Regression and Clinical prediction models

Session 1
Introduction and General considerations

Pedro E A A do Brasil
pedro.brasil@fiocruz.br
2023

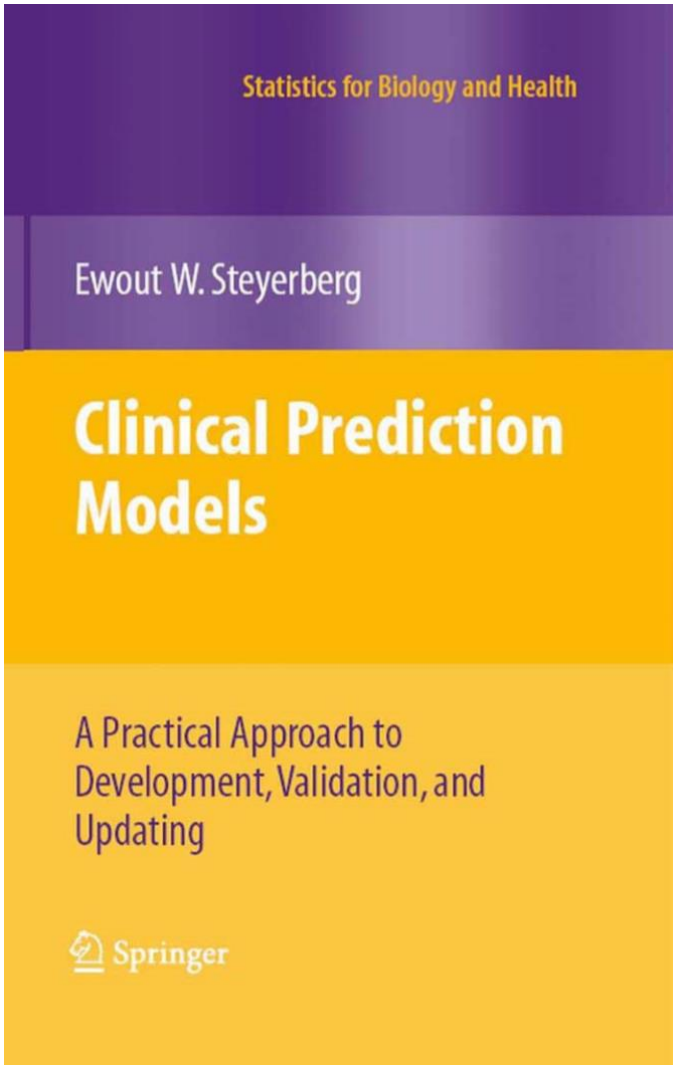
Course objectives

- The course is intended to introduce to MD and PhD students to practices and rationales of research where the aims are to plan, develop and validate tools for either clinical prediction aid or clinical decision aid.
- It is not expected that the audience have any previous knowledge about CPM.
- All examples will be from health research and students must have previous knowledge of statistics, clinical epidemiology and some familiarity with R-projects software.

Session objective

- In this session, some literature will be commented, and basic concepts involved in CPM research will be commented briefly. At the end, the students must be aware that additional reading may be required for their own study object, and know where to find them.

Main book

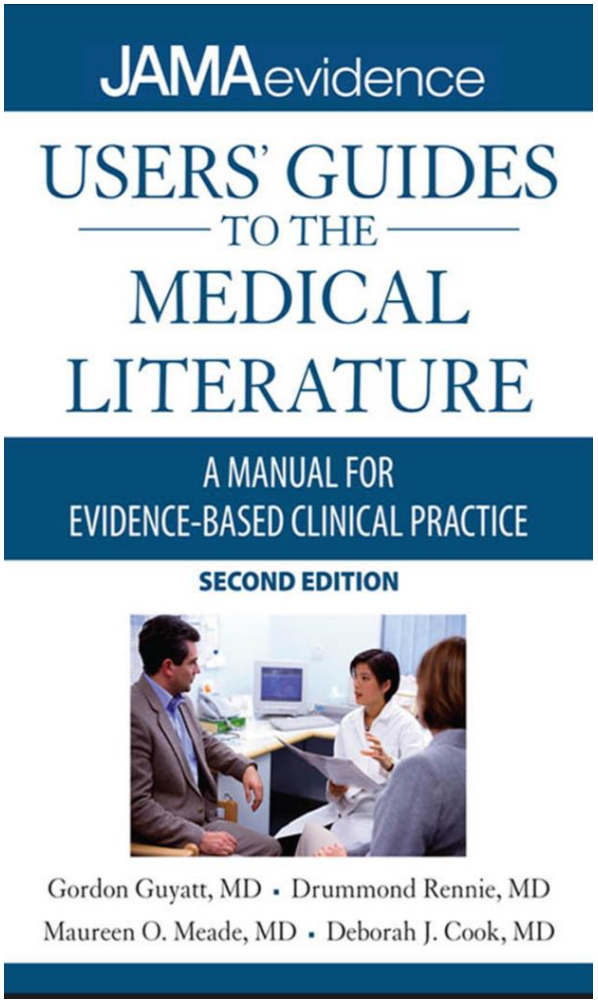


- 90% or more of the course is in this book.
- Good for the non initiated as it has exercises and in several parts it has a step-by-step guide.
- Good for the more experienced as it has R codes and outputs with examples and case studies
- Website with additional stuff, to reproduce case studies and tables or graphs in the book.

Additional book

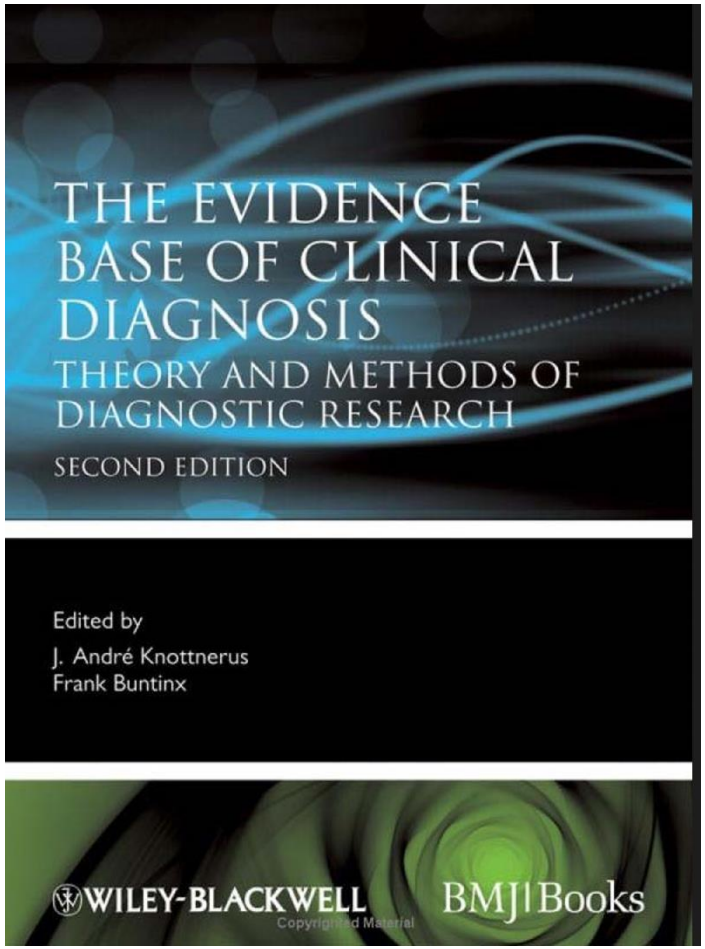
- For statistics readers. Lots of formulas, proofs and examples.
- Slowly progress through several issues of regressions analysis.
- Good for the non initiated as it has exercises and in several parts it has a step-by-step guide.
- Good for the more experienced as it has R codes and outputs with examples and case studies
- Website with additional stuff, to reproduce case studies and tables or graphs in the book.

Additional books



- A chapter dedicated to concepts and use of CPM in clinical practice.
- This is a very good reading for the non initiated
- The intended audience is health professionals that need to make decision on daily basis.
- It has examples on how to improve decisions with CPM.

Additional books



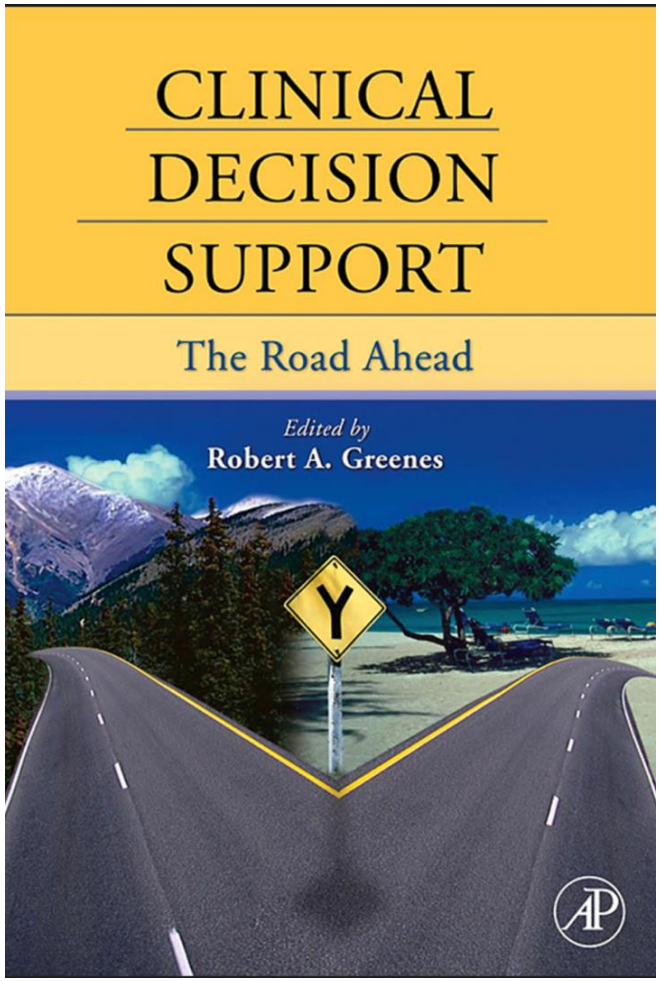
- A chapter dedicated to concepts, conducting and interpreting CPM.
- The mentioned chapter is an advanced topic of the book and concepts discussed in early chapters may be required.
- This is mainly dedicated to plan studies regarding diagnostic tests in helath.

Additional books

- **Ebell MH. Evidence-Based Diagnosis: A Handbook of Clinical Prediction Rules. 1º ed. Springer; 2001**

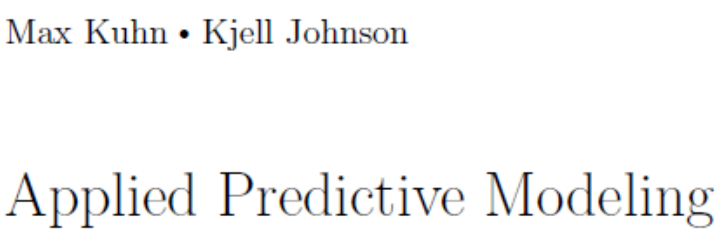
- A collection of several clinical prediction rules, teaching how to use them with comments and notes.
- Very nice for physicians who use CPM daily.
- It is more than 15 years old and it seems it has not been updated.

Additional books



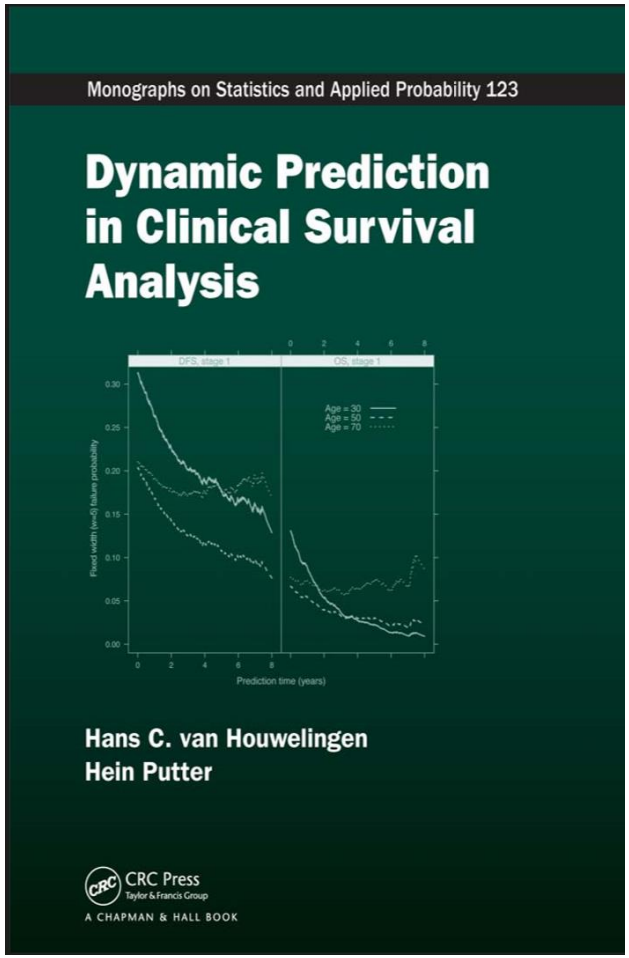
- It is strongly directed to unite several knowledges and practices through the use of electronic medical records from a variety of points of view.
- Prediction modeling is a chapter among several other topics related to decision support.

Additional books



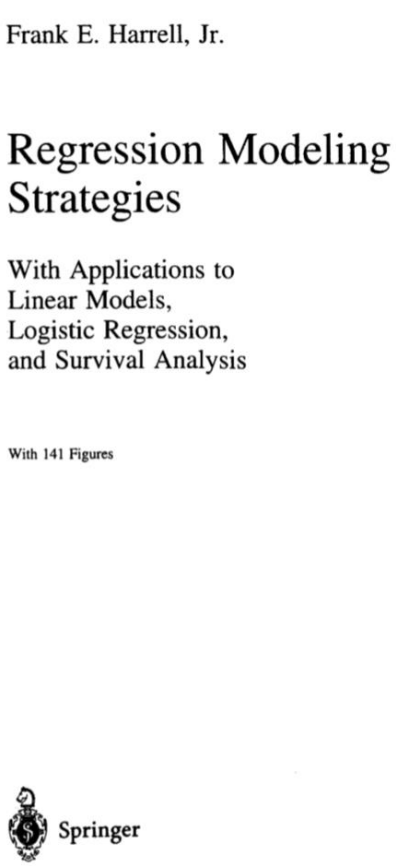
- Dedicated to hands-on data pilots.
- It has lots of examples with big data.
- It has several software codes. It recommends several websites as sources of examples. There is an R package with data to follow examples.

Additional books



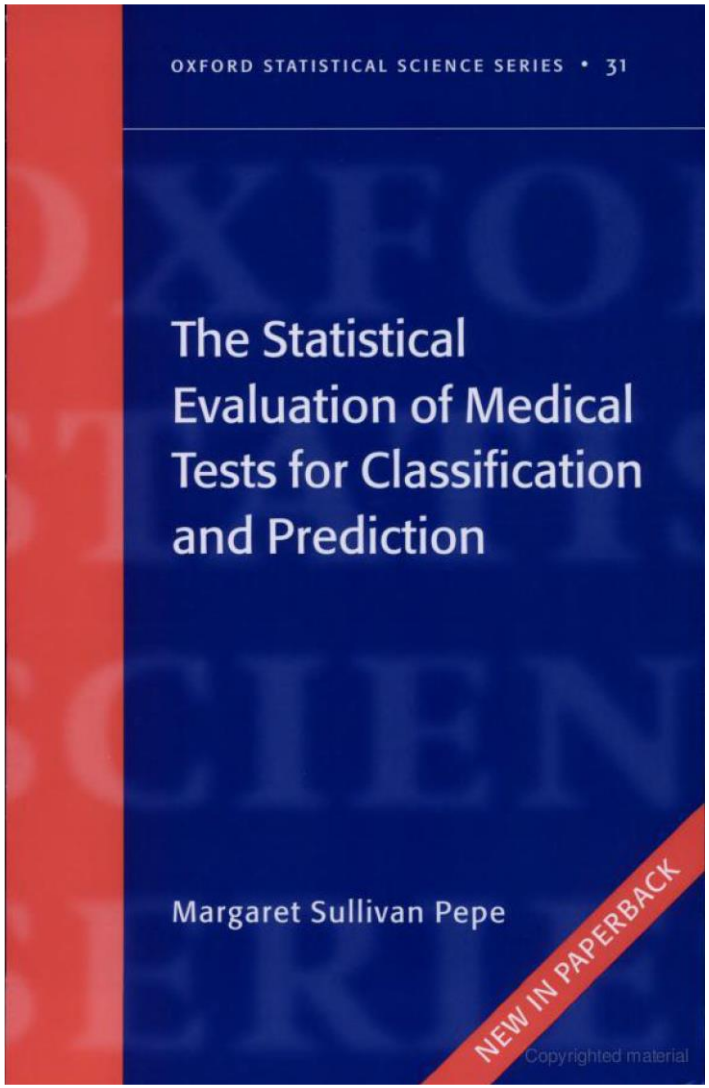
- Dedicated to statistical readers.
- It concerns only survival modeling, from simple to complex extensions.
- It has several formulas and codes. In its website it is possible to download the data and software to follow examples.

Additional books



- Dedicated to statistical readers.
- It requires strong statistics knowledge mainly related to regression.
- It presents current concepts of prediction modeling with logistic, survival and linear models.
- Its author has a website with many good stuff related to prediction modeling, and a R package devoted to this book.

Additional books



- It is dedicated to statistical readers.
- Have several case studies and examples of clinical problems
- Mainly dedicated to diagnostic test performance data analysis
- Does not have any example with software use neither a website with datasets nor software codes.

How this course works?

- The students must watch the videos exposing contents and the examples of data analysis.
- The scripts and data to reproduce these examples are provided at the website.
- There is a “real” dataset not used for examples that the students should use and exercise the steps of data analysis. The quizzes will be about the analysis of this data.

How this course works?

- The quizzes will be at the moodle platform and with several questions related to each chunk.
- To answer the questions, the students must check the “real” dataset analysis output.
- The classroom sessions are intended to discuss difficulties and to help on data analysis.

Concepts

- What is a prediction model?
  - CPRs attempt to increase the accuracy of clinicians' diagnostic and prognostic assessments. We define a CPR as a clinical tool that quantifies the individual contributions that various components of the medical history, physical examination, and basic laboratory results make toward the diagnosis, prognosis, or likely response to treatment in an *individual patient*. This definition is equally applicable to what have been called "**clinical prediction guides**" and "**clinical decision rules**."

Guyatt. Users' Guides to the Medical Literature: Essentials of Evidence-Based Clinical Practice, 2º ed. 2008.

Concepts

- What is a prediction model?
  - Clinical prediction models may provide the evidence-based input for shared decision-making, by providing estimates of the individual probabilities of risks and benefits. Clinical prediction models are also referred to as clinical prediction rules, prognostic models, or nomograms. Clinical prediction models combine a number of characteristics to predict a diagnostic or prognostic outcome. Typically, a limited number of predictors is considered.

Steyerberg EW. Clinical Prediction Models: A Practical Approach to Development, Validation, and Updating. 2008.

Concepts

- What is a prediction model?
  - Clinical prediction rules (CPRs) are tools that quantify the contribution of symptoms, clinical signs and available diagnostic tests, and in doing so stratify patients according to the probability of having a target disorder.

Knottnerus & Buntinx .*The Evidence Base of Clinical Diagnosis: Theory and methods of diagnostic research, 2nd Ed* 2009

Concepts

- Decision vs Prediction
  - "Clinical prediction" rules / models / guides have been used interchangeably with "Clinical decision" rules / models / guides
  - Predictions
    - Assigns probabilities of the outcome based on a model with certain information with a known amount of error.
  - Decisions
    - Alongside with prediction, there is a need to set or estimate decision limits/thresholds, where the appropriate course of action changes leading to recommendations based on the model.
    - Clinical decision models are also "Decision support tools"

Possible synonyms

- Clinical
- Prognostic
- Diagnostic

- Prediction
- Decision

- Model
- Rule
- Guide
- Tool

- Decision support tool
- Nomograms [MeSH]
- Decision Support Techniques [MeSH]
- Decision Support Systems, Clinical [MeSH]

Examples

- Breast cancer prognosis:
  - https://breast.predict.nhs.uk/tool

- Infectious diseases
  - https://pedrobrasil.shinyapps.io/INDWELL/

Concepts

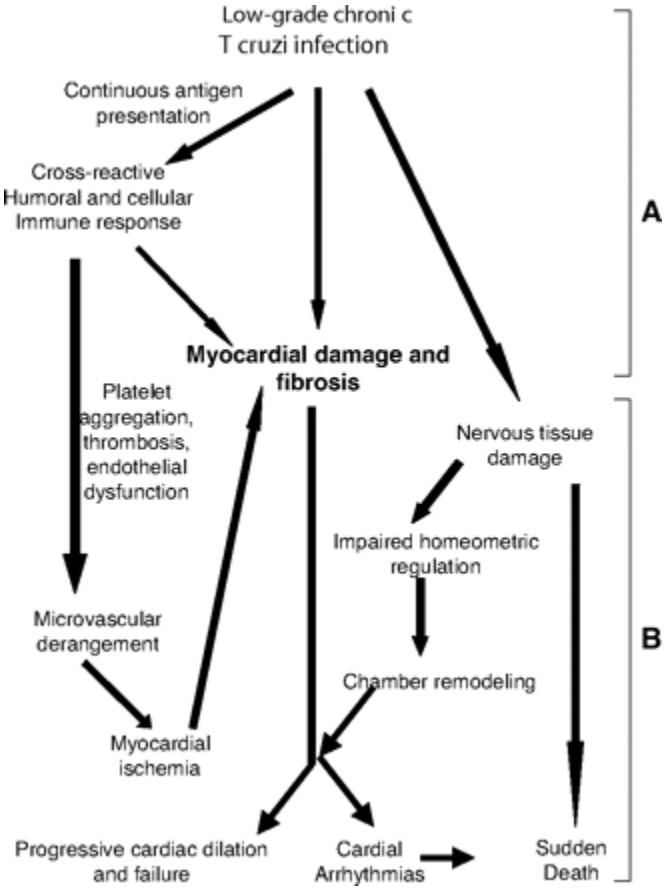
- Causality vs Prediction
  - Prediction is primarily an estimation problem. For example:
    - What is the risk of dying for this patient within 30 days after an acute myocardial infarction?
  - Prediction is also about testing of hypotheses. For example:
    - Is age a predictor of 30-day mortality after an acute myocardial infarction? predictor variables?

Concepts

- Causality vs Prediction
  - Hypothesis testing comes close to etiologic research, where biases such as confounding are among the major concerns of epidemiologists .
  - Statistical models may serve to address both estimation and hypothesis testing questions.

Causality model: example

Schematic view of main pathogenic mechanisms in chronic Chagas cardiomyopathy.



Marin-Neto. P**athogenesis of Chronic Chagas Heart Disease**
Circulation. 2007; 115: 1109-1123

- In causality, one defines or tests a predefined hypothetical model.
- The main interest is to find how causes / determinants relate to each other, to time and to the outcome.
- The independent effect of one cause is usually the aim.

Prediction model: example

- [1 point] age ≥60 years
- [1] blood pressure ≥140/90 mm Hg
- [1] unilateral weakness
- [1] speech impairment without weakness
- [2] duration ≥60 min
- [1] duration 10–59 min
- [1] diabetes

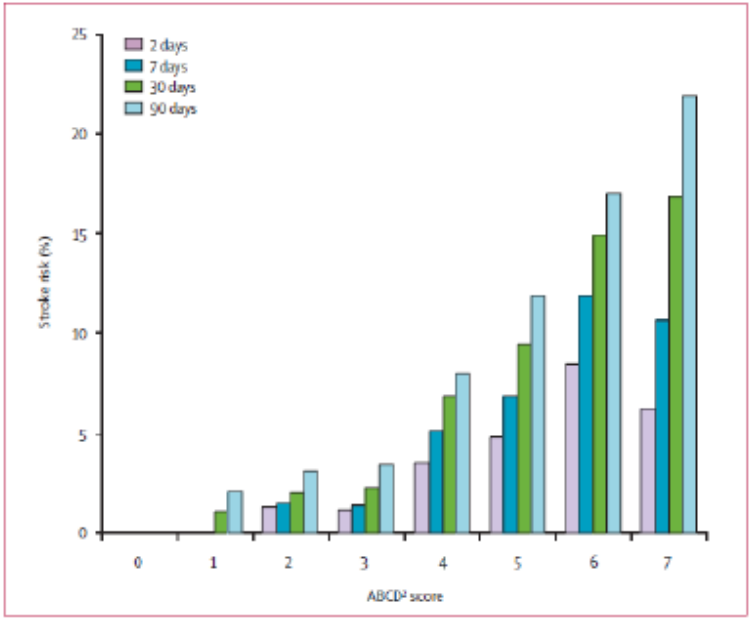


Figure: Short-term risk of stroke by ABCD² score in six groups combined (n=4799)

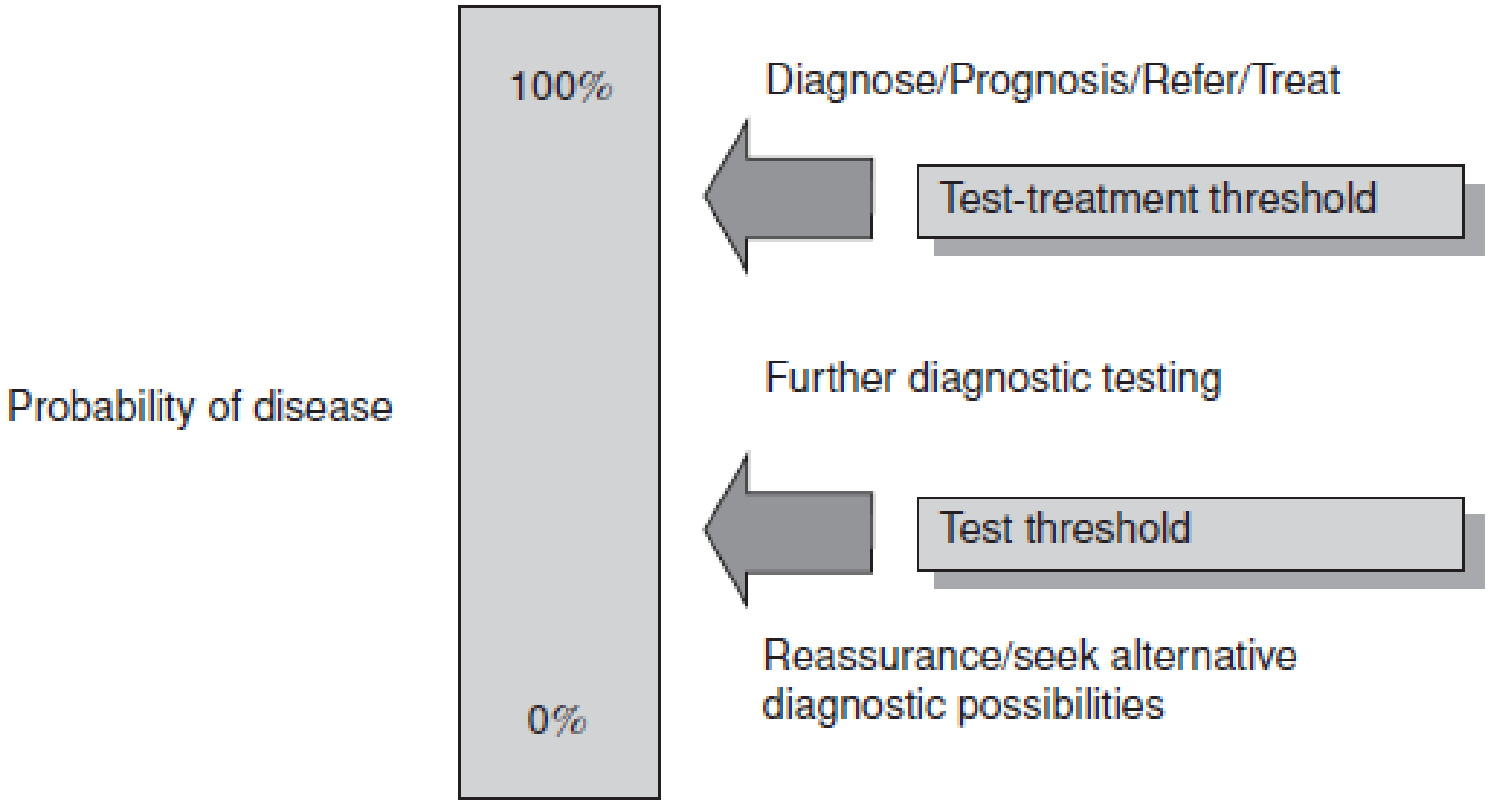
Johnston. Validation and refinement of scores to predict very early stroke risk after transient ischaemic attack. Lancet 2007; 369:283-92

- In prediction, one may not have a predefined model.
- The main interest is to increase accuracy of risk prediction and ultimately to recommend the most appropriate course of action.
- The predictors may not be part of the causality model.

Concepts

- Diagnostic & Prognostic & Treatment
  - The “prediction” may cause some confusion as many will intuitively understand that prediction is a sort of guess of something in the future, and may be applied only to prognosis.
  - The diagnostic prediction is the very same rationale to something ongoing that we are unable to apply a “gold standard” test to check the truth. Some stated that diagnostic prediction models are helpful to set priors, and decide whether further testing is required.
  - Prediction models may apply equally to diagnosis, prognosis, or treatment outcome.

Diagnostic probabilistic reasoning



Knottnerus & Buntinx .*The Evidence Base of Clinical Diagnosis: Theory and methods of diagnostic research, 2nd Ed* 2009
Pauker. The threshold approach to clinical decision making. The New England Journal of Medicine. 1980. 302:20;1109

Treatment probabilistic reasoning

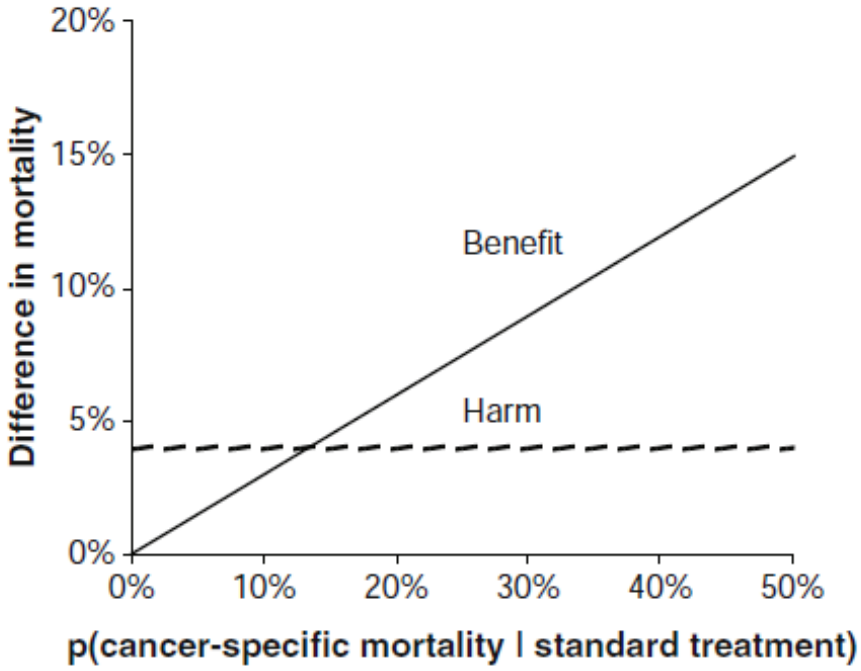


Fig. 2.3 Graphical illustration of weighing benefit and harm of treatment. Benefit of treatment (reduction in absolute risk) increases with cancer-specific mortality (relative risk set to 0.7). Harm of treatment (excess absolute risk, e.g. due to toxicity of treatment) is assumed to be constant at 4%. Net benefit occurs only when the cancer-specific mortality given standard treatment is above the threshold of 11%[451]

Steyerbeg. Clinical Prediction Models: A Practical Approach to Development, Validation, and Updating. Springer in 2009.

Applications of CPM

Table 2.1 Some areas of application of clinical prediction models

Application area	Example in this chapter
Public health	
Targeting of preventive interventions	
Incidence of disease	Models for (hereditary) breast cancer
Clinical practice	
Diagnostic work-up	
Test ordering	Probability of renal artery stenosis
Starting treatment	Probability of deep venous thrombosis
Therapeutic decision-making	
Surgical decision making	Replacement of risky heart valves
Intensity of treatment	More intensive chemotherapy in cancer patients
Delaying treatment	Spontaneous pregnancy chances
Research	
Inclusion in an RCT	Traumatic brain injury
Covariate adjustment in an RCT	Primary analysis of GUSTO-III
Confounder adjustment with a propensity score	Statin effects on mortality
Case-mix adjustment	Provider profiling

Steyerbeg. Clinical Prediction Models: A Practical Approach to Development, Validation, and Updating. Springer in 2009.

Concluding

- There are many types of use for prediction tools, more types of application can probably be thought of.
- Obtaining predictions from a model has to be separated from obtaining insights in the disease mechanisms and patho-physiological processes.
- Such insights are related to the estimated effects of predictors in a model. Often, prediction models serve the latter purpose too.

fim

Session 1
Introduction and General considerations

Pedro E A A do Brasil
pedro.brasil@ini.fiocruz.br
2015