

Swiss Re



Cancer: recent advances and implications for underwriting

Robert Rubens

Select 74

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Agenda

- Epidemiology - changing mortality
- Evidence-base for underwriting
 - breast cancer
 - ovarian cancer
 - melanoma
 - childhood cancer
 - Hodgkin's disease
- New treatments
- Implications for critical illness and disability insurance



Cancer:

% 5-year relative survival by year of diagnosis

	<u>1970</u>	<u>1980</u>	<u>1990</u>	<u>2000</u>
Breast	68	77	85	91
Hodgkin's disease	67	75	82	87
Testis	72	92	96	96
Melanoma	68	82	90	92
Prostate	63	74	90	99
Lung	10	14	14	16



Cancer registries

■ Advantages

- based on populations (large numbers)
- long follow-up

■ Disadvantages

- lack of precise prognostic subsets based on:
 - staging
 - histology
 - treatment



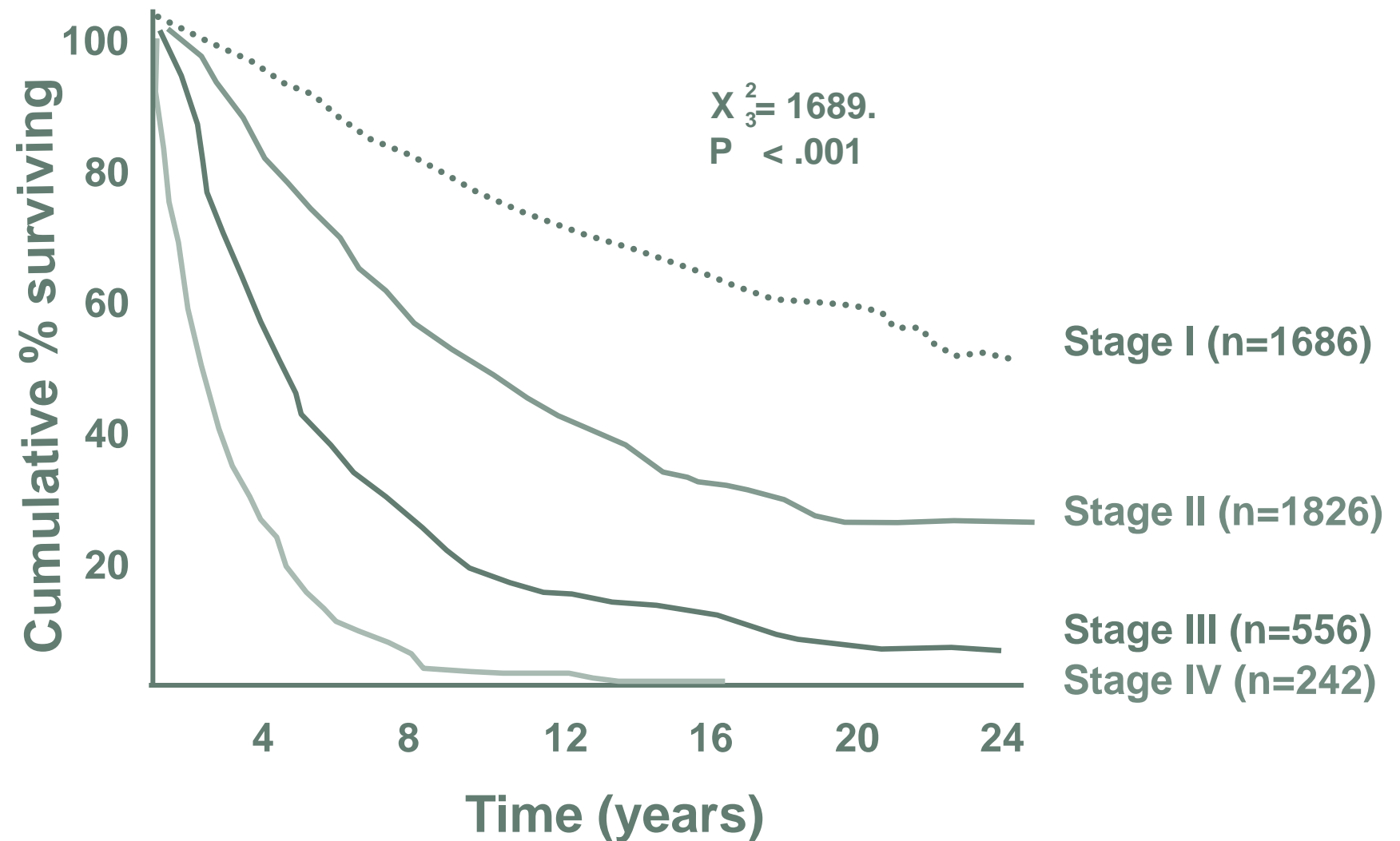
Institutional studies/clinical trials

- limited populations (may not be representative)
- strict selection criteria for clinical trials
- follow-up may be short
- precise definition of prognostic subsets



Survival: breast cancer

Guy's Hospital Breast Unit (1975 - 1999)





Breast cancer: determinants of outcome

- Staging
 - especially lymph node involvement
- Histological differentiation
- Tumour size
- Treatment



Staging of ovarian carcinoma:

Federation Internationale de Gynecologie et d'Obstetrique (FIGO)

- Stage 1 (growth limited to the ovaries)
 - Stage 1a - one ovary involved
 - Stage 1b - two ovaries involved
 - Stage 1c - one or both ovaries with ruptured capsule or ascites

- Stage 2 (pelvic extension)
 - Stage 2a - involvement of uterus and/or fallopian tubes
 - Stage 2b - involvement of other pelvic tissues
 - Stage 2c - pelvic extension with ruptured capsule or ascites

- Stage 3 (intra-abdominal extension outside the pelvis and/or involvement of retroperitoneal or inguinal lymph nodes)

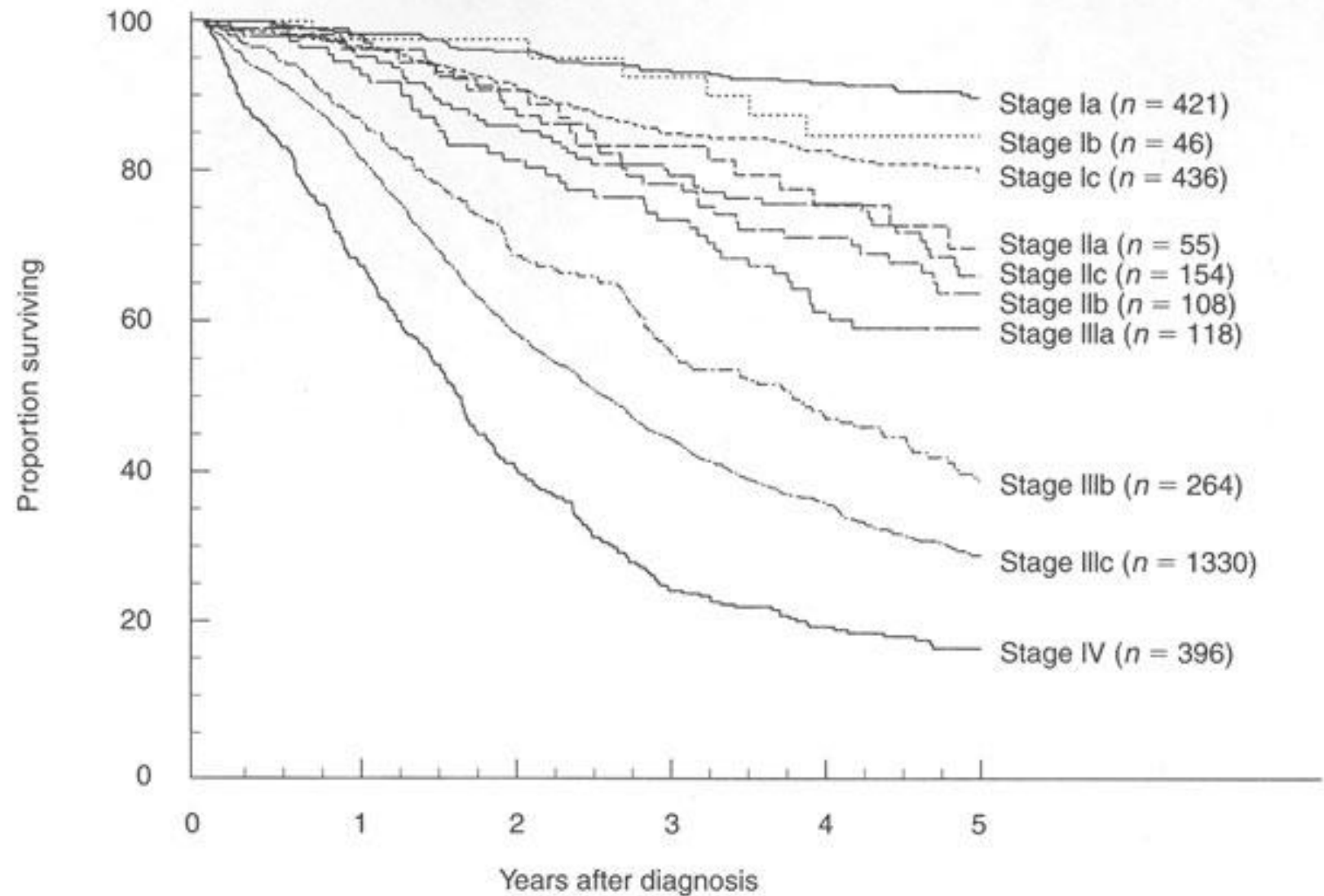
- Stage 4 (distant metastases)

Ovarian carcinoma: 5-year survival by ^{III}stage

Stage	Invasive cancer		Borderline tumours	
	Patients	% 5-yr survival	Patients	% 5-yr survival
Ia	421	89.9	296	95.6
Ib	46	84.7	28	95.9
Ic	436	80.0	90	96.3
IIa	55	69.9	6	100.0
IIb	108	63.7	7	85.7
IIc	154	66.5	14	59.5
IIIa	118	58.5	14	71.4
IIIb	264	39.9	22	62.0
IIIc	1330	28.7	25	45.0
IV	396	16.8	18	-



Carcinoma of the ovary - survival: patients treated 1993-5 (FIGO annual report 2002)



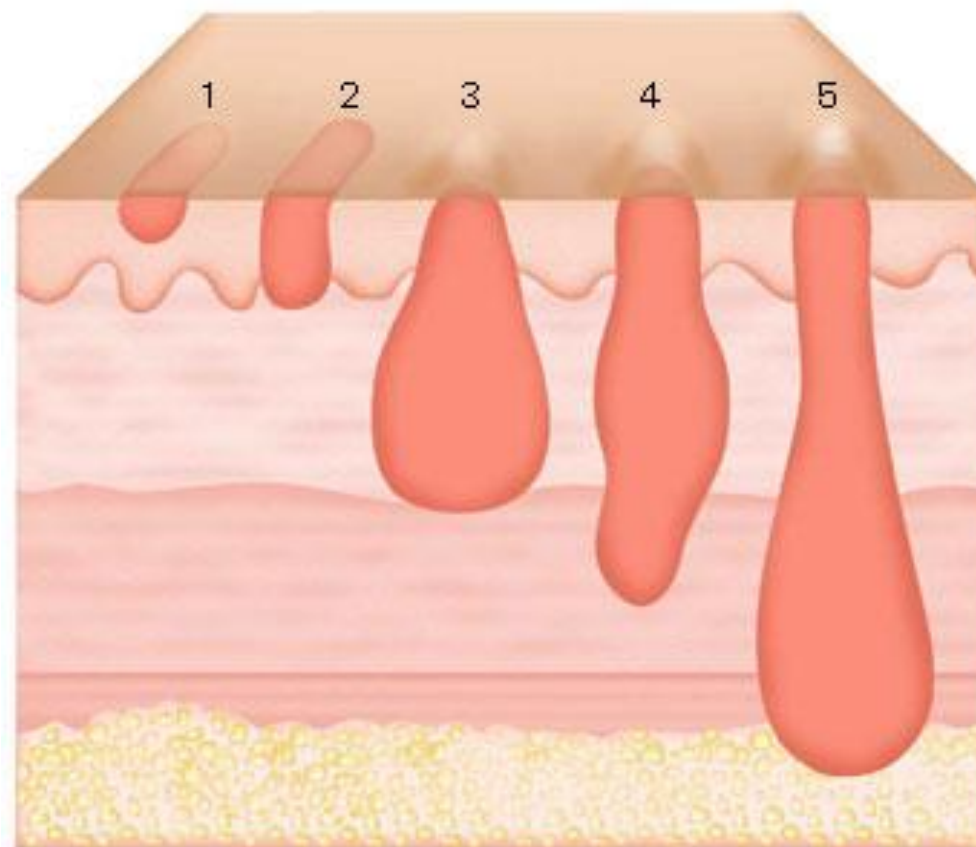


Melanoma: survival by thickness and ulceration

Thickness (mm)	n	% with ulceration	<u>5 yr survival (%)</u>		<u>10 yr survival (%)</u>	
			No ulceration	With ulceration	No ulceration	With ulceration
≤ 1	2113	0.05	95.7	79.1	92.0	69.1
1.01-2.00	1199	21	86.8	72.0	77.7	62.9
2.01-4.00	872	43	71.0	63.6	59.5	53.2
≥ 4	384	62	69.3	47.9	54.5	35.5



Melanoma: Clark levels



1. epidermis
2. basal lamina
3. papillary dermis
4. reticular dermis
5. subcutaneous fat

Artwork produced by the Department of Medical Illustration, Norfolk and Norwich University Hospital in association with Samantha J Elmhurst BA Hons.



Melanoma: American Joint Cancer Committee (AJCC) staging

Stage	TNM	Thickness	Description
0	TisN0M0	-	Level I
1A	T1aN0M0	≤ 1.0 mm	Without ulceration & level II/III
1B	T1bN0M0 T2aN0M0	≤ 1.00 mm 1.01-2.00 mm	With ulceration or level IV/V Without ulceration
2A	T2bN0M0 T3aN0M0	1.01-2.0 mm 2.01-4.0 mm	With ulceration Without ulceration
2B	T3bN0M0 T4aN0M0	2.01-4.0 mm > 4.0 mm	With ulceration Without ulceration
2C	T4bN0M0	> 4.0 mm	With ulceration
3	anyTN+M0		Regional node metastases
4	anyTanyNM+		Distant metastases



Melanoma: survival by stage

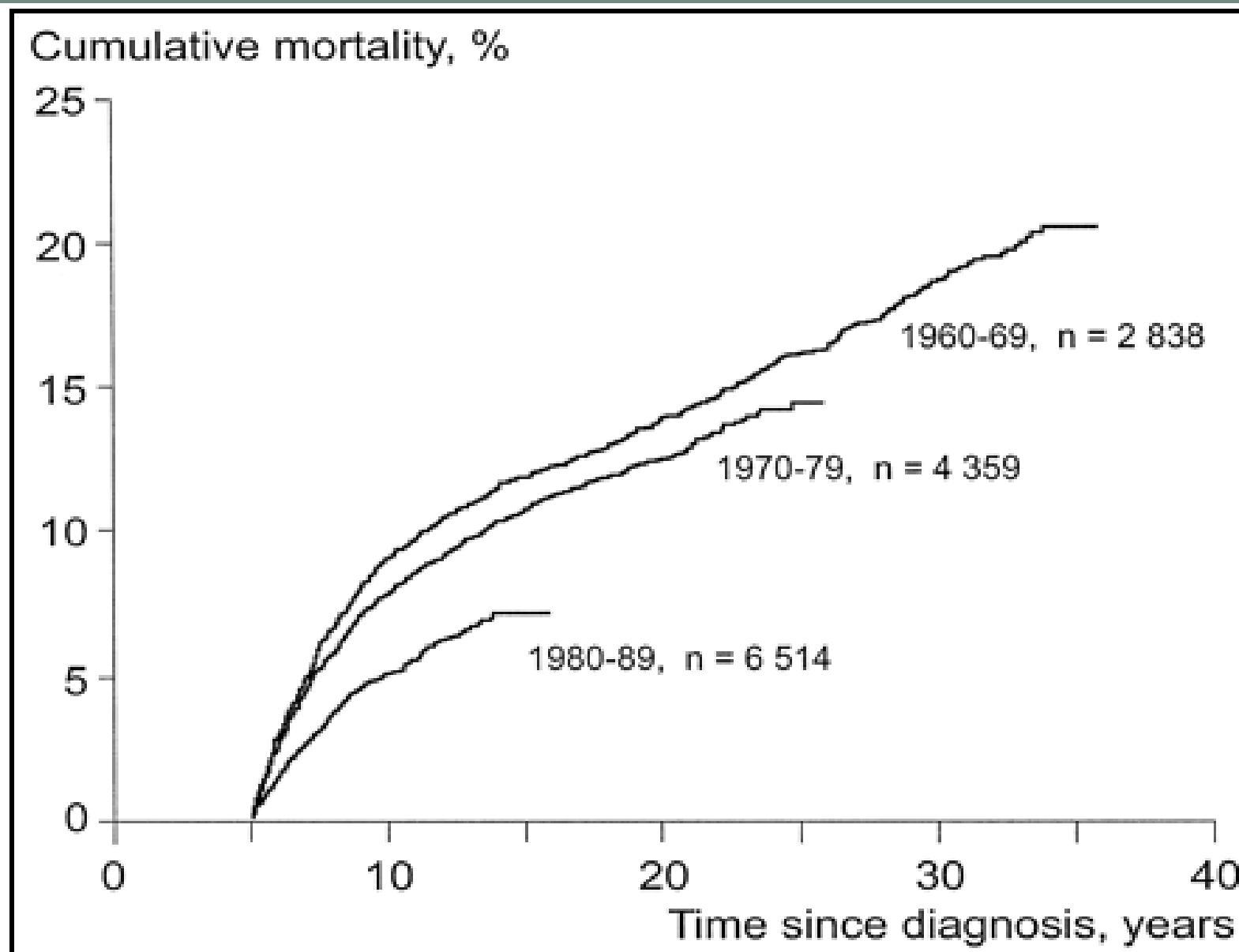
Stage	% survival		
	5 yrs	10 yr	15 yrs
1A	96	93	91
1B	84	77	72
2A	71	62	58
2B	67	56	50
2C	49	37	32



Childhood cancer: trends in survival in USA

Year of Diagnosis	5-yr relative survival
1975-77	58%
1978-80	63%
1981-86	67%
1987-89	71%
1990-95	77%
1996-2004	80%

Cumulative mortality in 5-year survivorsⁱⁱⁱ of childhood cancer by decade of diagnosis



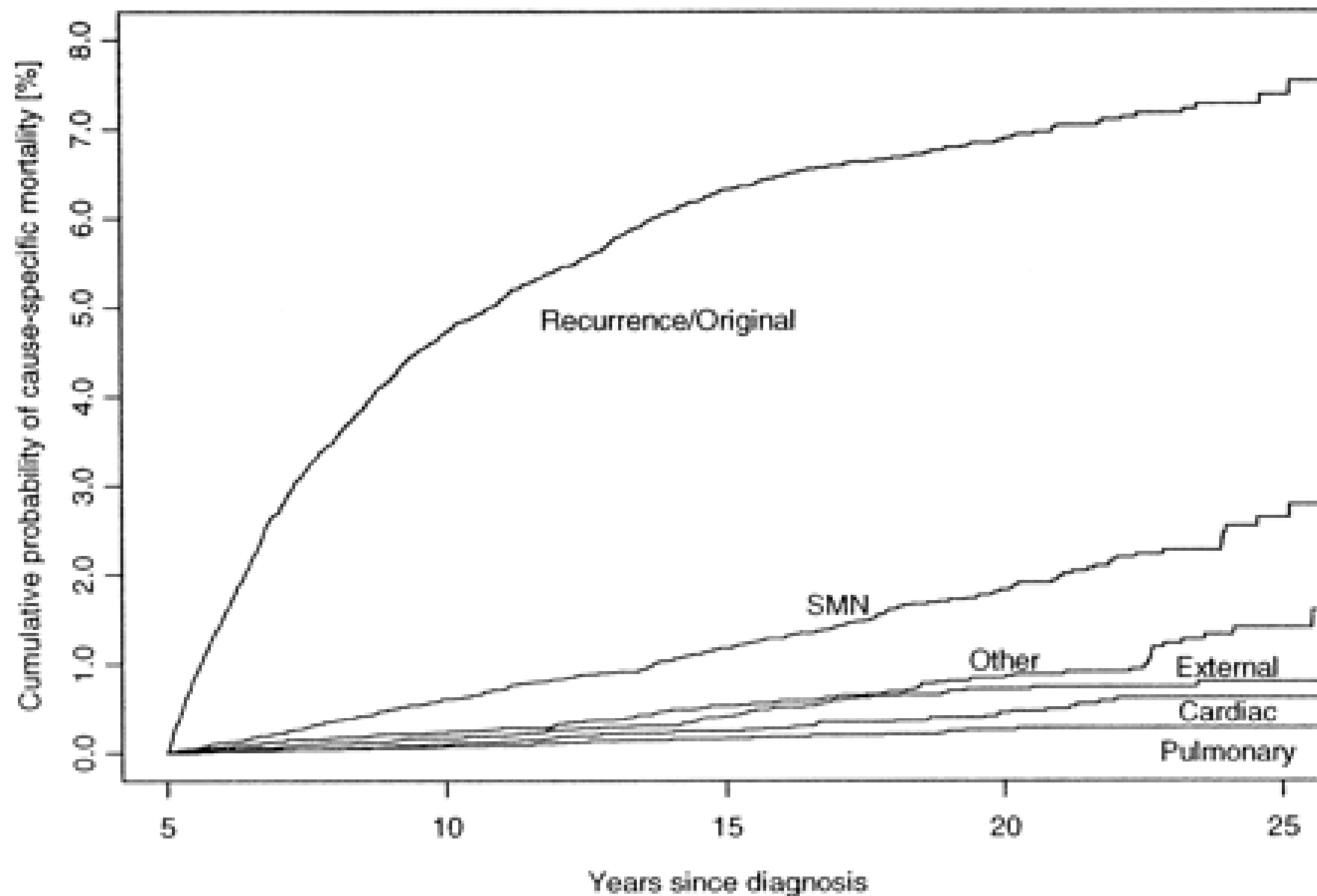


Childhood Cancer Survivors Study: causes of death in 5-year survivors (n=1848)

Recurrence	1246
Treatment related	394
– subsequent neoplasm	– 235
– cardiac	– 83
– pulmonary	– 33
– other	– 43
Non-treatment-related	208



CCSS: cause-specific mortality



Long-term consequences of cancer treatment

- Second cancers

- Non-carcinogenic
 - Cardiac

 - Pulmonary

 - Nephropathy

 - Neuropathy



Tissues particularly susceptible to radiation-induced cancer

- Bone marrow
- Thyroid
- Female breast

Carcinogenicity of chemotherapy

■ Leukaemia

- alkylating agents (eg cyclophosphamide)
- topoisomerase II inhibitors (eg etoposide, doxorubicin)

■ Bladder cancer

- cyclophosphamide

Relative risk of second cancers after Hodgkin's disease

Cancer type	Relative risk	95% confidence intervals	Absolute excess risk per 10⁴ per year
All	3.5	3.1 - 3.8	56.8
Acute (non-I) leukaemia	70.8	55.0 – 89.8	15.5
Non-Hodgkin Lymphoma	18.6	13.8 - 24.6	10.7
Lung	4.2	3.3 - 5.2	13.5
Other solid	1.9	1.6 - 2.3	15.8



Relative risk of second cancers after Hodgkin's disease in 10-year survivors

Cancer type	Relative risk	95% confidence intervals	Absolute excess risk per 10⁴ per year
All	4.7	3.8 – 5.7	112.1
Leukaemia	16.2	6.5 – 33.3	9.9
Non-Hodgkin Lymphoma	32.7	19.7 – 51.1	27.8
Lung	7.3	4.7 – 10.6	33.8
Other solid	2.8	2.0 – 3.8	40.6
Female breast	4.6	3.0 – 6.6	39.5

New specific anti-cancer treatments

1

- Inhibitors of growth factors
 - **imatininib** (Gleevec)
 - blocks the *bcr-abl* mutation in chronic myeloid leukaemia to inhibit the tyrosine kinase growth factor
 - active against gastrointestinal stromal tumours (GIST)



New specific anti-cancer treatments - 2

■ Anti-angiogenic agents

- **bevacizumab** (Avastin)
- prevents the formation of new blood vessels (angiogenesis) by blocking the action of vascular endothelial growth factor
- approved by FDA for metastatic colorectal and non-small cell lung cancer



Disability/income protection insurance

Paradoxically, improvements in cancer survival
may lead to worsening DI/IP claims experience



Morbidity from cancer

- The disease...its treatment
- Early...late
- Temporary...permanent
- Physical...psychosocial

Complications of cancer

- skeletal

- pain
- fracture
- vertebral collapse
- spinal cord compression
- cranial nerve palsies
- hypercalcaemia



Complications of cancer

- neurological

- epilepsy
- mental disturbance
- hemiplegia
- spinal cord compression/
paraplegia
- ataxia
- visual impairment
- deafness
- cranial nerve palsies
- peripheral neuropathy
- brachial plexopathy
- root pain

Non-malignant morbidity from chemotherapy

- Nephrotoxicity
 - cisplatin

- Cardiotoxicity
 - doxorubicin, epirubicin

- Pulmonary fibrosis
 - bleomycin, alkylating agents

- Neurotoxicity
 - vinca alkaloids, taxoids



Non-malignant morbidity from radiotherapy

- Cardiotoxicity
- Growth impairment
- Neurological disturbances (learning disorders)
- Abnormal pituitary function



Conclusions

- Mortality from cancer is decreasing
- This has significant implications for life, critical illness and disability underwriting
- The evidence-base for underwriting changes continually
- Underwriting manuals need to be updated regularly with ratings adjusted so as to be consistent with current evidence