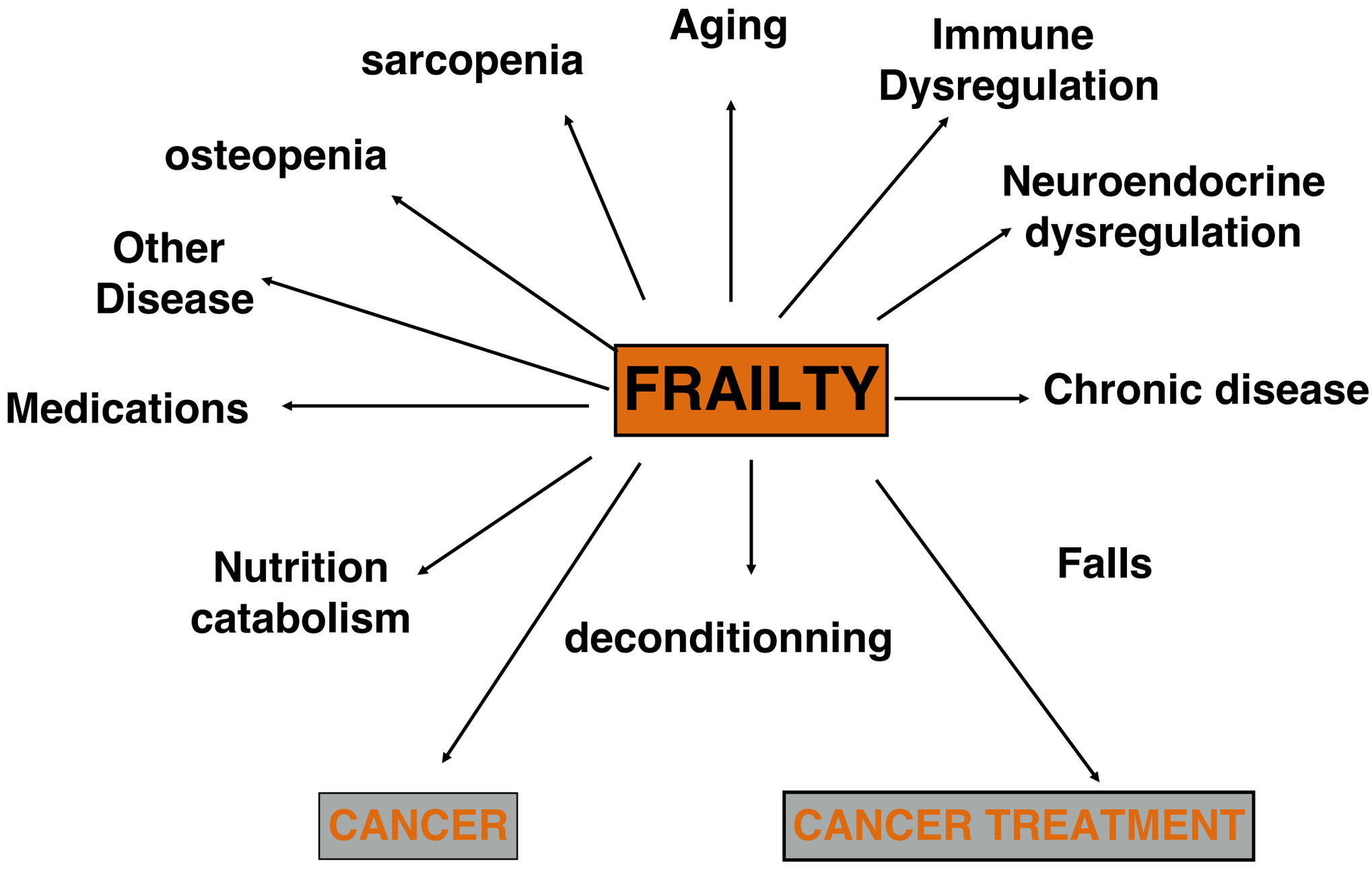
(start at 80 % and don't hesitate to use growth factors)

FRAIL:MAINLY PALLIATION

VULNERABLE:SPECIAL PRECAUTIONS

FOR THE LAST GROUP, IT IS IMPORTANT TO HAVE HELP WITH ADEQUATE TOOLS

CONTRIBUTORS TO FRAILTY



DIFFERENCE WITH AGE

Age changes the perspective of the cancer diagnosis

YOUNG ADULTS	OLDER ADULTS
single serious disease	coexist with multiple illnesses and significant morbidity
dominates the clinical picture	other morbid conditions may be beyond cancer
tolerates acute,severe side effects relatively welll	variable tolerability of specific treatment, may need more tailoring for different specific treatment
main goal:survival and cure	main goal: survival but vs QoL

GOALS OF CANCER TREATMENT IN OLDER PEOPLE

THE GOALS CAN VARY WIDELY:

- CURE
- PROLONGATION OF SURVIVAL
- PROLONGATION OF ACTIVE LIFE EXPECTANCY
- EFFECTIVE SYMPTOMS MANAGEMENT
- TO DO « NO »HARM
- BALANCE WITH QoL

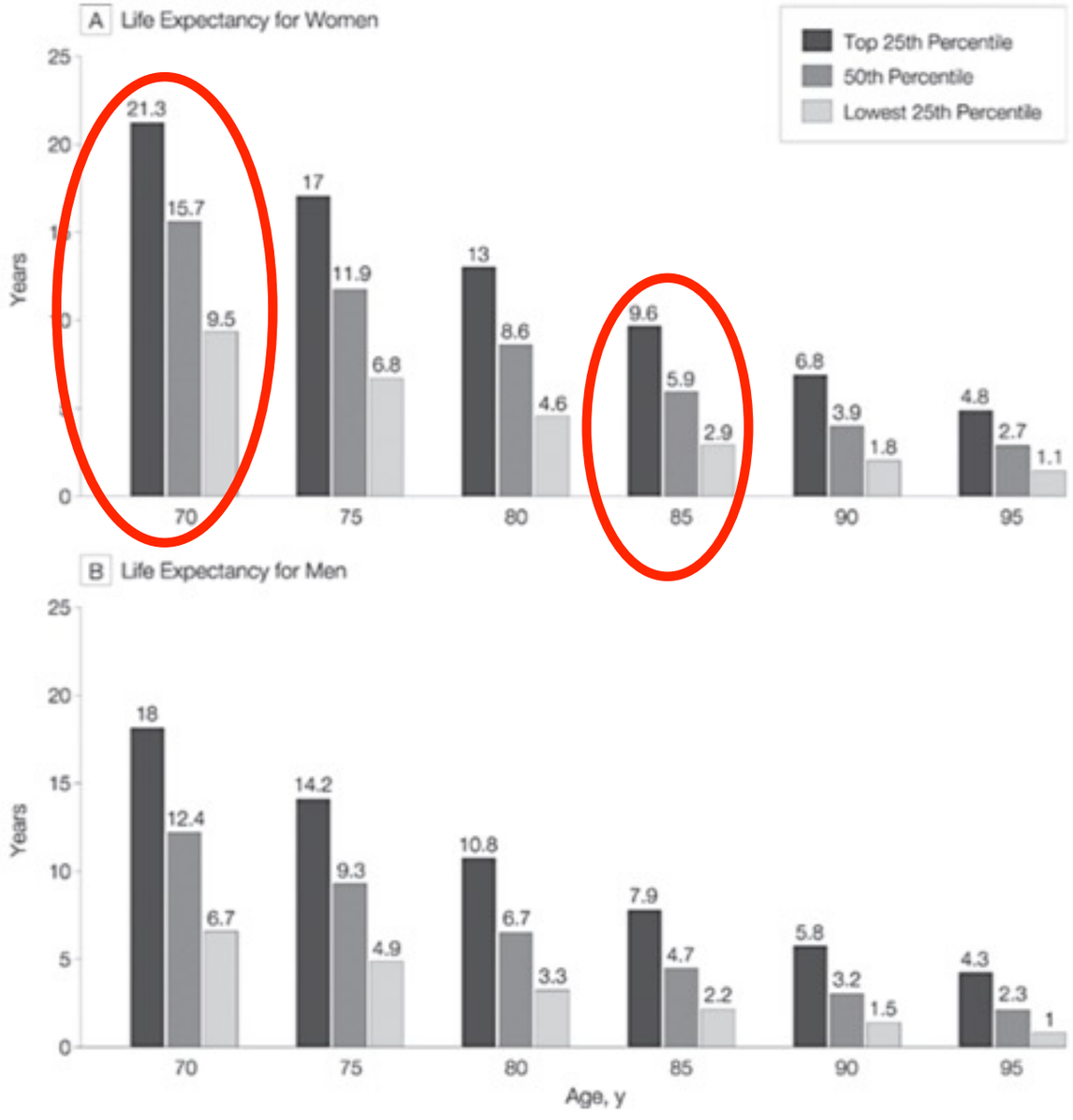
IMPORTANT QUESTIONS IN GERIATRIC ONCOLOGY

- IS THE PATIENT GOING TO DIE OF OR WITH CANCER ?
- IS THE PATIENT GOING TO LIFE ENOUGH TO SUFFER THE CONSEQUENCES OF CANCER ?
- IS THE PATIENT ABLE TO TOLERATE TREATMENT ?
- ARE THERE COMPLICATIONS OF TREATMENT THAT ARE MORE COMMON IN OLDER ?
- IS THE SOCIAL NETWORK OF THE PATIENT ABLE TO SUPPORT HER/HIM DURING THE TREATMENT
- HOW TO DEAL WITH THE HETEROGENEITY OF PATIENT
- WHEN SHOULD WE ADAPT THE TREATMENT

AGE IS IMPORTANT
BUT ALTHOUGH
FUNCTIONAL,SOCIAL AND MENTAL STATUS

WE ALSO NEED TO HAVE AN IDEA OF THE LIFE EXPECTANCY OF OLDER CANCER PATIENT TO BALANCE RISK AND BENEFIT OF THE TREATMENT

A 80 old woman may still have 4,6 to 13 year life expectancy



A fit patient of 85 year have the same survival that a frail patient of 70 years

JAMA. 2001;285(21):2750-2756.

WWW.EPROGNOSIS.ORG

COMBINED LEE SCHONBERG INDEX

variable	patient 1	patient 2
age	75	75
sex	F	F
smoking	NEVER SMOKED	FORMER
BMI	< 25	> 25
history of cancer	NO	YES
diabetes	NO	YES
COPD	NO	NO
hospitalizations past year	NO	YES once
self rated health	good	BAD
dependent ADL	NO	NO
difficulty walking 1/4 miles	NO	YES
5 and 10 year mortality risk	**9 % and 15 to 23 %**	**35 % and 70-82 %**

Common toxicities of TREATMENT ACUTE and late IN ALL AGE PATIENT

- nausea/vomiting,alopecia,mucositis,myelosuppresion..
- fatigue
- anxiety,depression
- neuropathy
- neucognitive dysfunction (chemo brain)
- ovarian failure and infertility
- menopausal symptoms
- sexual dysfunction weight gain
- bone loss
- arthralgia
- cardiac dysfunction
- secondary malignancies

BUT HOW TO PREDICT INCREASE TOXICITY FOR OLDER CANCER PATIENT

VOLUME 34 · NUMBER 20 · JULY 10, 2016

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Validation of a Prediction Tool for Chemotherapy Toxicity in Older Adults With Cancer

Arti Hurria, Supriya Mohile, Ajeet Gajra, Heidi Klepin, Hyman Muss, Andrew Chapman, Tao Feng, David Smith, Can-Lan Sun, Nienke De Glas, Harvey Jay Cohen, Vani Katheria, Caroline Doan, Laura Zavala, Abrahm Levi, Chie Akiba, and William P. Tew

CARG SCORE

This study externally validated a chemotherapy toxicity predictive model for older adults with cancer. This predictive model should be considered when discussing the risks and benefits of chemo- therapy with older adults.
Prediction Tool for Chemotherapy Toxicity in Older Adults With Cancer
CARG score
(Cancer and Aging Research Group)

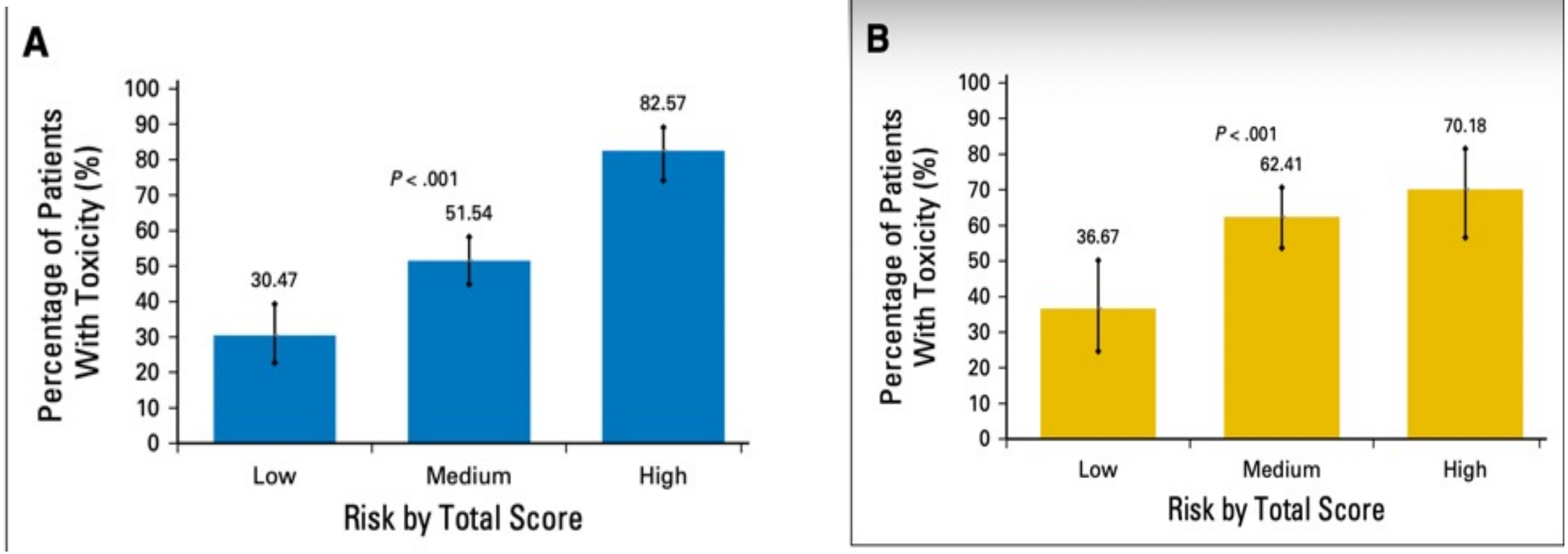
PREDICTORS OF GRADE 3-5 toxicity

CARG SCORE

Risk factors	0	1	2	3
AGE	<72 years		≥72 years	
CANCER TYPE	Other		GI or GU	
CHEMOTHERAPY DOSE				
Nb of chemotherapy drugs	Mono chemotherapy		Polychemo therapy	
HAEMOGLOBIN	≥11 g/dL (male) ≥10 g/dL (female)			<11 g/dL (male) <10 g/dL (female)
CREATININE CLEARANCE	≥34 mL/min			<34 mL/min
HEARING	Excellent or good		Fair, poor or totally deaf	
Nb OF FALL IN LAST 6 MONTHS	None			≥1
IADL:taking medications	Without help	With some help or completely unable		
Walking a block	Not limited at all		Limited a little or limited a lot	
MOS: Decreased social activity because of physical/emotional health	A little of the time or None of the time	Some of the time, Most of The time or all of the time		

PREDICTORS OF GRADE 3-5 toxicity

CARG SCORE



Risk strata versus toxicity percentage for the (A) development and (B) validation cohorts.

The CARG score (https://www.mycarg.org/?page_id=934)

Hurria, JCO, 2011

PREDICTORS OF GRADE 3-5 toxicity

CARG SCORE

The CARG score (https://www.mycarg.org/?page_id=934)

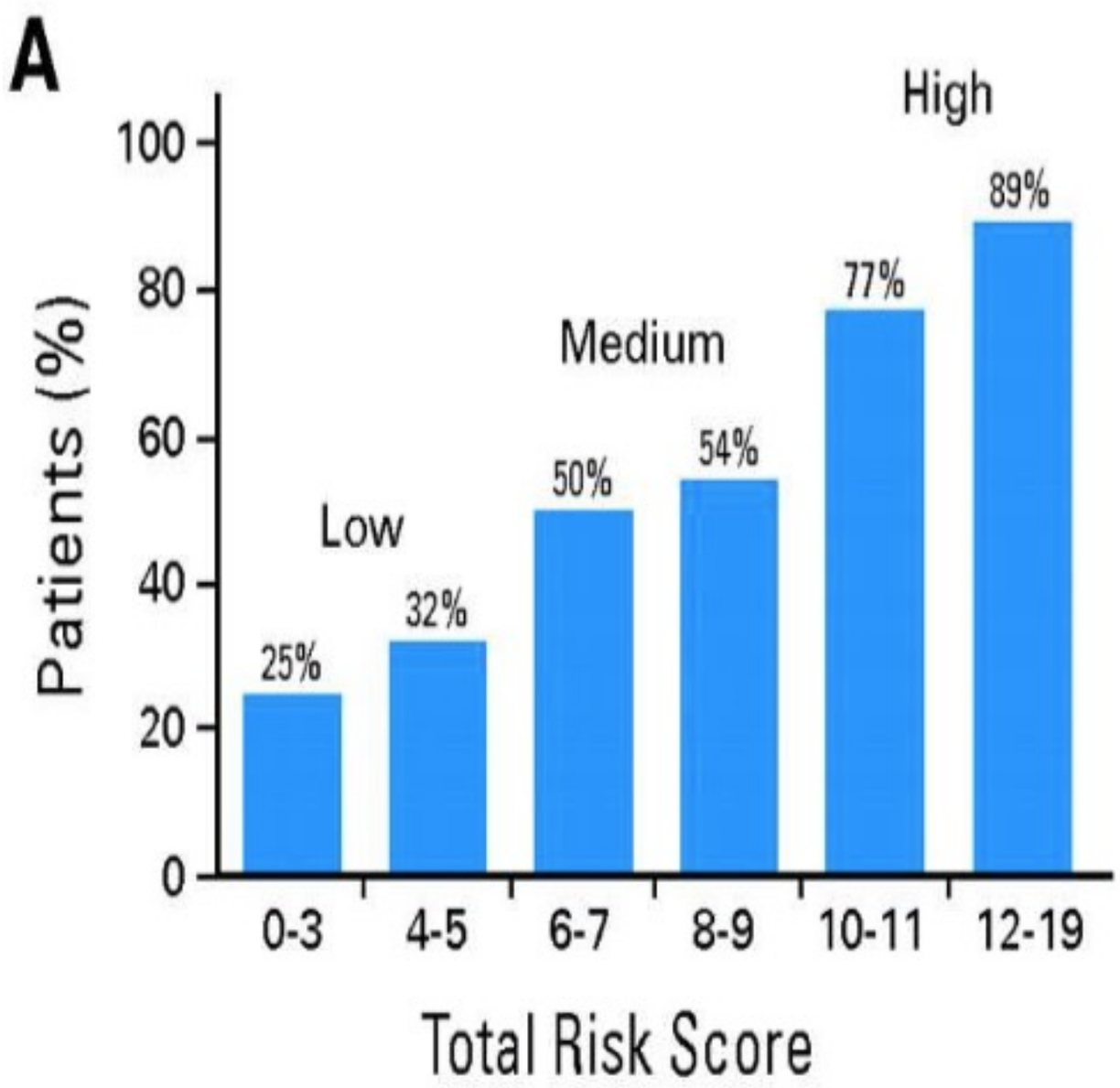
- **Estimates risk of grade 3-5 toxicity**
- **Categorizes patients into 3 risk groups: low,intermediate or high**
- **External validation**

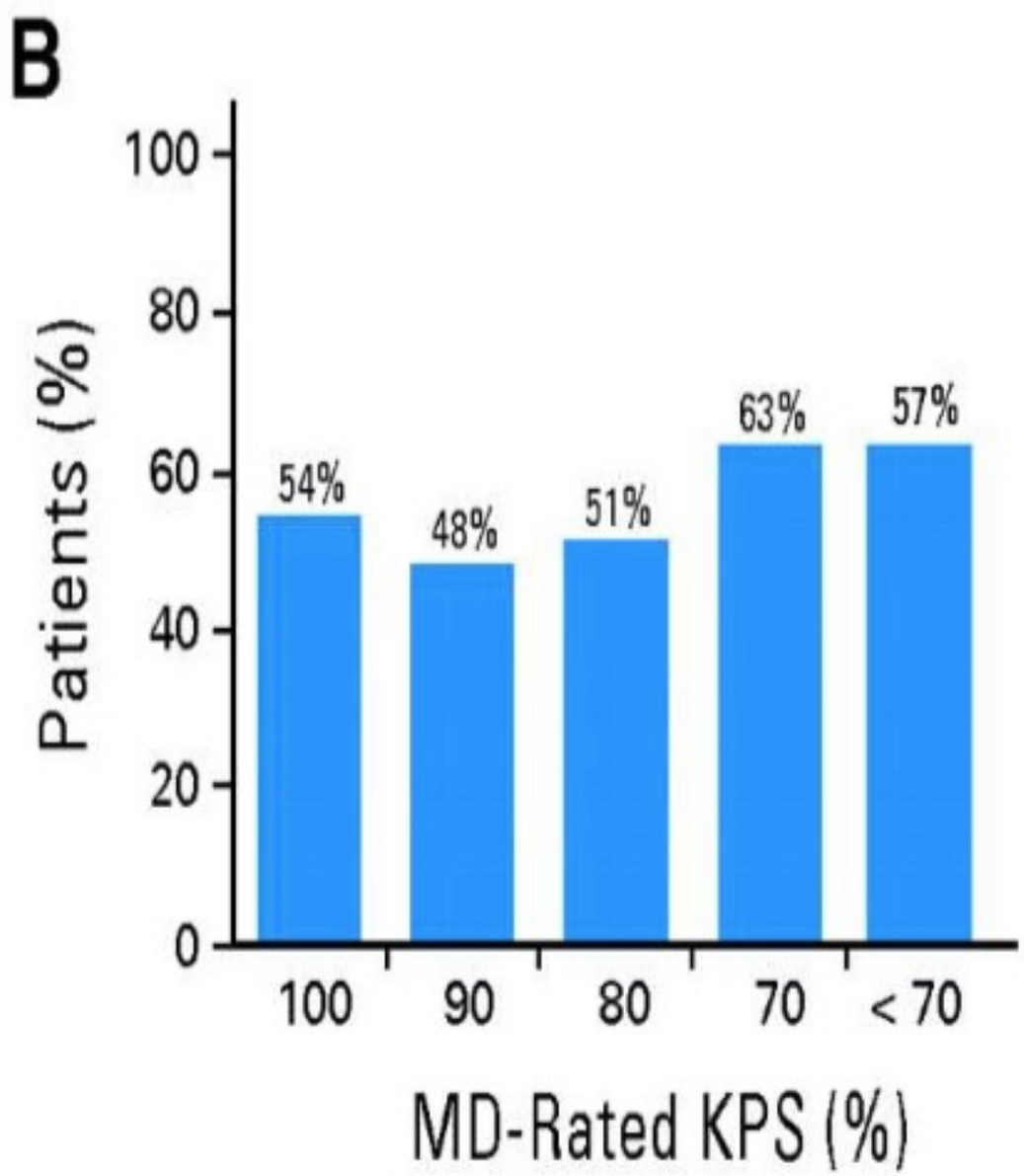
TOTAL RISK SCORE		% RISK OF GRADE 3-5 AES
LOW	0-3	25 %
	4-5	32 %
MEDIUM	6-7	50 %
	8-9	54 %
HIGH	10-11	77 %
	12-19	89 %

Hurria, JCO, 2011

CARG SCORE

Ability of (A) risk score versus (B) physician-rated Karnofsky performance status (KPS) to predict grade 3-5 chemotherapy toxicity





Hurria, JCO, 2011

GUIDELINES

????

VOLUME 25 · NUMBER 14 · MAY 10 2007

JOURNAL OF CLINICAL ONCOLOGY

REVIEW ARTICLE

International Society of Geriatric Oncology Chemotherapy Taskforce: Evaluation of Chemotherapy in Older Patients—An Analysis of the Medical Literature

Stuart M. Lichtman, Hans Wildiers, Etienne Chatelut, Christopher Steer, Daniel Budman, Vicki A. Morrison, Brigitte Tranchand, Iuliana Shapira, and Matti Aapro

ABSTRACT

The elderly comprise the majority of patients with cancer and are the recipients of the greatest amount of chemotherapy. Unfortunately, there is a lack of data to make evidence-based decisions with regard to chemotherapy. This is due to the minimal participation of older patients in clinical trials and that trials have not systematically evaluated chemotherapy. This article reviews the available information with regard to chemotherapy and aging provided by a task force of the International Society of Geriatric Oncology (SIOG). Due to the lack of prospective data, the conclusions and recommendations made are a consensus of the participants.

Potential Age-Related Factors Influence Pharmacokinetics

PARAMETER CHANGES	CLINICAL CONSEQUENCES
Absorption decreased	oral chemotherapy (eg.capecitabine) might be less effective in older
Volume of distribution	serum concentrations and toxicity of several chemotherapeutics might increase (eg.cisplatin,taxanes,etoposide,irinotecan)
Hepatic metabolism decreased	not well known,may affect serum concentrations of chemotherapeutics eliminated by hepatic metabolism (eg,taxanes,cyclophosphamides, anthracyclines)
Renal excretion decreased	dosing should be adapted to prevent recommendations to avoid excessive serum concentrations and toxicity from renal excreted chemotherapeutics (eg,carboplatin,topotecan,methotrexate)

Stuart M. Lichtman, JCO, 2007

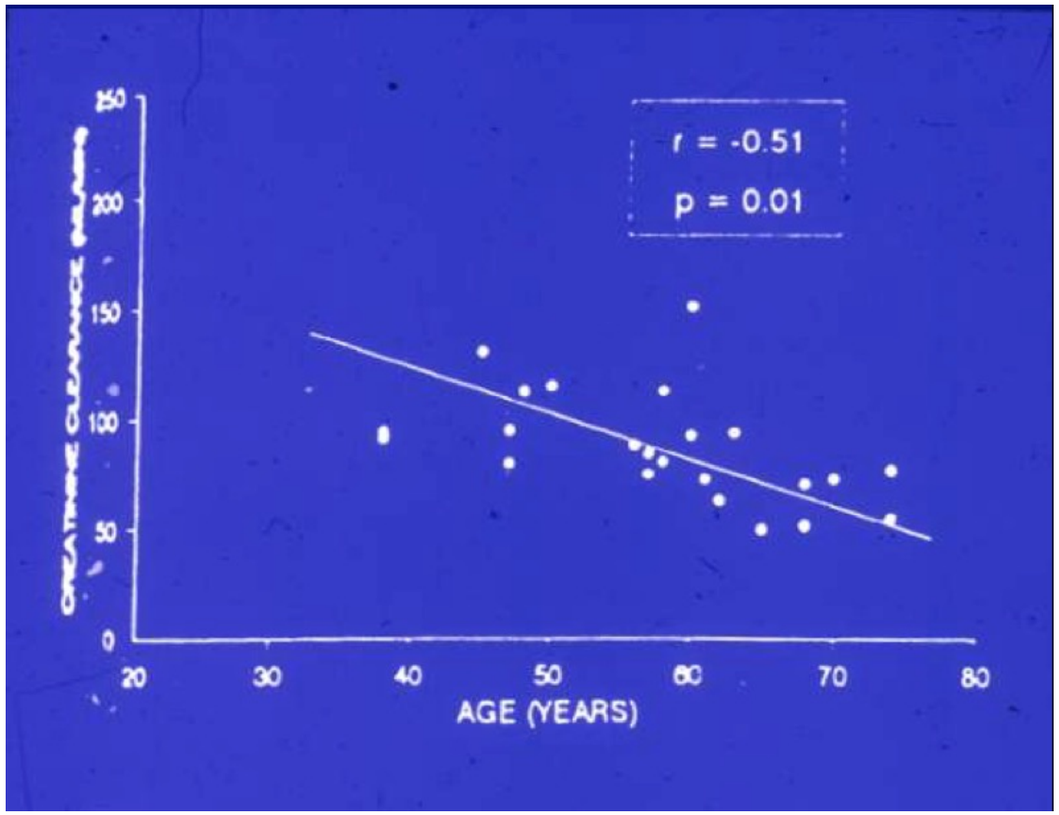
Potential Age-Related Factors Influence Pharmacokinetics

Decline in glomerular filtration rate (GFR) is one of the most predictable changes associated with aging

Additional effect of comorbid conditions on renal function

Drugs completely excreted through the kidneys:
- Methotrexate
- Carboplatin

Drugs partially excreted through the kidneys:
- Epipodophyllotoxins
- Fludarabine
- Capecitabine
- Pemetrexed



Drugs producing active or toxic metabolites excreted through the kidneys:
- Cytarabine (high doses)

CHEMOTHERAPY IN OLDERS

Stuart M. Lichtman, JCO, 2007

CISPLATIN

Increased toxicity because increasing AUC with age.

The maximum concentration of ultrafilterable platinum fraction has been shown to correlate significantly with nephrotoxicity

frequently, oral hydratation is lower; IV hydratation is important
it is recommended to reduce doses and increase duration of perfusion

IRINOTECAN

More grade 3/4 toxicities in >70 years

Delayed diarrhea was increased in patients with advanced age; It is recommended that patients older than 70 years, patients with prior pelvic irradiation, or those with poor performance status start at reduced doses

CHEMOTHERAPY IN OLDER

5-FU

Meta-analysis and retrospective studies: same benefit and same toxicity for older patient than younger

The data suggests no reason to reduce the dose for intravenous

fluoropyrimidines, unless there is severe renal dysfunction or comorbidity

CAPECITABINE

The pharmacokinetics of capecitabine are not affected by age in patients with normal renal function. Studies in elderly breast cancer patients showed that the dose of capecitabine might be reduced from 1,250 mg/m² to 1,000 mg/m², with equal efficacy but reduced toxicity The dose of capecitabine should be adjusted to CrCl, and a starting dose of no more than 1,000 mg/m² twice daily be strongly considered.

Stuart M. Lichtman, JCO, 2007

CHEMOTHERAPY IN OLDER

•

GEMCITABINE

monotherapy=minimal toxicity in older patient

OXALIPLATINE

The kidneys eliminate approximately 30% to 50% of the drug. Clearance of total and free platinum is decreased in patients with renal impairment. Few studies have been performed specifically in the elderly population. There is no data to support dose reduction based on age alone. Patients with a severe decrease in GFR should have dose reduction

Stuart M. Lichtman, JCO, 2007

CHEMOTHERAPY AND OLDER

JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

PACLITAXEL, drug used in many cancers

Prospective Evaluation of the Relationship of Patient Age and Paclitaxel Clinical Pharmacology: Cancer and Leukemia Group B (CALGB 9762)

Stuart M. Lichtman, Donna Hollis, Antonius A. Miller, Gary L. Rosner, Chris A. Rhoades, Eric P. Lester, Frederick Millard, John Byrd, Stephen A. Cullinan, D. Marc Rosen, Robert A. Parise, Mark J. Ratain, and Merrill J. Egorin

be aware of clearance reduction with age that can increase toxicity;be careful if hepatic alteration

Table 4. Adverse Events by Cohort

Age Cohort (years)	Percentage of Patients With Specified Adverse Event				
	ANC = 476/μL		Hospitalized for Toxicity	Intravenous Antibiotics	Temp > 38°C
	≥ Grade 3	Grade 4			
55-64	22	12	4	8.5	8.5
65-74	35	15	6	4.0	2.0
≥ 75	49	14	5	3	5.3
P_{trend}	.006	.74	.82	.21	.45

Abbreviation: ANC, absolute neutrophil count.

CHEMOTHERAPY IN OLDER: COMORBIDITY

DRUG	SPECIAL CONSIDERATION IN RELATION TO COMORBIDITY
ANTHRACYCLINES	**AVOID USE IN PATIENT WITH A EF < 50%**
CYCLOPHOSPHAMIDE	ELIMINATION DECREASED IN PATIENTS WITH IMPAIRED RENAL FUNCTION
METHOTREXATE	**DOSE ADJUSTMENTS BASED ON RENAL FUNCTION** **PATIENTS WITH PLEURAL EFFUSIONS AND ASCITES AT RISK FOR PROLONGED DRUG ELIMINATION AND TOXICITY**
FLUOURACIL	FU INDUCED CARDIOTOXICITY
VINCA ALCALOIDS	**MONITOR CAREFULLY FOR NEUROPATHY**
TAXANES	HEPATIC IMPAIREMENT INCREASED TOXICITY
TRASTUZUMAB	**CARDIOTOXICITY**

INDIVIDUALIZED TREATMENT IS IMPORTANT

CGA

ELDERLY AND CANCER

INCORRECT HYDRATATION

IMPORTANCE OF SUPPORTIVE CARE(anti-nausea,growth factor)

CHOICE OF CHEMOTHERAPY WITH LOWER TOXICITY **DATA??????**

POLYPHARMACyY AND INTERACTION

MODIFIED RENAL EXCRETION

POOR DATA
LOW NUMBER OF CLINICAL TRIALS IN ELDERLY

COMPLIANCE

GUIDE LINES (SIOG)

PATIENT PREFERENCE

MORE CLINICAL TRIALS

End Points and Trial Design in Geriatric Oncology Research: A Joint European Organisation for Research and Treatment of Cancer–Alliance for Clinical Trials in Oncology–International Society of Geriatric Oncology Position Article

Hans Wildiers, Murielle Mauer, Athanasios Pallis, Arti Hurria, Supriya G. Mohile, Andrea Luciani, Giuseppe Curigliano, Martine Extermann, Stuart M. Lichtman, Karla Ballman, Harvey Jay Cohen, Hyman Muss, and Ulrich Wedding

Table 2. Issues in Clinical Trial Design for Older Patients With Cancer

Issue
RCTs remain gold standard when possible
Clinical trials should preferably integrate whole age range, including fit and frail older individuals
Elderly-specific clinical trials in older patients with cancer are required if standard therapy is different from that for younger patients
Trials of treatment strategy comparing different strategies (eg, therapy *v* best supportive care) should be encouraged
Randomized phase II or even single-arm phase II trials in specific subsets of older patients can provide insight into range of efficacy and toxicity in older populations but ideally should be confirmed in large phase III trials, which might be hard to perform for various reasons (eg, insufficient interest from sponsors/investors, difficulty in finding sufficient numbers of patients)
Not all questions can be answered with randomized trials, and large observational cohort studies or registries in community can provide further insight for frail population with less selection bias (preferably in parallel with or linked to RCTs)
Comparable/uniform geriatric assessment should be integrated into future trials in geriatric oncology
Regulatory authorities should require evaluation of efficacy and safety of new drugs in older and frail patients as well as in younger patients

Abbreviation: RCT, randomized clinical trial.

JCO 2013

GO DEPEND ALSO ON TUMOUR SUBTYPE

SPECIFIC TUMOUR TYPE and OLDER PATIENT HEMATOLOGY

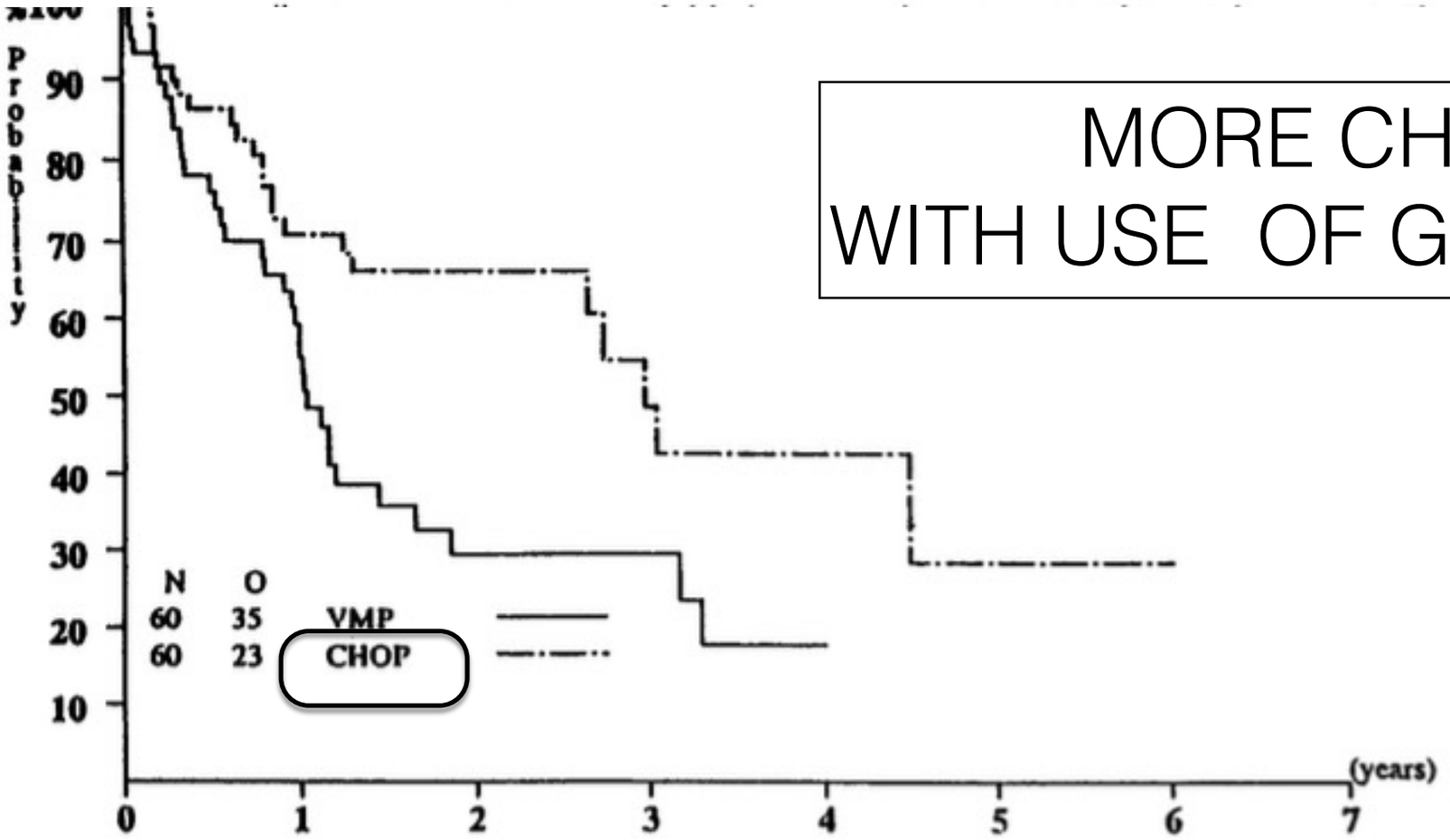
Non-Hodgkin's Lymphomas in 137 Patients Aged 70 Years or Older: A Retrospective European Organization for Research and Treatment of Cancer Lymphoma Group Study

By U. Tirelli, V. Zagonel, D. Serraino, J. Thomas, B. Hoerni, A. Tangury, U. Ruhl, P. Bey, N. Tubiana, W.P.M. Breed, K.J. Roozendaal, A. Hagenbeek, P.S. Hupperets, and R. Somers

We are aware that this retrospective study cannot lead to any definitive conclusion about whether aggressive or more conservative treatment should be used in the treatment of unfavorable NHL in the elderly. However, the present study does suggest that unfavorable NHL occurs frequently in elderly patients and that severe and lethal side effects are, in a relevant percentage of patients, associated with standard intensive chemotherapy regimens, especially if used at full dosage.

Journal of Clinical Oncology, Vol 6, No 11 (November), 1988: pp 1708-1713

CHOP Is the Standard Regimen in Patients ≥ 70 Years of Age With Intermediate-Grade and High-Grade Non-Hodgkin's Lymphoma: Results of a Randomized Study of the European Organization for Research and Treatment of Cancer Lymphoma Cooperative Study Group



MORE CHEMO BUT
WITH USE OF GROWTH FACTOR

Fig 2. Kaplan-Meier curve of OS by treatment regimen. Log-rank $P = .004$.

Journal of Clinical Oncology, Vol 16, No 1 (January), 1998: pp 27-34

SPECIFIC TUMOUR TYPE and OLDER PATIENT

colorectal cancer

SCREENING IF LIFE EXPECTANCY > 5 years

SCREENING and OLDER PATIENT

Impact of Age and Comorbidity on Colorectal Cancer Screening Among Older Veterans

Ann Intern Med. 2009 April 7; 150(7): 465–473.

Patients—27,068 patients > 70 years who had an outpatient visit in 2000 and an outpatient visit at 1 of 4 VA's during 2001–2002 and due for screening.

Measurements—The main outcome was receipt of fecal occult blood testing (FOBT), colonoscopy, sigmoidoscopy, or barium enema during 2001–2002 based on national VA and Medicare claims. Charlson comorbidity scores were used to stratify patients into 3 groups ranging from no comorbidity (score=0) to severe comorbidity (score > 4) and 5-year mortality was determined for each group.

Results—46% of patients were screened during 2001–2002. Only 47% of patients with no comorbidity were screened despite having life expectancies > 5 years (5-year mortality=19%). While the incidence of screening declined with age and worsening comorbidity, it was still 41% for patients with severe comorbidity who had life expectancies < 5 years (5-year mortality=55%).

Conclusions—Advancing age was inversely associated with colorectal cancer screening while comorbidity was a weaker predictor. More attention to comorbidity is needed to better target screening to older patients with substantial life expectancies and avoid screening older patients with limited life expectancies.

SCREENING

Should Colorectal Cancer Screening Be Considered in Elderly Persons Without Previous Screening?

A Cost-Effectiveness Analysis

SREENING IN >75 YEARS IF NO PREVIOUS SCREENING

Background: The U.S. Preventive Services Task Force recommends against routine screening for colorectal cancer (CRC) in adequately screened persons older than 75 years but does not address the appropriateness of screening in elderly persons without previous screening.

Table 4. **Results Summary of CRC Screening Indicated in Elderly Persons Without Previous Screening**

Comorbid Condition Level*	Age up to Which CRC Screening Should Be Considered, *y*	Screening Strategy Indicated, by Age										
		76 y	77 y	78 y	79 y	80 y	81 y	82 y	83 y	84 y	85 y	86 y
No comorbid conditions	86	COL	COL	COL	COL	COL	COL	COL	COL	SIG	FIT	FIT
Moderate comorbid conditions	83	COL	COL	COL	COL	COL	SIG	FIT	FIT			
Severe comorbid conditions	80	COL	COL	SIG	FIT	FIT						

Ann Intern Med. 2014;160:750-759.

SURGERY

IF « FIT »PATIENT, SURVIVAL IS THE SAME AS FOR YOUNGER PATIENT: TREATMENT SOULD BE OPTIMAL

BUT SURVIVAL MAY BE WORSE BECAUSE OF DIFFERENT FACTORS (more advanced stage at diagnosis,more morbidities in the post operative time, post treatment decisions, pre-op comorbidities..)

If liver metastasis,treatment should also be optimal but morbidity and mortality are superior (4,5 % vs 1,5 %)

RADIOTHERAPY

Age impacts the pattern of care for elderly patients with rectal cancer

Florence Guillerme · Jean Baptiste Clavier · Hélène Nehme-Schuster · Valérie Leroy · Damien Heitz · Catherine Schumacher · Méher Ben Abdelghani · Cécile Brigand · Jean Emmanuel Kurtz · Georges Noël

Table 2 Administered treatment performed

	<75 years (n=127)	≥75 years (n=113)	p
Surgery	92 % (116)	80 % (90)	0.0142
Chemotherapy	55 % (70)	39 % (44)	0.017
Conventional RT	61 % (78)	49 % (55)	0.064
Adaptive treatment	46 % (59)	66 % (75)	0.0027
Toxicity > G2	7 % (9)	9 % (10)	0.79
Iatrogenic deaths	2 % (2)	6 % (7)	0.12
Six months deaths	9 % (11)	16 % (18)	0.12

MORE USE OF 5X5 SHORT SCHEDULE ALMOST IF UNFIT PATIENT

J Colorectal Dis (2014) 29:157–163

ADJUVANT CHEMOTHERAPY

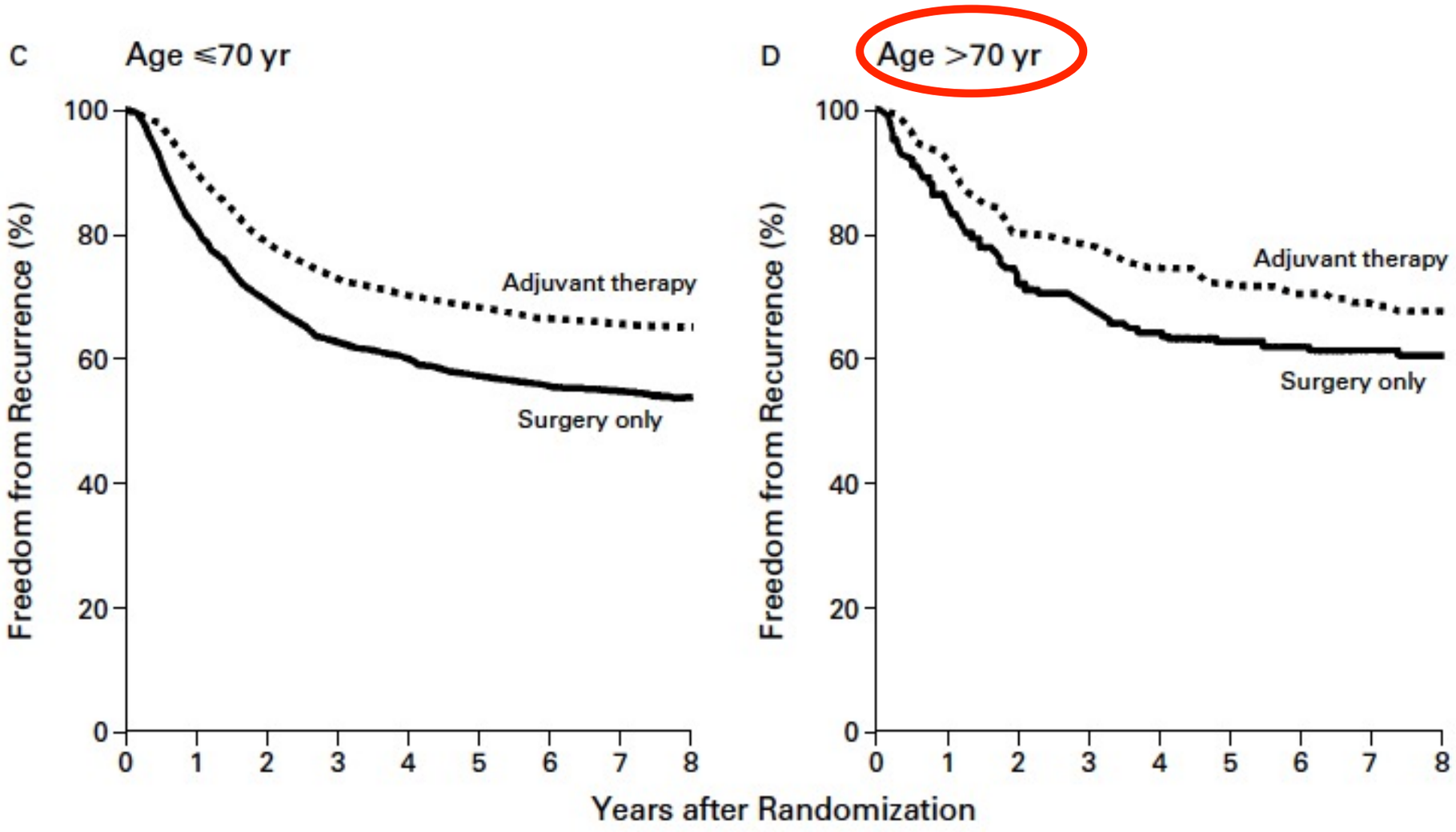
- In Europe (2008 DATA) 436 000 new cases of CCR
- average age onset=71 years
- 40 % present at stage III
- 80 % recurrence by 3 years;90 % by 5 years

- **NO QUESTION ABOUT THE NEED FOR FU BASED**
- **ADJUVANT CHEMOTHERAPY**
    - **SAVE LIFE IN STAGE 3 REGARLESS OF AGE (25 TO 30 %)**
    - **REASONNABLY WELL TOLERATED**
    - **UNDERUSED IN OLDER**

FOLFOX INCREASE BENEFIT of 5 % in younger
AND IS MORE TOXIC

WHAT MAY WE DO IN OLDER??

ADJUVANT CHEMOTHERAPY



CONCLUSION:Selected elderly patients with colon cancer can receive the same benefit from fluorouracil based adjuvant therapy as their younger counterparts, without a significant increase in toxic effects.

Sargent NEJM,2001

ADJUVANT CHEMOTHERAPY

sub group study

ADJUVANT FOLFOX vs FUFOL

Table 3. Cox Analysis HR for DFS, TTR, and OS According to Stage and Age

FOLFOX4 *v* FL by Subgroup	No. of Patients	Five-Year DFS			Five-Year TTR			Six-Year OS		
		HR	95% CI	*P*	HR	95% CI	*P*	HR	95% CI	*P*
Stage III	1,347	0.78	0.65 to 0.93	.005	0.74	0.61 to 0.89	.001	0.80	0.65 to 0.97	.023
Stage II	899	0.84	0.62 to 1.14	.258	0.70	0.49 to 0.99	.045	1.00	0.7 to 1.41	.986
High risk	569	0.72	0.51 to 1.01	.062	0.62	0.41 to 0.92	.002	0.91	0.61 to 1.36	.648
Low risk	330	1.36	0.76 to 2.45	.305	1.01	0.5 to 2.05	.972	1.36	0.67 to 2.5	.399
Age < 70 years, all stages	1,931	0.78	0.66 to 0.92	.003	0.74	0.62 to 0.88	.001	0.80	0.66 to 0.97	.020
Age 70-75 years, all stages	315	0.93	0.64 to 1.35	.710	0.72	0.47 to 1.11	.140	1.10	0.73 to 1.65	.661

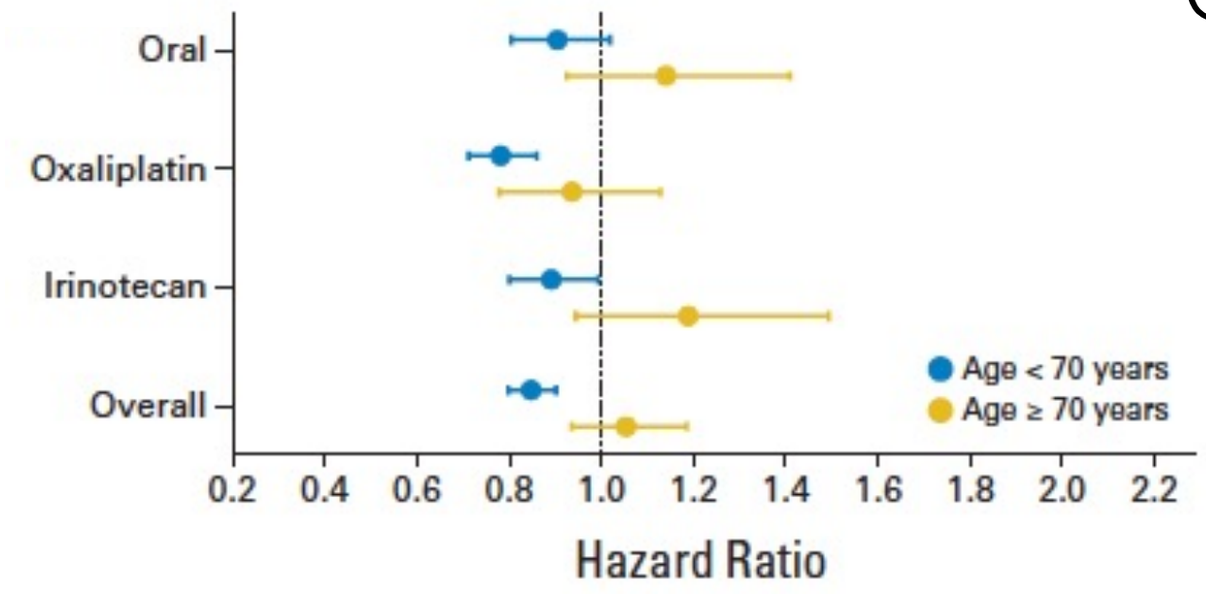
Abbreviations: DFS, disease-free survival; FL, fluorouracil with leucovorin; FOLFOX4, infusional fluorouracil, leucovorin, and oxaliplatin; HR, hazard ratio; OS, overall survival; TTR, time to recurrence.

N=2246 patients;315 :70-75 year
In this group no statistical benefit (OS/DFS)
for adjunction of oxaliplatin in adjuvant treatment
for older patient (>70 years)

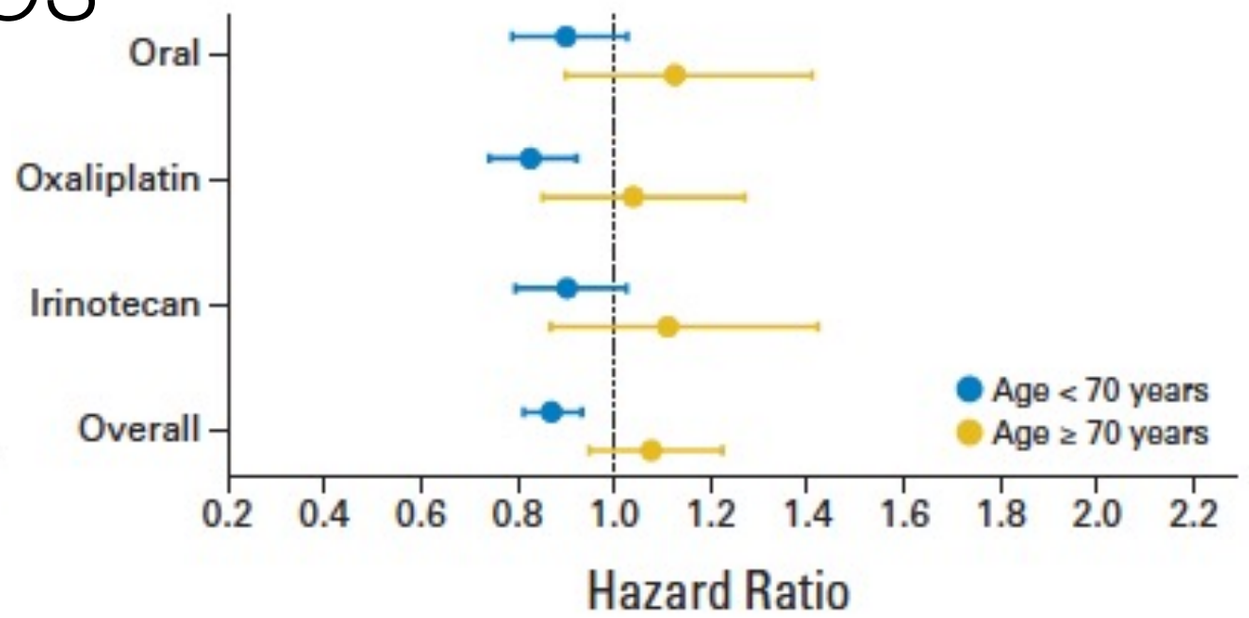
Tournigand,JCO,2012

ADJUVANT CHEMOTHERAPY

DFS



OS



Benefit of oxaliplatin (DFS OS) in younger < 70 years.
In a subset of patients > 70 years oxaliplatin
may add a benefit in DFS.
Data support FU monotherapy in older patient

McCleary,JCO,2013

ADJUVANT CHEMOTHERAPY

POPULATION BASED ANALYSIS

Table 3. Benefit of Adjuvant Oxaliplatin Among Elderly Patients With Stage III Colon Cancer

Patient Group and Survival	Oxaliplatin *v* Nonoxaliplatin Adjuvant Chemotherapy					
	SEER-Medicare		NYSCR-Medicare		NCCN*	
	Nonoxaliplatin (n = 1,163)	Oxaliplatin (n = 610)	Nonoxaliplatin (n = 325)	Oxaliplatin (n = 124)	Nonoxaliplatin (n = 42)	Oxaliplatin (n = 66)
PS matched	512	512	110	110	NA	NA
3-year OS, unmatched cohort, %	65	74	59	66	88	84
3-year OS, PS-matched cohort, %	68	73	61	66	NA	NA
Crude mortality unmatched						
HR	1	0.71	1	0.83	1	1.25
95% CI		0.60 to 0.85		0.56 to 1.22		0.43 to 3.68
PS matched mortality						*
HR	1	0.84	1	0.82	1	1.84
95% CI		0.69 to 1.04		0.51 to 1.33		0.48 to 7.05
Trimmed, PS matched mortality					NA	NA
HR	1	0.87	1	0.88		
95% CI		0.69 to 1.10		0.51 to 1.53		

Data Source
SEER-Medicare
NY-Medicare
NY-Medicaid
CanCORS
NCCN

5489 patients > 75 year with stage III resected colon cancer
Benefit of chemotherapy as in clinical trial with younger (24 % reduction in the risk of death)
Oxaliplatin treatment was associated with 3 % increase in OS
greater number of outpatient AEs in patient older than 75 years receiving FOLFOX
But no more hospitalization or death

Sarnoff,JCO,2012

ADJUVANT CHEMOTHERAPY

TOXICITY
MOSAIC DATA

	5FU/LV		FOLFOX	
	ALL GRADE	SEVERE OR LIFE THREATENING	ALL GRADE	SEVERE OR LIFE THREATENING
Paresthesia	16 %	<1 %	92 %	12 %
Neutropenia	40 %	4 %	79 %	41 %
Vomiting	24 %	1 %	47 %	6 %
Diarrhea	48 %	7 %	56 %	11 %

ADJUVANT FOLFOX in older may increase os
but we need to discuss
with the patient the toxicity profile and decide
on an individual basis

Work in Progress

PRODIGE 34 – FFCD 1402 – ADAGE
Adjuvant chemotherapy in elderly patients with resected stage III colon cancer: A randomized phase 3 trial

ADAGE is an academic, multi-centre, randomized phase III study comparing 3-year DFS of two therapeutic strategies in two groups of elderly patients with completely resected colon cancer. Patients are selected for one of the two groups by the physician, based on a multidisciplinary evaluation involving a geriatrician

Group 1 (defined as "able" to be treated with bi-chemotherapy)
Arm A: LV5FU2 or capecitabine / Arm B: FOLFOX or XELOX

Group 2 (defined as "unable" to be treated with bi-chemotherapy)
Arm C: Observation /Arm D: LV5FU2 or capecitabine

SPECIFIC TUMOUR TYPE and OLDER PATIENT

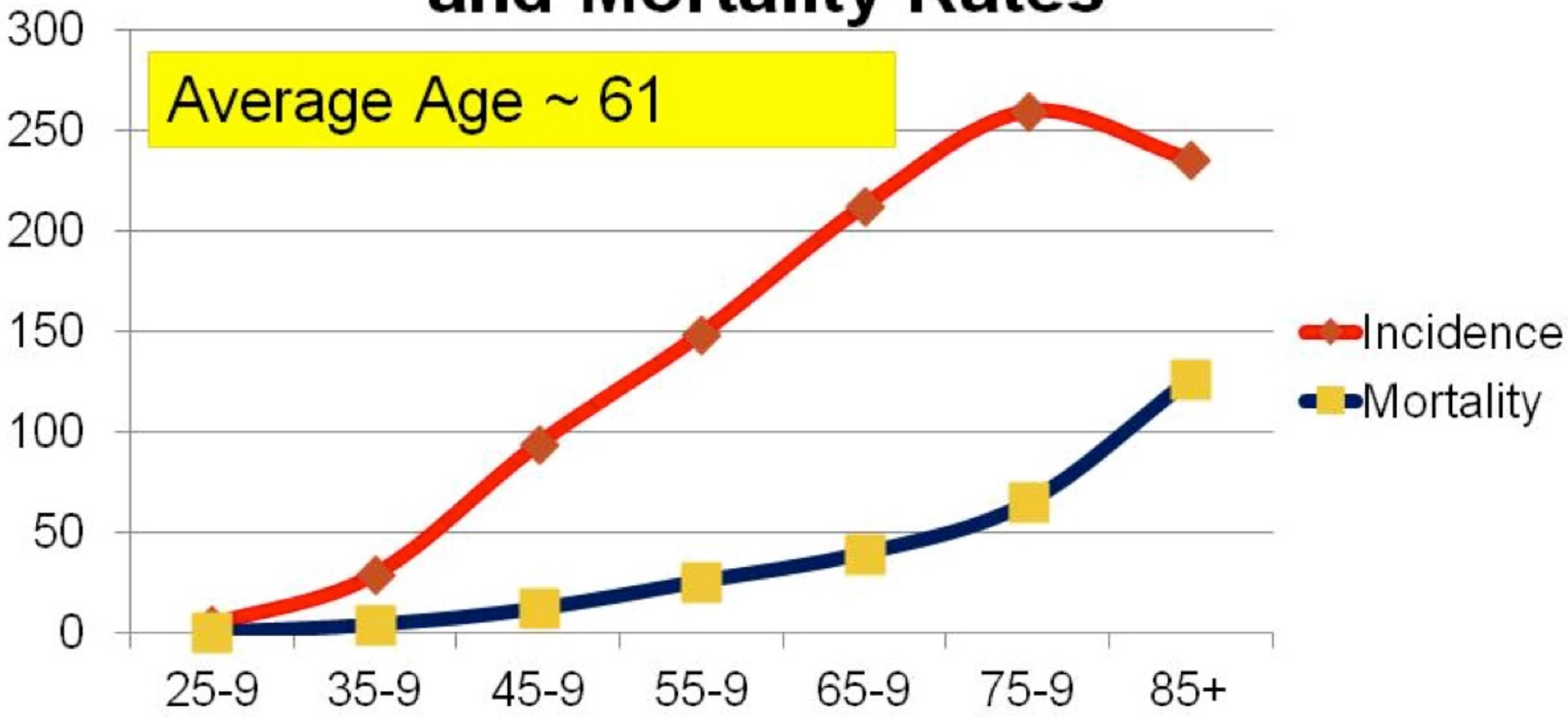
breast cancer

Updated recommendations regarding the management of older patients with breast cancer: a joint paper from the European Society of Breast Cancer Specialists (EUSOMA) and the International Society of Geriatric Oncology (SIOG)

Laura Biganzoli, Nicolò Matteo Luca Battisti, Hans Wildiers, Amelia McCartney, Giuseppe Colloca, Ian H Kunkler, Maria-João Cardoso, Kwok-Leung Cheung, Nienke Aafke de Glas, Rubina M Trimboli, Beatriz Korc-Grodzicki, Enrique Soto-Perez-de-Celis, Antonio Ponti, Janice Tsang, Lorenza Marotti, Karen Benn, Matti S Aapro, Etienne G C Brain

Lancet Oncol 2021; 22: e327–40

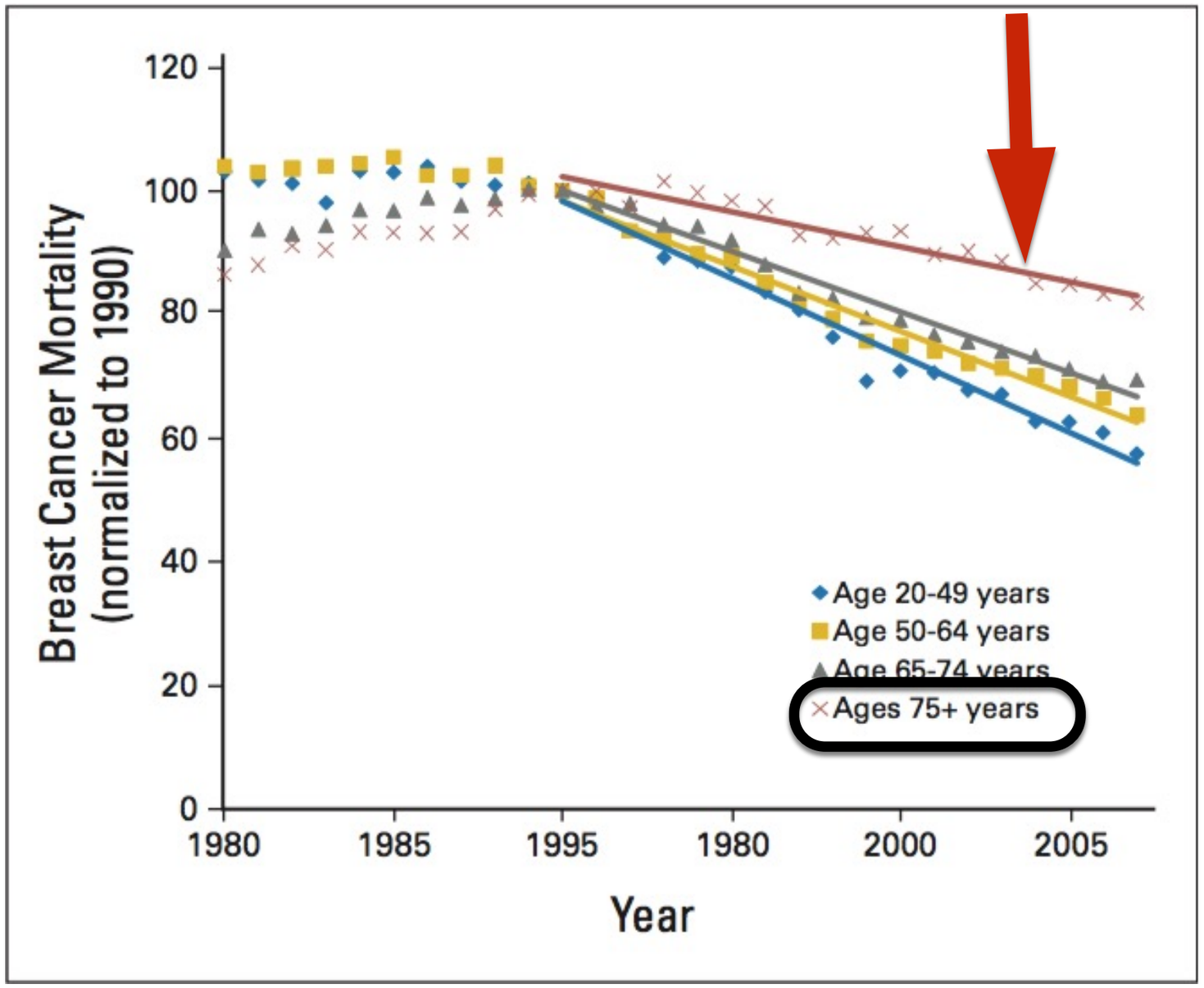
SEER 2002-2006: Breast Cancer Incidence and Mortality Rates



http://seer.cancer.gov/cgi-bin/csr/1975_2006/search.pl

AS FOR COLORECTAL,LUNG,PROSTATE…
.INCREASING INCIDENCE AND MORTALITY WITH AGE

Breast cancer outcome
is better in women age less than 75 years

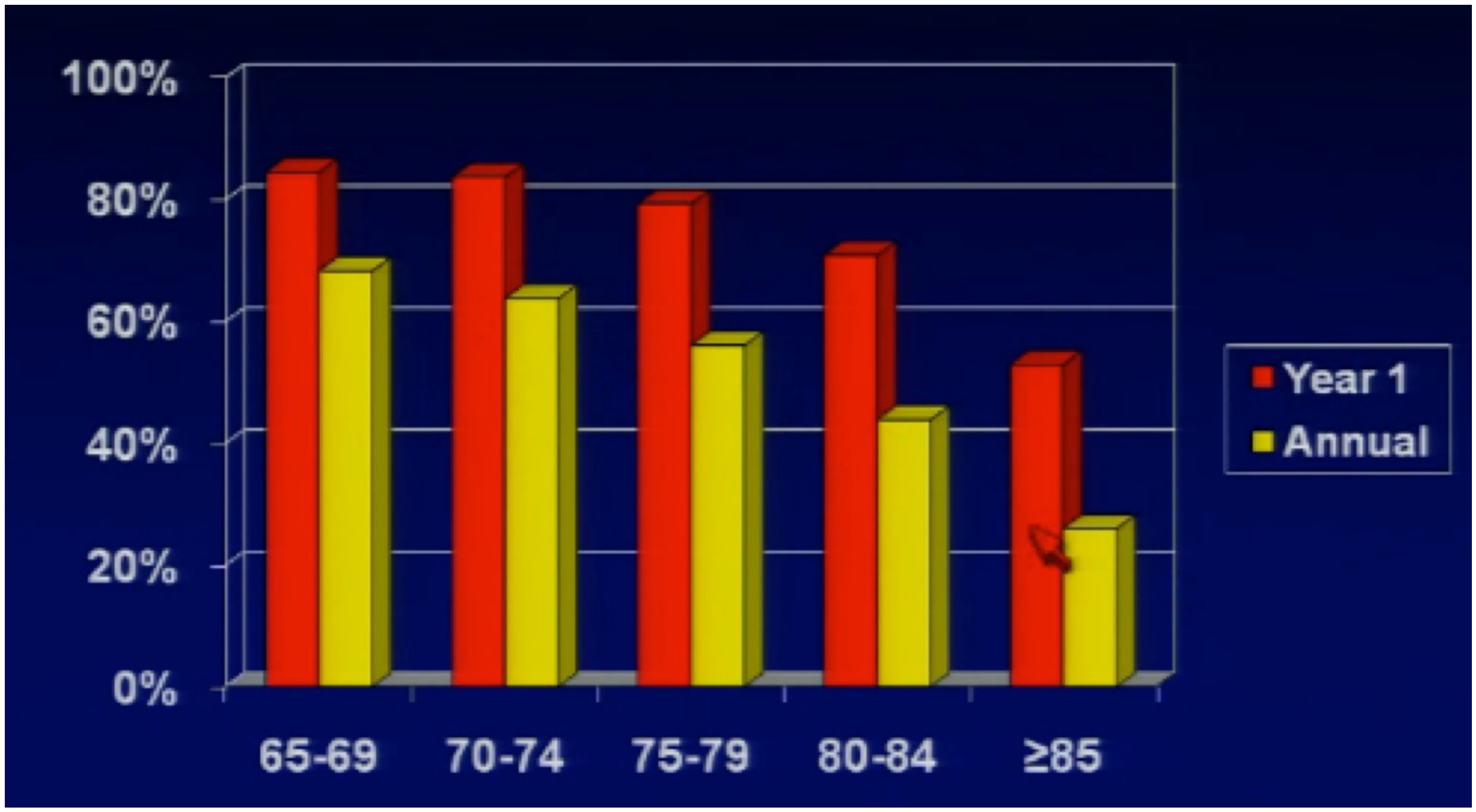


BECAUSE OF UNDER TREATMENT?:
BETTER SELECTION IS IMPORTANT

Smith,JCO,2011

WHO NEEDS LESS OR MORE TREATMENT ?

OLDER BREAST CANCER SURVIVORS LESS LIKELY TO GET MAMMOGRAPHY



Keating,JCO,2006

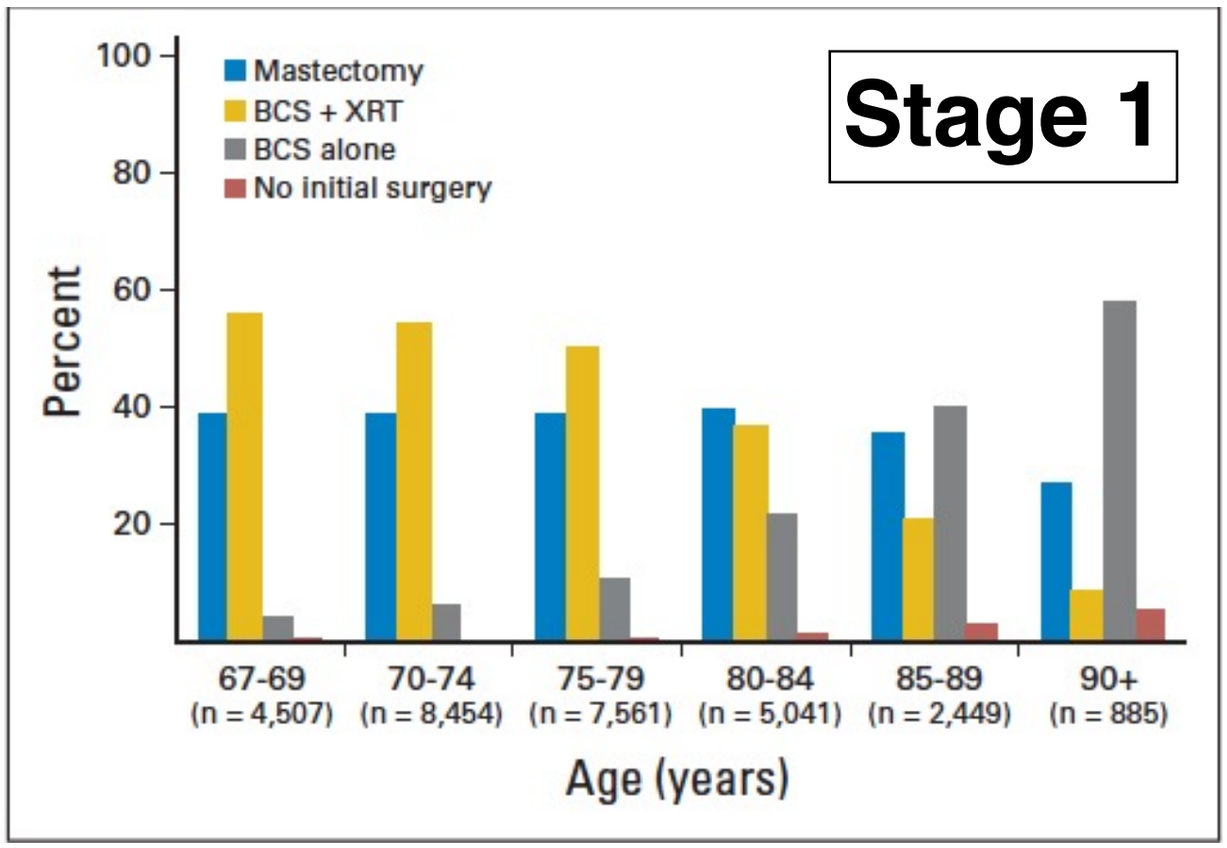
RECOMMENDATIONS FOR SCREENING
NCCN

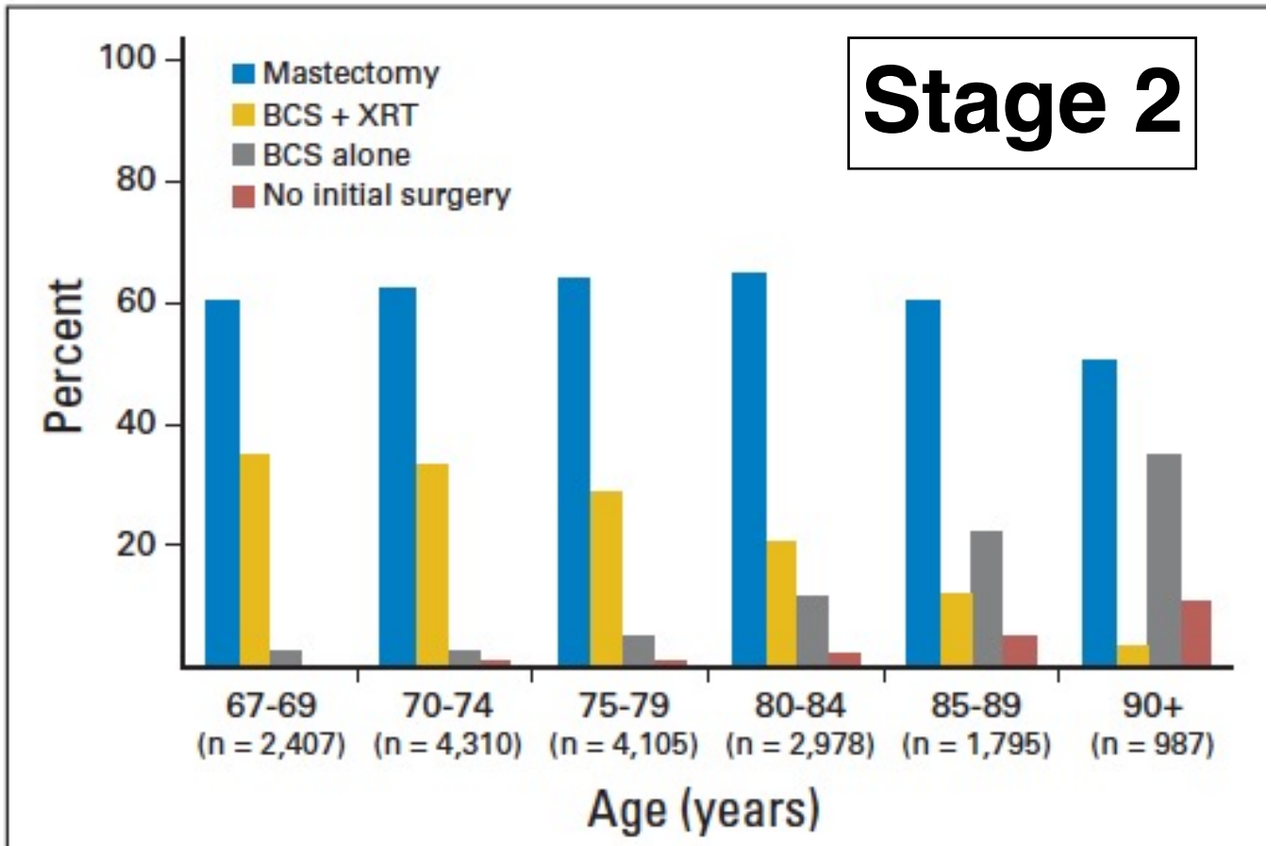
Age to Stop Mammographic Screening:

There are limited RCT data regarding screening of elderly women, because most trials for breast screening have used a cutoff age of 65 or 70 years.[101-103] However, observational studies and computer models show mortality benefit to age 80 to 84.[69,80] Considering the high incidence of breast cancer in the elderly population, the screening guidelines used for women who are age 40 or older are recommended in the elderly as well. Clinicians should always use judgment when applying screening guidelines. The mortality benefit of screening mammography is often

delayed for 5 to 7 years in RCTs that emphasize the importance of life expectancy and overall health when considering age to stop screening. Mammography screening should be individualized, weighing its potential benefits/risks in the context of the patient's overall health and estimated longevity.[104] If a patient has severe comorbid conditions limiting her life expectancy and no intervention would occur based on the screening findings, then the patient should not undergo screening, regardless of her age.[104,105]

OLDER PATIENTS LESS LIKELY TO UNDERGO SURGERY





REGARDLESS OF STAGE

Schonberg,JCO,2010

RECOMMENDATIONS FOR SURGERY AND RADIOTHERAPY

MINIMIZE THE MORBIDITY OF TREATMENT

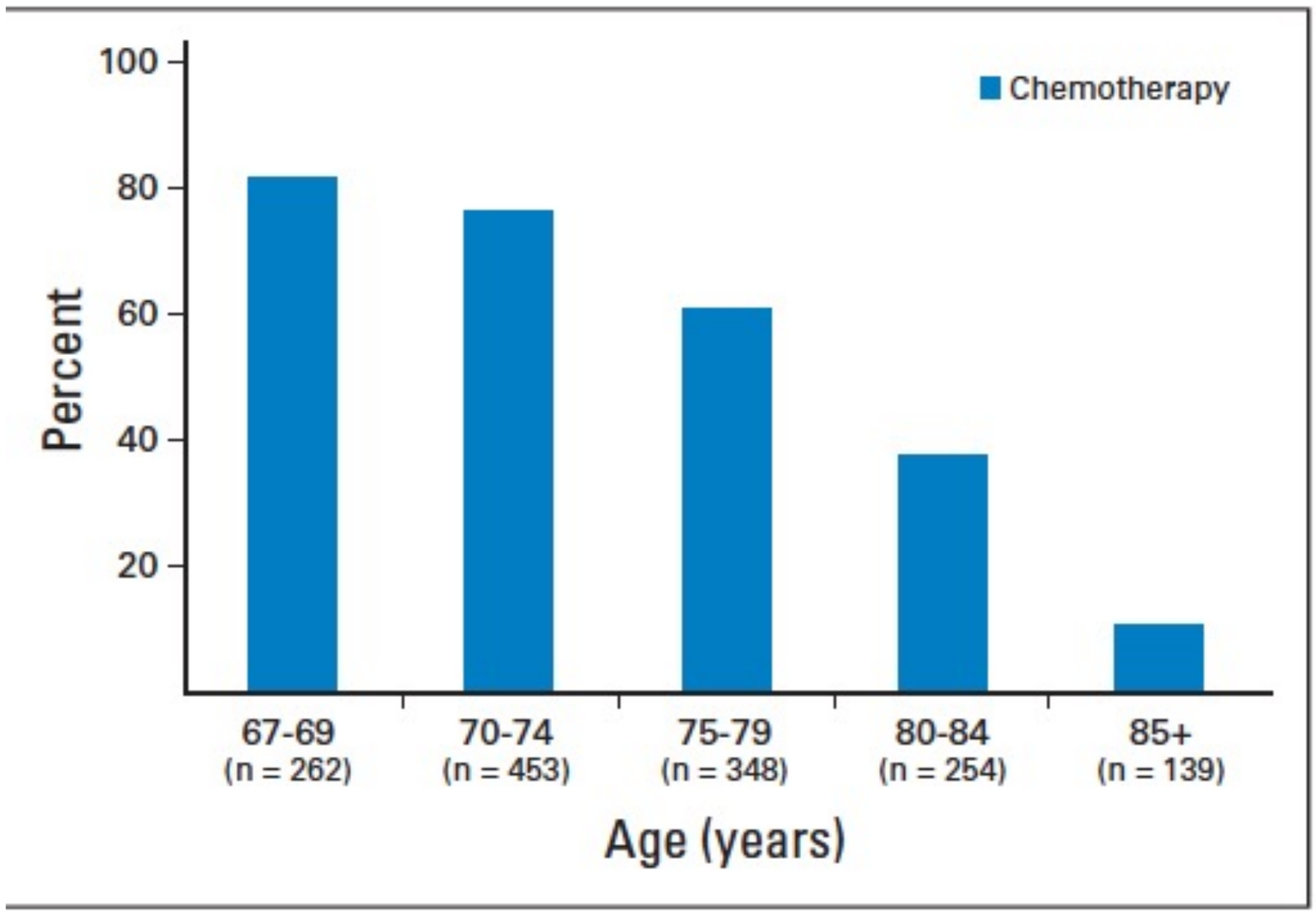
- **LUMPECTOMY WITH MINIMAL MARGINS**
- **HORMONAL THERAPY**

SOME SPECIAL CIRCUMSTANCES

- **PREOP HORMONAL TREATMENT**
- **MASTECTOMY**
- **SENTINEL NODE**
- **CHEMOTHERAPY**
- **RADIATION**

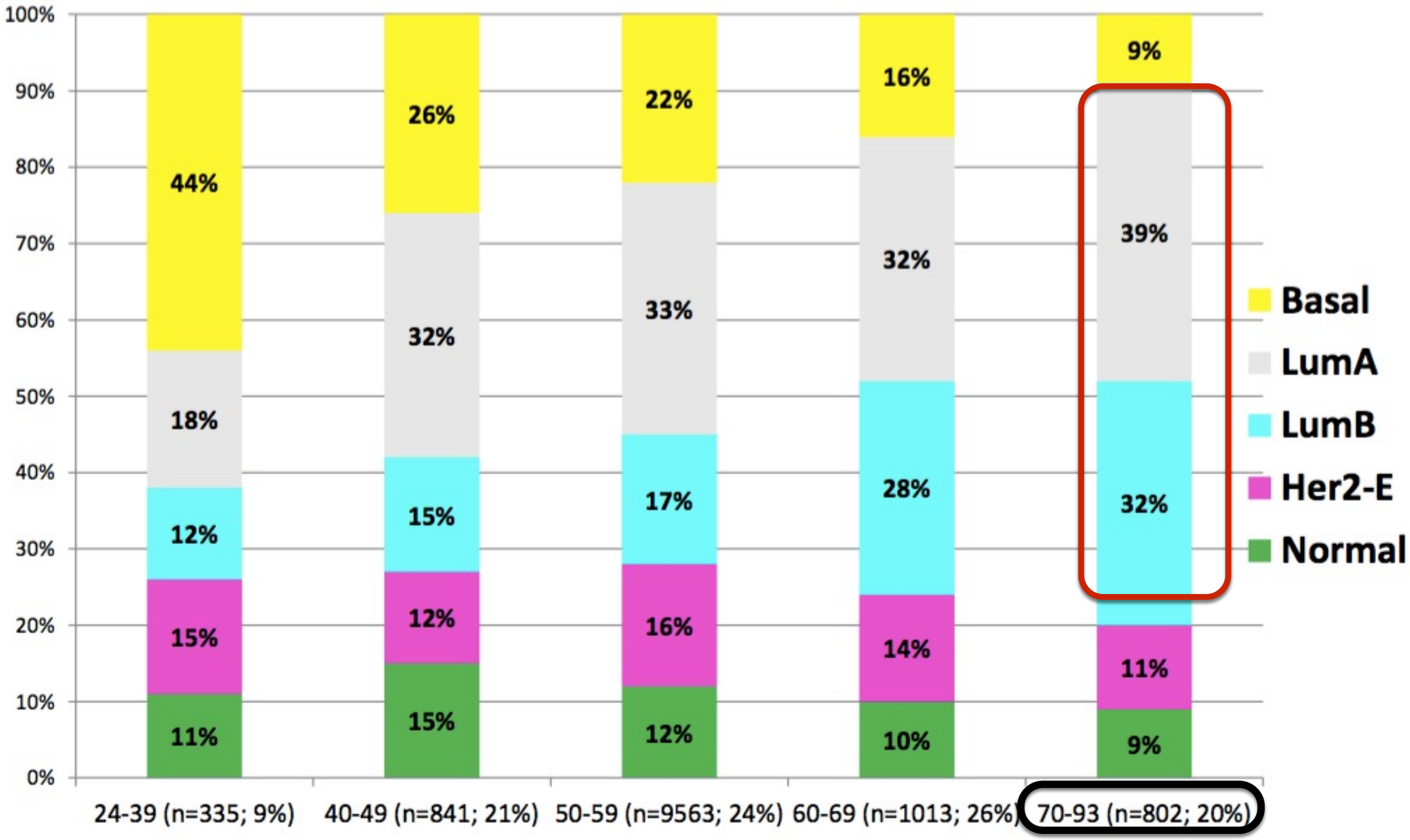
FOR STAGE I AND ER +
LUMPECTOMY AND HORMONAL THERAPY
AVOID RADIOTHERAPY FRO PATIENTS > 70 YEARS

OLDER PATIENT
LESS LIKELY TO RECEIVE CHEMOTHERAPY



Schonberg,JCO,2010

BREAST CANCER SUBTYPES:
THE INCIDENCE OF MORE FAVORABLE SUBTYPES INCREASE WITH AGE



Jenkins et Al. PAM 50 Subtypes,Abstract,ASCO 2012

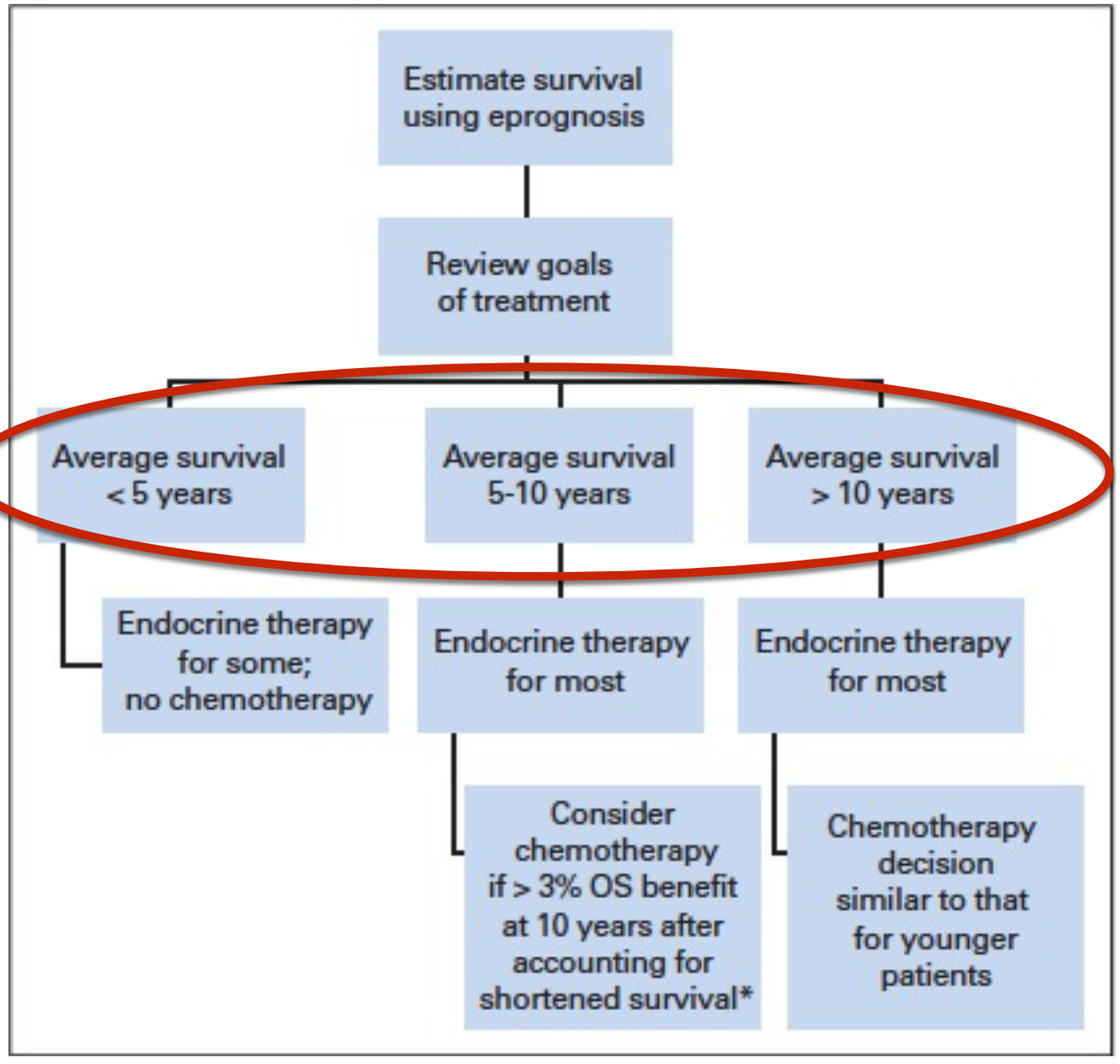
ER and/or PgR + and HER2 -

- Most common phenotype of breast cancer
- increase with age
- about 75 % of older > 75 years
- variable course:
    - luminal A and B
    - most recurrences after 5 years (**life expectancy help for decisions!!**)
    - **Endocrine therapy** mainstay for most

<u>importance of adherence</u>:
20-50 % stop medications
early stoppage related to toxicity,cost and being unaware of value of treatment
we must discuss toxicity before treatment
ask if they are taking drugs
have support for those who are not compliant

ER and/or PgR + and HER2 -: chemotherapy ?

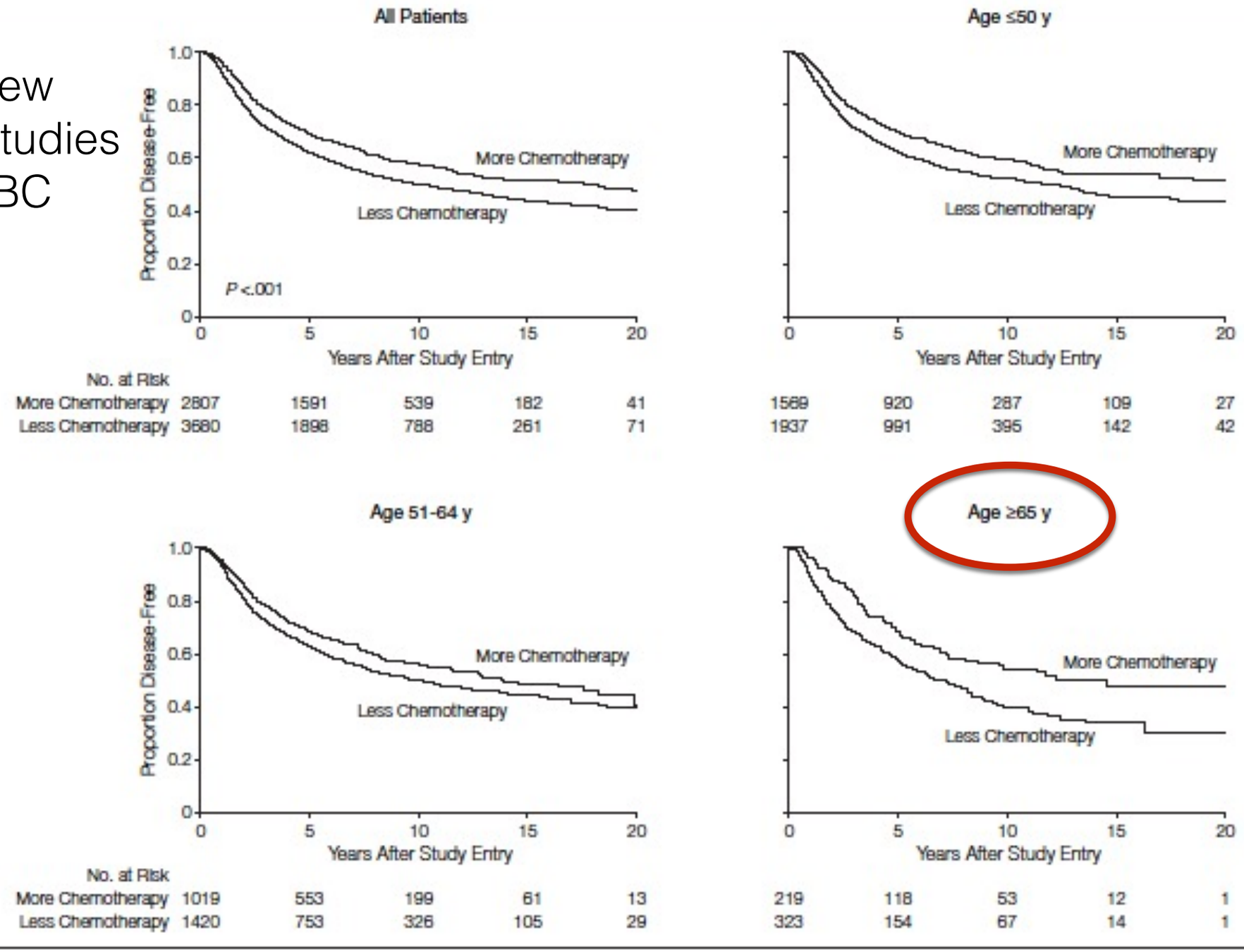
- **Life expectancy** is key in decision
- very small benefit if nodes negative
- tools like oncotype and Adjuvantonline may provide information
- consider chemo if **≥ 4 nodes positive**



Muss,JCO, 2014

Breast cancer Nodes positive: chemotherapy in older

Retrospective review
data from 4 random studies
N=6487 nodes + BC
2% > 70 years



Conclusion Age alone should not be a contraindication to the use of optimal chemotherapy regimens in older women who are in good general health.

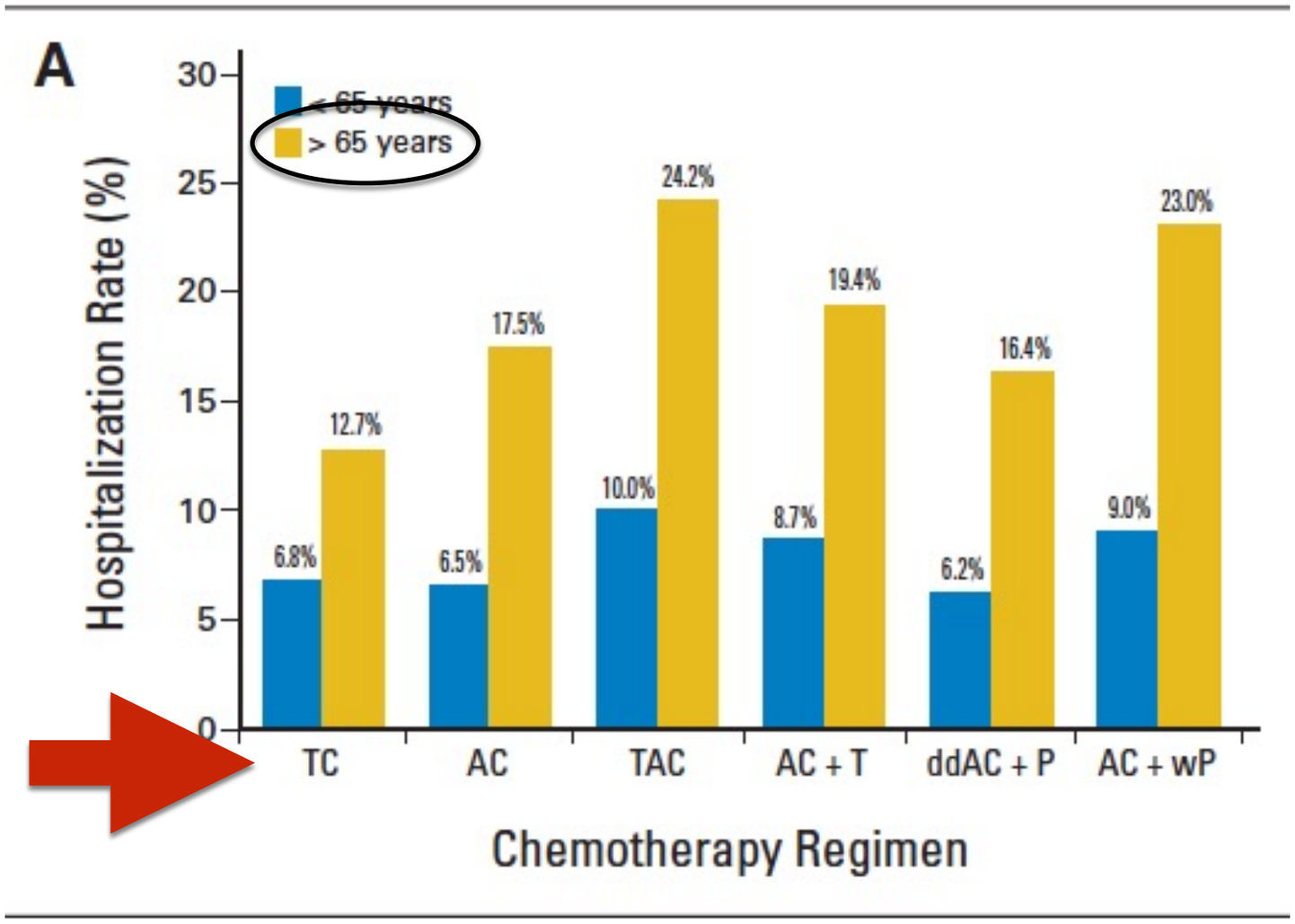
JAMA. 2005;293:1073-1081 www.jama.com

Muss,JAMA,2005

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Risk of Hospitalization According to Chemotherapy Regimen in Early-Stage Breast Cancer

Carlos H. Barcenas, Jiangong Niu, Ning Zhang, Yufeng Zhang, Thomas A. Buchholz, Linda S. Elting, Gabriel N. Hortobagyi, Benjamin D. Smith, and Sharon H. Giordano



More hospitalisation in olders
the best schedule seems TC 4 cycles
with growth factor support

BE CAREFULL WITH ANTHRACYCLINE

Triple negative breast cancer: chemotherapy is the only treatment

- About 10 % of BC in older
- Biology similar irrespective of age
- Most recurrence within 5 years
- More chemo is better
    - taxanes and anthracycline
- Proven benefit of chemo even in older
- Estimating life expectancy and toxicities

studies in older

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 14, 2009 VOL. 360 NO. 20

Adjuvant Chemotherapy in Older Women with Early-Stage Breast Cancer

Hyman B. Muss, M.D., Donald A. Berry, Ph.D., Constance T. Cirrincione, M.S., Maria Theodoulou, M.D.,

65 and older
≥ 1 cm and any N
Hormonal RX per MD
companion trials
QoL,compliance and
tumor biology

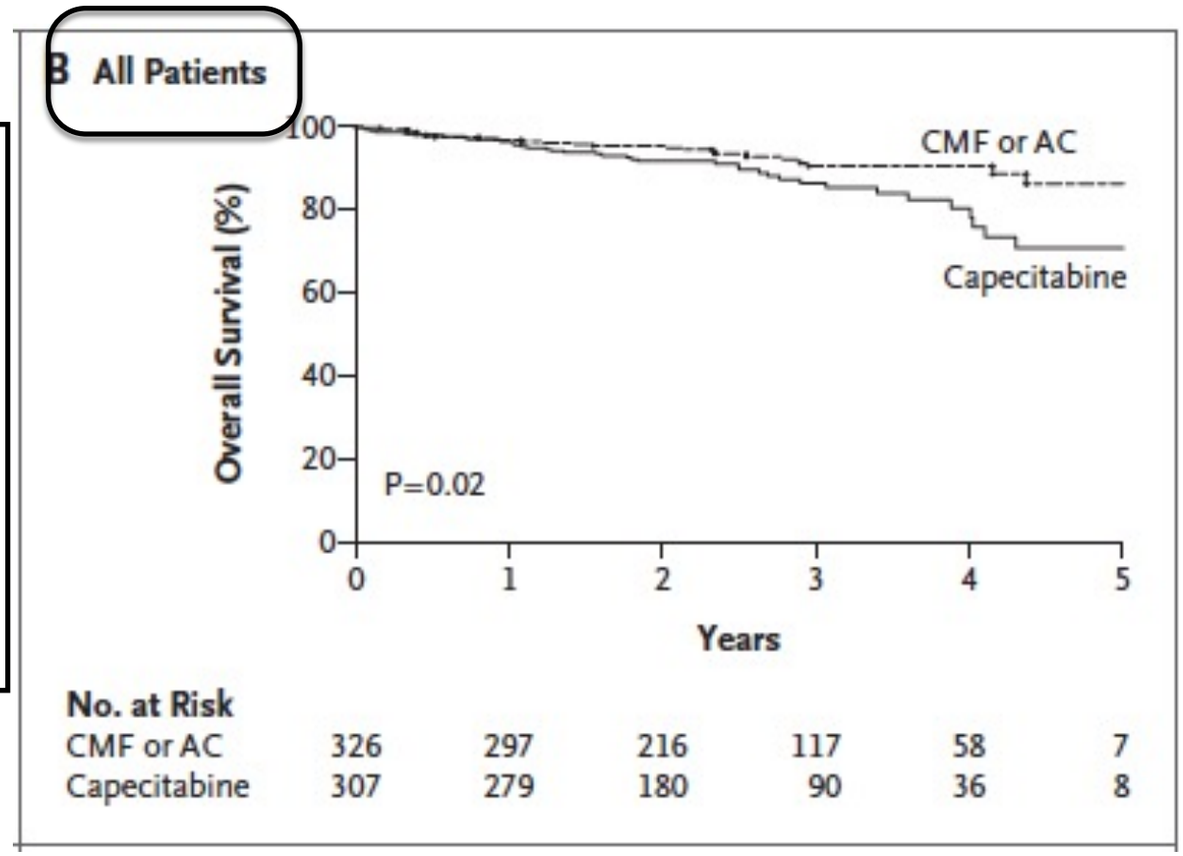
R

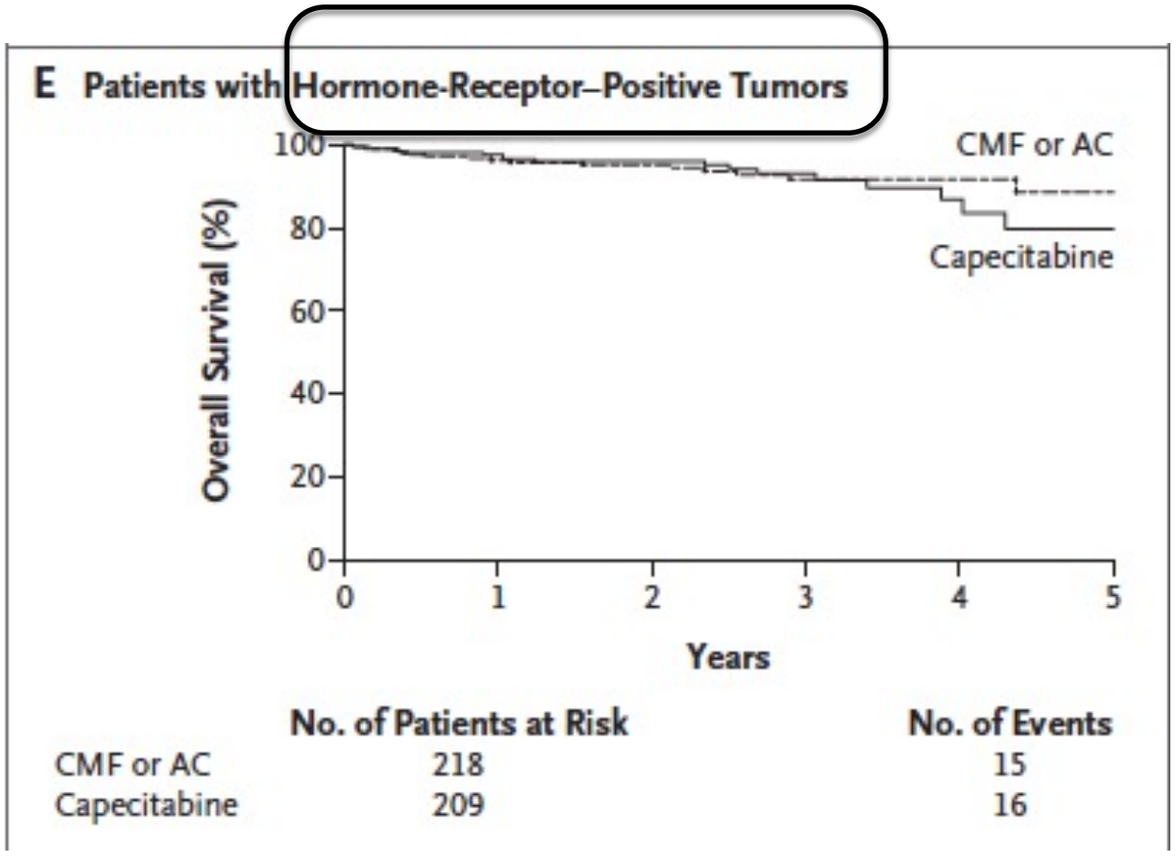
CMF X 6 or AC X 4
(1)

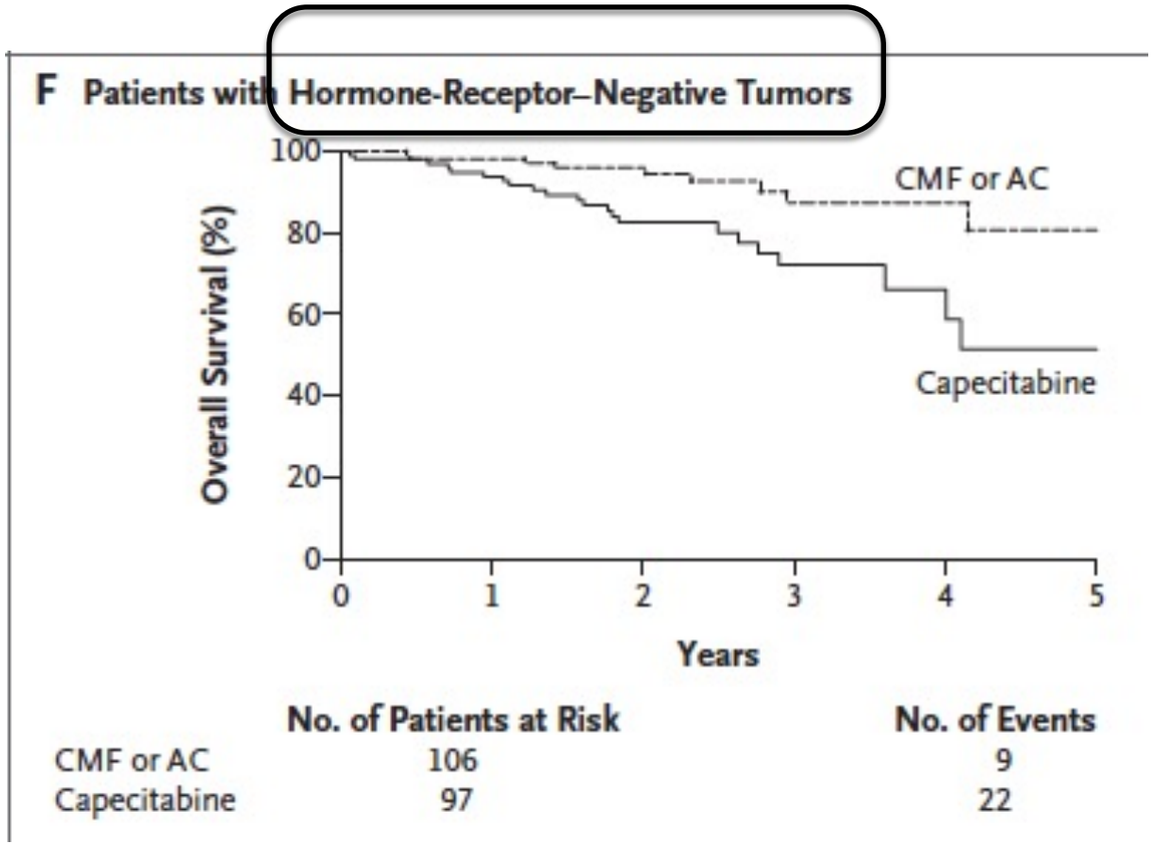
CAPECITABINE X 6 (2)

1) More intensive chemo
2) Less intensive and oral drug

Standard treatment is superior to less chemo and benefit is more important in triple negative BC







Muss,NEJM,2009

HER2 + breast cancer: chemotherapy and targeted treatment

- Anti-HER2 therapy changes the prognosis
- ER and PR are important
    - ER and PR negative: worst
    - ER and / or PR positive: better
- No good data on anti-HER2 alone
- Trastuzumab cardiac toxicity matters !:increasing with age
- « onco-Cardiology » is a new era of interest (proactive ACE inhibitors and Beta-blockers
- Data on less chemo for older ? (no anthracycline)

CONCLUSIONS

WE NEED COLLABORATION FOR THE EVALUATION OF OLDER PATIENT

TOOLS FOR SELECTION OF PATIENTS NEEDING GA EVALUATION OF LIFE EXPECTANCY IS IMPORTANT

FOR DIFFERENT CANCERS,DATA GENERALLY
SHOW THAT FOR FIT PATIENT SAME GUIDELINES FOR PATIENT < 70 AND >70 YEARS

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Department of Medical Oncology
Prof Jerusalemy
Breast and GI tumors
CHU ST LIEGE
BELGIUM

SOME WEBSITES HELPIN FOR EVALUATION IN GERIATRIC ONCOLOGY

Site	Description	Link
ASCO University	Series of online modules exploring different care options for older patients, including those with breast cancer; also has MOC course on geriatric oncology	http://university.asco.org/geriatric-oncology
SIOG	International organization focusing on geriatric oncology; Web site has useful links to geriatric oncology guidelines and other educational materials	http://www.siog.org
Adjuvant! Online	Calculates benefits of adjuvant therapy for patients with breast cancer; can add estimates of comorbidity to calculations	https://www.adjuvantonline.com/index.jsp
PREDICT	UK-derived calculator that calculates benefits of adjuvant therapy for patients with breast cancer; does not allow for comorbidity; can calculate benefits for patients with HER2-positive tumors	http://www.predict.nhs.uk
ePrognosis	Series of calculators based on systematic review of literature allowing for estimation of life expectancy in older adults	http://eprognosis.ucsf.edu/default.php
POGOe	Comprehensive site with free collection of expert-contributed geriatric materials for educators and learners	http://www.pogoe.org/about
CARG	Group of researchers with major interest in geriatric oncology research; opportunities for mentoring; online chemotherapy toxicity calculator and geriatric assessment tools	http://www.mycarg.org
Moffitt Cancer Center Senior Adult Oncology Program Tools	Online tools for estimating chemotherapy toxicity (CRASH score) and other geriatric calculators	http://moffitt.org/cancer-types–treatment/cancers-we-treat/senior-adult-oncology-program-tools
Lineberger Comprehensive Cancer Center Geriatric Oncology	Free PowerPoint slide sets of core lectures in geriatrics as well as resources and links	http://unclineberger.org/geriatric

Muss,JCO, 2014

SOME FURTHER READINGS

- international Society of Geriatric Oncology consensus on geriatric assessment in older patients with cancer.Wildiers H.J Clin Oncol. 2014 Aug 20;32(24):2595-603
- Screening tools for multidimensional health problems warranting a geriatric assessment in older cancer patients: an update on SIOG recommendations.Decoster L,.Ann Oncol. 2015 Feb;26(2):288-300
- updated recommendations regarding the management of older patients with breast cancer: a joint paper from the European Society of Breast Cancer Specialists (EUSOMA) and the International Society of Geriatric Oncology (SIOG).Biganzoli L.Lancet Oncol. 2021 Jul;22(7):e327-e340.