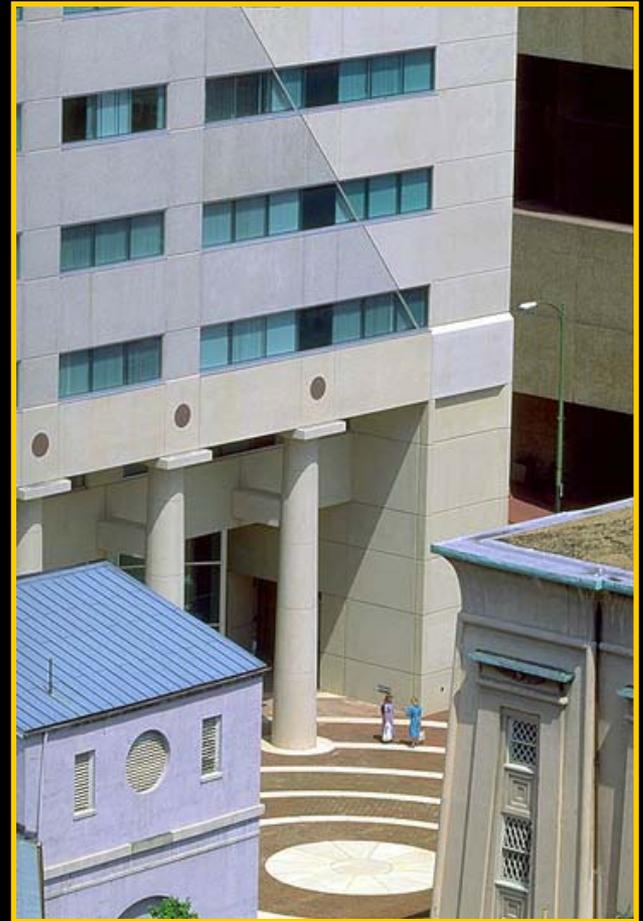


Prognosis

VCU School of Medicine

M1 Population Medicine Class

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The physician who cannot inform his patient what would be the probable issue of his complaint, if allowed to follow its natural course, is not qualified to prescribe any rational treatment for its cure.

Hippocrates 460-375 BC

*Extent and determinants of error in
doctor's prognoses in terminally ill
patients: prospective cohort study*

Christakis N, Lamont E. *BMJ*. Vol 329.469-73.2000

Extent and determinants of error in doctors' prognoses in terminally ill patients: prospective cohort study

- Objective
 - To describe doctors' prognostic accuracy in terminally ill patients
 - Prospective cohort study in five outpatient hospice programs in Chicago
- Participants
 - 343 doctors provided survival estimates for 468 terminally ill patients at the time of hospice referral

Extent and determinants of error in doctors' prognoses in terminally ill patients: prospective cohort study

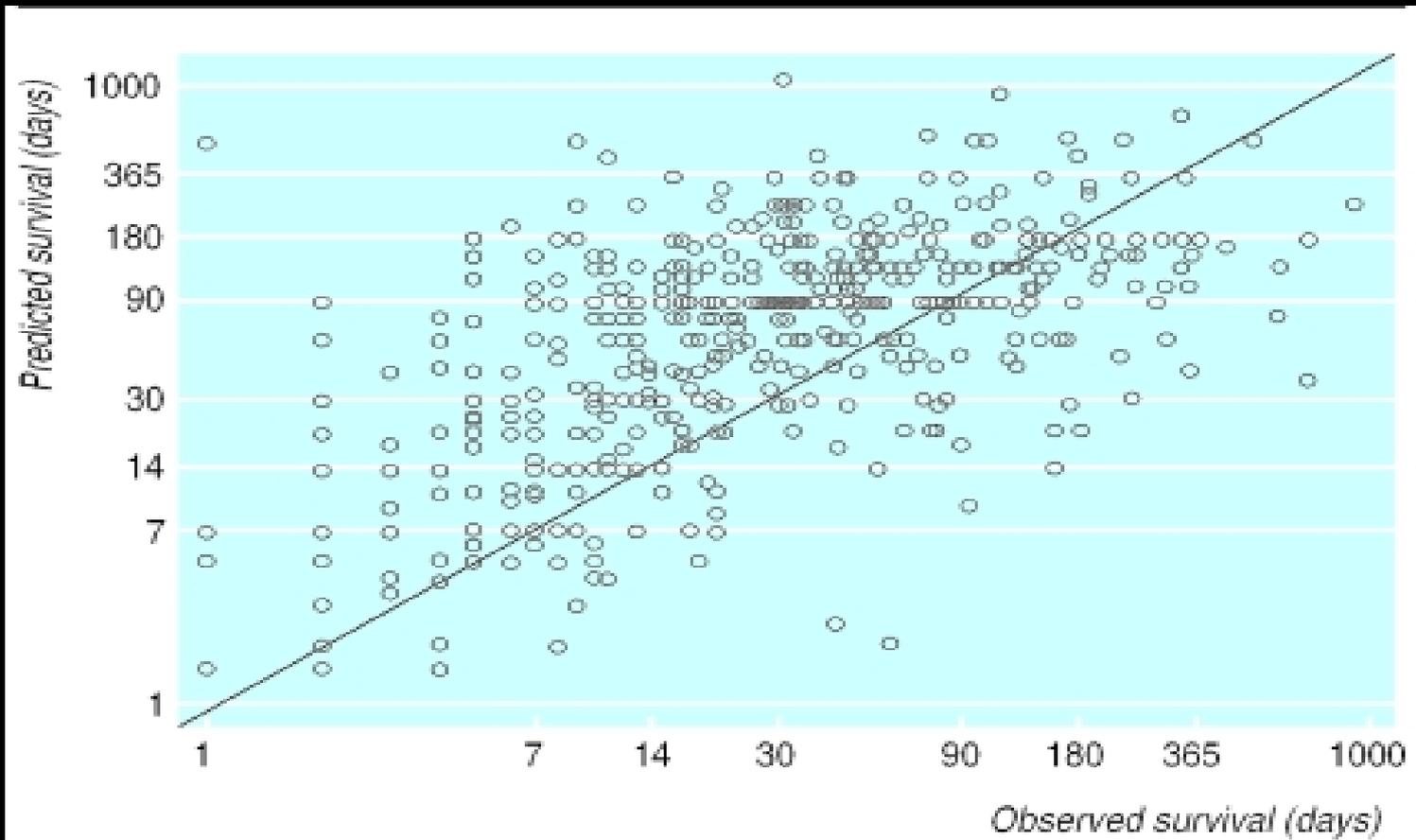
- Cohort
 - Five outpatient hospice programs in Chicago in 1996
- Referring doctors were contacted and administered a four minute telephone survey
 - Estimate of how long the patient had to live
- Additional data collected
 - Patient demographic, diagnoses
 - Physician specialty, years in practice, and board certification from public records.
 - Dates of patients' deaths obtained from public death registries or the hospices

Extent and determinants of error in doctors' prognoses in terminally ill patients: prospective cohort study

Median Survival	24 days
Accurate Prediction	20% (92/468)
Over-optimistic	63% (295/468)
Over-pessimistic	17% (81/468)

Physicians overestimated survival by a factor of 5.3

Few patient or doctor characteristics were associated with prognostic accuracy



Predicted versus observed survival in 468 terminally ill hospice patients. Diagonal line represents perfect prediction. Patients above diagonal are those in whom survival was overestimated; patients below line are those in whom survival was underestimated

Extent and determinants of error in doctors' prognoses in terminally ill patients: prospective cohort study

- Doctors are inaccurate in their prognoses for terminally ill patients
 - The error is systematically optimistic
- The prognostic inaccuracy is, in general, not restricted to certain kinds of doctors or patients
- This may be adversely affecting the quality of care given to patients near the end of life

Commentary: Prognoses should be based on proved indices not intuition

- *The accurate prediction of survival is important for several reasons. Excessive optimism may cause us to wait too long to refer people for palliative care, we may delay the use of narcotic drugs for pain relief, and we may persist in unpleasant and pointless treatments aimed at curing or prolonging life when it would be kinder to stop*

Commentary: Prognoses should be based on proved indices not intuition

- *In the long term it may be possible to extract from the research those criteria that will enable us to make more reliable clinical predictions. Until that time arrives we would do better to stop guessing and, when predictions are needed, to make use of these indices.*

Doctors' prognostic estimates are a central element of both patient and physician decision making, especially at the end of life

How can medicine scientifically address the issue of prognosis such that both physicians and patients are better informed?

Studies of Prognosis

Prognostic
factors for
outcome

Outcomes

Morbidity

Mortality

Recovery

Disease Onset

Risk
Factors

Study Types

- Case control studies
- Cohort studies

Elements of Prognostic Studies

- Population based
 - Representative sample of people afflicted with a disease
 - Unbiased
- Zero time
 - Time of onset of disease or symptoms
 - Must be well defined
 - Onset or inception of disease
 - Participants should all be enrolled and observed from the same time
 - Maximizes precision

Elements of Prognostic Studies

- Follow up
 - Appropriate length of follow up depends upon the disease and anticipated outcomes
 - Patients must be followed long enough for the clinically important outcome events to occur
 - Inadequate follow up time
 - Observed rate of a given outcome will likely underestimate it's true rate

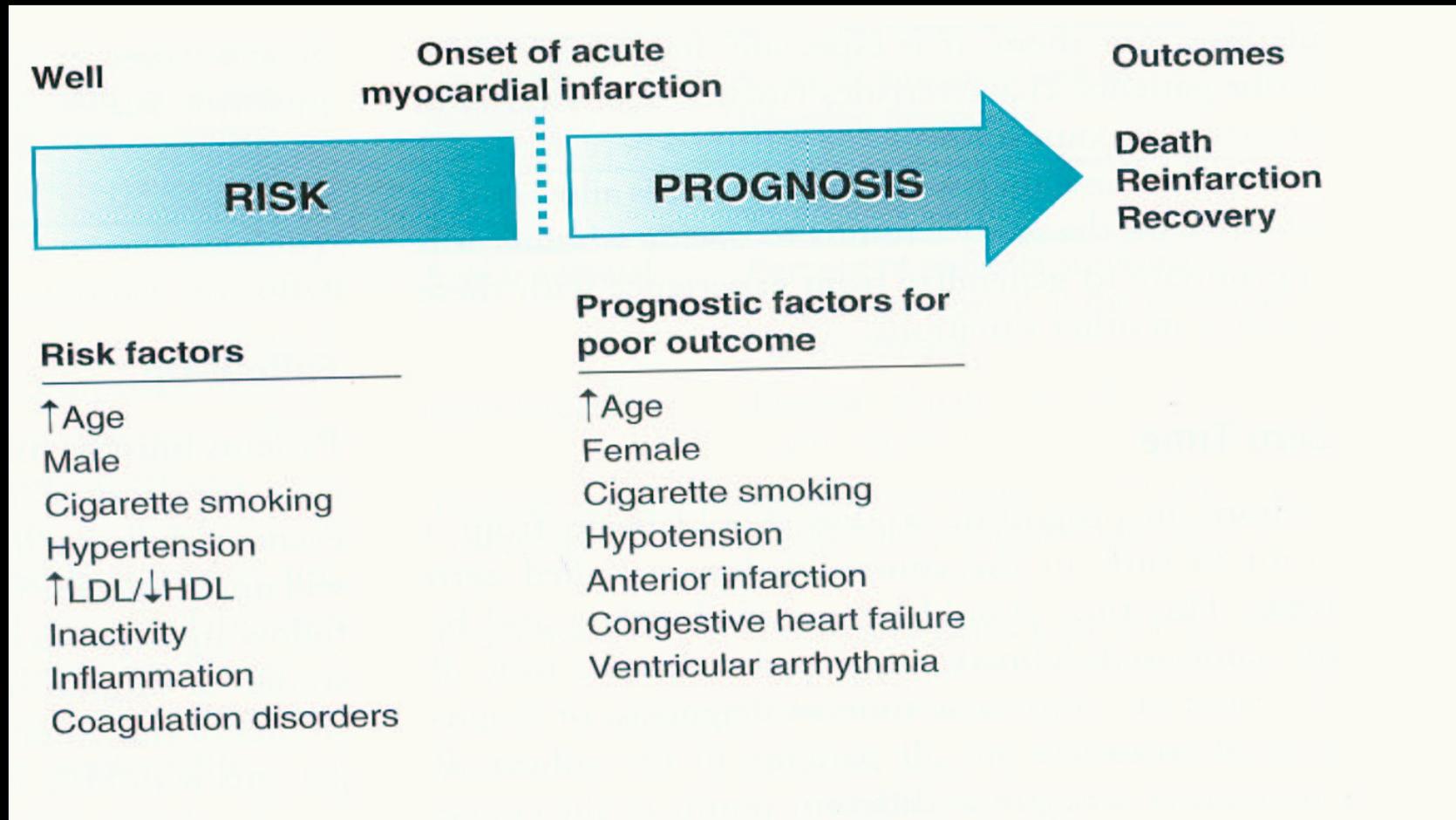
Important Definitions

- Clinical course
 - The evolution (prognosis) of a disease has come under medical care and has been treated in a variety of ways that affect the subsequent course of events
- Natural History
 - The evolution (prognosis) of disease without medical intervention

Risk vs. Prognostic Factors

	Risk factors	Prognostic factors
Patient Population	Healthy Population	Sick Population
Outcome	Disease onset	Morbidity Mortality
Rates	Rare event	Relatively frequent events

Risk and Prognostic Factors



Outcomes of Disease: The 5 D's

- Important Clinical Outcomes of Concern:
 - Death
 - Disease
 - Discomfort
 - Disability
 - Dissatisfaction

Important Rates Used to Describe Prognosis

- 5 year survival: percent of patients surviving 5 years from some point in the course of their disease
- Case fatality: percent of patients with a disease who die with it
- Disease-specific mortality: number of people per 100,000 population dying of a specific disease

Important Rates Used to Describe Prognosis

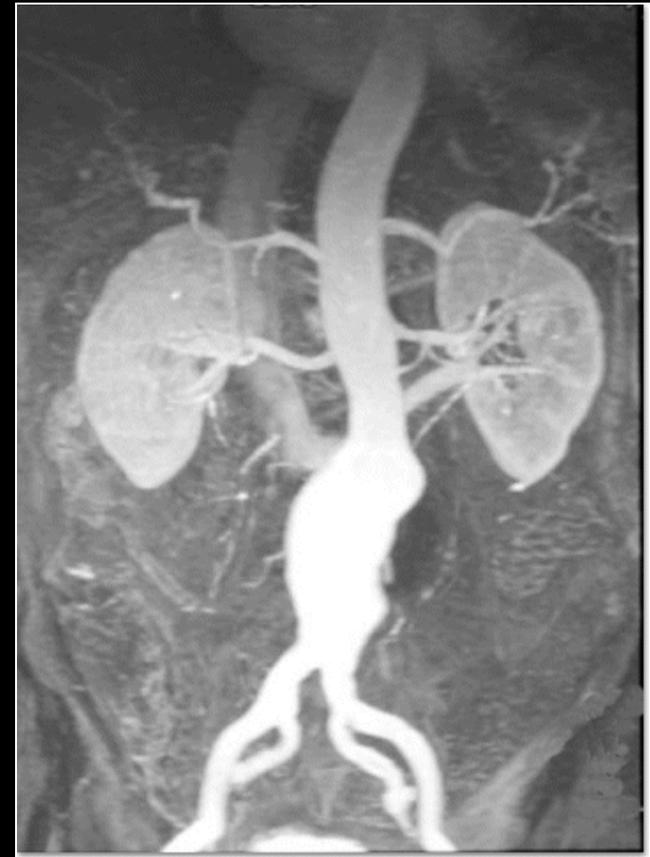
- Response: percent of patients showing a clinical improvement following a therapeutic intervention
- Remission: percent of patients entering a phase in which disease is no longer detectable
- Recurrence: percent of patients entering a phase in which disease is no longer undetectable

Some real life examples....



Case 1

- 63 year old Caucasian man
- HTN and DM
- Palpable abdominal mass confirmed by CT scan
- AAA 8 cm in size
- What is his prognosis?



Rupture rate of large abdominal aortic aneurysms in patients refusing or unfit for elective repair

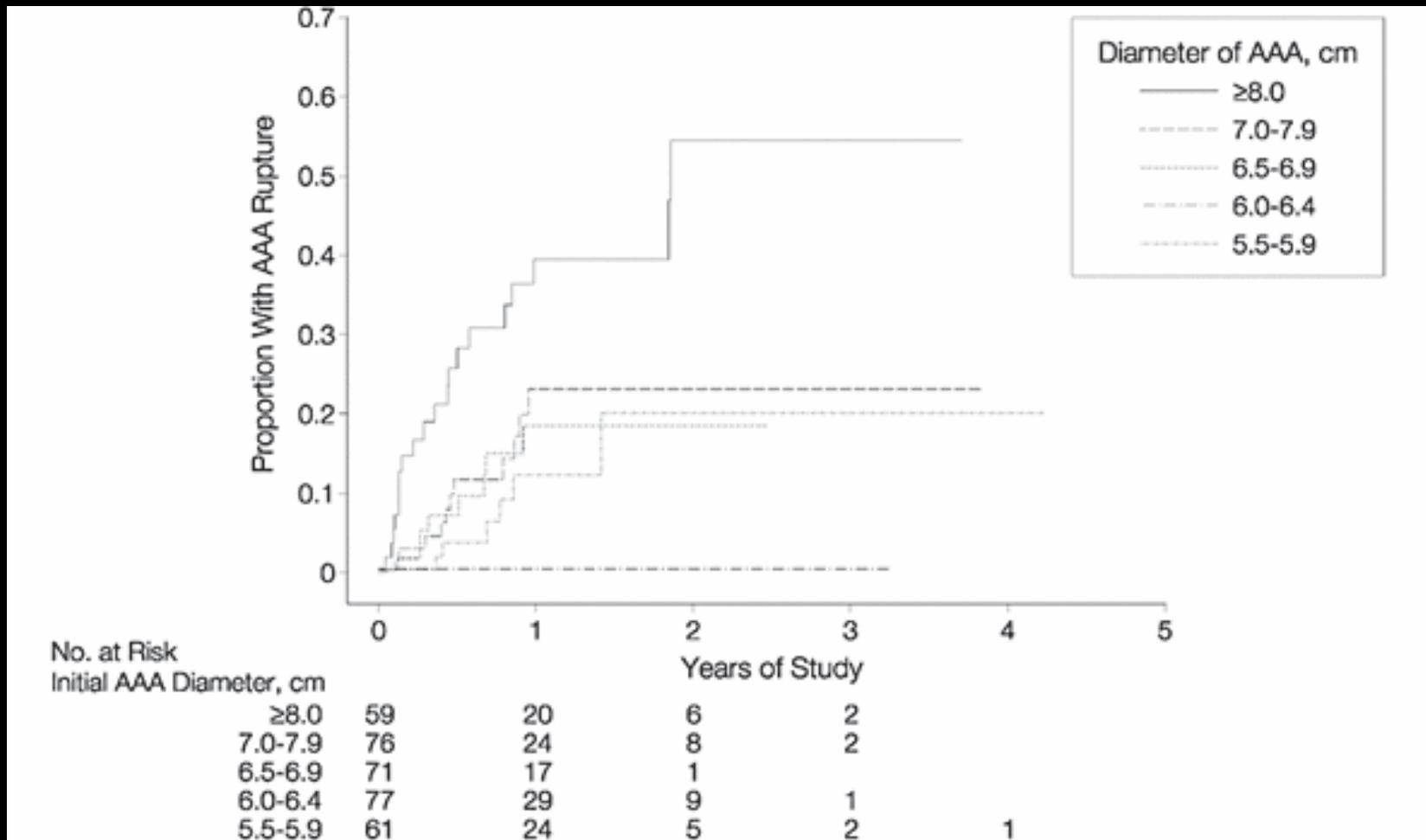
- Background:
 - Among patients with abdominal aortic aneurysm (AAA) who have high operative risk, repair is usually deferred until the AAA reaches a diameter at which rupture risk is thought to outweigh operative risk
 - Few data exist on rupture risk of large AAA
- Objective:
 - To determine the incidence of rupture in patients with large AAA

Rupture rate of large abdominal aortic aneurysms in patients refusing or unfit for elective repair

- Method and Outcomes

- Prospective cohort study in 47 Veterans Affairs medical centers
- Veterans (n = 198) with AAA of at least 5.5 cm for whom elective AAA repair was not planned because of medical contraindication or patient refusal
- Incidence of AAA rupture by strata of initial and attained diameter

Cumulative Incidence of Probable Rupture by Attained AAA Diameter



Lederle, F. A. et al. JAMA 2002;287:2968-2972.

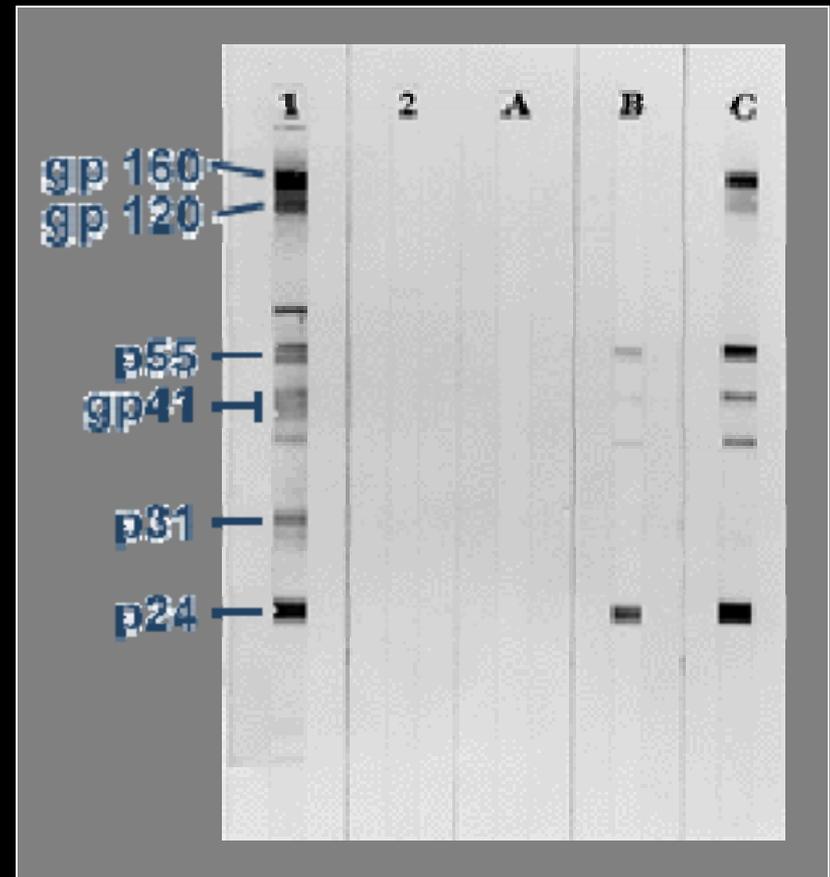
Rupture rate of large abdominal aortic aneurysms in patients refusing or unfit for elective repair

- Conclusion

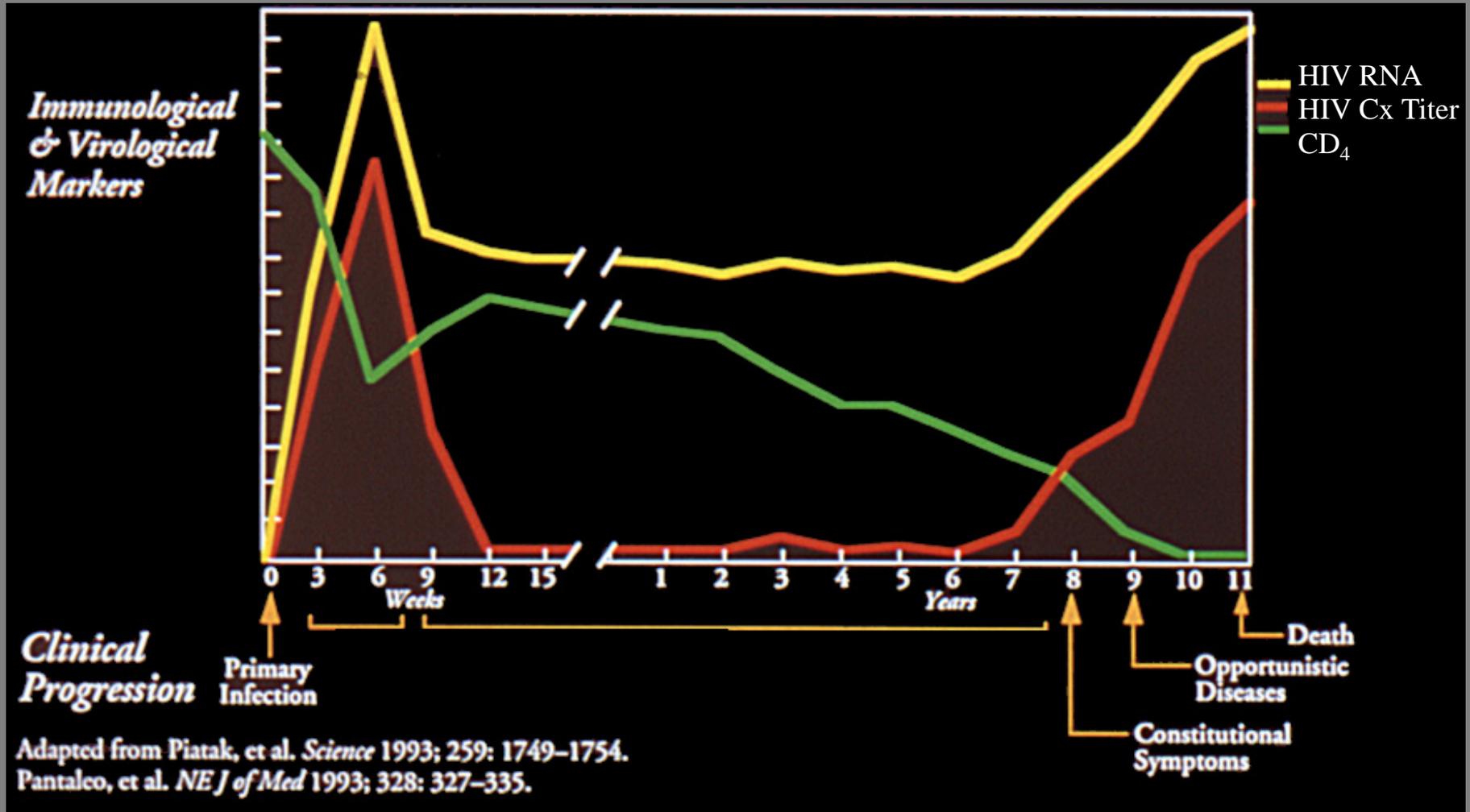
- The rupture rate is substantial in high-operative-risk patients with AAA of at least 5.5 cm in diameter and increases with larger diameter

Case 2

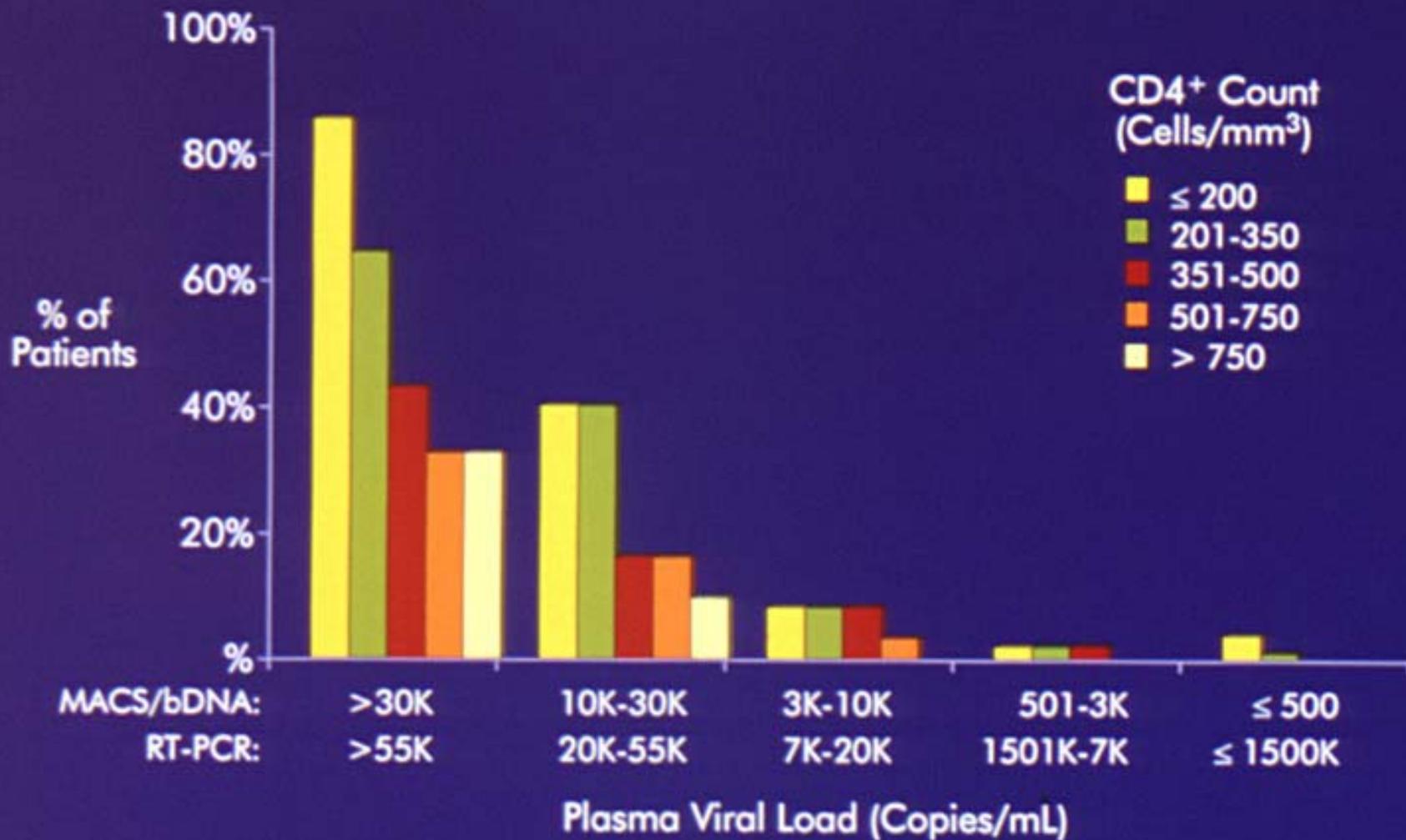
- 23 year old woman, IVDA
- Admitted to the hospital for bacterial pneumonia.
- Diagnosed with HIV
- What is her prognosis?
- When should HIV therapy be started?



Time Course of HIV Infection: Immunological and Virological Markers



Likelihood of Developing AIDS Within 3 Years

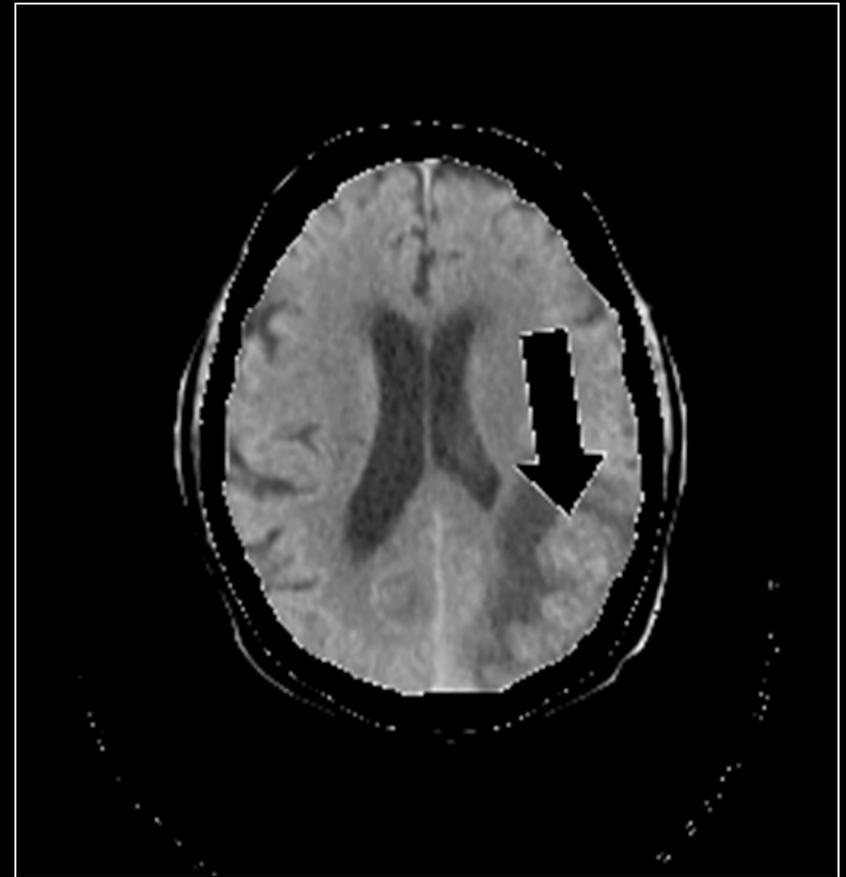


When To Start Treatment? – Summary of Current Guidelines

Guidelines	symptoms or CD4 <200	CD4 200- 350	CD4 >350
DHHS: 7/14/03 update < www.aidsinfo.nih.gov >	treat	offer treatment	defer if VL <55K; treat or defer if VL >55K
IAS-USA: JAMA 2002	treat	consider treatment	consider if VL >50-100K

Case 3

- 87 year old caucasian man
- HTN
- Recently admitted for an ischemic stroke
- Will the addition of lipid lowering therapy affect prognosis?

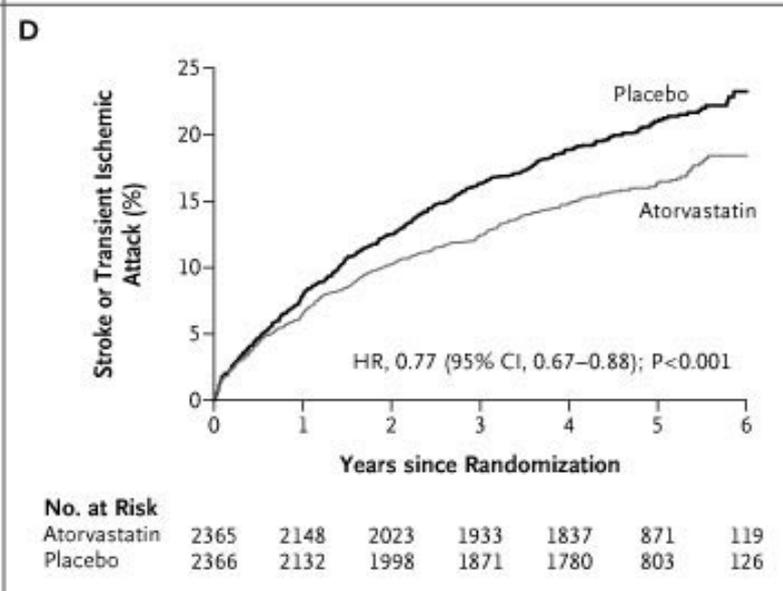
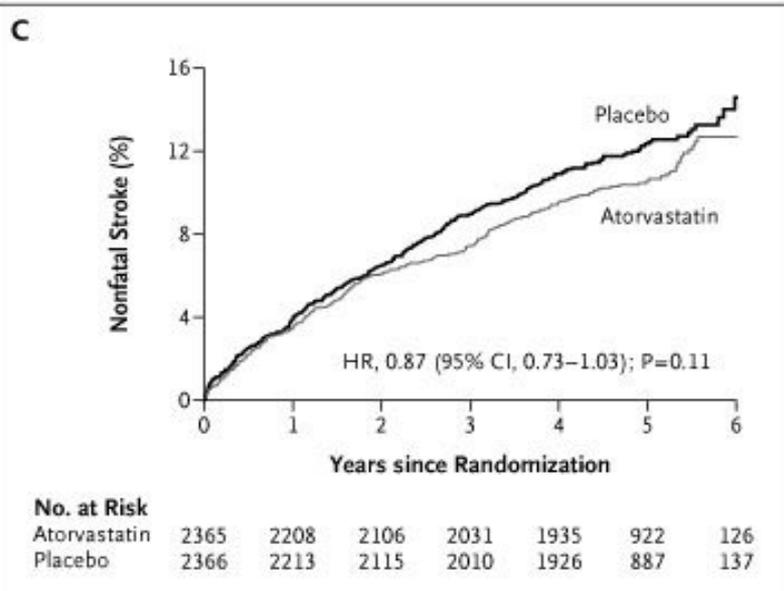
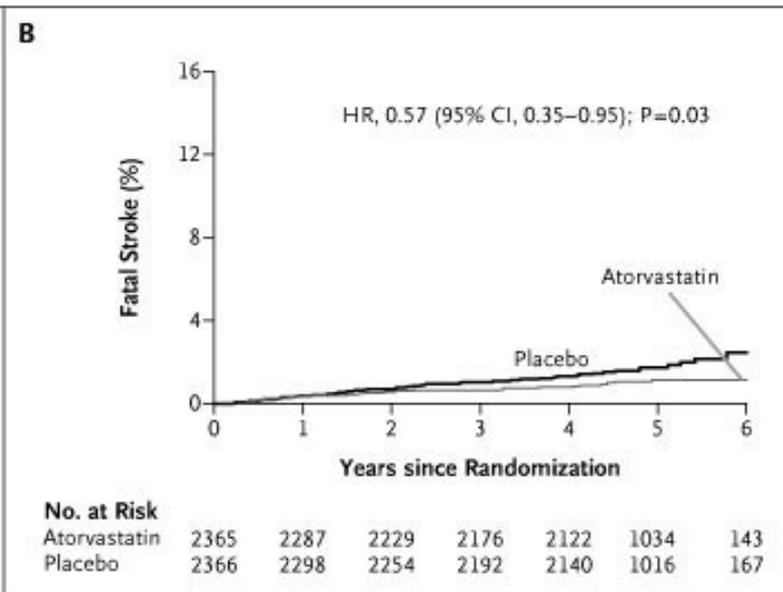
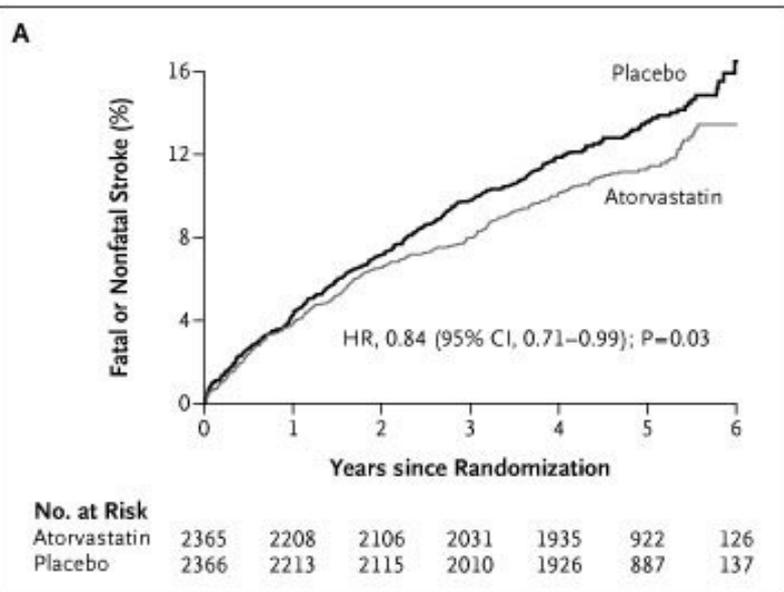


High-Dose Atorvastatin after Stroke or Transient Ischemic Attack

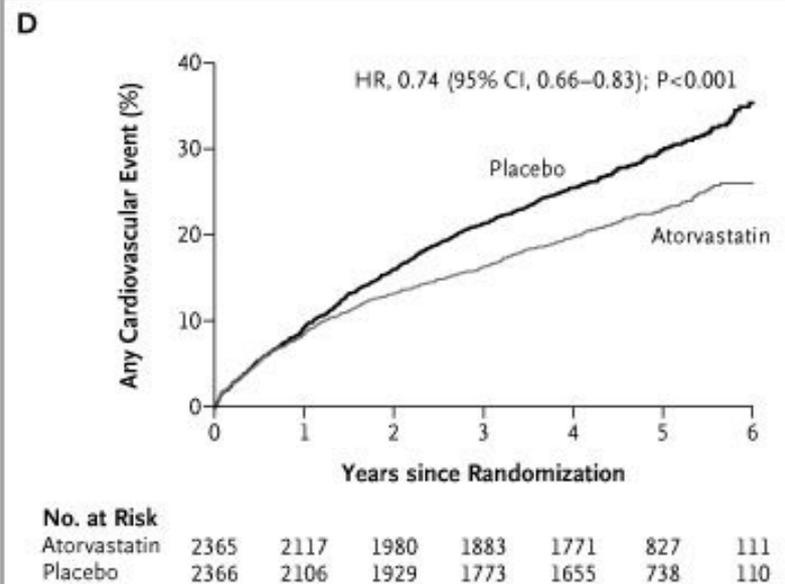
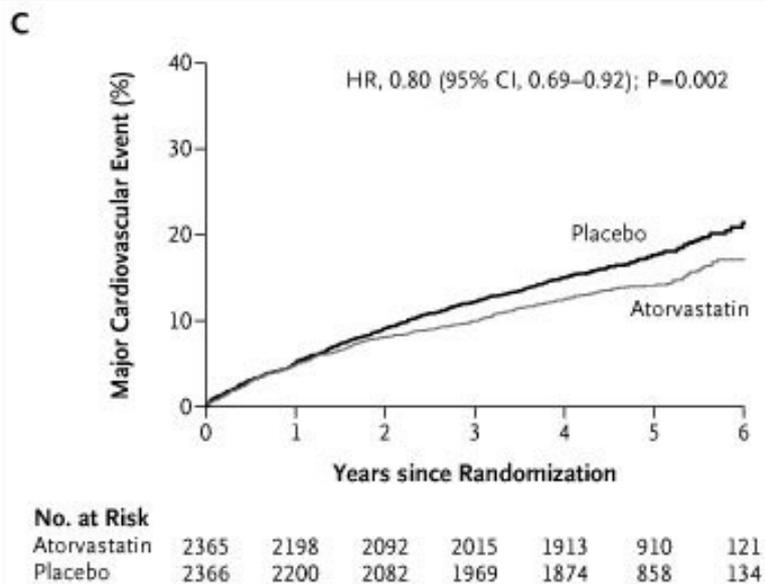
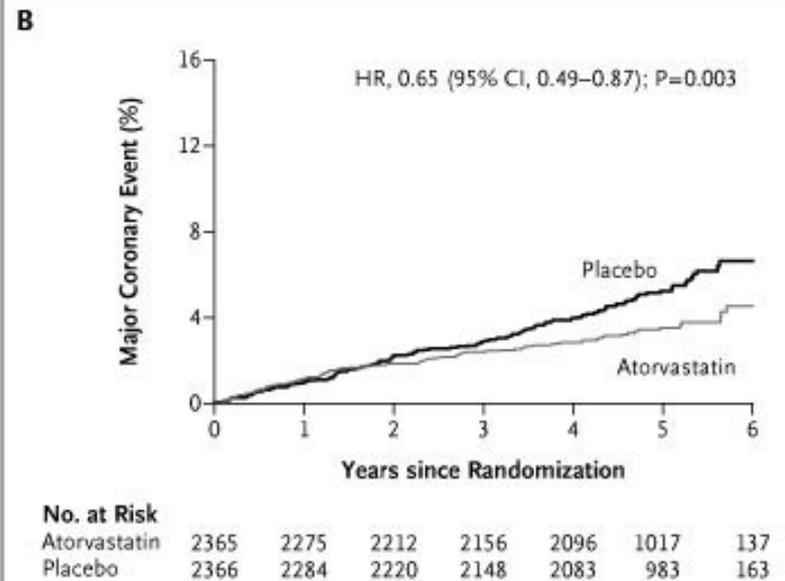
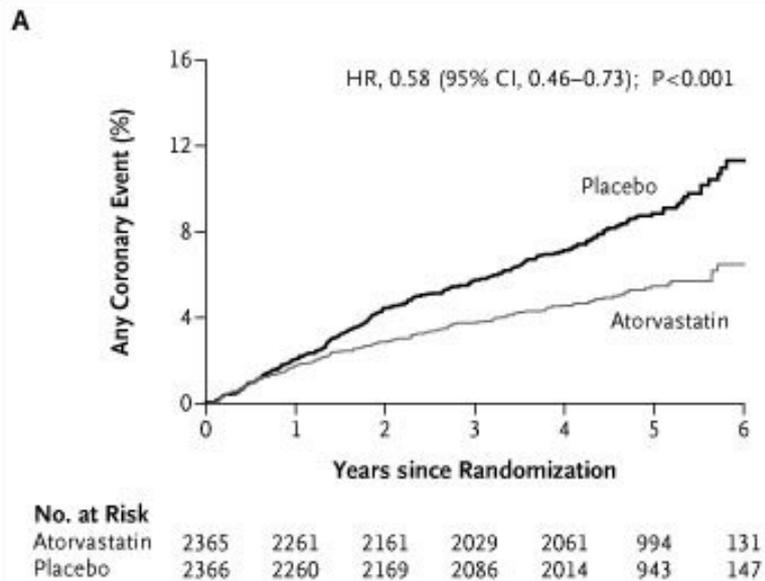
- Statins reduce the incidence of strokes among patients at increased risk for cardiovascular disease
- Whether they reduce the risk of stroke after a recent stroke or transient ischemic attack (TIA) remains unknown

High-Dose Atorvastatin after Stroke or Transient Ischemic Attack

- Method
 - 4731 patients with prior stroke or TIA within one to six months before study entry and no known coronary heart disease
 - Randomly assigned to double-blind treatment with 80 mg of atorvastatin per day or placebo.
 - Primary end point- first nonfatal or fatal stroke



Stroke or TIA



Cardiovascular Events

High-Dose Atorvastatin after Stroke or Transient Ischemic Attack

- Conclusion

- In patients with recent stroke or TIA and without known coronary heart disease, 80 mg of atorvastatin per day reduced the overall incidence of strokes and of cardiovascular events

Clinical Prediction Rules

- Prediction rules estimate the probability of outcomes according to a set of patient characteristics
 - Outcomes include
 - Morbidity, mortality, adverse events etc

Clinical Prediction Rules

- **Clinical prediction rule** is type of medical research study in which researchers try to identify the best combination of medical sign, symptoms, and other findings in predicting the probability of a specific disease or outcome

Clinical Prediction Rules

- Investigators identify a consecutive group of patients who are suspected of having a specific disease or outcome
- Data collected on signs, symptoms, laboratory values etc
- Logistic regression/multivariate analysis used to develop prediction rule on a cohort retrospectively
- Prediction rule is then validated prospectively
- Prediction rules are meant to assist in clinical decision making

Predicting Mortality Among Patients Hospitalized for Heart Failure

- A predictive model of mortality in heart failure may be useful for clinicians to improve communication with and care of hospitalized patients
- Objective:
 - To identify predictors of mortality and to develop and validate a model using information available at hospital presentation

Predicting Mortality Among Patients Hospitalized for Heart Failure

- Retrospective study of 4031 community-based patients presenting with heart failure at multiple hospitals in Ontario, Canada
 - 2624 patients in the derivation cohort from 1999-2001
 - 1407 patients in the validation cohort from 1997-1999

Clinical Prediction Rules

Table 4. Heart Failure Risk Scoring System*

Variable	No. of Points	
	30-Day Score†	1-Year Score‡
Age, y	+Age (in years)	+Age (in years)
Respiratory rate, min (minimal 20; maximum 45)§	+Rate (in breaths/min)	+Rate (in breaths/min)
Systolic blood pressure, mm Hg		
≥180	-60	-50
160-179	-55	-45
140-159	-50	-40
120-139	-45	-35
100-119	-40	-30
90-99	-35	-25
<90	-30	-20
Urea nitrogen (maximum, 60 mg/dL)§¶	+Level (in mg/dL)	+Level (in mg/dL)
Sodium concentration <136 mEq/L	+10	+10
Cerebrovascular disease	+10	+10
Dementia	+20	+15
Chronic obstructive pulmonary disease	+10	+10
Hepatic cirrhosis	+25	+35
Cancer	+15	+15
Hemoglobin <10.0 g/dL (<100 g/L)	NA	+10

Abbreviation: NA, not applicable to 30-day model.

*An electronic version of the risk scoring system is available at: <http://www.ccort.ca/CHFriskmodel.asp>.

†Calculated as age + respiratory rate + systolic blood pressure + urea nitrogen + sodium points + cerebrovascular disease points + dementia points + chronic obstructive pulmonary disease points + hepatic cirrhosis points + cancer points.

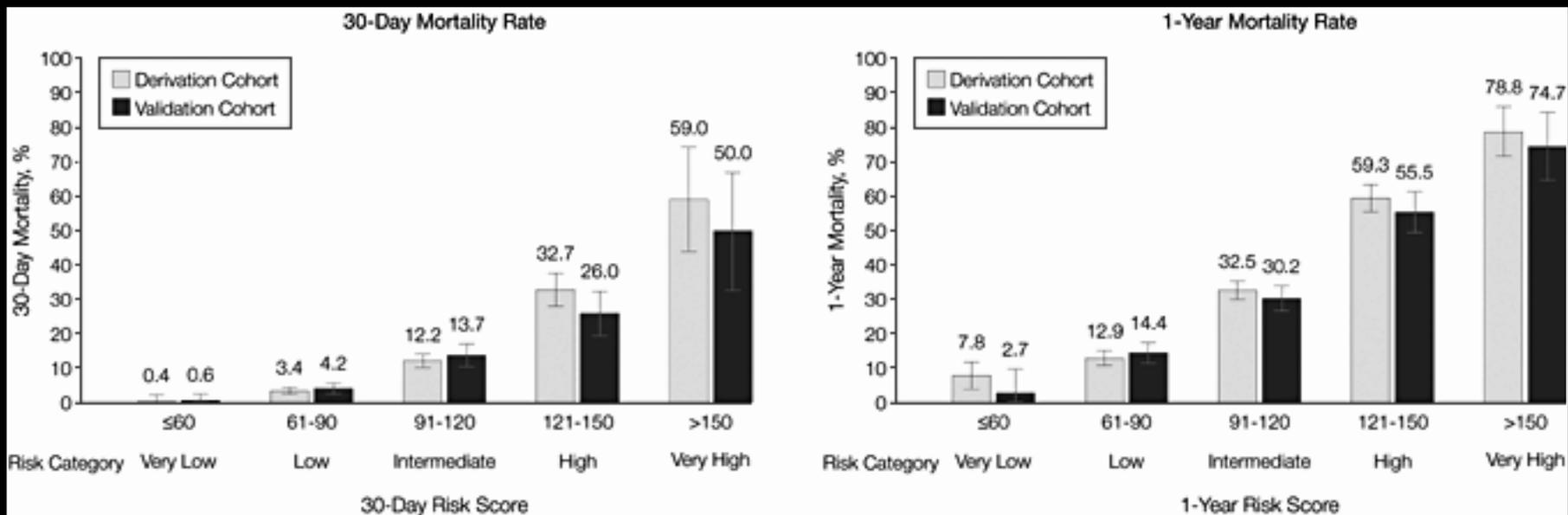
‡Calculated as age + respiratory rate + systolic blood pressure + urea nitrogen + sodium points + cerebrovascular disease points + dementia points + chronic obstructive pulmonary disease points + hepatic cirrhosis points + cancer points + hemoglobin points.

§Values higher than maximum or lower than minimum are assigned the listed maximum or minimum values.

||Increases were protective in both mortality models. Points are subtracted for higher blood pressure measurements.

¶Maximum value is equivalent to 21 mmol/L. Score calculated using value in mg/dL.

Clinical Prediction Rules



A Prediction Rule to Identify Low-Risk Patients with Community-Acquired Pneumonia

- There is considerable variability in rates of hospitalization of patients with community-acquired pneumonia, in part because of physicians' uncertainty in assessing the severity of illness at presentation
- Purpose
 - to develop a prediction rule for prognosis that would accurately identify patients with community-acquired pneumonia who are at low risk of dying within 30 days of presentation

A Prediction Rule to Identify Low-Risk Patients with Community-Acquired Pneumonia

- Data collected on 14,199 adult inpatients with community-acquired pneumonia
- A prediction rule was derived that stratified patients into five classes with respect to the risk of death within 30 days
- The rule was validated with 1991 data on 38,039 inpatients

Pneumonia Severity Index

Characteristic	Points assigned
Demographic factor	
Age	
Men	Age (yrs)
Women	Age (yrs) – 10
Nursing-home resident	+10
Co-existing 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 breaths/min	+20
Systolic blood pressure < 90 mm Hg	+20
Temperature < 35°C (95°F) or $\geq 40^\circ\text{C}$ (104°F)	+15
Pulse ≥ 125 beats/min	+10
Laboratory and radiographic findings (if study performed)	
Arterial blood pH < 7.35	+30
Blood urea nitrogen level ≥ 30 mg/dL	+20
Sodium level < 130 mmol/L	+20
Glucose level ≥ 250 mg/dL	+10
Hematocrit < 30%	+10
Partial pressure of arterial O ₂ < 60 mm Hg or O ₂ Sat < 90%	+10
Pleural effusion	+10

Pneumonia Severity Index

Class	Points	Mortality*
I	<51	0.1%
II	51-70	0.6%
III	71-90	0.9%
IV	91-130	9.5%
V	>130	26.7%

* From the PORT study validation cohort

Reference: Fine MJ, et. al. A prediction rule to identify low-risk patients with community acquired pneumonia *NEJM* 1997; 336: 243)

Prediction rule accurately identified the patients with community-acquired pneumonia at low risk for death and other adverse outcomes

The prediction rule may help physicians make more rational decisions about hospitalization for patients with pneumonia

Conclusion

- Doctors' prognostic estimates are a central element of both patient and physician decision making
- Doctors are inaccurate in their prognoses, especially if they rely on intuition and not evidence based practice
- Studies of prognosis are important for accurate decision making
- Prognostic factors can be different than risk factors

Conclusion

- Prognostic (cohort studies) should be:
 - Population based
 - A representative sample of people afflicted with a disease
 - Of similar time onset of disease or symptoms

Conclusion

- Important analyses of prognosis include:
 - Clinical prediction rules
- Important prognostic outcomes of interest include
 - Death
 - Disease
 - Discomfort
 - Disability
 - Dissatisfaction

The End