SEMINARI DEL GRG *2005*
13 MAGGIO 2005

CASI CLINICI IN GERIATRIA

LA PROGNOSI COME INDICATORE PER LE SCELTE TERAPEUTICHE

ANGELO BIANCHETTI

- PROGNOSI
  - Dal greco *prógnōsis* = previsione
- PROGNOSTICO
  - Dal greco *prognōstikós* = atto a conoscere prima

Dizionario della lingua Italiana Sabatini Coletti, 2004

Ippocrate

460-370 a.C.

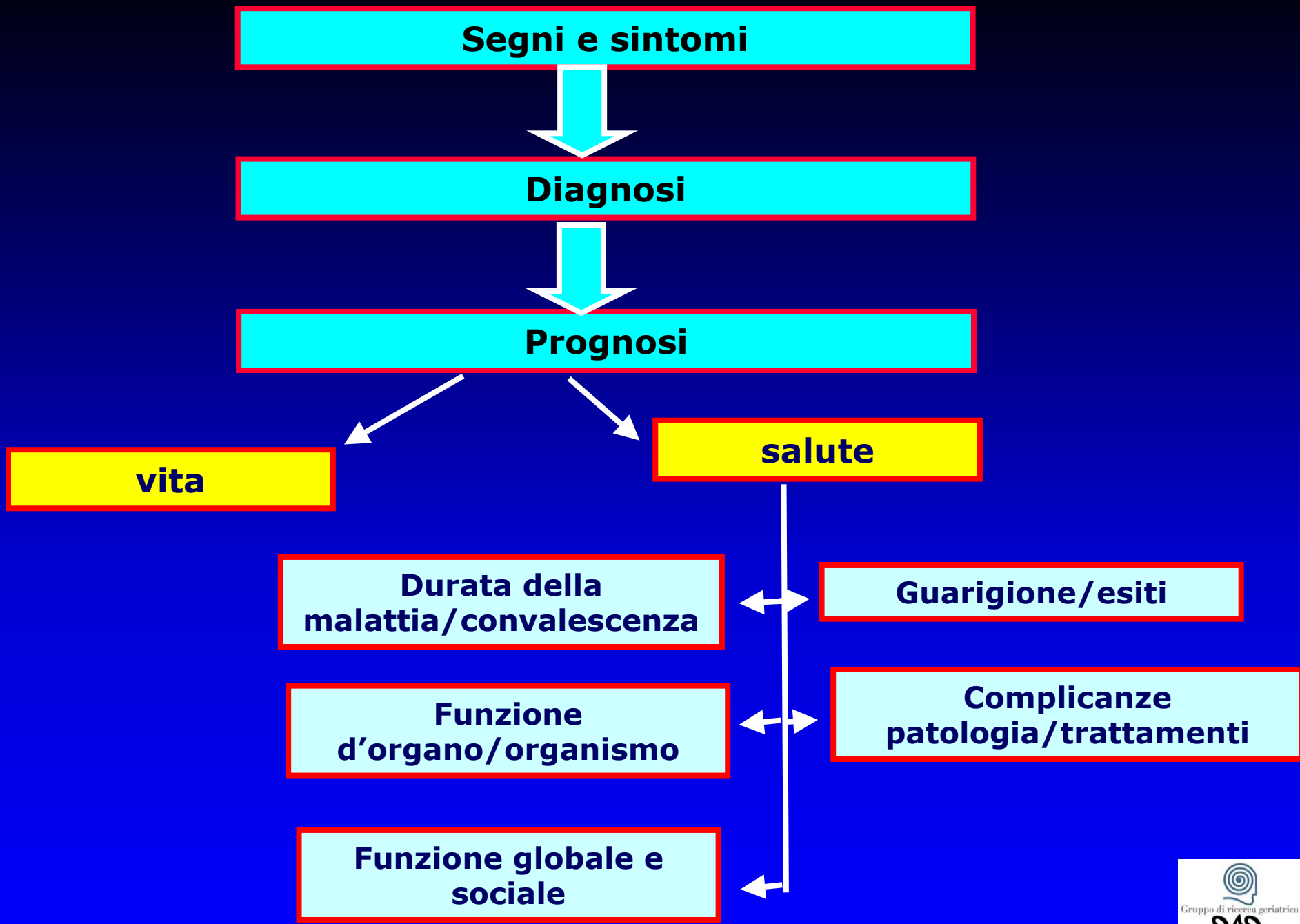
- Nel *Prognostico* , libro del *Corpus Hippocraticum*, viene introdotta la teoria dell'osservazione delle manifestazioni del malato (segni e sintomi), essenziale per compiere una diagnosi corretta e per potere prevedere il decorso di una malattia.
- Ippocrate contrappone al "divinare" (*manteuesqai*) il "congetturare" (*tekmairesqai*) in base ai sintomi (*shmeia*) del male.
- Nel secondo capitolo del *Prognostico* vengono descritti i segni infausti (sudore freddo, anemizzazione delle mani, cianosi delle unghie e stato di agitazione), quella che è passata alla storia come *facies hippocratica*

Prognosi

- Valutazione del medico sul decorso di una malattia in un determinato paziente.
- La prognosi presenta un carattere di probabilità.
- La prognosi può riguardare la vita del paziente o le condizioni di salute nelle quali questi verrà a trovarsi quando la fase acuta della malattia sarà terminata.

Dizionario del Benessere e della Salute, (a cura di) Saccomani R, UTET, 2004

Gruppo di ricerca geriatrica


Segni e sintomi
Diagnosi
Prognosi
vita
salute
Durata della malattia/convalescenza
Guarigione/esiti
Funzione d'organo/organismo
Complicanze patologia/trattamenti
Funzione globale e sociale

Elementi determinanti la prognosi

MALATTIA

- Diagnosi etiologica
- Criteri di gravità clinico-biologica
- Trattamenti disponibili

POLMONITE (CAP)

- Mortalità in relazione all'etiologia
  - P aeruginosa 50%
  - S aureus 35%
  - Acinetobacter spp 30%

PORT (Pneumonia Patient Outcomes Research Team)

TABLE 2. POINT SCORING SYSTEM FOR STEP 2 OF THE PREDICTION RULE FOR ASSIGNMENT TO RISK CLASSES II, III, IV, AND V.

CHARACTERISTIC	POINTS ASSIGNED*
Demographic factor	
Age	
Men	Age (yr)
Women	Age (yr) − 10
Nursing home resident	+10
Coexisting illnesses†	
Neoplastic disease	+30
Liver disease	+20
Congestive heart failure	+10
Cerebrovascular disease	+10
Renal disease	+10
Physical-examination findings	
Altered mental status‡	+20
Respiratory rate ≥30/min	+20
Systolic blood pressure <90 mm Hg	+20
Temperature <35°C or ≥40°C	+15
Pulse ≥125/min	+10
Laboratory and radiographic findings	
Arterial pH <7.35	+30
Blood urea nitrogen ≥30 mg/dl (11 mmol/liter)	+20
Sodium <130 mmol/liter	+20
Glucose ≥250 mg/dl (14 mmol/liter)	+10
Hematocrit <30%	+10
Partial pressure of arterial oxygen <60 mm Hg§	+10
Pleural effusion	+10

NEJM, 1997

Gruppo di ricerca geriatrica

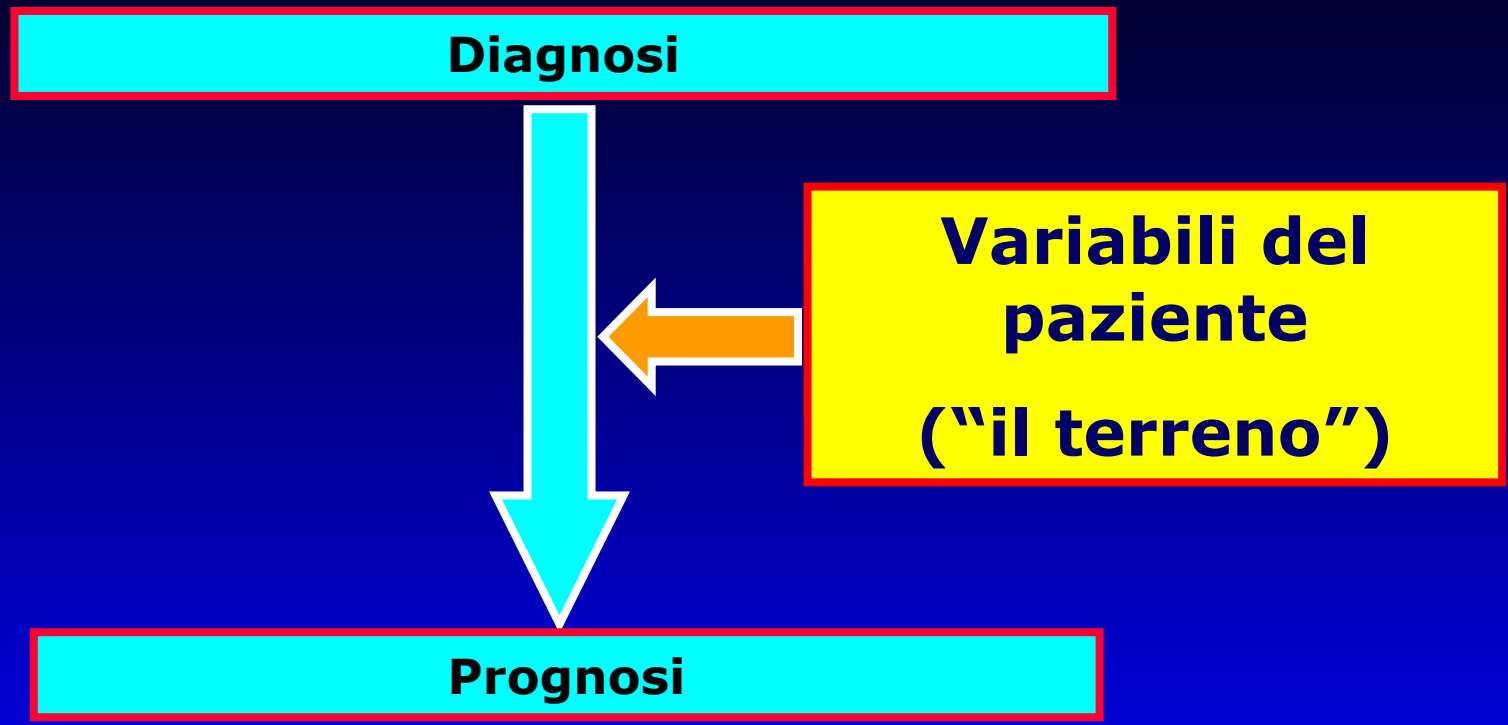
TABLE 3. COMPARISON OF RISK-CLASS–SPECIFIC MORTALITY RATES IN THE DERIVATION AND VALIDATION COHORTS.*

RISK CLASS (NO. OF POINTS)†	MEDISGROUPS DERIVATION COHORT		MEDISGROUPS VALIDATION COHORT		PNEUMONIA PORT VALIDATION COHORT					
					INPATIENTS		OUTPATIENTS		ALL PATIENTS	
	no. of patients	% who died	no. of patients	% who died	no. of patients	% who died	no. of patients	% who died	no. of patients	% who died
I	1,372	0.4	3,034	0.1	185	0.5	587	0.0	772	0.1
II (≤70)	2,412	0.7	5,778	0.6	233	0.9	244	0.4	477	0.6
III (71–90)	2,632	2.8	6,790	2.8	254	1.2	72	0.0	326	0.9
IV (91–130)	4,697	8.5	13,104	8.2	446	9.0	40	12.5	486	9.3
V (>130)	3,086	31.1	9,333	29.2	225	27.1	1	0.0	226	27.0
Total	14,199	10.2	38,039	10.6	1343	8.0	944	0.6	2287	5.2

*There were no statistically significant differences in overall mortality or mortality within risk class among patients in the MedisGroups derivation, MedisGroups validation, or overall Pneumonia PORT validation cohort. The P values for the comparisons of mortality across risk classes are as follows: class I, P = 0.22; class II, P = 0.67; class III, P = 0.12; class IV, P = 0.69; and class V, P = 0.09.

La prognosi in geriatria

- Questo modello si applica anche al vecchio?
- Con quali aggiustamenti?



Elementi determinanti la prognosi

PAZIENTE ("il terreno")

- Età

CAP (BTS guidelines)

- Age has consistently been shown to be significantly associated with mortality in studies from a variety of countries.
- However, recent studies of CAP in the elderly (>65 years) have suggested that, within this population, age by itself is not of prognostic importance [**IIb-II**].

CAP (ATS guidelines)

- The role of age in the prediction of organisms causing CAP is not clear
- In the elderly seem more frequent the emergence of drug-resistant pneumococcus CAP (inconclusive data)
- In the elderly (or pt. with coexistent diseases) routine laboratory tests to assess severity of CAP are recommended
- Advanced age and coexisting illness are important factors that affect the clinical presentation of pneumonia.
- The Pneumonia PORT rule assigns points in a way that heavily weights age, requiring much more severe physiologic abnormalities in young

ICU mortality in the elderly

- Although some studies report overall increased ICU mortality among the elderly, others fail to demonstrates consistent evidence of uniformly poor survival, even in patients over 80 years.

Lewy CR, Hazzard Principles of Geriatric Medicine, 2003

Speranza di vita nel 2000

Età	donne	uomini
Alla nascita	74.1	79.5
A 65 anni	16.3	19.2
A 75 anni	10.2	12.1
A 85 anni	5.6	6.7

Da: National Vital Statistics Report, 2001

Elementi determinanti la prognosi

PAZIENTE ("il terreno")

- Età

- Riduzione spettanza di vita
- Influenza la presentazione della malattia (e la diagnosi)
- Influenza l'epidemiologia
- Richiede un più attento monitoraggio clinico
- I trattamenti possono più facilmente essere meno efficaci
- A parità di severità biologica di malattia la severità clinica può essere maggiore
- Più frequenti le complicanze della malattia/trattamenti

Elementi determinanti la prognosi

PAZIENTE ("il terreno")

- Età
- Comorbidità
- Funzioni mentali

CAP (BTS guidelines)

- Concomitant congestive cardiac failure, coronary artery disease, stroke, diabetes mellitus, chronic lung disease, cancer and other coexisting illnesses have been shown to predict death in patients with CAP **[IIb-III]**
- However, the magnitude of the contribution of these coexisting illnesses to disease severity is difficult to ascertain due to variations in disease definition and problems in determining the severity of these conditions themselves.
- This may partly explain the low predictive power of the presence of coexisting illnesses as a risk factor for death on multivariate analysis, despite the large number of studies that have demonstrated significance on univariate

Ann Intern Med. 1995 Feb 1;122(3):191-203.

The SUPPORT prognostic model.

Objective estimates of survival for seriously ill hospitalized adults.

Knaus WA, Harrell FE Jr, Lynn J, Goldman L, Phillips RS, Connors AF Jr, Dawson NV, Fulkerson WJ Jr, Califf RM, Desbiens N, Layde P, Oye RK, Bellamy PE, Hakim RB, Wagner DP.

S*tudy to* **U***nderstand* **P***rognoses and* **P***references for* **O***utcomes and* **R***isks of* **T***reatments*

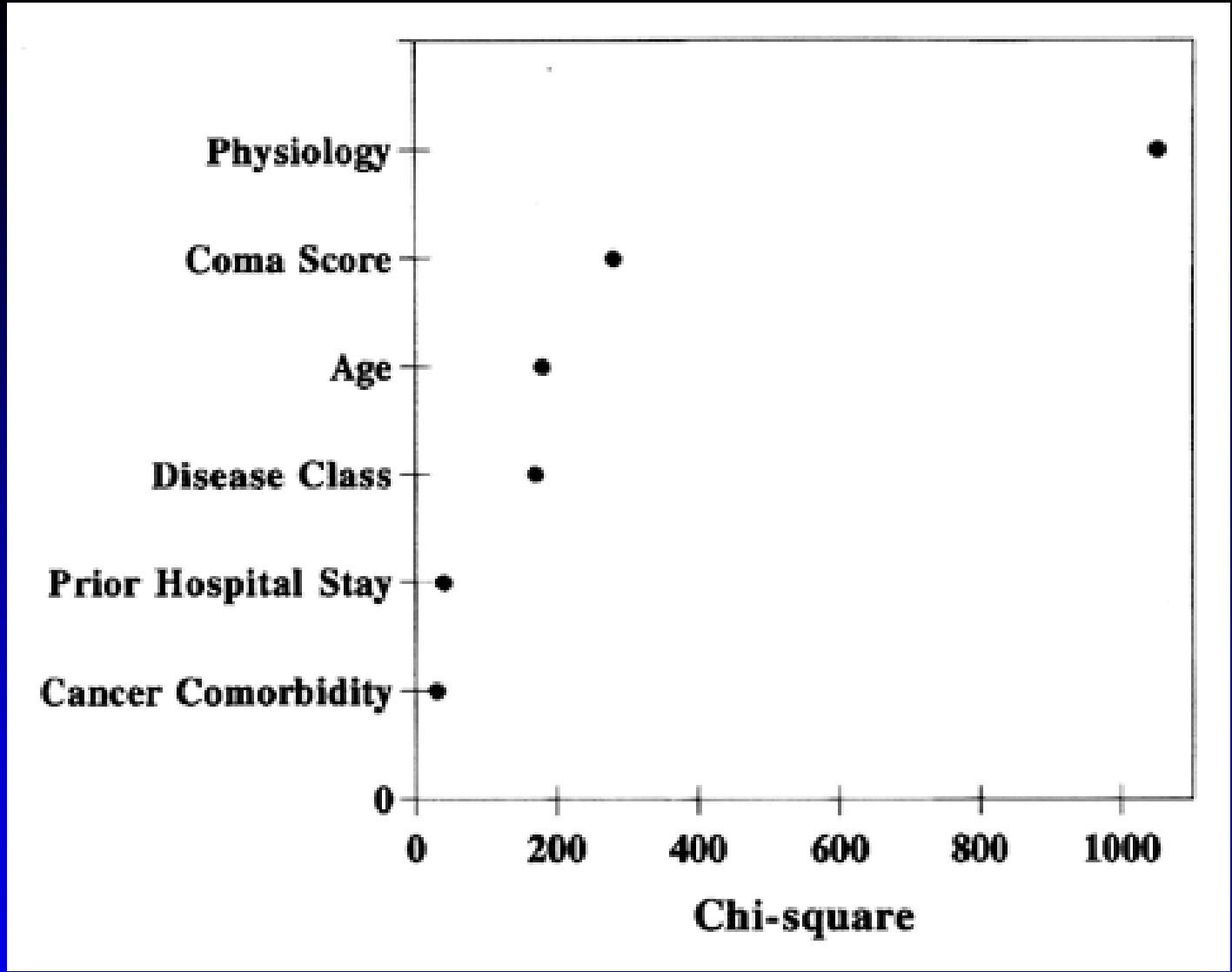


Figure 1. Relative contributions of major prognostic elements in the SUPPORT model as measured by the amount of chi-square accounted for by each element. Physiology = all physiologic measures except Glasgow coma scale; cancer comorbidity = presence of cancer in addition to disease category; previous hospital stay = days in the hospital before study entry

ICU mortality in the elderly

- Factors independently associated with increased mortality were gender, functional status, CHF, cancer, elevate creatinine, low albumin, number of days in hospital before ICU admission, neurological status.

Lewy CR, Hazzard Principles of Geriatric Medicine, 2003

The importance of co-existent disease in the occurrence of postoperative complications and one-year recovery in patients undergoing total hip replacement. Comorbidity and outcomes after hip replacement.

Greenfield S, Apolone G, McNeil BJ, Cleary PD.
Med Care 1993 Feb;31(2):141-54

Co-existent or comorbid diseases are appreciated as prognostic factors in studies of quality and effectiveness of care when mortality is the end point. The need to measure and adjust for comorbidity in studies of postoperative hospital complications or long-term recovery from surgery has not been documented.
After controlling for gender, age, education, and marital status, ICED remained a significant predictor of functional status at 1 year. Furthermore, differences among hospitals in functional outcomes disappeared when the ICED was included in the model to adjust for patient characteristics at the time of surgery.
A measure of co-existent disease was crucial in explaining differences among hospitals in recovery from total hip replacement patients.

Outcomes up to 5 Years After Severe, Acute Respiratory Failure*

Allan Garlandet al, for the SUPPORT Investigators

Chest. 2004;126:1897-1904

- The median survival time after hospital discharge for ARF was > 5.3 years.
- The posthospital survival time was shorter for those with older age, male gender, several preexisting comorbid conditions, worse prehospital functional status, greater acute physiologic derangement, and a do-not-resuscitate order while in the hospital, and for those discharged to a location other than home.
- Five months after hospital discharge, 48% of survivors needed help with at least one activity of daily living, and 27% rated their QOL as poo

Med Decis Making. 2005 Mar-Apr;25(2):210-21.

Withholding or starting antibiotic treatment in patients with dementia and pneumonia: prediction of mortality with physicians' judgment of illness severity and with specific prognostic models.

van der Steen JT, Ooms ME, van der Wal G, Ribbe MW.

- Pneumonia patients treated without (n = 165) or with antibiotics (n = 541) were enrolled in a prospective cohort study in 61 nursing homes.
- Mortality was 83% in untreated patients and 15% in treated patients.
- In both groups predictors of mortality were physicians' clinical judgment, respiratory rate, fluid intake, and eating dependency

CAP (BTS guidelines)

- An altered mental state has been identified as an independent risk factor for mortality in large studies, even in the elderly [Ib-III].

Dementia: The leading predictor of death in a defined elderly population

The Cache County Study

J.T. Tschanz, PhD; C. Corcoran, PhD; I. Skoog, MD, PhD; A.S. Khachaturian, PhD; J. Herrick, MS; K.M. Hayden, PhD; K.A. Welsh–Bohmer, PhD; T. Calvert, RN, BA; M.C. Norton, PhD; P. Zandi, PhD; and J.C.S. Breitner, MD, MPH; and the Cache County Study Group*

Abstract—*Objective:* To examine the relative risk and population attributable risk (PAR) of death with dementia of varying type and severity and other risk factors in a population of exceptional longevity. *Methods:* Deaths were monitored over 5 years using vital statistics records and newspaper obituaries in 355 individuals with prevalent dementia and 4,328 without in Cache County, UT. Mean age was 83.3 (SD 7.0) years with dementia and 73.7 (SD 6.8) years without. History of coronary artery disease, hypertension, diabetes, and other life-shortening illness was ascertained from interviews. *Results:* Death certificates implicated dementia as an important cause of death, but other data suggested a stronger association. Adjusted Cox relative hazard and PAR of death were higher with dementia than with any other illness studied. Relative hazard of death with dementia was highest at ages 65 to 74, but the high prevalence of dementia after age 85 resulted in 27% PAR among the oldest old. Mortality increased substantially with severity of dementia. Alzheimer disease shortened survival time most dramatically in younger participants, but vascular dementia posed a greater mortality risk among the oldest old. *Conclusion:* In this population, dementia was the strongest predictor of mortality, with a risk two to three times those of other life-shortening illnesses.

NEUROLOGY 2004;62:1156–1162

Table 3 Point estimates of the relative risks and population attributable risk for predictors of mortality

Risk factor	RR (95% CI)	n (%) with risk factor age 65–74	PAR, %	n (%) with risk factor age 75–84	PAR, %	n (%) with risk factor age 85+	PAR, %	n (%) with risk factor (total)	PAR, % (total)
Dementia, all ages	2.99 (2.53–3.53)	—	—	—	—	—	—	355 (10.0)*	16.6
Age 65–74	7.26 (4.50–11.69)	39 (2.7)*	14.5	—	—	—	—	—	—
Age 75–84	3.55 (2.76–4.55)	—	—	153 (11.8)*	23.1	—	—	—	—
Age ≥85	2.20 (1.70–2.84)	—	—	—	—	163 (30.1)*	26.5	—	—
Education, y	0.98 (0.96–1.01)	NA	NA	NA	NA	NA	NA	NA	NA
APOE ε4/ε*x*	1.06 (0.92–1.22)	714 (30.7)	NA	493 (28.3)	NA	124 (22.3)	NA	1,331 (28.4)	NA
APOE ε4/ε4†	1.49 (1.05–2.12)	68 (2.9)	1.40	41 (2.4)	1.16	12 (2.2)	1.07	121 (2.6)	1.31
Asthma	1.05 (0.83–1.32)	205 (8.7)	NA	167 (9.6)	NA	36 (6.3)	NA	408 (8.7)	NA
Cerebrovascular disease†	1.25 (1.03–1.50)	155 (6.6)	1.60	190 (10.9)	2.63	78 (13.8)	3.28	423 (9.1)	2.19
Coronary heart disease†	1.35 (1.16–1.59)	327 (13.9)	4.69	320 (18.4)	6.15	93 (16.4)	5.49	740 (15.9)	5.33
Hypercholesterolemia	0.90 (0.75–1.09)	509 (21.7)	NA	301 (17.30)	NA	39 (7.2)	NA	849 (18.5)	NA
Diabetes†	1.86 (1.57–2.20)	228 (9.7)	7.67	184 (10.6)	8.32	63 (11.0)	8.61	475 (10.2)	8.03
Head injury	0.87 (0.74–1.02)	528 (22.4)	NA	332 (19.0)	NA	103 (18.1)	NA	963 (20.6)	NA
Hypertension	1.14 (0.99–1.30)	915 (38.8)	NA	750 (43.0)	NA	238 (42.3)	NA	1903 (40.8)	5.22
Parkinson disease†	1.90 (1.39–2.59)	35 (1.5)	1.33	53 (3.0)	2.63	10 (1.7)	1.51	98 (2.1)	1.85
Pneumonia†	1.33 (1.05–1.68)	131 (5.5)	1.77	135 (7.8)	2.49	44 (7.7)	2.46	310 (6.6)	2.11
Ulcer	1.06 (0.92–1.23)	611 (25.8)	NA	452 (26.0)	NA	124 (21.7)	NA	1187 (25.4)	NA
Pulmonary disease†	1.40 (1.11–1.77)	162 (6.8)	2.70	142 (8.2)	3.19	36 (6.3)	2.47	340 (7.3)	2.85

This table provides point estimates of the relative risks (RR) for mortality associated with dementia and other medical risk factors, obtained from a multivariable Cox proportional hazards model. Only the highly significant two-way interaction between age and dementia was retained. For all other risk factors, the estimated hazards ratios collapsed across all age groups are presented. The percentages of individuals in the population with the risk factor and the corresponding population attributable risk (PAR) are also shown.

* Prevalence figures for dementia reflect estimates based on correction for insensitivity of screening methods and incomplete participation through all study stages.

† $p < 0.05$.

NA = not applicable (PAR not calculated for continuous variables or those with hazards ratios of <1 or not significant at $p = 0.05$).

Table 4 Mortality risk associated with dementia categorized by severity and type

Risk factor	Ages 65–74			Ages 75–84			Ages 85+		
	Adj. RR (95% CI)	n (%) of population	PAR, %	Adj. RR (95% CI)	n (%) of population	PAR, %	Adj. RR (95% CI)	n (%) of population	PAR, %
All dementia	7.26 (4.5–11.7)	39 (2.7)*	14.5	3.55 (2.76–4.55)	153 (11.8)*	23.1	2.20 (1.70–2.84)	163 (30.1)*	26.5
Dementia severity									
Mild	5.75 (2.70–12.25)	14 (0.6)	2.8	2.44 (1.69–3.54)	62 (3.6)	4.9	1.80 (1.24–2.60)	51 (8.9)	6.6
Moderate	7.45 (3.46–16.06)	9 (0.4)	2.5	3.36 (2.16–5.22)	30 (1.7)	3.9	2.25 (1.51–3.36)	53 (9.2)	10.3
Severe	18.59 (8.53–40.51)	13 (0.5)	8.1	7.04 (4.78–10.37)	54 (3.1)	15.8	3.45 (2.04–5.84)	52 (9.1)	18.2
Dementia type									
AD	11.30 (5.70–22.40)	20 (1.4)	12.5	4.30 (3.12–5.92)	91 (7.0)	18.7	2.12 (1.50–2.90)	96 (17.7)	16.5
VaD	6.92 (2.79–17.20)	7 (0.5)	2.8	3.14 (1.84–5.38)	23 (1.9)	3.9	2.20 (1.26–3.84)	24 (4.3)	4.9
Mixed AD/VaD	9.00 (2.18–37.03)	4 (0.2)	1.9	3.12 (1.36–7.18)	10 (0.8)	1.6	2.24 (1.17–4.27)	17 (3.0)	3.6
Other dementia	3.43 (1.09–10.81)	8 (0.6)	1.4	2.66 (1.59–4.44)	29 (2.2)	3.5	2.42 (1.50–3.91)	26 (5.2)	6.8

This table presents the adjusted relative risks (Adj. RR) for mortality associated with all dementia and with dementia categorized by severity and type, as estimated from a multivariable Cox proportional hazards model. The percentages of affected individuals in the population (prevalence) and the corresponding population attributable risk (PAR) are also shown.

* Prevalence figures for dementia reflect estimates based on correction for insensitivity of screening methods and incomplete participation through all study stages.

AD = Alzheimer disease; VaD = vascular dementia.

Brookmeye R, Corrada MM, Curriero FC, Kawas C.

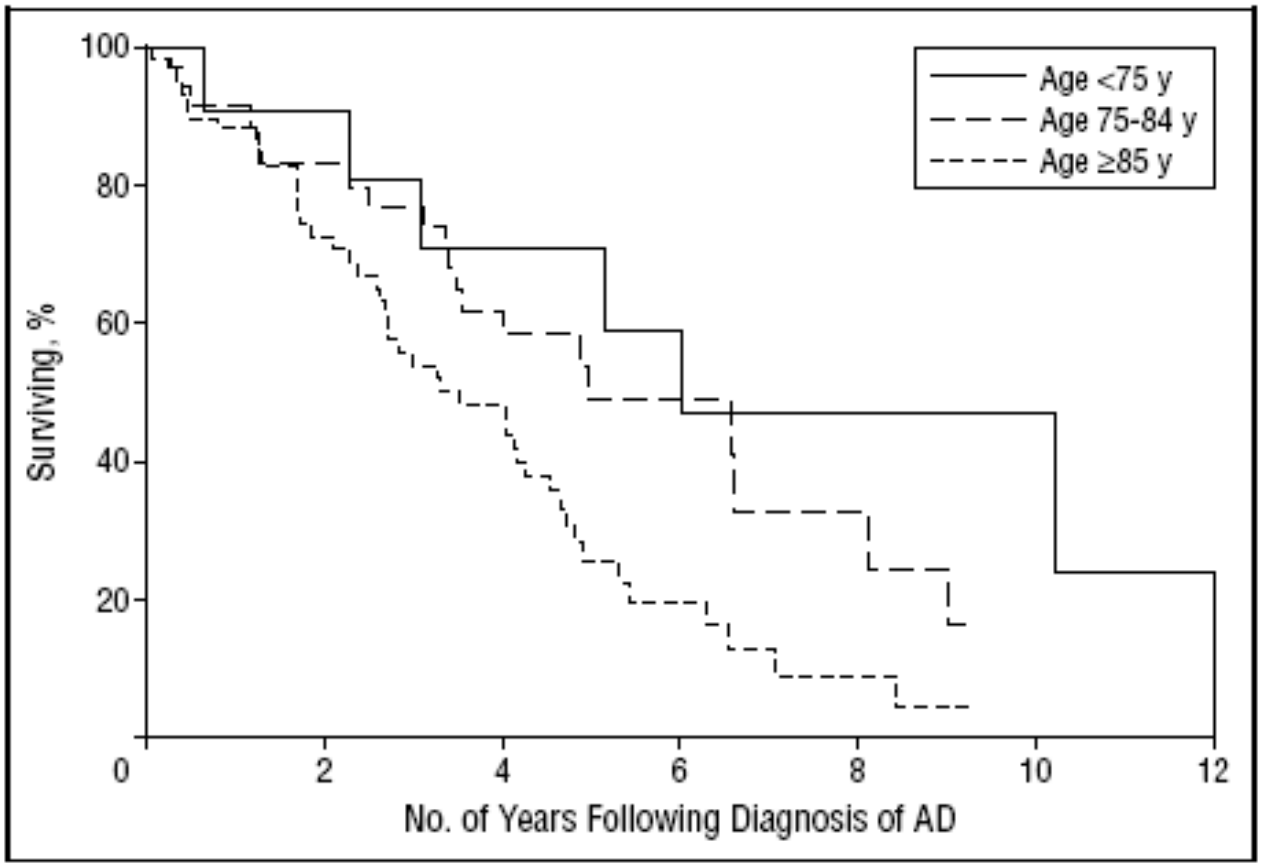
Survival Following a Diagnosis of Alzheimer Disease.

Arch Neurol. 2002;59:1764-1767

- La sopravvivenza dopo la diagnosi di malattia di Alzheimer dipende sostanzialmente dall'età del paziente.
- La sopravvivenza è mediamente di 9 anni per le persone a cui la diagnosi è stata effettata a 65 anni, mentre è di 3 anni per le persone a cui la diagnosi è stata posta a 90 anni.
- Le persone a cui la diagnosi è posta a 65 anni hanno una riduzione della spettanza di vita attesa di circa il 67%, mentre per le persone di 90 anni la riduzione di spettanza di vita è del 39%.

Brookmeye R, Corrada MM, Curriero FC, Kawas C. Survival Following a Diagnosis of Alzheimer Disease.

Arch Neurol. 2002;59:1764-1767



Kaplan-Meier survival curves following the diagnosis of Alzheimer disease stratified by patient's age at the time of the diagnosis.

Life expectancy in older persons

Years still to live

	Men						Women					
Age	**70**	**75**	**80**	**85**	**90**	**95**	**70**	**75**	**80**	**85**	**90**	**95**
Healthy	18.0	14.2	10.8	7.9	5.8	4.3	21.3	17.0	13.0	9.6	6.8	4.8
Average	12.4	9.3	6.7	4.7	3.2	2.3	15.7	11.9	8.6	5.9	3.9	2.7
Frail	6.7	4.9	3.3	2.2	1.5	1.0	9.5	6.8	4.6	2.9	1.8	1.7

Based on NCMS Life Tables of the United States 1997,
Adapted from Walter LC and Covinsky KE . JAMA 2001:285; 2750-6

Delirium

- Pazienti con delirium hanno un tassso maggiore di mortalità rispetto ai pazienti senza delirium, sia durante l'ospedalizzazione (16% vs 5%; OR 3.4, 95% CI 1.3-8.6) che a sei mesi dalla dimissione (31% vs 15%; OR 2.5, 95% CI 1.3-4.7)
- Pazienti con delirium rimangono ospedalizzati più a lungo (21 giorni contro 11 giorni; p<.001). All'analisi multivariata, il delirium era l'unico predittore di durata dell'ospedalizzazione. (p<.001).
- Il delirium è il più forte predittore di rischio di sviluppare una complicanza durante il ricovero ospedaliero.
- I pazienti con delirium hanno una probabilità p

J Am Geriatr Soc 199

Elementi determinanti la prognosi

PAZIENTE ("il terreno")

- Comorbidità
- Funzioni mentali

- La comorbidità peggiora la prognosi in relazione alla severità della patologia
- La demenza è la patologia cronica che ha maggior impatto sulla sopravvivenza, soprattutto negli "young-elderly"
- Le alterazioni dello stato mentale sono un fattore indipendente di mortalità, di complicanze e di disabilità

Elementi determinanti la prognosi

PAZIENTE ("il terreno")

- Età
- Comorbidità
- Funzioni mentali
- Stato funzionale

Outcome predictors of pneumonia in elderly patients: importance of functional assessment.

Torres OH, Munoz J, Ruiz D, Ris J, Gich I, Coma E, Gurgui M, Vazquez G.

J Am Geriatr Soc. 2004 Oct;52(10):1603-9

- Functional status was an independent predictor for short- and long-term mortality in hospitalized patients whereas CAP severity predicted functional decline.

Gruppo di ricerca geriatrica

Table. Cox Regression Analysis of Associations Between Groups of Risk and 6-Month Mortality Among Acutely Hospitalized Elderly Patients (N = 840)*

	No. (Events)	RR (95% CI)
Prognostic Index†		
Group 1 (0-1 point)	344 (11)	Reference
Group 2 (2-3 points)	303 (31)	2.1 (1.0-4.6)
Group 3 (4-6 points)	128 (32)	6.9 (3.3-14.6)
Group 4 (≥6 points)	65 (30)	18.3 (8.8-37.9)

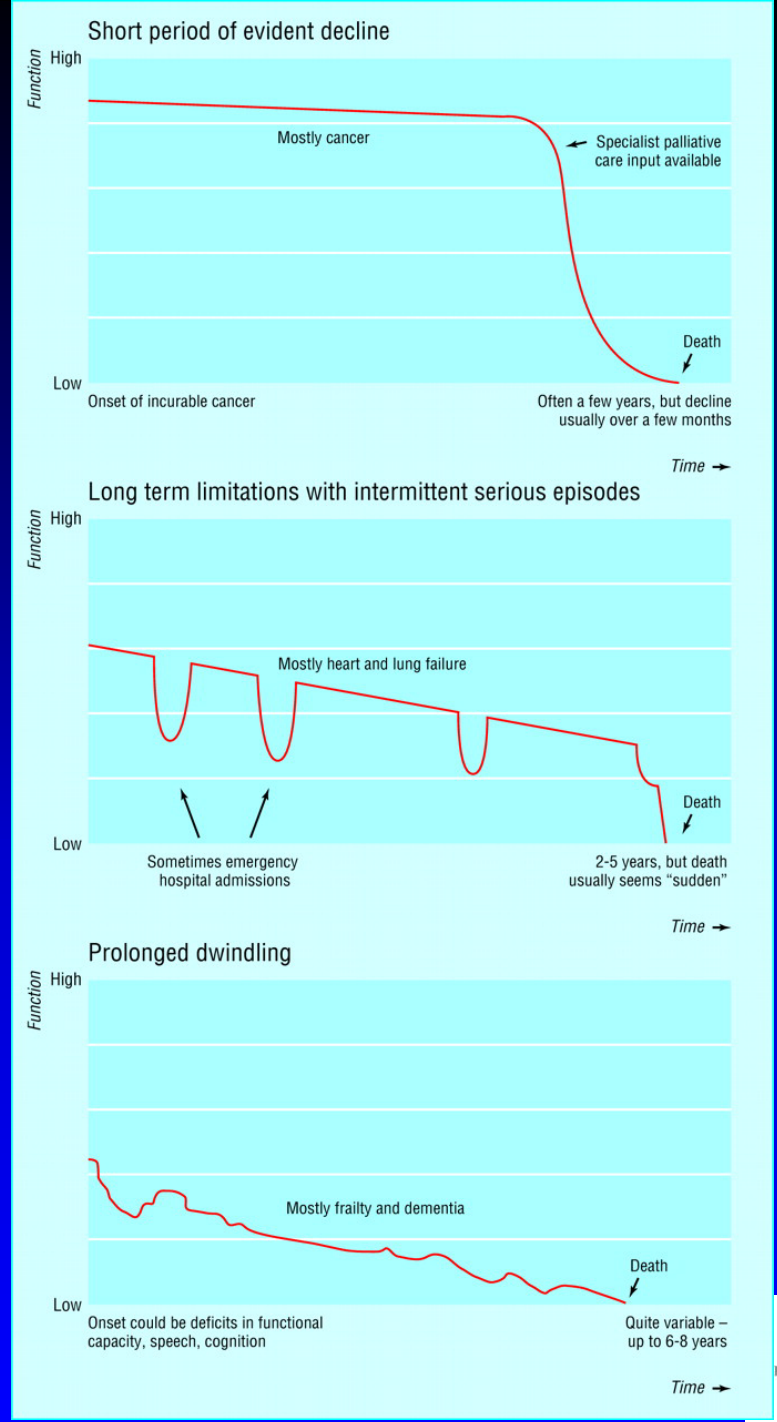
*RR indicates relative risk; CI, confidence interval.

†Independent risk factors for mortality identified in computing the prognostic index were: male sex (1 point); number of dependent activities of daily living (ADLs) at discharge (1-4 ADLs, 2 points; all 5 ADLs, 5 points); congestive heart failure (2 points); cancer (solitary, 3 points; metastatic, 8 points); creatinine level >3.0 mg/dL (265 µmol/L) (2 points); and low albumin level (3.0-3.4 g/dL, 1 point; <3.0 g/dL, 2 points).[1]

Prediction of 6-Month Mortality Among Older Hospitalized Adults

Rozzini et al. JAMA. 2001;286:1315-1316

Typical illness trajectories for people with progressive chronic illness. Adapted from Lynn and Adamson, 2003.7



(BMJ 2005;330:1007-1011)

Life expectancy in older persons

Years still to live

	Men						Women					
Age	**70**	**75**	**80**	**85**	**90**	**95**	**70**	**75**	**80**	**85**	**90**	**95**
Healthy	18.0	14.2	10.8	7.9	5.8	4.3	21.3	17.0	13.0	9.6	6.8	4.8
Average	12.4	9.3	6.7	4.7	3.2	2.3	15.7	11.9	8.6	5.9	3.9	2.7
Frail	6.7	4.9	3.3	2.2	1.5	1.0	9.5	6.8	4.6	2.9	1.8	1.7

Based on NCMS Life Tables of the United States 1997,
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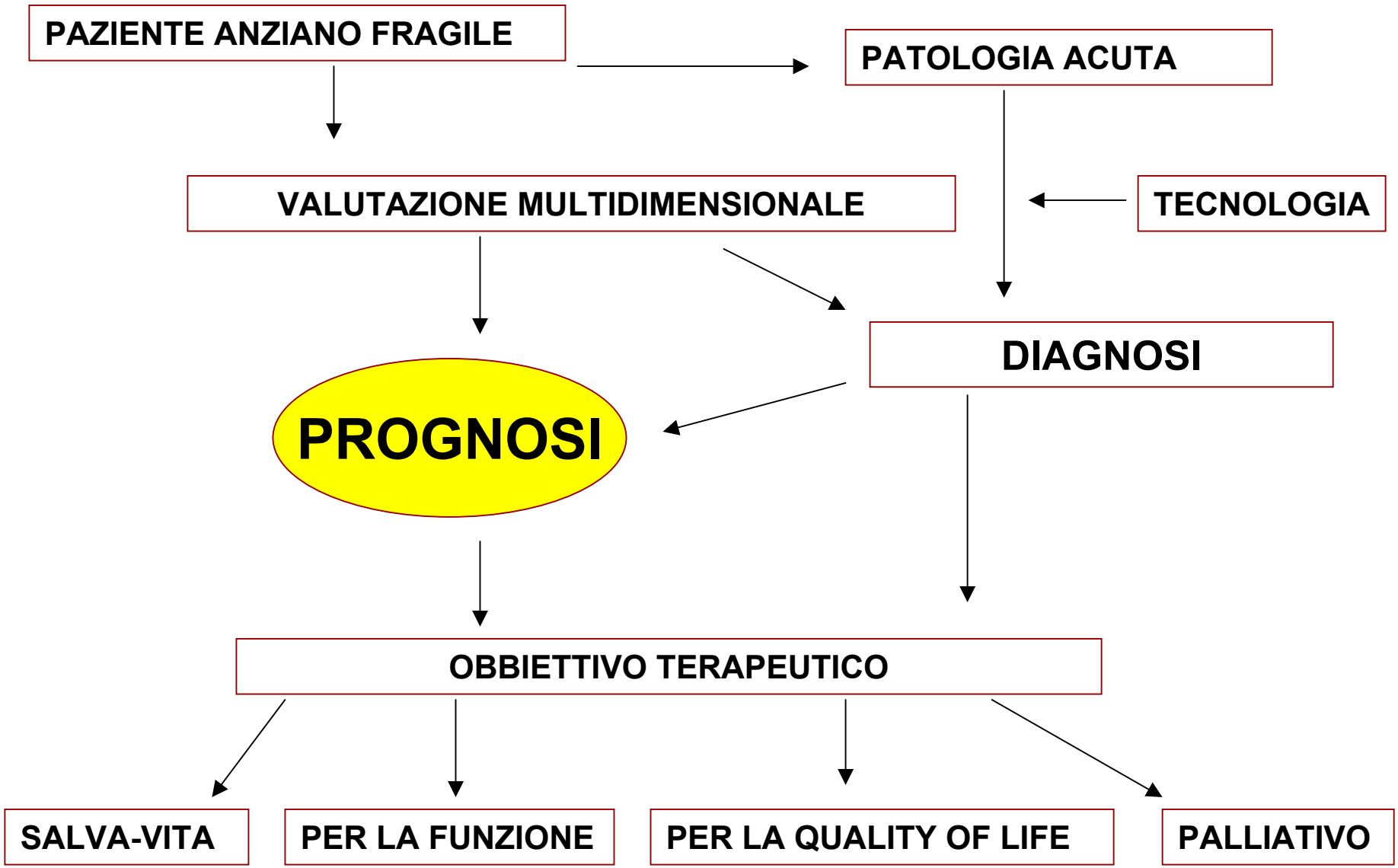
MODELLO OPERATIVO GERIATRICO



By Piera Ranieri

La vita è breve, l'arte lunga, l'esperienza ingannevole, il giudizio difficile.

Ippocrate