



Geriatric Oncology

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THE UNIVERSITY OF LIVERPOOL



Multidisciplinary Cancer Management Course

1. Epidemiology



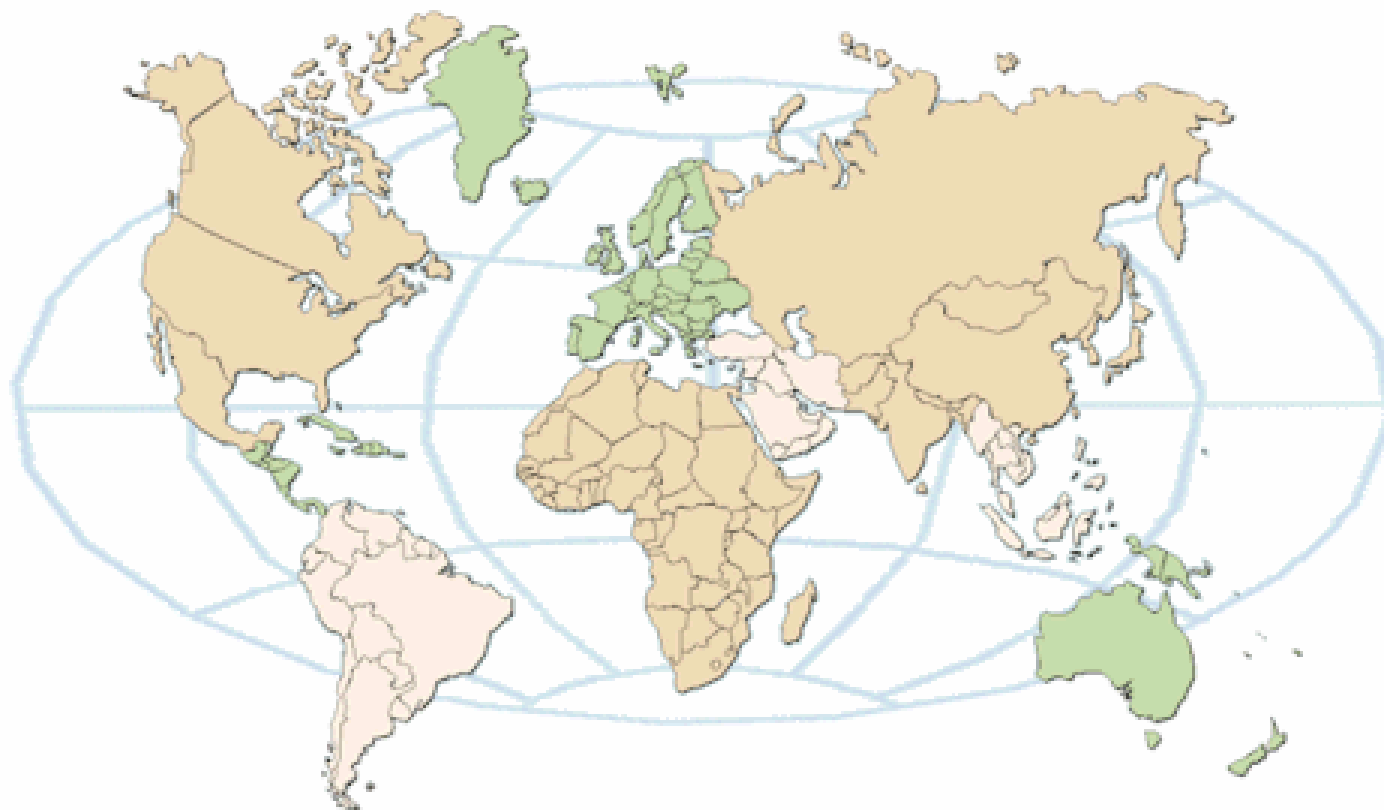
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Epidemiology - EU

- Life expectancy: 40 yrs 1900
 80 yrs 2000
- >60yr subjects increase at a 1% rate/yr
- >65yr 1990 13%
 2000 21%
 2035 40%
- geriatric population has x 3 over of the last century

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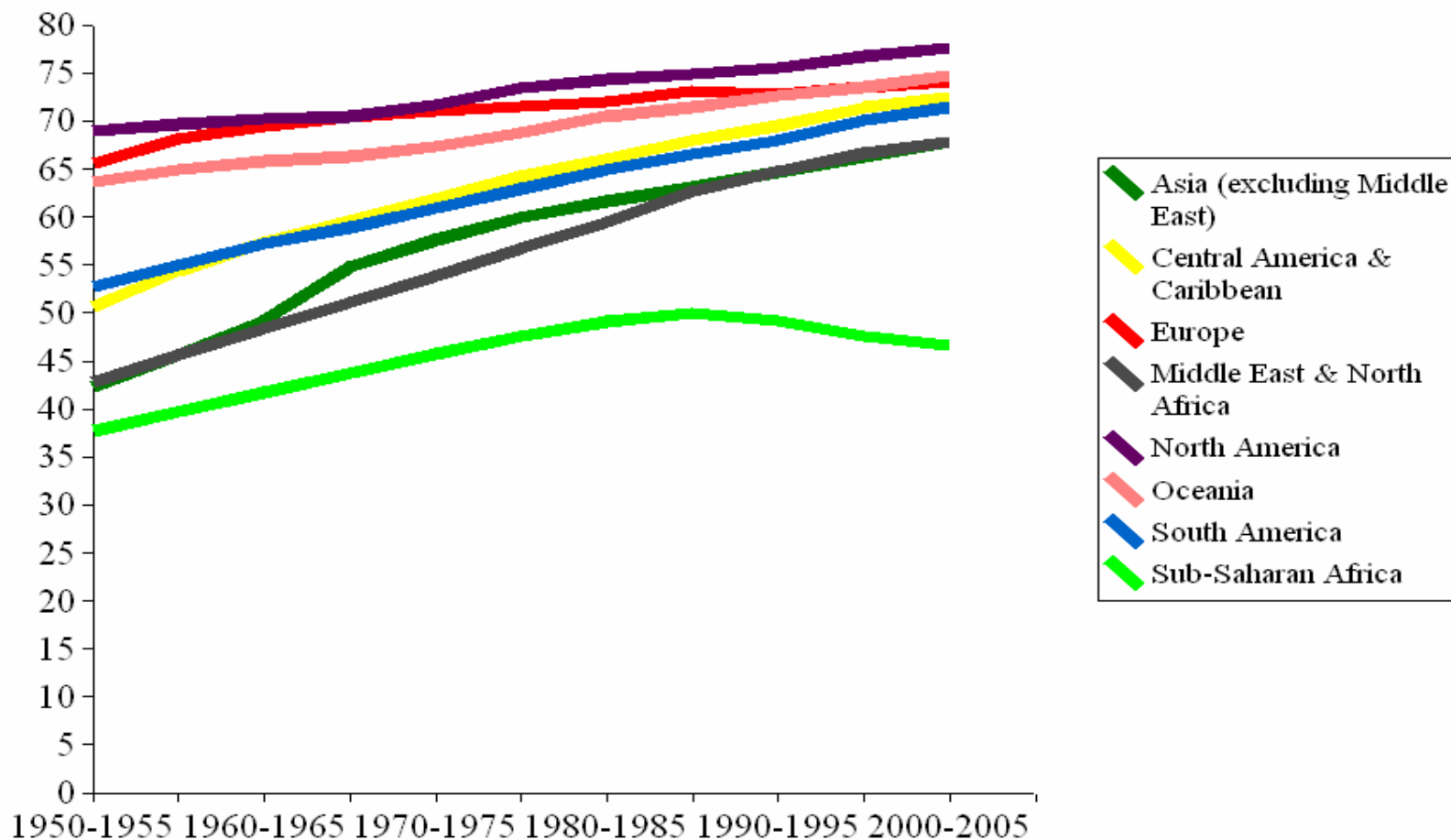
Life Expectancy at Birth (2006 - World)



male: 63 years
female: 67 years

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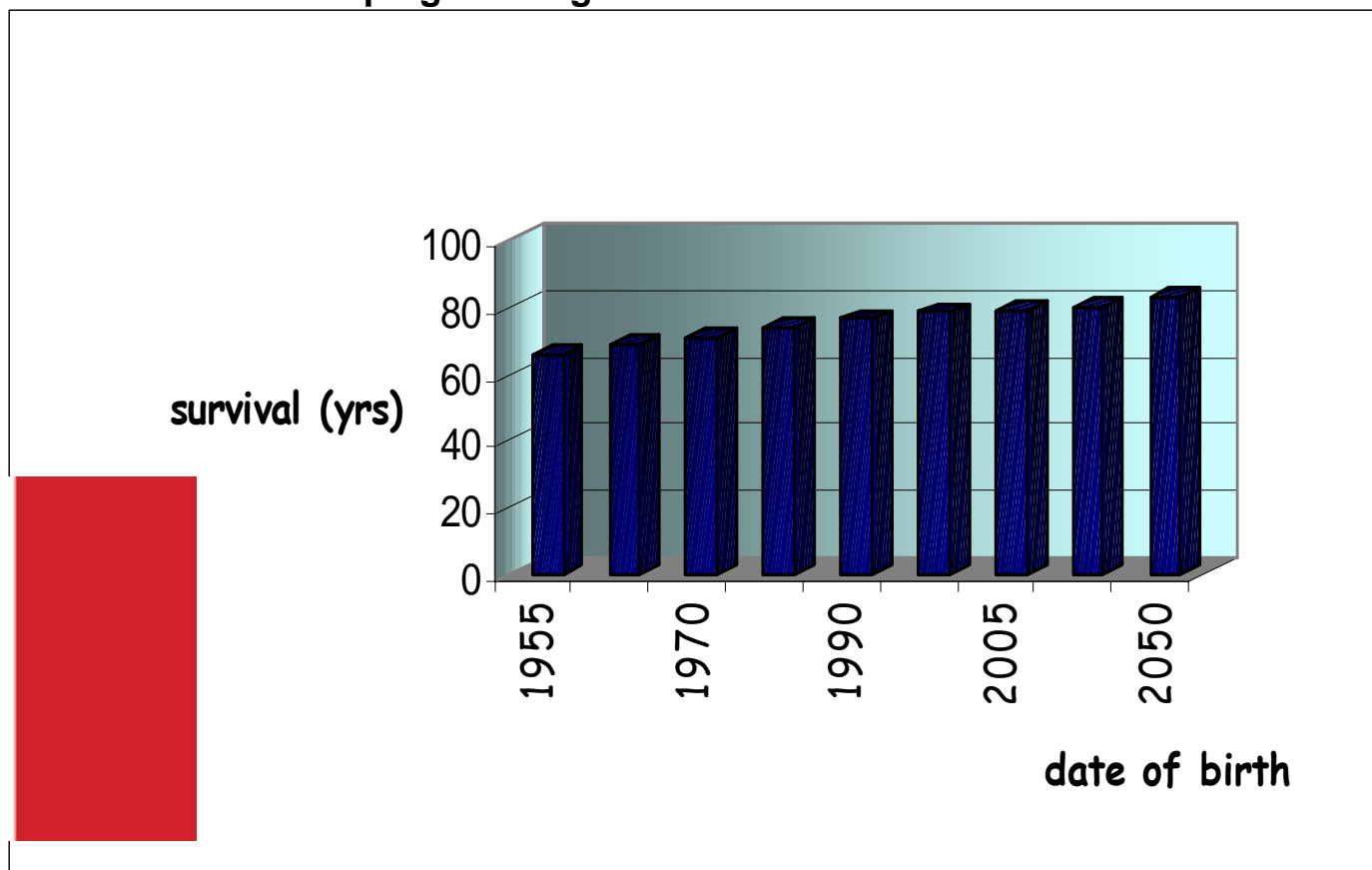
Life expectancy 1950-2005



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Life Expectancy at Birth (2006 - Italy)

<http://globalis.gvu.unu.edu/>



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Life Expectancy at Birth (2006)



male: 76 years
female: 81 years



male: 75 years
female: 81 years

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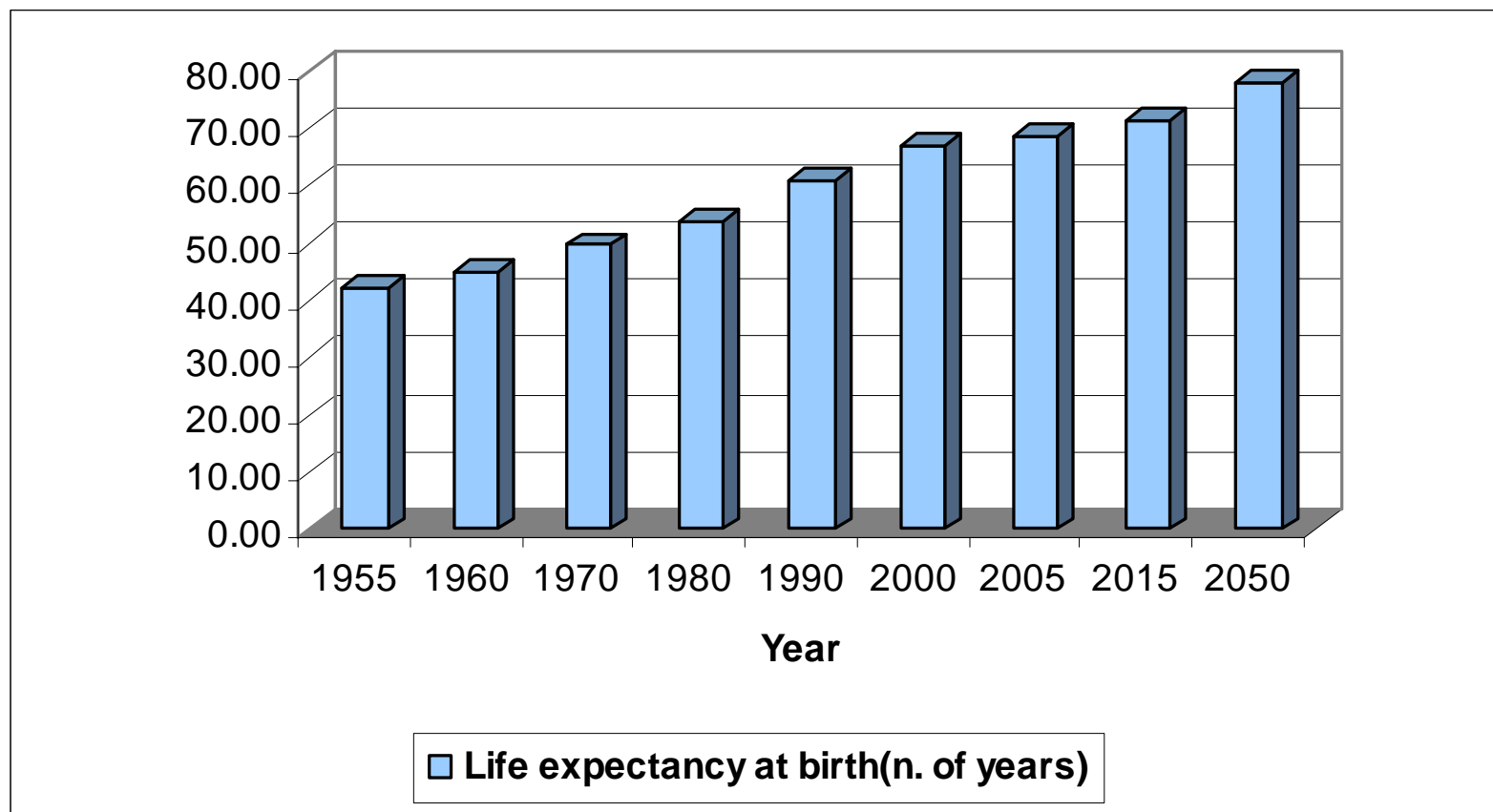
Life Expectancy at Birth (2006 - Egypt)



male: 69 years
female: 74 years (2006 est.)

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Life Expectancy at Birth (2006 - Egypt)



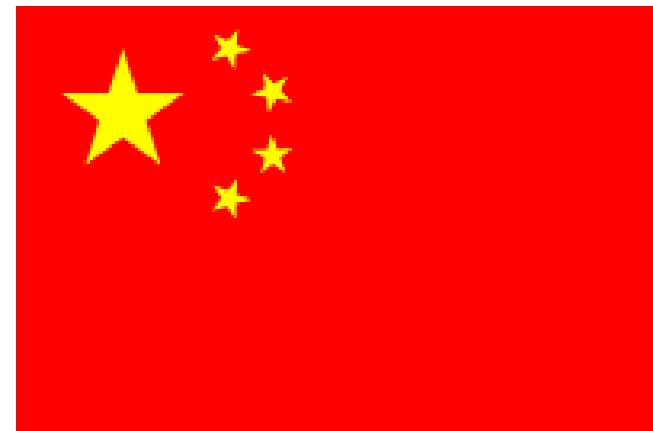
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Life Expectancy at Birth (2006 - emerging countries)



male: 64 years
female: 65 years (2006 est.)

male: 71 years
female: 74.5 years



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Burden of the problem

Median survival	1900	1990
males	46 yrs	71 yrs
females	49 yrs	78 yrs

In the last 20 yrs 1983 - 2003

>65 yrs x 2

>85 yrs x 4

2/3 cancer deaths occur >65yrs

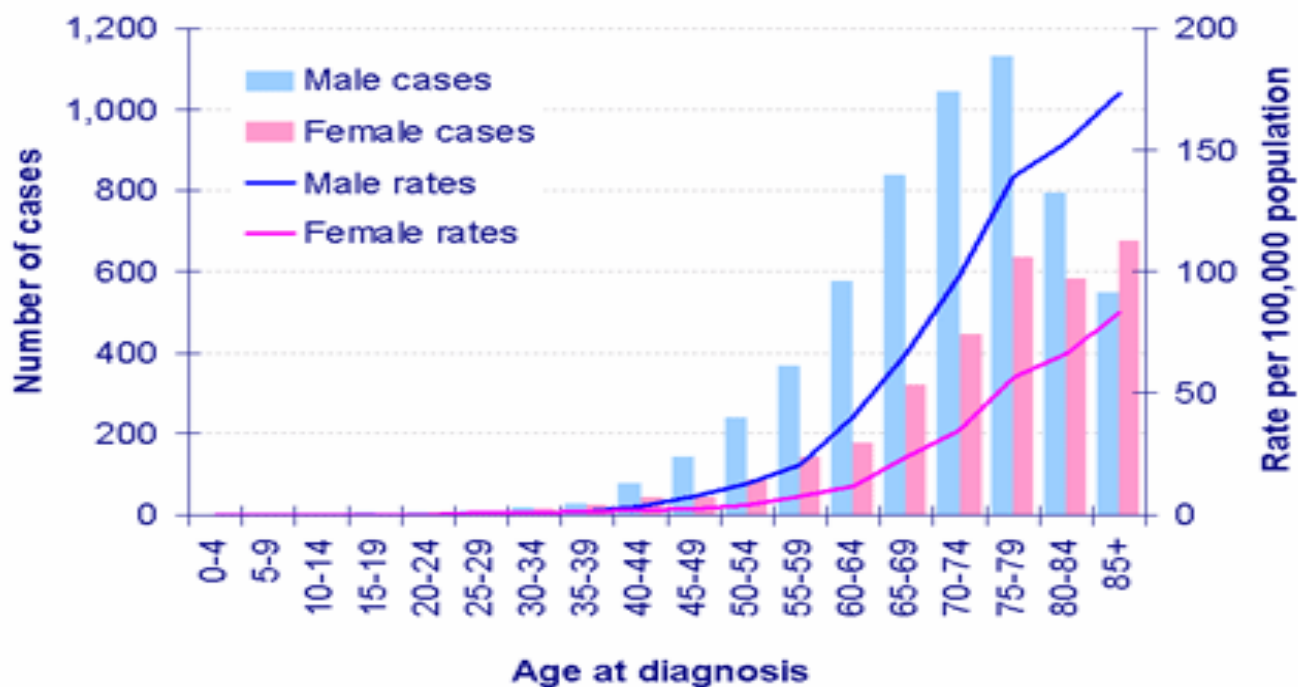
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2. Cancer & Age



Age-specific Gastric ca. - UK

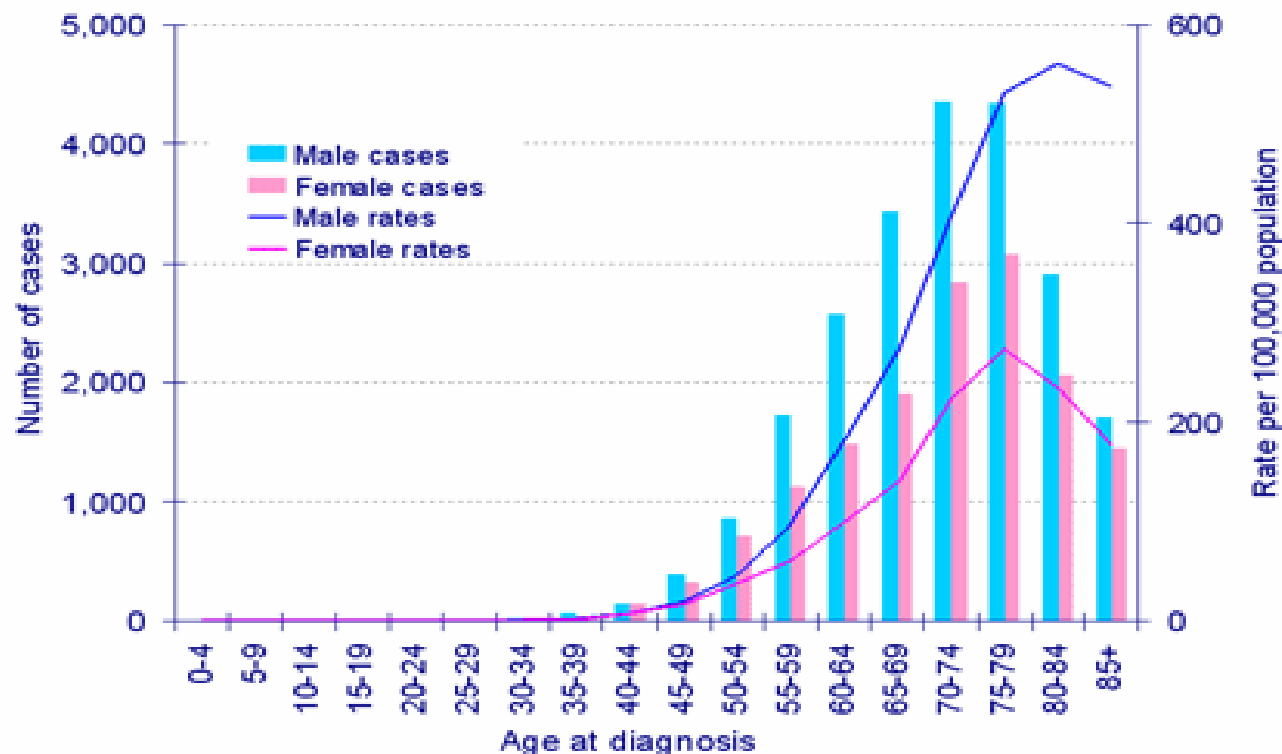
Figure 1.1: Numbers of new cases and age-specific incidence rates by sex, stomach cancer, UK 2002



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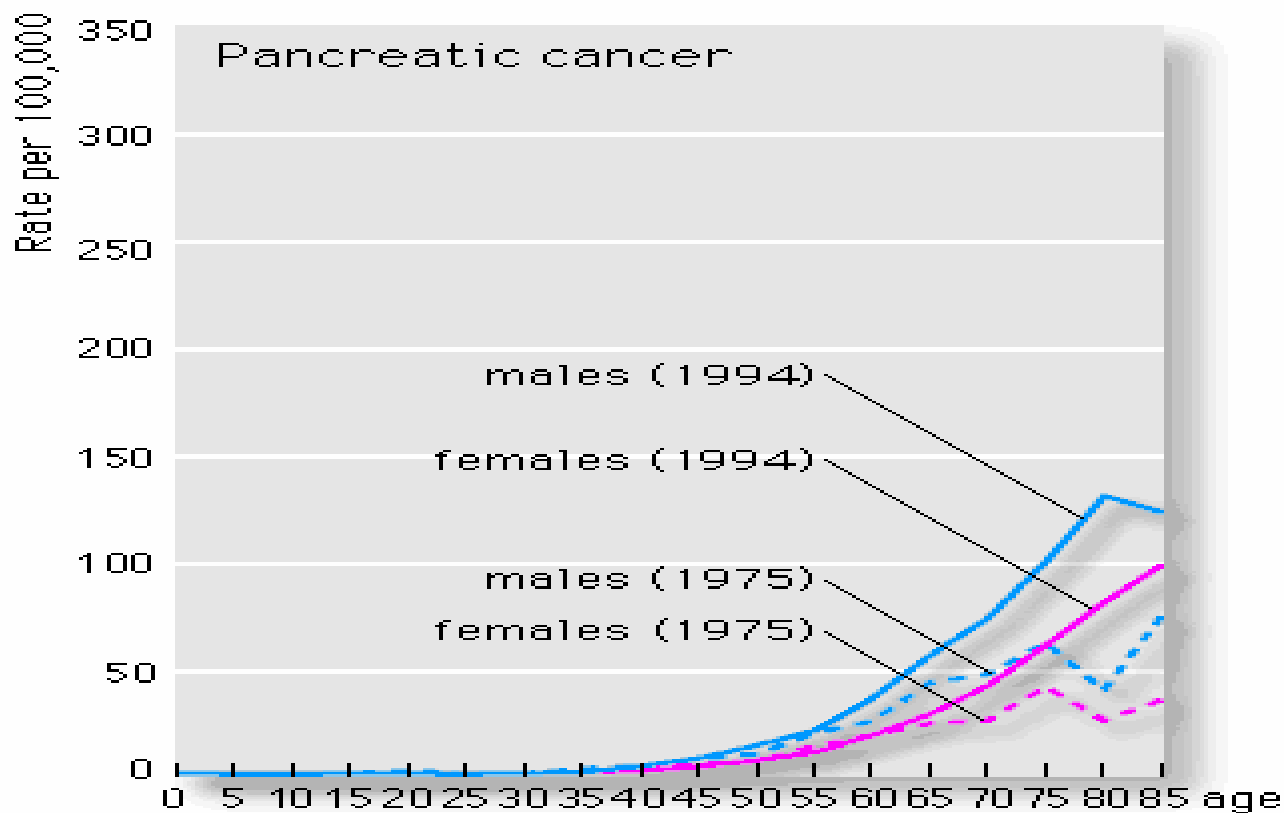
Age-specific Lung ca. - UK

Figure 1.1: Numbers of new cases and age-specific incidence rates by sex, lung cancer, UK 2002

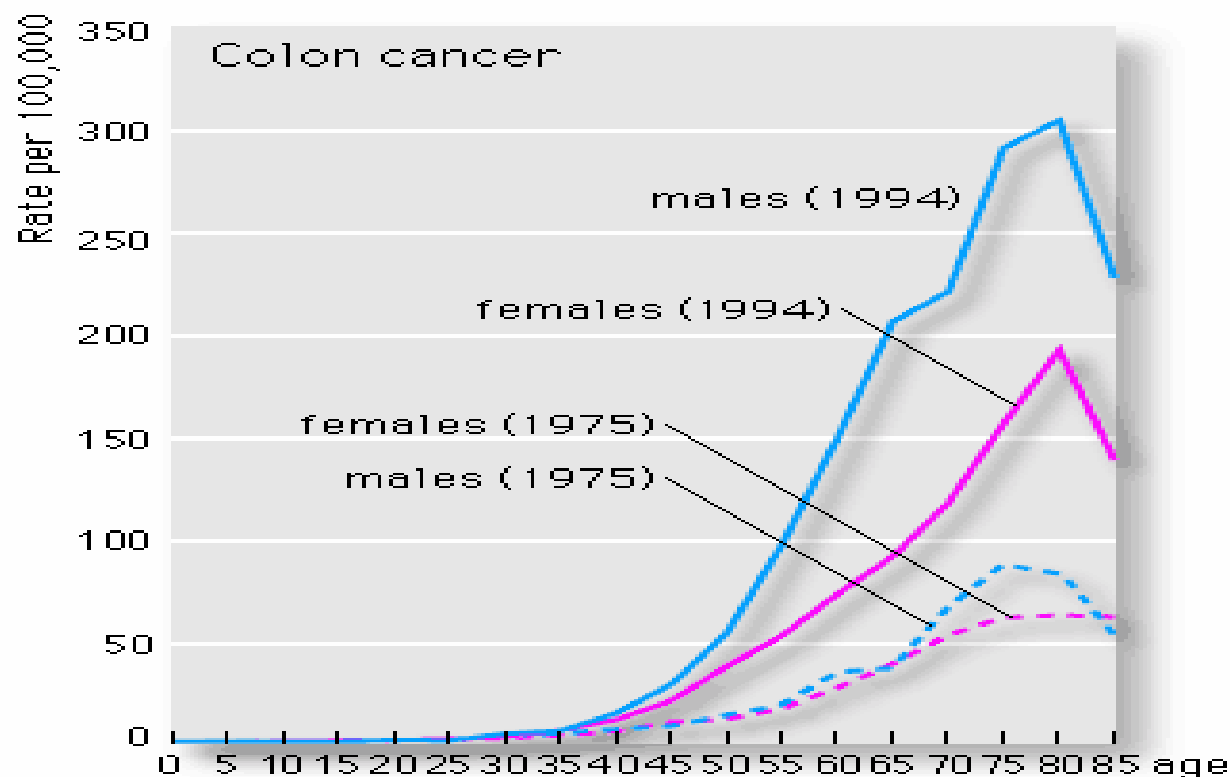


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Age-specific Pancreatic ca. - Japan



Age-specific Colon ca. - Japan



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With the exception of cervical ca.
all cancers prevail in the elderly population

Probability of Developing Invasive Cancers Over Selected Age Intervals, by Sex, US, 1998-2000*

		Birth to 39 (%)	40 to 59 (%)	60 to 79 (%)	Birth to Death (%)
All Sites†	Male	1.36 (1 in 73)	8.03 (1 in 12)	33.92 (1 in 3)	44.77 (1 in 2)
	Female	1.92 (1 in 52)	9.01 (1 in 11)	22.61 (1 in 4)	38.03 (1 in 3)
Bladder‡	Male	.02 (1 in 4603)	.40 (1 in 250)	2.36 (1 in 42)	3.46 (1 in 29)
	Female	.01 (1 in 9557)	.12 (1 in 831)	.64 (1 in 157)	1.10 (1 in 91)
Breast	Female	.44 (1 in 229)	4.14 (1 in 24)	7.53 (1 in 13)	13.36 (1 in 7)
Colon & rectum	Male	.06 (1 in 1678)	.86 (1 in 116)	3.94 (1 in 25)	5.88 (1 in 17)
	Female	.06 (1 in 1651)	.67 (1 in 150)	3.05 (1 in 33)	5.49 (1 in 18)
Leukemia	Male	.15 (1 in 649)	.20 (1 in 495)	.82 (1 in 122)	1.45 (1 in 70)
	Female	.13 (1 in 789)	.14 (1 in 706)	.46 (1 in 219)	1.00 (1 in 100)
Lung & bronchus	Male	.03 (1 in 3439)	1.02 (1 in 98)	5.80 (1 in 17)	7.69 (1 in 13)
	Female	.03 (1 in 3046)	.79 (1 in 126)	3.93 (1 in 25)	5.73 (1 in 17)
Melanoma of skin	Male	.12 (1 in 809)	.49 (1 in 205)	.97 (1 in 103)	1.81 (1 in 55)
	Female	.19 (1 in 532)	.39 (1 in 255)	.51 (1 in 197)	1.22 (1 in 82)
Non-Hodgkin lymphoma	Male	.14 (1 in 739)	.45 (1 in 224)	1.27 (1 in 79)	2.10 (1 in 48)
	Female	.08 (1 in 1258)	.30 (1 in 332)	.98 (1 in 102)	1.76 (1 in 57)
Prostate	Male	.01 (1 in 12833)	2.28 (1 in 44)	14.20 (1 in 7)	17.15 (1 in 6)
Uterine cervix	Female	.16 (1 in 632)	.31 (1 in 322)	.27 (1 in 368)	.78 (1 in 128)
Uterine corpus	Female	.05 (1 in 1832)	.69 (1 in 144)	1.57 (1 in 64)	2.60 (1 in 38)

*For those free of cancer at beginning of age interval. Based on cancer cases diagnosed during 1998-2000. The "1 in" statistic and the inverse of the percentage may not be equivalent due to rounding.

†All sites exclude basal and squamous cell skin cancers and in situ carcinomas except urinary bladder. ‡Includes invasive and in situ cancer cases.

Source: DEVCAN: Probability of Developing or Dying of Cancer Software, Version 5.1. Statistical Research and Applications Branch, National Cancer Institute, 2003. <http://srab.cancer.gov/devcan>

American Cancer Society, Surveillance Research, 2004

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3. Who is “Elderly”



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Definition of “Elderly”

- 65yrs Int. Conference Harmonisation
- 70yrs 90% subjects present signs of ageing
- 85yrs significant increase of functional impairments, >3 comorbidities, presence of “geriatric syndrome”
- No biological marker has proven reliable in drawing a cut-off line

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Age-related biological differences

comorbidities: 80% elderly cancer patients have comorbid conditions

age (yrs)	n. of comorbidities
55-64	2.9
65-74	3.6
≥75	4.2

polipharmacy:

drug interaction
anaesthesiological issues
pharmacokinetics

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Age-related biological differences

Growth rate

Doubling time

Hormonal receptor status

Ploidy

% cells in S-phase

Angiogenesis

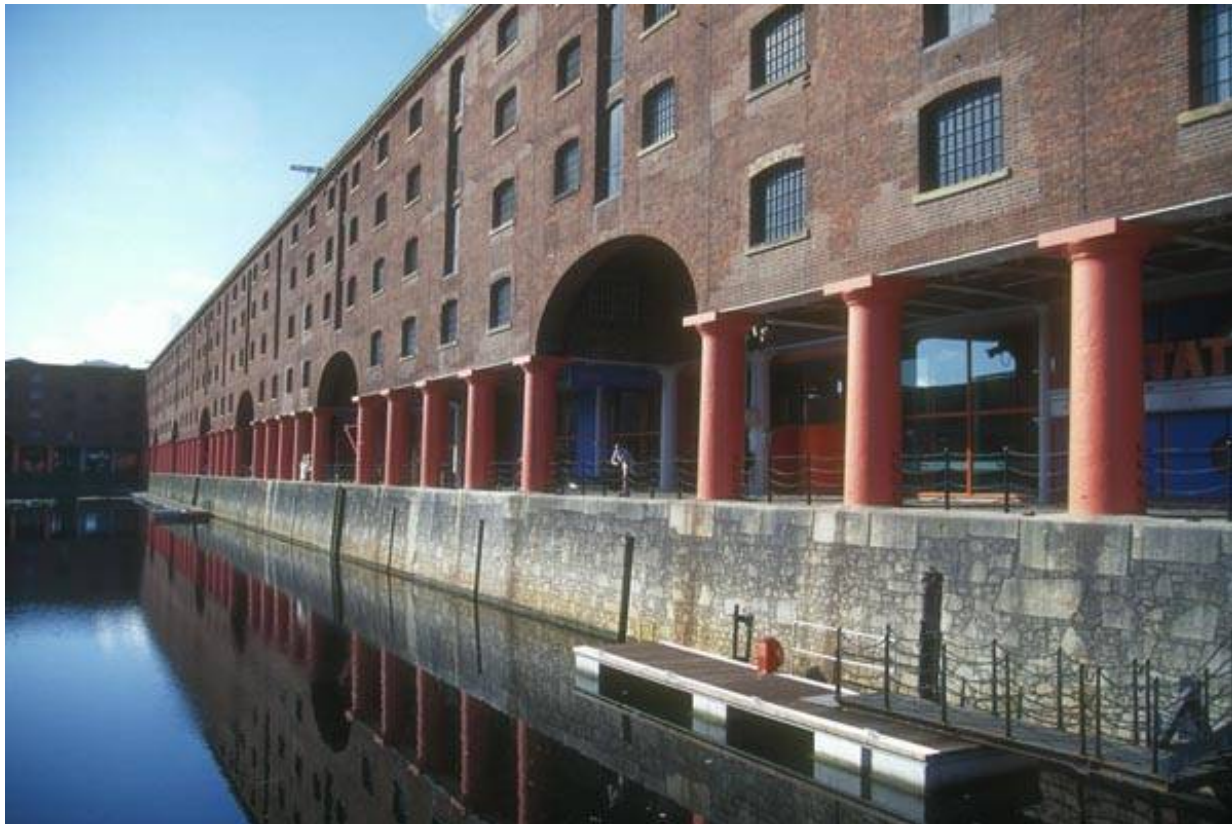
p53 expression

Extra-cellular matrix protein expression

Unwinding proteins

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4. Under-Management



Evidence of under-Staging

Inaccurate staging &
lack of histo/cytological diagnosis
are frequent
among onco-geriatric series

de Rijke JM. Ann Oncol 1996

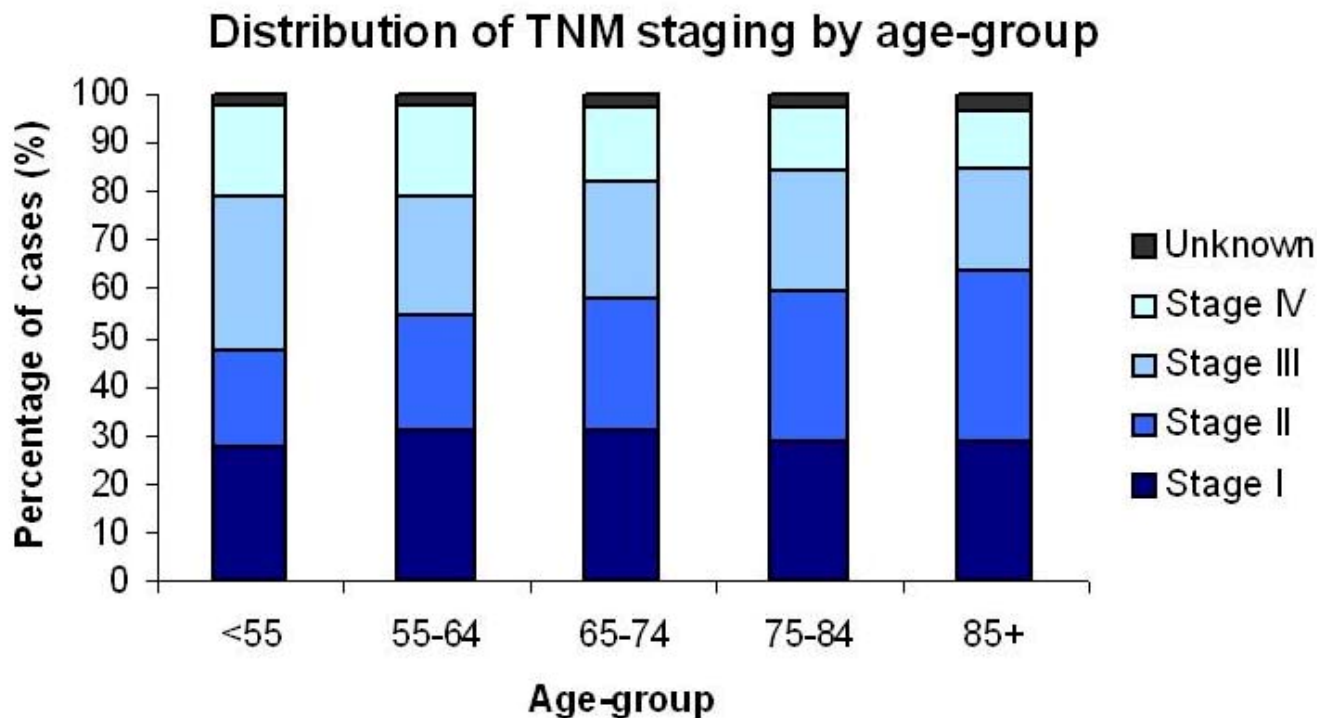
de Rijke JM. Eur J Cancer 2002

de Rijke JM. Cancer 2000

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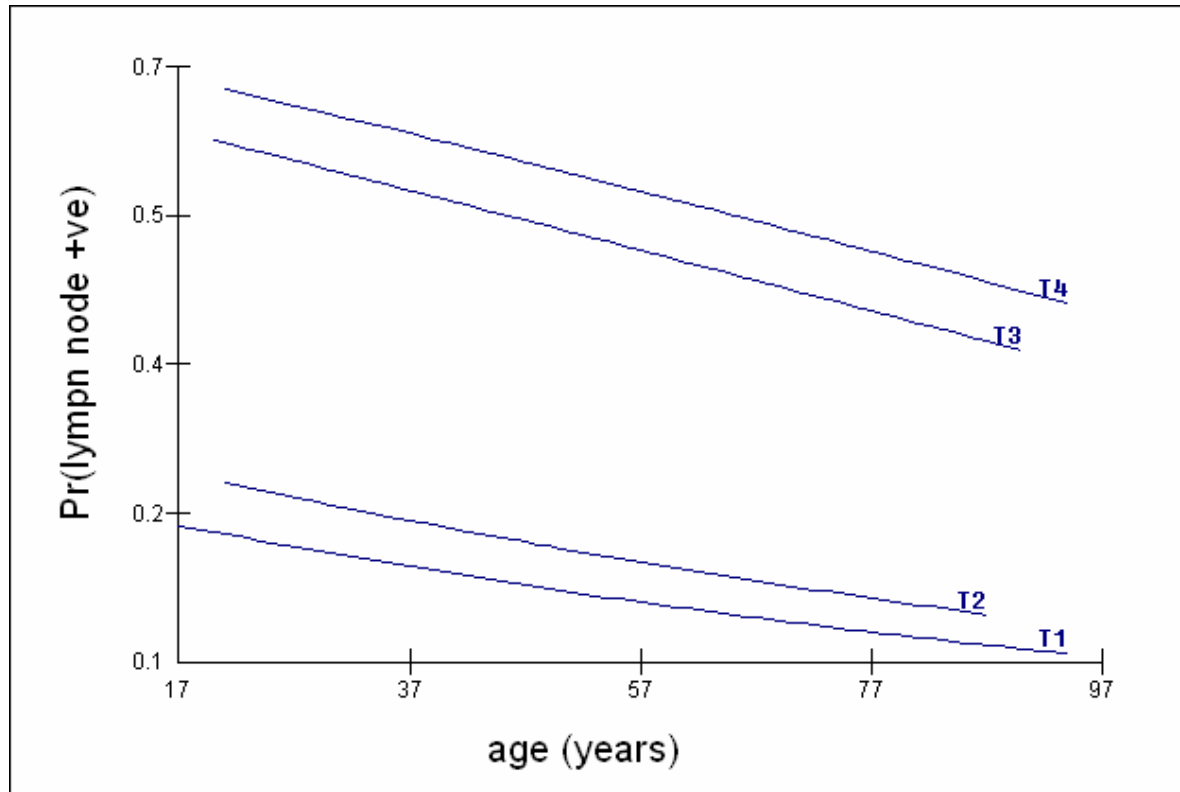
Evidence of under-Staging

Colorectal Cancer - UK: stage distribution



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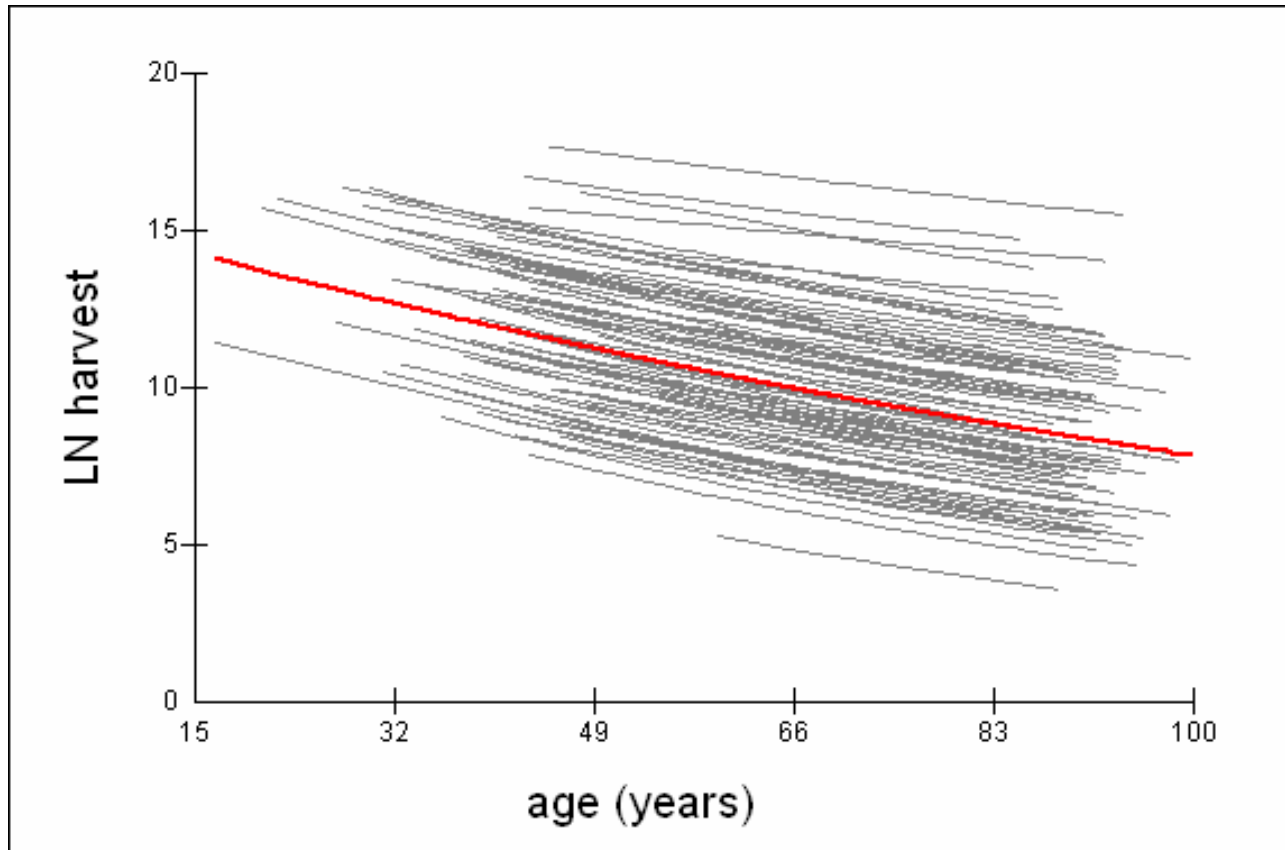
Evidence of under-Staging lymph node involvement and age



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Evidence of under-Staging

Colorectal Cancer - UK: n. nodes retrieved



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Evidence of under-Staging

Cancer in old age—is it inadequately investigated and treated?

N J Turner, R A Haward, G P Mulley, P J Selby

Proportion (%) of cancers confirmed by histology, cancer patients with no definitive treatment, and cancer patients surviving five years, by age group, Yorkshire 1989-93

Site	Confirmed by histology			No definitive treatment			Five year survival*		
	0-64	65-74	75+	0-64	65-74	75+	0-64	65-74	75+
Breast	97	91	63	1	4	11	71	68	54
Colon	95	89	75	9	16	31	43	39	37
Lung	80	70	44	32	48	76	8	5	2
Prostate	94	91	78	6	8	15	46	46	42
Skin (non-melanoma)	98	98	96	1	1	2	98	99	100
Stomach	90	86	70	32	44	66	16	11	9

* Excludes deaths from other causes.

bmj.com

NJ Turner BMJ 1999

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5. Poor Surgery



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Breast Cancer

Surgery is the standard and offers good results

Kessler HJ. Am J Surg 1978

Primary endocrine treatment first described in the
early '80s

Preece PE. BMJ 1982

Sole use of Tamoxifen...

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Tam, an anti-oestrogen drug...

Treatment well tolerated

The cancer would shrink or fail to progress in 80%
women

**TAM became a standard treatment for BC in the
elderly:**

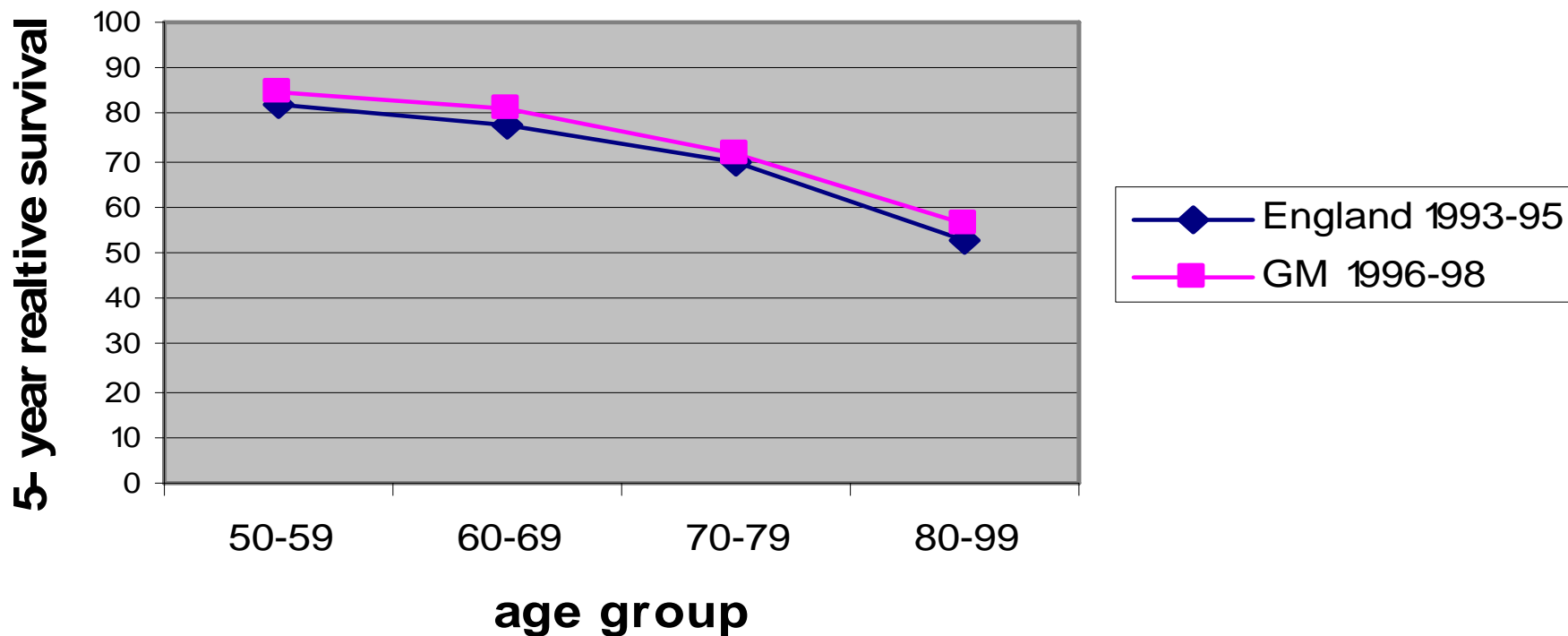


42% pts >70yrs

55% pts >80yrs

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5-year Relative Survival in England & Greater Manchester



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Colorectal Cancer

Obstruction alone (40%) or associated with other signs is the most frequent presenting complaint

Limpert P. Crit Rev Oncol Hem 2003

Operative mortality is higher in Elderly patients undergoing emergency surgery (60%E vs. 25%Y)

Hessman O. Eur J Surg Oncol 1997

+ high complications rate, stoma, longer hospital stay and increased costs

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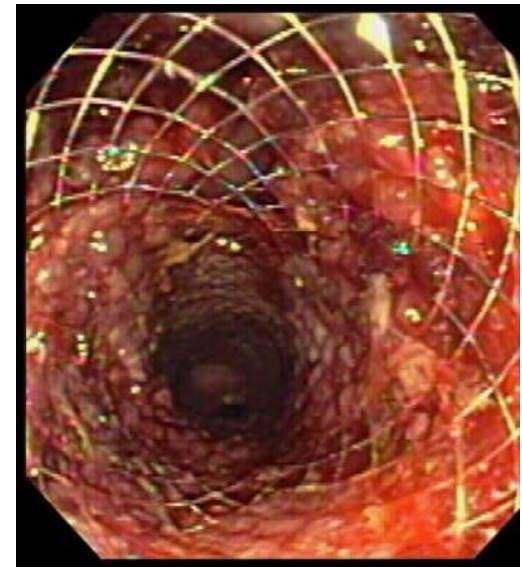
Colorectal Stents

first introduced in the 90's

93% success rate
"bridge-to-surgery"

92% treatment under elective
conditions

1% death rate



Mainar A. Radiology 1999

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Colorectal Stents

2 systematic reviews (2002-2004)

826 pts: decompression 88%
 mortality 0.4%

Khot UP. BJS 2002

1198 pts: decompression 94%
 mortality 0.6%

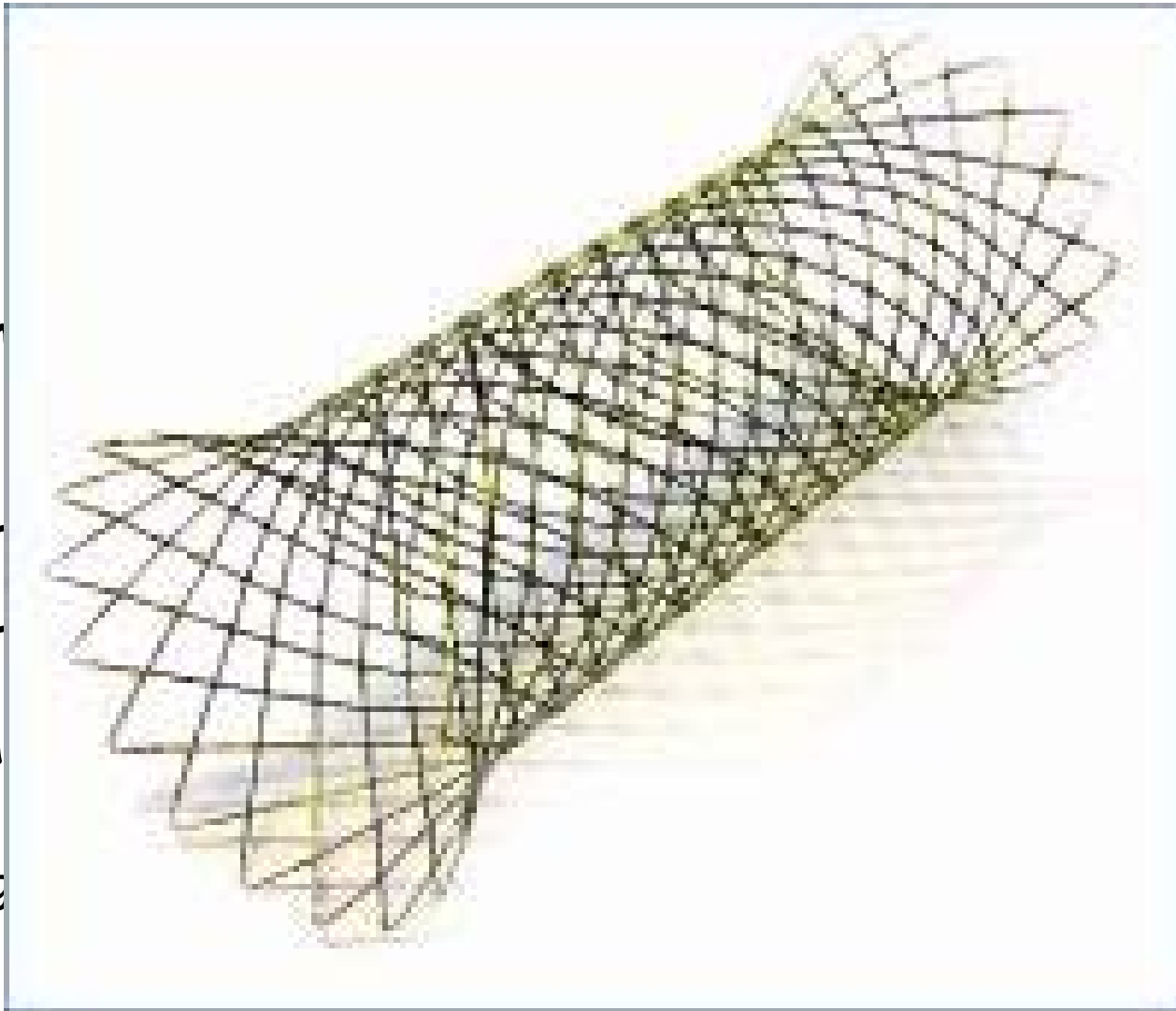
Sebastian S. Am J Gastr 2004

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Case-r

- less
- shor
- shor
- high

Kan Chung



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6. What patients want?



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what patients want?

Older patients

show a more positive attitude in the face of a diagnosis of cancer

Hoskins CN. Oncol Nurs Forum 1997

Baider L. Crit Rev Oncol Hematol 2003

desire involvement in their decision making process regarding cancer treatment

Sandison AJ. Br J Surg 1996

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7. Tailored Treatment



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What kind of Surgery?

Breast sparing surgery has not been validated in and Fisher's findings have not been validated amongst elderly patients (>70 excluded)

Elderly patients not entered into clinical trials

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What kind of Surgery?

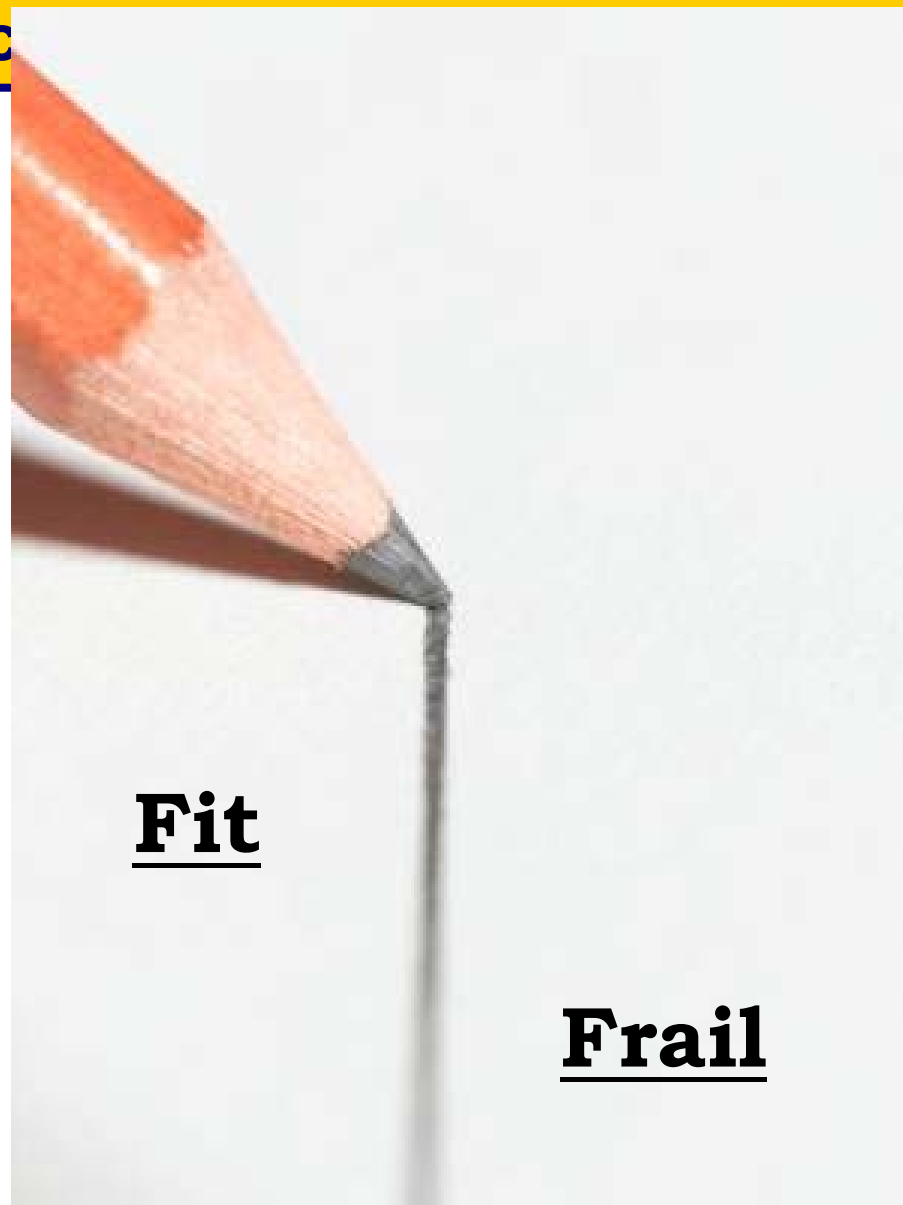
Quality of Life to be prioritised rather than survival expansion

Audisio RA. UICC Manual 2005

Clinical decisions based on a rule of thumb

Audisio RA. SIOG Position paper EJC 2004

Where to draw the line ?



Fit

Frail

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Preoperative Assessment of Cancer in the Elderly

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PACE

1) Comprehensive Geriatric Assessment (CGA)

CGA adds information to Eastern Cooperative Oncology Group performance status in elderly cancer patients

Repetto L et al. J Clin Oncol 2002; 20: 494-502

+

2) ASA - Possum - P-Possum

+

3) pathological /surgical data

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PACE

morbidity

PACE Item	Odds ratio	95% confidence		<i>p</i>
PS (2-4)	2.60	1.36	4.94	0.004
MMS (deficit)	1.46	0.79	2.69	0.229
ADL (dependent)	2.11	1.19	3.75	0.011
IADL (dependent)	1.97	1.29	3.02	0.002
GDS	1.50	0.95	3.35	0.082
BFI	1.71	1.07	2.72	0.024
ASA	1.08	0.65	2.03	0.636

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PACE

morbidity
multivariate analysis

PACE	OR	95% confidence		<i>p</i>
IADL	1.97	1.29	3.02	0.002
BFI	1.71	1.07	2.72	0.024

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PACE

Hospital stay

PACE Item	OR	95% confidence		<i>p</i>
PS (2-4)	1.40	0.68	2.86	0.358
MMS (deficit)	0.85	0.43	1.67	0.628
ADL (dependent)	3.27	1.63	6.55	0.001
IADL (dependent)	1.53	0.96	2.44	0.075
GDS	1.45	0.89	2.36	0.134
BFI	1.43	0.84	2.45	0.134
ASA	0.80	0.51	1.25	0.323

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PACE

Hospital Stay
multivariate analysis

PACE	OR	95% confidence		<i>p</i>
ADL	3.23	1.61	4.37	<0.0005

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Tailoring treatment entails the assessment of:

- Frailty & Life Expectancy
- Patients' expectations
- QoL: dying with cancer vs. dying of cancer

8. Conclusions



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Conclusions

3. Who is elderly?

4. Under-management

5. Poor surgery

Thank you

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ANDREA VERONESI

Division of Medical Oncology C,

Centro di Riferimento Oncologico, Aviano, Italy

Board of Founders of ICEDOC's Experts in Cancer without Borders

Scientific Advisor of SEMCO

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Pharmacology and aging

- Aging brings about a progressive decrease in physiologic reserve that affects each individual at a unique pace.
- The physiologic decline begins in the 3rd decade of life
- It may not be apparent at rest, but becomes apparent in stress conditions, such as cancer and treatment
- A number of age-related changes in drug absorption, distribution, excretion

Absorption

- Decreased GI motility
- Decreased splanchnic blood flow
- Decreased secretion of digestive enzymes
- Mucosal atrophy

Distribution

- Increase in body fat, decrease in lean mass and total body water
- Rise in the volume of distribution for lipid soluble drugs, decrease for hydrophilic drugs
- Hypoalbuminemia causes increase of unbound concentration of albumin-bound drugs

Excretion (I) Liver

- Hepatic mass and blood flow decrease with age
- Impact of age upon P450 activity
- In 226 pts, the P450 content in the liver decreased by 30% over 70 years of age

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Excretion (II) Kidney

- Over a life span, renal mass decreases by 25-30% and renal blood flow decreases by 1% per year after 50
- Decline in GFR about 0.75 mL/min per year after age 40
- Often no increase in serum creatinine due to simultaneous loss of muscle mass
- Cockcroft and other formulas to be taken with some caution

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Preventing toxicity of drugs with predominant renal excretion (I)

- Hydration status should be optimized and renal function evaluated to establish possible need for dose adjustment.
- Serum creatinine alone is insufficient in evaluating renal function.
- More accurate tools, including creatinine clearance methods such as Cockcroft-Gault, are available and generally provide accurate indices of a patient's renal function status. However, in older patients, these equations are not as precise as in a younger population.

Preventing toxicity of drugs with predominant renal excretion (II)

- When dealing with extremes of obesity and cachexia or very high and low creatinine values, no single tool is completely accurate.
- Preference should be given to agents that are less likely to be influenced by renal clearance.
- Preference should be given to agents that are less toxic to the kidneys or for which there are ways to prevent renal toxicity.

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Impact of age on PK of some CT drugs

- Paclitaxel: Increased AUC, decreased clearance
- Docetaxel: No difference
- Vinorelbine: Increased AUC, decreased clearance
- Methotrexate: Decreased clearance
- Etoposide: Increased blood concentration
- Doxorubicin: lower clearance
- Oxaliplatin: no difference

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Main drug-related toxicities

- Bone-marrow (anthracyclines, alkylating agents, taxanes, vinorelbine)
- Mucosae (anthracyclines, alkylating agents, fluoropyrimidine, vinorelbine)
- Heart (anthracyclines)
- Peripheral nervous system (taxanes, vinorelbine)
- Hand-foot syndrome (fluoropyrimidine, taxanes)

One question:

Is advanced age associated with increased toxicity per se or through PK mechanisms?

In other words:

If an elderly patient has normal excretory function and hemoglobin and albumin levels, can we proceed without dose adjustment?

Answer (tentative):

Consider that not all toxicities are mediated by PK (e.g., bone marrow, neurotoxicity)

Geriatric assessment can capture features that independently predict morbidity and mortality (comorbidities, functional, cognitive, nutritional and psychological status)

The case of breast cancer: which adjuvant therapy in the elderly?

- Life-expectancy.
- Risk of cancer recurrence without and with treatment.
- Presence and degree of comorbid conditions.
- Geriatric assessment.
- Treatment related toxicities.
- Patient preferences.

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Baseline life expectancy for women with various ages and comorbidity levels

Life expectancy (years)

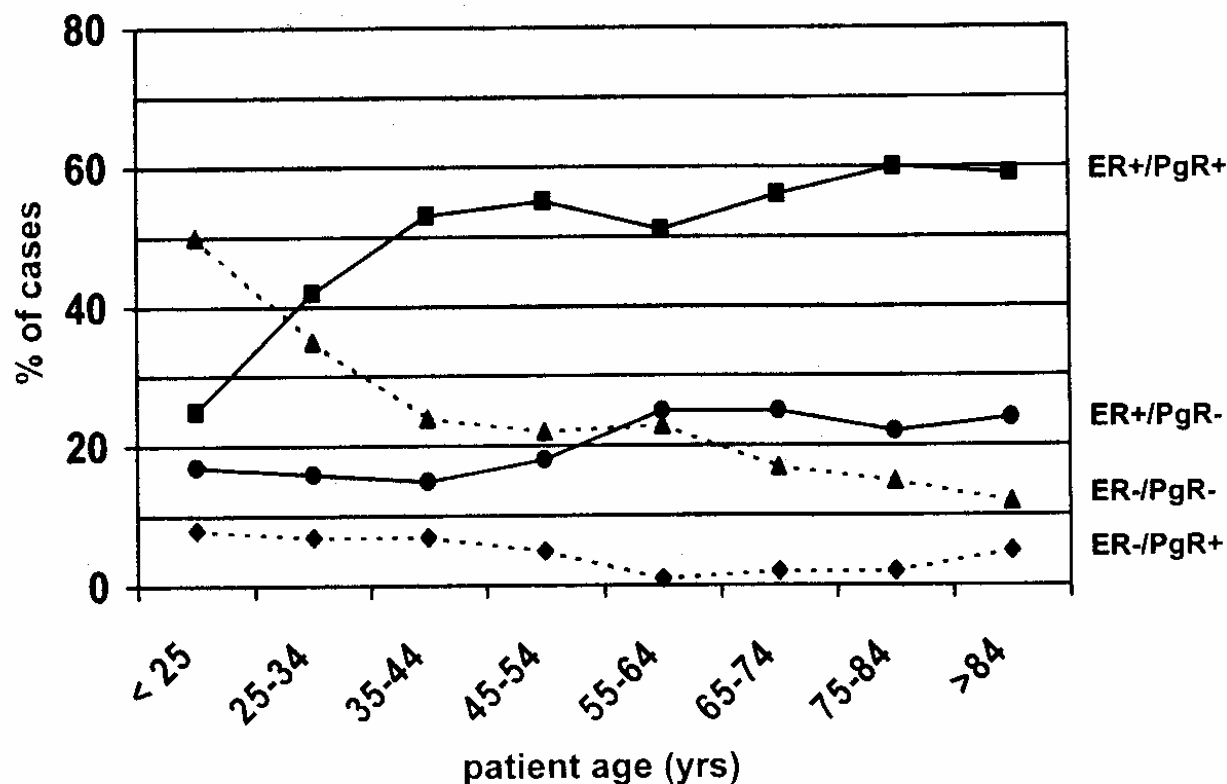
Age (years)	Healthy	Average	Sick
65	20.0	18.5	9.7
70	15.8	14.8	8.6
75	12.1	11.5	7.3
80	8.8	8.4	5.9
85	6.1	5.9	4.5

Extermann et al, JCO, 2000.

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ER and PgR status as a function of patient age in 13,517 breast cancer

(Daidone et al, Crit Rev Oncol Hemato 2003)



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Adjuvant endocrine therapy outcome

EBCTCG, Lancet 1998 and 2005

	10 yrs (1998)		15 yrs (2005)	
Age	DFS	OS	DFS	OS
<50	47	30	44	39
50-59	45	20	34	24
60-69	54	33	45	35
70+	54	34	51	37

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Adjuvant chemotherapy outcome

EBCTCG, Lancet 1998 and 2005

	10 yrs (1998)		15 yrs (2005)	
Age	DFS	OS	DFS	OS
<50	34	27	36	30
50-59	22	14	23	15
60-69	18	8	13	9
70+	-	-	-	-

REASONS FOR PAUCITY OF DATA

- Exclusion criteria for age in clinical trials
- Physician bias : patients will not benefit, will not tolerate, or both
- Patients and family members: refuse chemotherapy when it is offered

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International Breast Cancer Study Group Trial VII

- Around 600 women with N+ operated breast cancer were randomized to:
- TAM alone (213 <65aa; 93 \geq 65aa)
- or
- TAM+CMF(223 <65aa; 79 \geq 65aa) for 3 cycles

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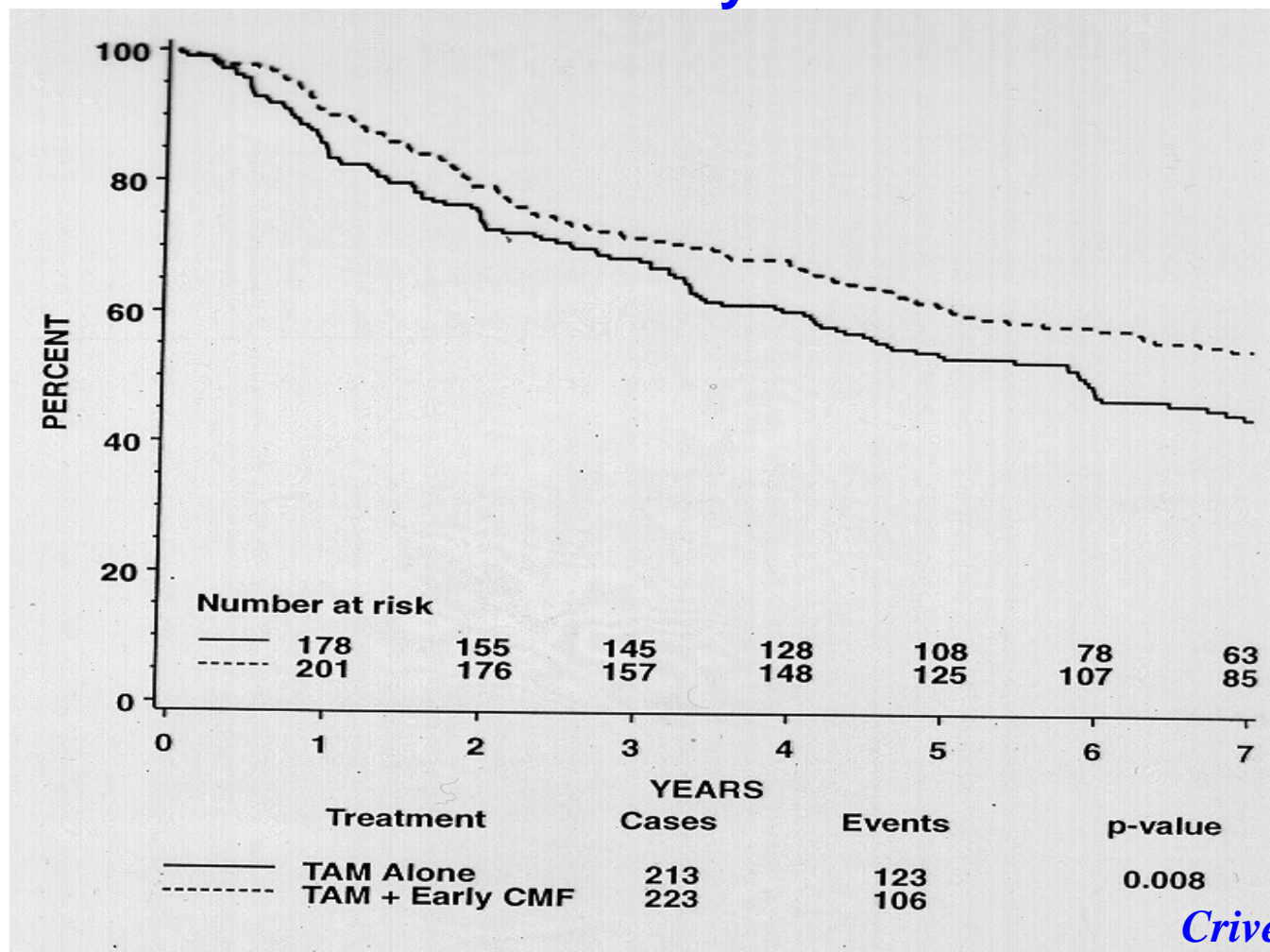
Distribution of worst grade of toxicity according to type of toxicity and age category for 299 assessable patients who received CMF chemotherapy. IBCSG Study VII

	Hematologic T.		Mucosal T		Other T.		Worst Grade 3/4 Any Toxicity	
	<65	>65	<65	>65	<65	>65	<65	>65
Age at entry								
No. of patients	223	76	223	76	223	76	223	76
Percent of patients with:								
Grade 0	12.6	9.2	72.2	55.3	15.3	18.4	3.6	2.6
Grade 1	53.4	30.3	19.3	27.6	45.3	50.0	37.7	23.7
Grade 2	29.6	51.3	7.6	13.2	36.8	25.0	51.6	56.6
Grade 3	4.5	9.2	0.9	4.0	2.7	6.6	7.2	17.1
<i>p-value</i>	0.0002		0.004		0.0335		0.004	

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Disease-Free Survival by Treatment

AGE < 65

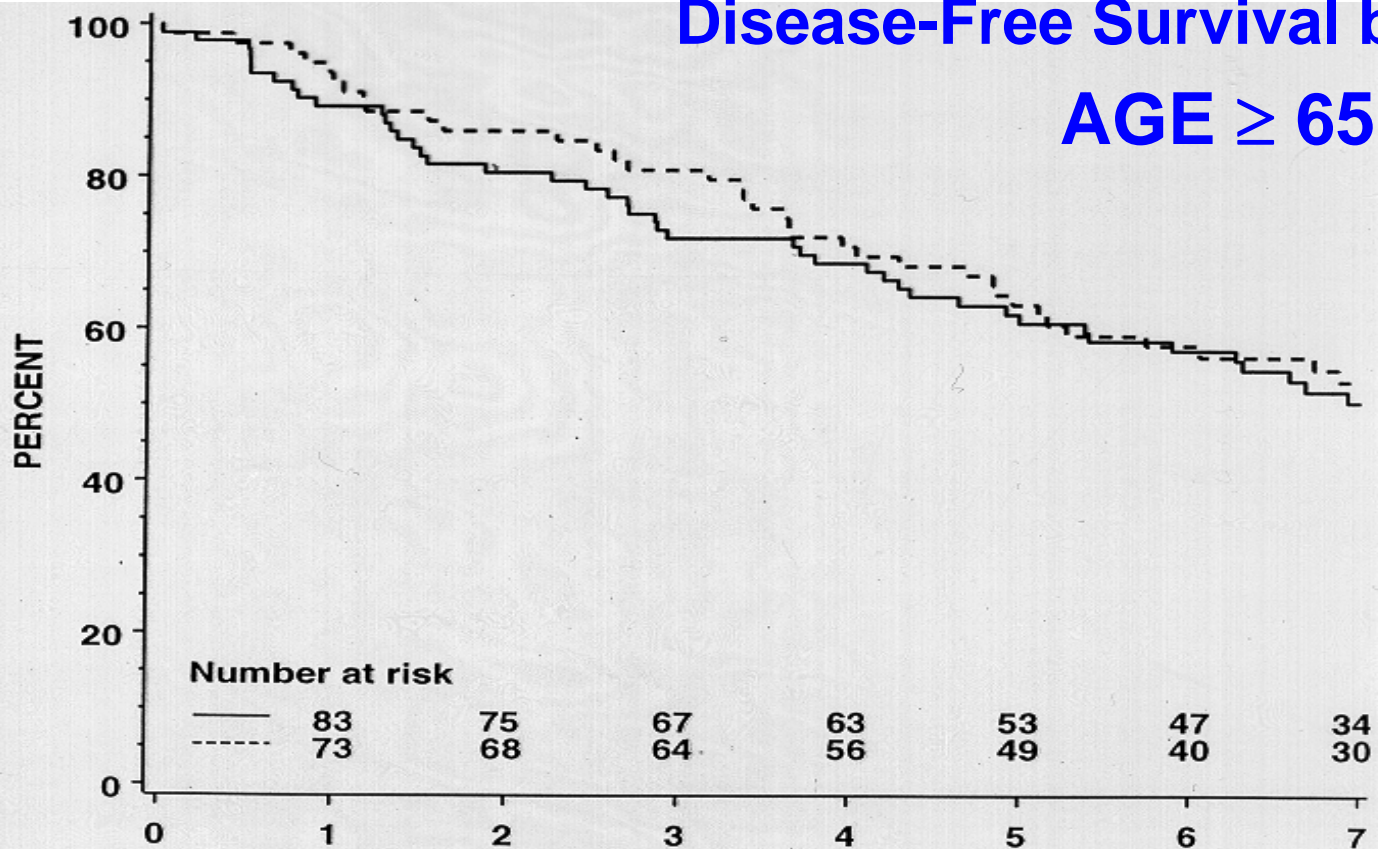


Crivellari et al, JCO 2000

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Disease-Free Survival by Treatment

AGE ≥ 65



Treatment	Cases	Events	p-value
TAM Alone	93	48	0.99
TAM + Early CMF	79	41	

Crivellari et al, JCO 2000

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Trials Evaluating Additive Value of Anthracycline-Based regimens to Tamoxifen in Postmenopausal Patients with Node-Positive Breast Cancer

GROUP	NUMBER OF PATIENTS	REGIMEN	MEDIAN FOLLOW-UP	DFS	OS
FARGEOT	338	Tamoxifen vs.Epirubicin/Tamoxifen	6 years	Benefit	No benefit
WILS	604	Tamoxifen vs.Tamoxifen/Epirubicin	5.7 years	Benefit	No Benefit
FISHER	1124	Tamoxifen vs. AC/Tam vs.PAF/Tam	3 years	Benefit	Benefit with Doxorubicin/ Cyclophosphamide
ALBAIN	1477	Tamoxifen vs.CAF/Tam vs. CAF followed by Tam	8.5 years	Benefit only for N >3	Benefit
FARGEOT	335	Tamoxifen vs.FEC/Tam	4 years	Benefit	NA

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Chemotherapy Adjuvant Study for Women at Advanced Age (CASA)

- Phase III Trial Evaluating the Role of Adjuvant Pegylated Liposomal Doxorubicin (PLD, Caelyx®, Doxil®) for Women (age 66 years or older) with Endocrine **Non-Responsive** Breast Cancer Who Are **NOT Suitable** for Being Offered a “Standard Chemotherapy Regimen”
- Two Individual Complementary Randomization Options:
 - Option 1: CASA-nil (PLD versus nil)
 - Option 2: CASA-CM (PLD versus CM)
- Coordinating Group: IBCSG

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Summing up:

- Few trials in the elderly
- In elderly trials, selection bias
- In selected patients, treatment as effective but more toxic
- Population studies suggest that a minor group (30%-40%) is treated and that age (and comorbidities) represent a strong deterrent to adjuvant treatment
- A standard treatment in high-risk cases impacts upon survival

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Geriatric Oncology

The Message of **SEMCO (South and East Mediterranean College of Oncology)** on the occasion of the **ASCO-SEMCO Multidisciplinary Cancer Management Course**
5-6 April 2007 - Cairo, Egypt

By : **Riccardo A. Audisio***, UK
& **Andrea Veronesi***, Italy
& **Ahmed Elzawawy***, Egypt

* & from **SEMCO & ICEDOC's Experts in Cancer Without Borders**
www.icedoc.org

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- **SEMCO** region is a wide region with different economic profiles and varieties of health problems and services.

Hence, in general, it could become an area of important studies in health and medical education.

- Cancer in the elderly is becoming an increasing problem in the **SEMCO** region. Although the problem is not accurately sized, cancer in the elderly has become a problem **today, and a larger one in the future**. So, Health professionals should be prepared!

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- **Lack** of studies and educational programs for different aspects of cancer in the elderly in the SEMCO region.
- There is **a list** of aspects and sciences related to Cancer in the Elderly e.g. **epidemiology, clinic-pathological studies, pharmacology and pharmacokinetics, cancer management in the elderly and different treatment modalities, Palliative care, socio-economic aspects and Psychology of the elderly and before and with all... Oncology nursing!**
- Once again, we stress on the **multidisciplinary management!**

Multidisciplinary Cancer Management Course

- Today, in this event, SEMCO raises the flag for the birth of ***"Geriatric Oncology and comprehensive Cancer care in the elderly with multidisciplinary approaches"*** in the ***South and East Mediterranean region.***
- We call authorities, Health and Educational bodies, organizations and colleagues in the region to pay more attention to this topic in the years to come.

Multidisciplinary Cancer Management Course

SEMCO with alliances and collaborators will consider different aspects of Cancer Management in Geriatrics among its upcoming educational conferences and studies.

Till our next SEMCO & Alliances meetings..... Wishing more progress for all of you and warmest regards.....
Thank you !

(Don't miss WWW.ICEDOC.ORG)