UMC Utrecht

# Prediction modelling: Where are we now and where do we need to go?


## Karel GM Moons

UMC Utrecht

Julius Center for Health Sciences and Primary Care/
Dutch Cochrane Center

www.juliuscenter.nl


University Medical Center Utrecht

**Experiences from various consortia and series of papers:**

- BMJ 2009 – series on prognostic modelling
- Plos Med + BMJ 2013 -- PROGRESS series
- HEART 2012 2 papers
- TRIPOD reporting guideline

*Ladies and Gentlemen, Choose Your Models*

Models are fine and statistics are dandy
But don't choose too quickly just cause they're handy
Stick to a model that's been through the mill
Don't try something new just for the thrill
A new shiny model is full of allure
But making it work is no sinecure.

The more complex the merrier does not follow
The voluminous output may be hard to swallow
Too many variables and too few cases
Is too much like duelling at ten paces

What's fit may be error rather than trend
And shrinkage will get you in the end.

Know what you're doing and do it well
Replictable findings are easy to sell
Be willing to progress one step at a time
A counterfeit dollar's worth less than a dime
Now that I've warned you I'm ready to stop
And let you get back to tending the shop.

PERSONNEL PSYCHOLOGY
1975, 28, 1–18.

# UNDERPREDICTION FROM OVERFITTING: 45 YEARS OF SHRINKAGE[1]

ROBERT J. WHERRY, SR.

# Prediction

- Prediction = foreseeing / foretelling

  … (the probability) of something that is yet unknown

- In medicine:

  1. Probability of a future event/outcome = **prognosis**

  2. Probability of the result of a more invasive/costly reference (gold) standard that is not yet done = **diagnosis**

# What is a prediction model?

Any combination >= 2 predictors/variables/covariates/ determinants → which convert observed values to an absolute probability…

- … of having a particular disease/disorder → **diagnosis**
- … of developing particular event/outcome within a certain time (hours, days, weeks, years)→ **prognosis**
  - Not necessarily patients –- subjects at risk of developing outcome

# Prediction is done with predictors...

- **= variables measured in subject→ obtained from:**
  - Patient history
  - Physical examination
  - Imaging tests
  - Elektrofysiology (ECG, EEG)
  - Blood/urine markers
  - Omics markers
  - Disease characteristics
  - Undergone therapies

# Practice

- **Hardly any diagnosis/prognosis based on single variable (test/marker)**
  - doctors measure many variables → combine them→ estimate diagnostic + prognostic probabilities

- **Desired knowledge/evidence for professionals:**
  - Does new test/marker has added value to what already know from my patient?
    - Combination of test results = multivariable prediction models

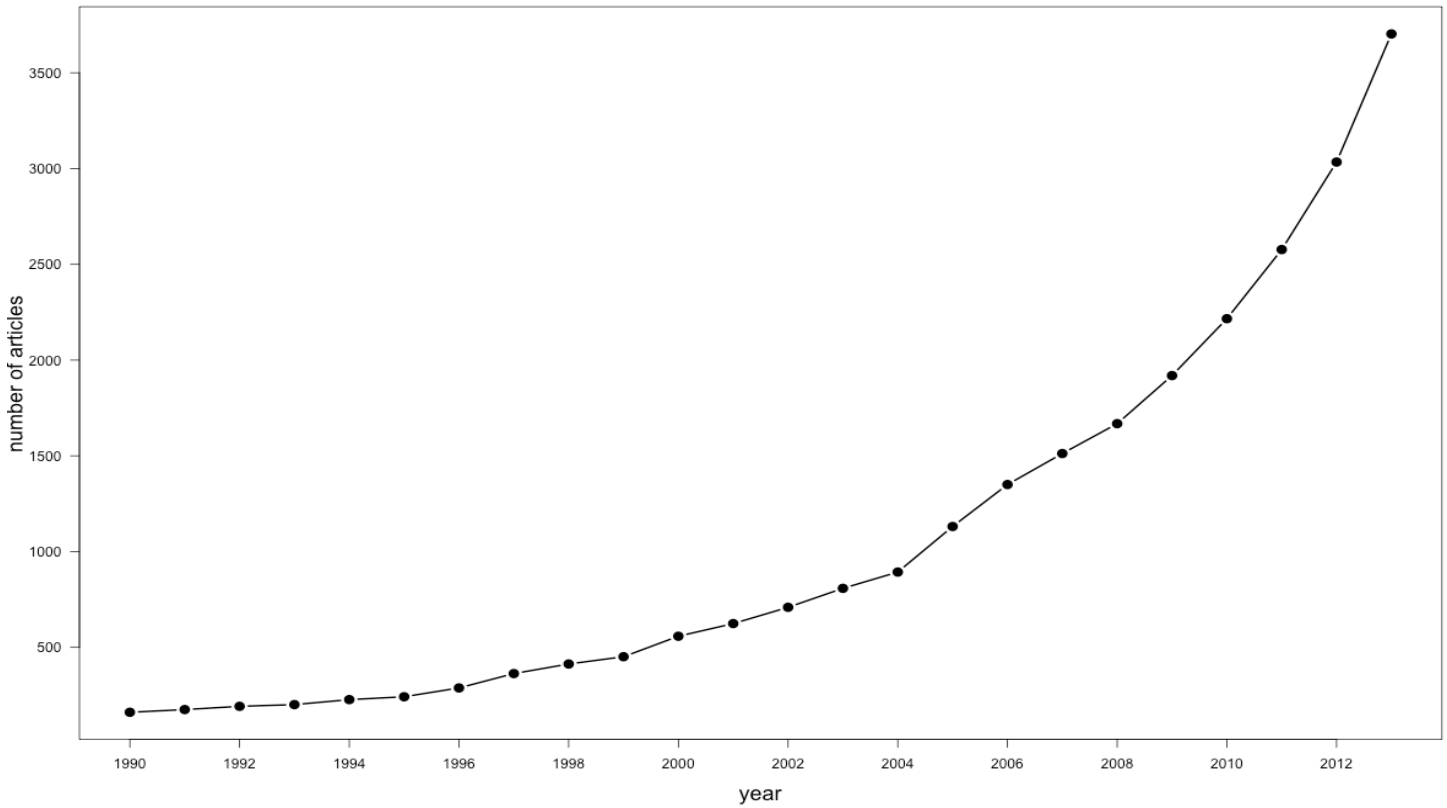
# Apgar Score in neonates

(JAMA 1958)


**Table 9–1.** Apgar scoring.

| Signs | 0 | 1 | 2 |
|---|---|---|---|
| Heartbeat per minute | Absent | Slow (<100) | Over 100 |
| Respiratory effort | Absent | Slow, irregular | Good, crying |
| Muscle tone | Limp | Some flexion of extremities | Active motion |
| Reflex irritability | No response | Grimace | Cry or cough |
| Color | Blue or pale | Body pink, extremities blue | Completely pink |

# Multivariable Prediction models are hot!




- 10,000s (!) prediction models
- Numerous models for same outcome or target population

# Systematic reviews of prediction models

- >110 models for prostate cancer (Shariat 2008)
- >100 models for Traumatic Brain Injury (Perel 2006)
- 83 models for stroke (Counsell 2001)
- 54 models for breast cancer (Altman 2009)
- 43 models for type 2 diabetes (Collins 2011; Dieren 2012)
- 31 models for osteoporotic fracture (Steurer 2011)
- 29 models in reproductive medicine (Leushuis 2009)
- 26 models for hospital readmission (Kansagara 2011)
- >25 models for length of stay in cardiac surgery (Ettema 2010)

- >350 models for prediction of CVD outcomes in general population (Damen, BMJ 2016)

# Why using prediction models?

- … Not meant to replace physicians, but to complement their clinical intuition!!!!!!

- Assumption:
  - They provide accurately + objectively estimated probabilities…
  - …to improve medical decision making …
  - … and thus subject's outcomes
  - … and thus cost-effectiveness of health care

# What evidence do we need before using prediction models?

## 4 steps in prediction modelling

***BMJ series 2009; HEART series 2012; PROGRESS series BMJ + PLOS MED 2013, TRIPOD Ann Intern Med 2015***

- 1. Developing prediction model from a particular (your) dataset
- 2. Validate/test the predictive accuracy of previously developed model in (data of) other subjects
- 3. Adjust/tailor model to local situation/care setting using the validation dataset
- 4. Quantify impact of using a model on decision making and patient outcomes

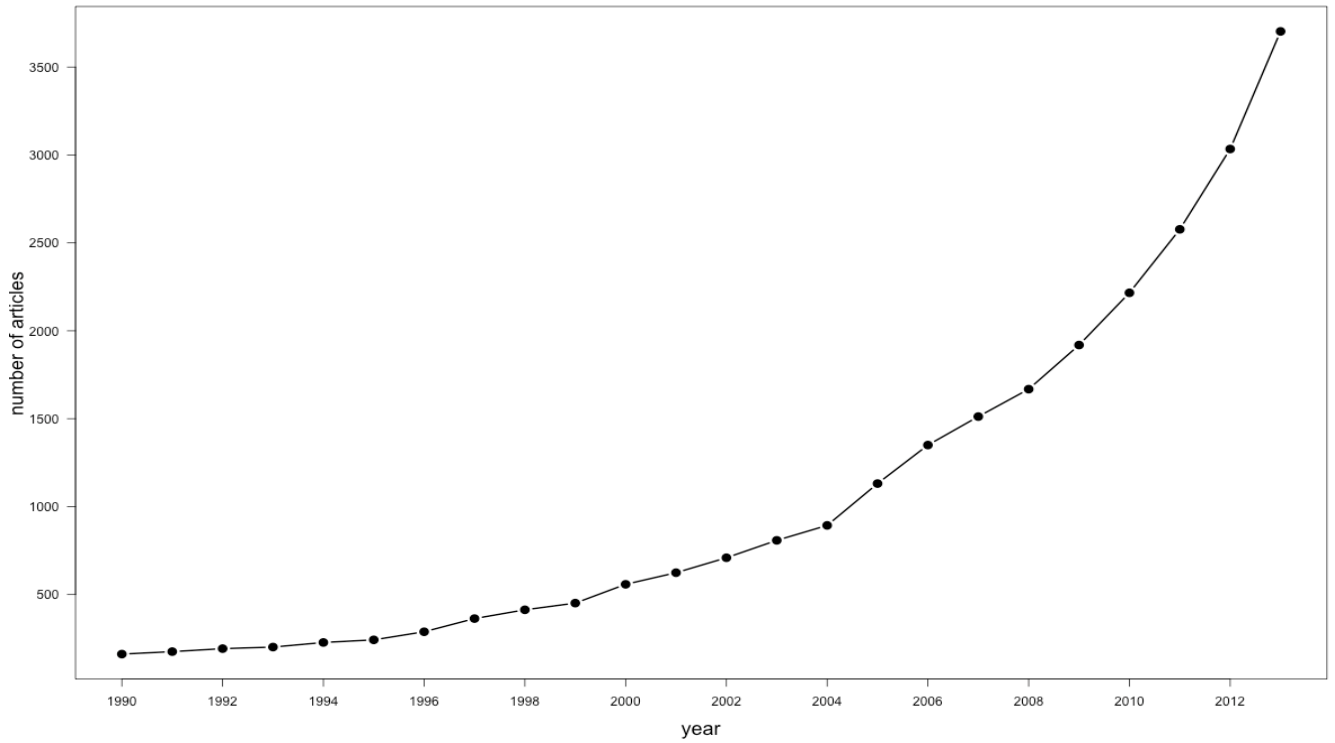
## 1. Developing a prediction model from your dataset

# Don't

**Don't develop a model from your data – skip this phase**

1. **Suppress your reflex**
   - Hard: we finally learned 'trics' to develop models (standard software)
   - 'Own' model makes us famous (Apgar; Goldman; Gail; Wells)
     - Validation of somebody else's model is only to support citation index of others

# Prediction modelling is hot!




**Majority is newly developed models – few validation studies**

# Numerous systematic Reviews

- Regardless clinical domain: numerous models developed → few validated
- Too much focus on developing → hardly on validation
- Like biomarker world: discovery driven → validation uninteresting ('losers'/non-innovative)
- But: with all these models for same outcome or target population: we/professionals have 'no clue' which model to use in which situation
  - Is our healthcare better of with yet another developed model?

## So when we are behind our dataset and aimed to develop a prediction model

**… Starts with …**

**…NOT developing a model…**

**… First search, review and validate existing models for your domain, target population or outcome at interest**

# When behind our dataset and aimed to develop a prediction model

- There are (almost) always existing models that apply to your patient population/outcome
  - We hardly search for existing models to first test on our datasets
  - We rather pursue to develop yet another (own) model

- Test and directly compare (!) the predictive performance of these models on your data set = (external) validation


*BMJ* 2012;344:e3186 doi: 10.1136/bmj.e3186 (Published 24 May 2012)


EDITORIALS

Gary S Collins *senior medical statistician*[1],

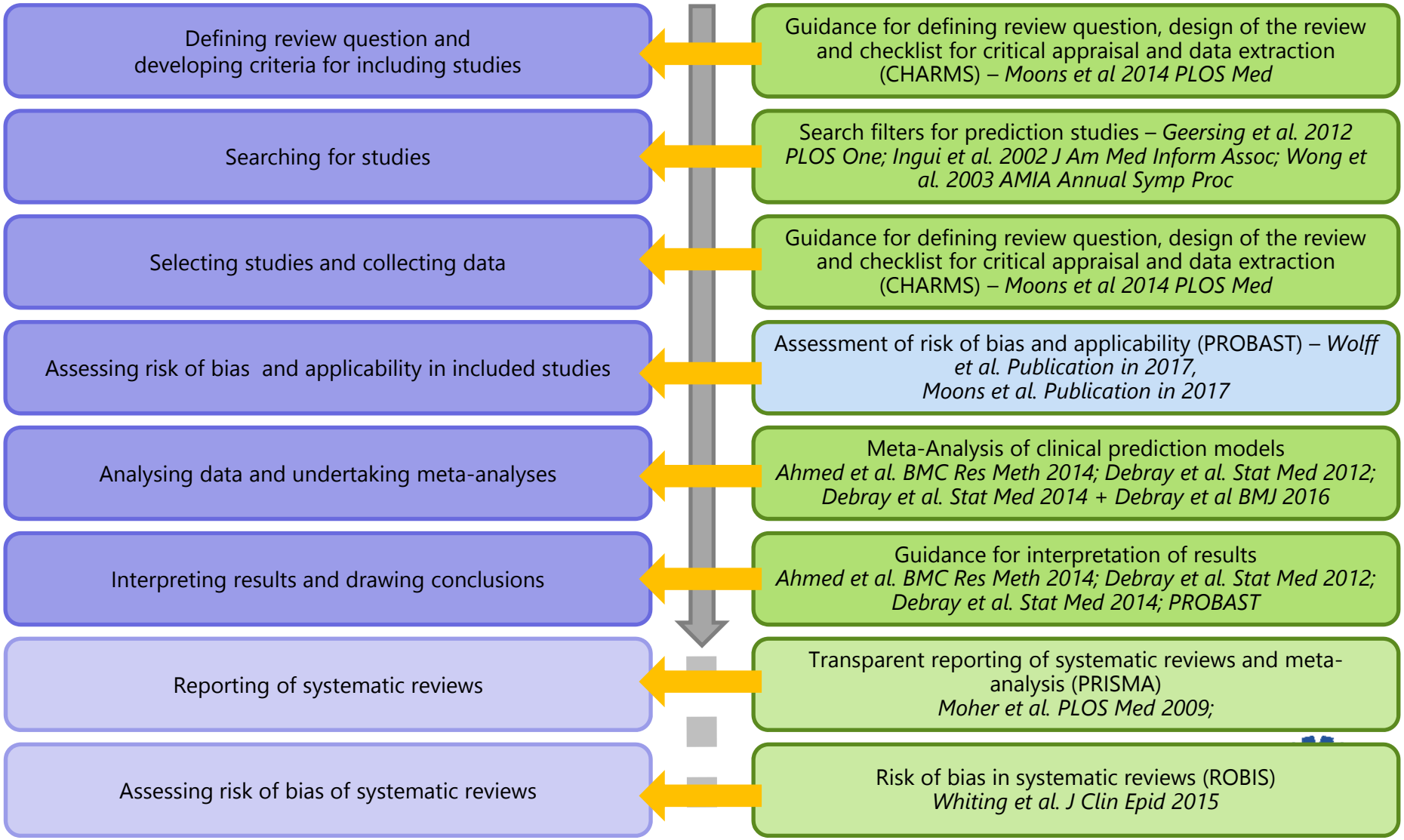
**Comparing risk prediction models**

Should be routine when deriving a new model for the same purpose

# Conducting a systematic review: generally 6 steps

1. Well-formulated review question
2. Extensive search and selection of primary studies
3. Objective extraction of data
4. Critical appraisal of methodological quality
5. Synthesis of data (meta-analysis)
6. Interpretation, conclusions, recommendations

# Conducting systematic reviews of prediction model studies




*Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 - http://handbook.cochrane.org/*

OPEN ACCESS Freely available online

PLOS | MEDICINE

Guidelines and Guidance

## Critical Appraisal and Data Extraction for Systematic Reviews of Prediction Modelling Studies: The CHARMS Checklist

Karel G. M. Moons[1¶*], Joris A. H. de Groot[1¶], Walter Bouwmeester[1], Yvonne Vergouwe[1], Susan Mallett[2], Douglas G. Altman[3], Johannes B. Reitsma[1], Gary S. Collins[3]

**PROBAST**
**Prediction model Risk Of Bias ASsessment Tool**

**2017 (pilot available)**

OPEN ACCESS Freely available online

PLOS one

## Search Filters for Finding Prognostic and Diagnostic Prediction Studies in Medline to Enhance Systematic Reviews

Geert-Jan Geersing[1*], Walter Bouwmeester[1], Peter Zuithoff[1], Rene Spijker[2,4], Mariska Leeflang[3,4],

## A guide to systematic review and meta-analysis of prediction model performance

BMJ 2017

Thomas P.A. Debray[†], Johanna A. A. G. Damen[†], Kym I. E. Snell, Joie Ensor, Lotty Hooft, Johannes B Reitsma, Richard D. Riley[†], Karel G. M. Moons[†]

## Meta-analysis and aggregation of multiple published prediction models

Thomas P. A. Debray,[a*†] Hendrik Koffijberg,[a] Daan Nieboer,[b] Yvonne Vergouwe,[b] Ewout W. Steyerberg[b] and Karel G. M. Moons[a]

Cochrane Netherlands

Cochrane Methods Prognosis

# Basic & Advanced Courses

MSC EPIDEMIOLOGY

## Systematic Reviews, Meta Analysis

## Face to Face & Online

### Accessible from all over the world
### More than 50 courses…

- Systematic Reviews of Randomised Intervention Studies
- Systematic Reviews of Diagnostic Studies
- Systematic Reviews of Prognostic Studies
- Meta Analysis with Individual Participants Data
- ….and many more

**www.msc-epidemiology.eu** **www.msc-epidemiology.online**

UMC Utrecht Julius Center

Universiteit Utrecht

elevate

# Hence …

… prognostic/prediction studies are hot

... SR's and notably MA of prognostic studies as well

- highly desired and well received by journals/policy makers →

- it is time to systematically summarise the existing prognostic evidence in the field before we start developing 'your own model'

## You are still behind your dataset and aimed to develop a prediction model

You have done your review

Selected the (most) relevant models for your interest

Published your review in a MAJOR journal

(Most prediction model papers do not appear in such journals!)

And then…..

# What evidence do we need before using prediction models?

**4 Steps in prediction modelling**

***BMJ series 2009; HEART series 2012; PROGRESS series BMJ + PLOS MED 2013, TRIPOD Ann Intern Med 2015***

- 1. Developing prediction model from a particular dataset

- 2. Validate/test predictive accuracy of previously developed model in your data

- 3. Adjust/tailor model to local situation/care setting using the validation dataset

- 4. Quantify impact of using a model on decision making and patient outcomes

# Validating

- Test and directly compare (!) the predictive performance of the retrieved/selected models on your data set = (external) validation

*BMJ* 2012;344:e3186 doi: 10.1136/bmj.e3186 (Published 24 May 2012)


EDITORIALS

Gary S Collins *senior medical statistician*[1],

**Comparing risk prediction models**

Should be routine when deriving a new model for the same purpose

# 2. Model validation studies: Don'ts

*BMJ series 2009; HEART series 2012; PROGRES series BMJ + PLOS MED 2013*

- Aim: to demonstrate predictive performance of competing models in (data of) subjects that were not used to develop model – direct comparison!
  - Calibration, discrimination, (re)classification

- Validating model(s) is not …
  - …Repeat the analysis in your data → whether you find same predictors, regression coefficients, predictive performance

  or

  - …Fit the previously found predictors and compare performance with development set

# 2. Model validation studies: Do's

*BMJ series 2009; HEART series 2012; PROGRES series BMJ + PLOS MED 2013*

- Use original developed model → apply 'as is' to your data → compare predicted with observed outcomes
  - Discrimination, calibration and (re)classification

- Validation studies require that developed prediction models properly reported
  - Original beta's – plus intercept / baseline hazard
    - Not just simplified score (too often done)
  - Clear definition and measurement method of predictors + outcome
  - Someone can indeed validate and use the model

Annals of Internal Medicine RESEARCH AND REPORTING METHODS

# Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD): The TRIPOD Statement

Gary S. Collins, PhD; Johannes B. Reitsma, MD, PhD; Douglas G. Altman, DSc; and Karel G.M. Moons, PhD *Ann Intern Med.* 2015;162:55-63. doi:10.7326/M14-0

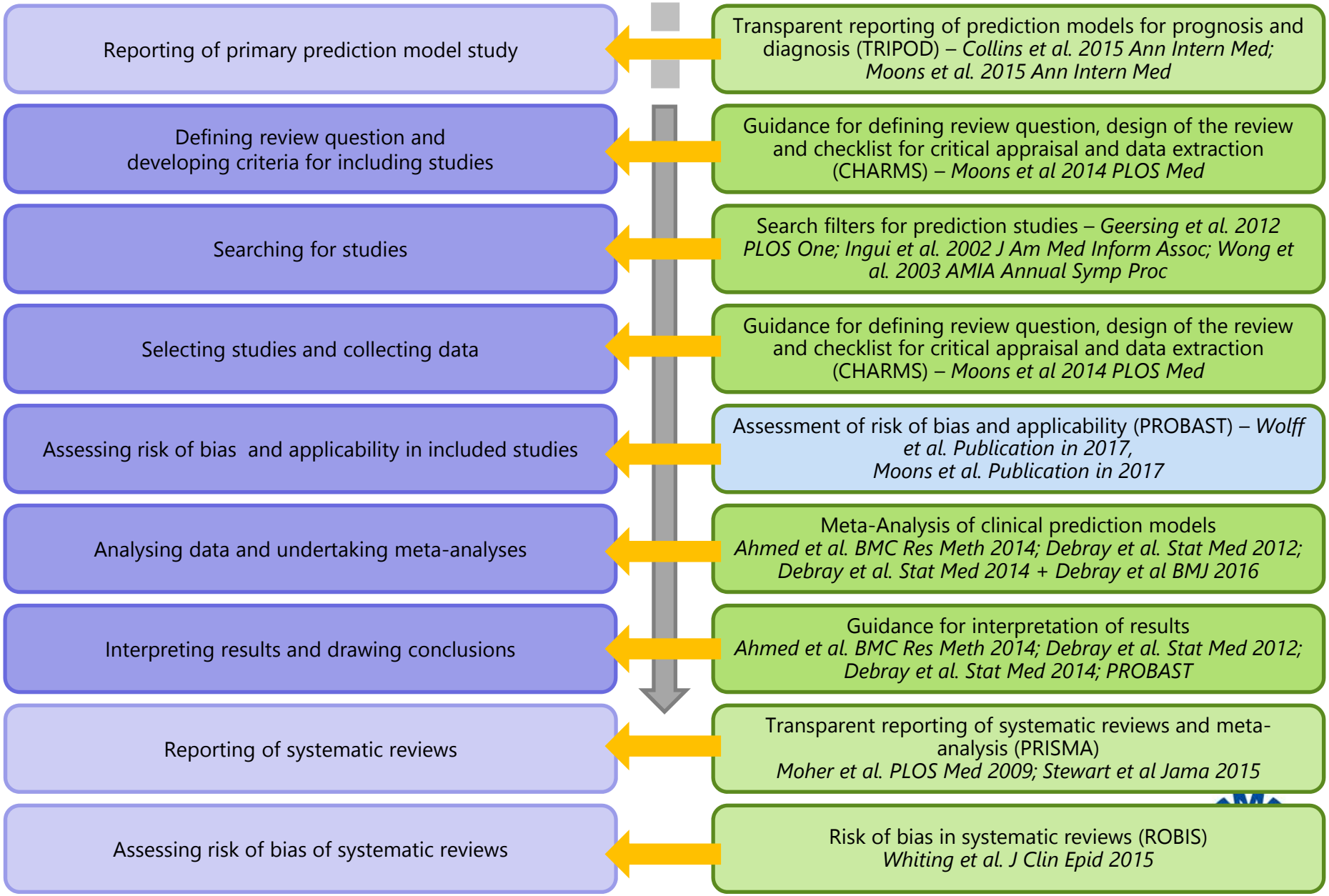
Annals of Internal Medicine RESEARCH AND REPORTING METHODS

# Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD): Explanation and Elaboration

*Ann Intern Med.* 2015;162:W1-W73. doi:10.7326/M14-0698

Karel G.M. Moons, PhD; Douglas G. Altman, DSc; Johannes B. Reitsma, MD, PhD; John P.A. Ioannidis, MD, DSc; Petra Macaskill, PhD; Ewout W. Steyerberg, PhD; Andrew J. Vickers, PhD; David F. Ransohoff, MD; and Gary S. Collins, PhD

www.tripod-statement.org




*Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 - http://handbook.cochrane.org/*

# Types of Validation Studies

*BMJ series 2009; HEART series 2012; PROGRES series BMJ + PLOS MED 2013*

## 1. Temporal validation

- Often same setting, measurement methods, investigators only later in time
  - Many similarities → very 'high' chance of good performance
- If large dataset: Split over time
- Don't randomly split – no difference but chance

# Types of Validation Studies

*BMJ series 2009; HEART series 2012; PROGRES series BMJ + PLOS MED 2013*

## 2. Geographic validation

- Validation in other centers/region; often other investigators
- Often other measurement methods
- If multicenter or combination of datasets (= IPD meta analysis)
  - split sample by center/region – see later

## 3. Setting/domain/subgroup validation

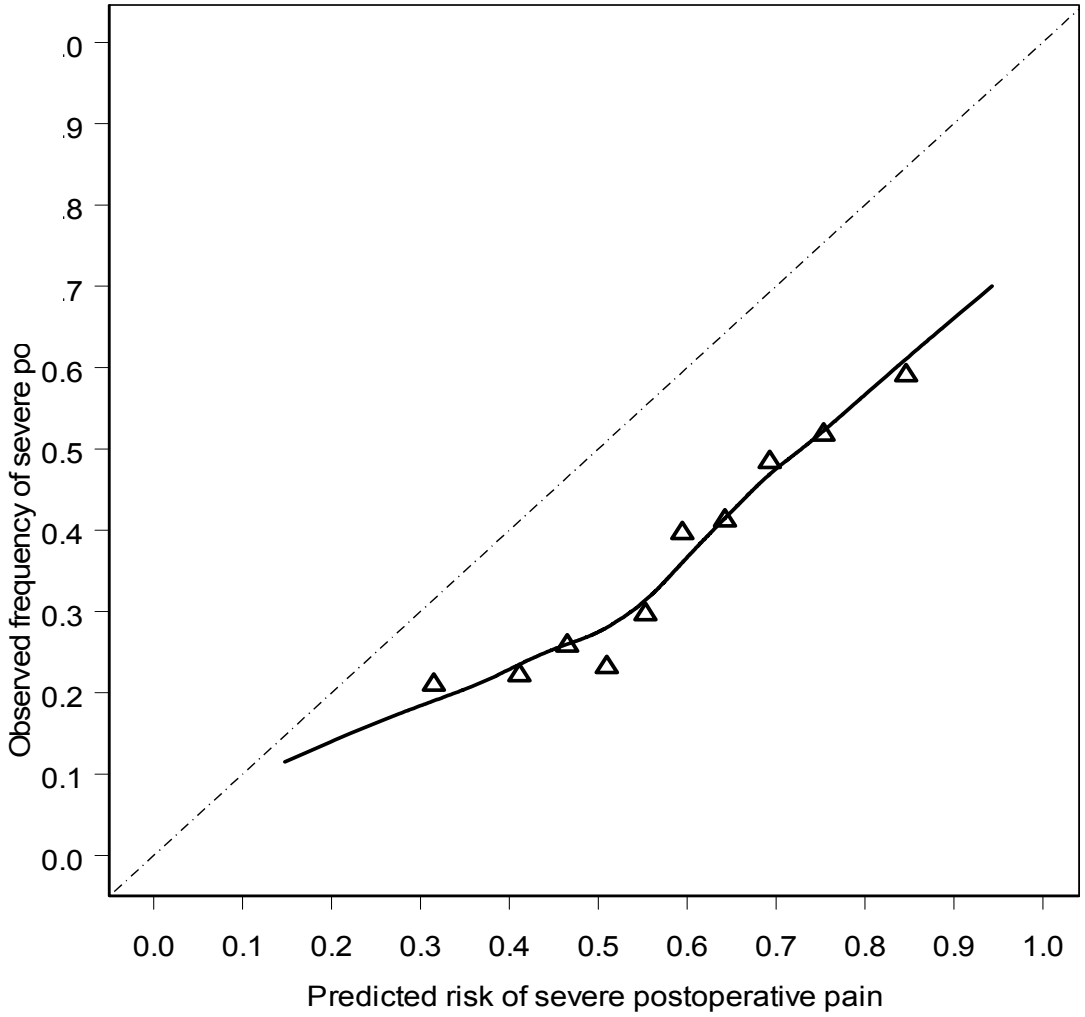
- Secondary → primary care
- Adults → children
- Men → women
- first VT → recurrent VT

# Types of Validation Studies

*BMJ series 2009; HEART series 2012; PROGRES series BMJ + PLOS MED 2013*

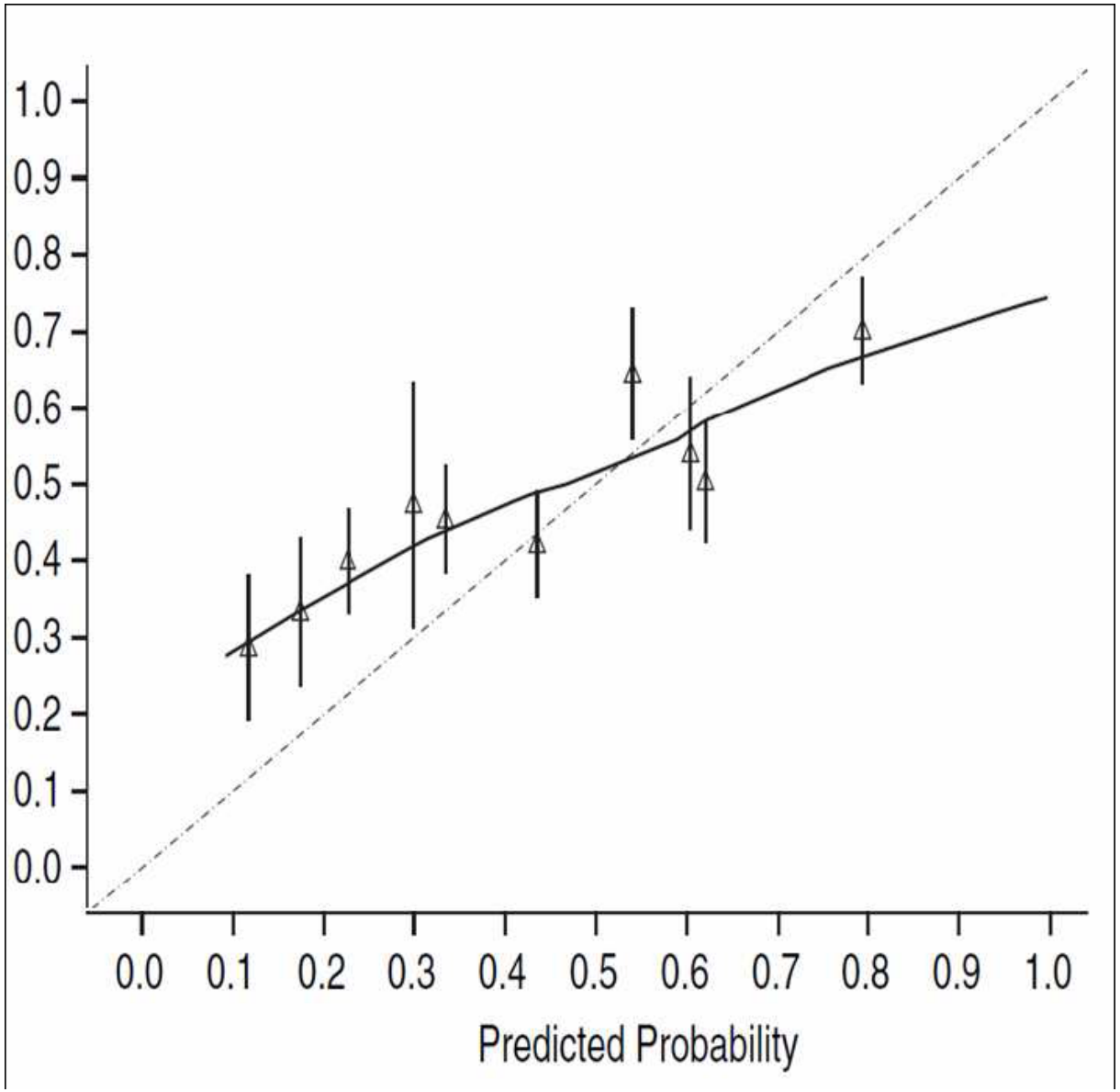
- **Aim of validation studies is not to find similar predictive accuracy as in development set…**
  - But to find satisfactory performance in validation set
  - AUC of 0.60 is not per se bad
    - Depends on accepted consequences of false predictions/decisions
    - You can always find low or high risk group –- despite small
- **YES: commonly find poorer performance when validating existing model in your data**
  - Still suppress reflex to develop a new model – be patient!

# Typical Model Validation Result




- Systematically too high predictions
  - **Higher outcome frequency in development set**
    - **Intercept/baseline hazard too high for new subjects**

# Typical Model Validation Result




## Slope plot < 1.0

- Low prob too low
- High prob too high
  - **Typical overfitted model in development set**
  - **Too extreme regression coefficients (OR/HR)**

# Poor validation = expected

**Reilly Ann Int Med 2009; Moons BMJ 2009 + Heart 2012;Steyerberg Plos Med 2013**

- Different outcome occurrence
  - Due to differences/changes in care often lower over time
  - Treatments (See Romin's talk)
- Different patients (case mix)
- Different interpretation/use of predictors or (incorrect) proxies of predictors
- Improvement in measurements over time: e.g. imaging tests
  - Previous CTs less accurate than spiral CT for PE detection
- Original model missed important predictor

ELSEVIER

Journal of Clinical Epidemiology ■ (2014) ■

ORIGINAL ARTICLE

# A new framework to enhance the interpretation of external validation studies of clinical prediction models

Thomas P.A. Debray[a,*], Yvonne Vergouwe[b], Hendrik Koffijberg[a], Daan Nieboer[b], Ewout W. Steyerberg[b,1], Karel G.M. Moons[a,1]

# External validation of clinical prediction models using big datasets from e-health records or IPD meta-analysis: opportunities and challenges

Richard D Riley,[1] Joie Ensor,[1] Kym I E Snell,[2] Thomas P A Debray,[3,4] Doug G Altman,[5] Karel G M Moons,[3,4] Gary S Collins[5]

# Multivariate meta-analysis of individual participant data helped externally validate the performance and implementation of a prediction model

Kym I.E. Snell[a], Harry Hua[b], Thomas P.A. Debray[c,d], Joie Ensor[e], Maxime P. Look[f], Karel G.M. Moons[c,d], Richard D. Riley[e,*]

# Poor validation = expected

**(Reilly Ann Int Med 2009; Moons BMJ 2009 + Heart 2012;Steyerberg Plos Med 2013 )**

- No matter what reason for poor validation – developing immediately another model =
  - Neglecting previous models/studies
  - Prediction research becomes completely particularistic
    - Every country, setting, hospital, subgroup 'own' model
  - Validation data sets often smaller → even less generalisable models
  - Perhaps new model needed: but likely not!
- Easy to adjust existing model using validation dataset
  - rather than fitting new model → notably when validation set is small(er)

# What evidence do we need to start using prediction models in practice?

**Steps in prediction modelling**

***BMJ series 2009; HEART series 2012; PROGRESS series BMJ + PLOS MED 2013, TRIPOD Ann Intern Med 2015***

- 1. Developing prediction model from a particular dataset
- 2. Validate/test the predictive accuracy of previously developed model in (data of) other subjects
- 3. Adjust/tailor model to local situation/care setting using the validation dataset
- 4. Quantify impact of using a model on decision making and patient outcomes

# 3. Adjusting prediction models

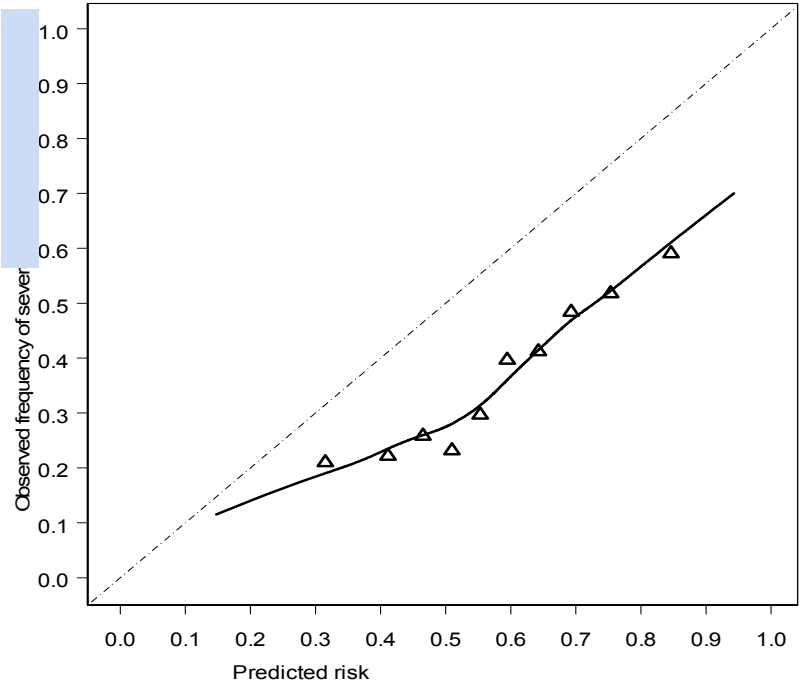
*Houwelingen Stat Med 2000; Steyerberg Stat Med 2004; KJM Janssen JCE 2008+CJA 2008; D Toll JCE 2008; Moons Heart 2012)*

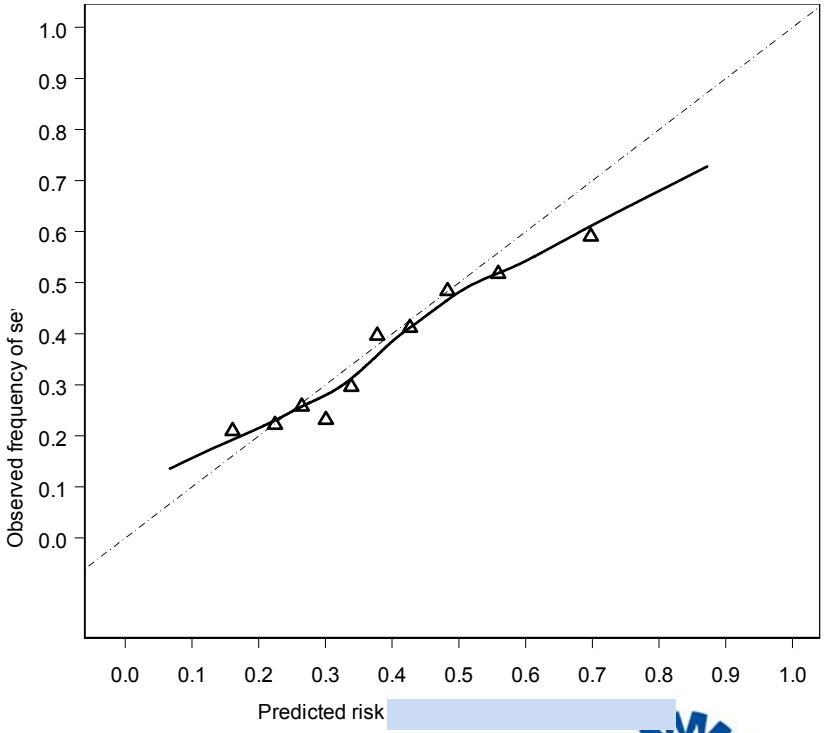
- **Adjusting can be simple and ranges from:**
  - Simple adjustment of base line risk/hazard (intercept)
  - Adjusting regression coefficients of predictors in model
  - Adding previously missed or new predictors/biomarkers
  - Refitting

# 3. Adjusting prediction models

*Houwelingen Stat Med 2000; Steyerberg Stat Med 2004; KJM Janssen JCE 2008+CJA 2008; D Toll JCE 2008; Moons Heart 2012*

- Adjusting for difference in overall outcome frequency (intercept adjustment) is often sufficient




- If (also) slope different → adjust predictor weights

# 3. Adjusting prediction models

*Houwelingen Stat Med 2000; Steyerberg Stat Med 2004; KJM Janssen JCE 2008+CJA 2008; D Toll JCE 2008; Moons Heart 2012*

- **Updating is particularly important when:**
  - new predictors found → added to existing models
    - CRP to Framingham risk model
  - new era / new setting

- **Updating done after (!) models (external) validation → if unsatisfactory accuracy in new subjects**
    - **Not recommend updating without first validating**

**If validation of existing models in our data is unsatisfactory …**

**…and updating could not fix the job…then**

**… Develop our new model**

# What evidence do we need before using prediction models?

**4 Steps in prediction modelling**

***BMJ series 2009; HEART series 2012; PROGRESS series BMJ + PLOS MED 2013, TRIPOD Ann Intern Med 2015***

- 1. Developing prediction model from a particular dataset

- 2. Validate/test the predictive accuracy of previously developed model in (data of) other subjects
- 3. Adjust/tailor model to local situation/care setting using the validation dataset
- 4. Quantify impact of using a model on decision making and patient outcomes

# 1. Developing a prediction model

No real challenges anymore

Much literature:

*Design: Book Grobbee & Hoes 2009; BMJ series 2009; Heart series 2012; PROGRESS series 2013; TRIPOD 2015.*

*Analysis: Royston  BMJ 2009 + Books by Harrell 2001; Steyerberg 2008; Royston & Sauerbrei 2009.*

# Basic & Advanced Courses

MSC EPIDEMIOLOGY

## Face to Face & Online

### Accessible from all over the world
### More than 50 courses…

- Basic and Modern Statistical methods
- Advanced Diagnostic Research
- Prognostic research
- Meta Analysis with Individual Participants Data

www.msc-epidemiology.eu

www.msc-epidemiology.online

UMC Utrecht Julius Center

Universiteit Utrecht

elevate

# What evidence do we need before using prediction models?

**4 Steps in prediction modelling**

***BMJ series 2009; HEART series 2012; PROGRES series BMJ + PLOS MED 2013, TRIPOD (Ann Intern Med 2015)***

- 1. Developing prediction model
- 2. Validate the predictive accuracy of developed model in (data of) other subjects
- 3. Adjust/tailor model to local situation/care setting

- 4. Quantify impact of using a model on decision making and patient outcomes

# 4. Model impact studies

*Campbell BMJ 2000; Reilly+Evans Ann Int M. 2006; Moons BMJ 2009 + Heart 2012*

- **Aim: Whether actual use of prediction model truly improves …**
  - … Decision making behaviour (treatment indications) …
  - … Patient outcome or healthcare costs …

  … as compared to not using such model

- **Impact studies are comparative, intervention studies**
  - Intervention = model use + subsequent (treatment) actions based on model predictions
  - In sharp (!) contrast to previous prediction modeling phases

# 4. Model impact studies

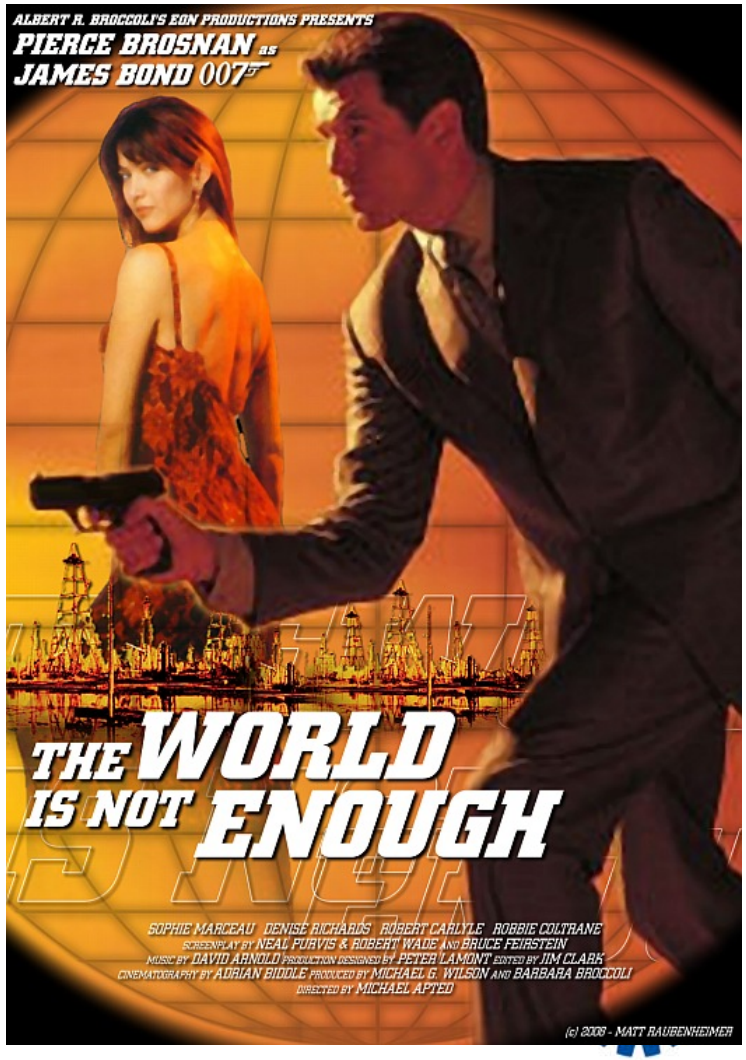
***Campbell BMJ 2000; Reilly+Evans Ann Int M. 2006; Moons BMJ 2009 + Heart 2012***

- Quantifying effects on patient outcomes:
  - Reflex = randomized comparison
  - This time good reflex: best design indeed RCT
    - Preferably cluster RCT (e.g. stepped wedge) trial

# 4. Model impact studies

***Campbell BMJ 2000; Reilly+Evans Ann Int M. 2006; Moons BMJ 2009 + Heart 2012***

- **Disadvantages (Cluster) RCTs:**
  - Long duration → Certainly if patient outcomes occur late in time
  - Large studies (costs)
  - Prediction model always studied in combination with current treatments
    - If new treatment → new RCT
- **10.000's clinical prediction models → increase per day**
- **Not enough resources - budget + subjects to study them all in long term, expensive cluster RCT**



# 4. Model impact studies

***Moons BMJ 2009 + Heart 2012; Hendriksen JTH 2013***

- Need alternative approaches to separate caff from wheat
- To determine which models are completely useless and which may …
  - …Change decision making
  - … Change patient outcomes
- Simple approaches to determine whether a model may/may not change decision making + patient outcomes

# 4. Model impact studies

***Moons BMJ 2009 + Heart 2012; Hendriksen JTH 2013***

- **1. Cross sectional randomised study**
  - Treatment decision = outcome (no f-up)
  - Outcome never changes if physicians/patients don't change behavior based on model predictions

# 4. Model impact studies

***Moons BMJ 2009 + Heart 2012; Hendriksen JTH 2013***

- **2. Risk-Benefit modelling study**
  - Linked evidence approach -- combining Model's predictive accuracy studies + Treatment effect evidence
  - → To quantify effect of actually using the model with model-directed therapies → on patient outcome (+ cost-effectiveness)

ELSEVIER

Journal of Clinical Epidemiology 62 (2009) 1248–1252

Journal of Clinical Epidemiology

SYSTEMATIC REVIEW

Decision analysis to complete diagnostic research by closing the gap between test characteristics and cost-effectiveness

Joanna D. Schaafsma[a,*], Yolanda van der Graaf[b], Gabriel J.E. Rinkel[a], Erik Buskens[b,c]

Koffijberg *et al. BMC Medical Research Methodology* 2013, **13**:12
http://www.biomedcentral.com/1471-2288/13/12

BMC Medical Research Methodology

RESEARCH ARTICLE Open Access

From accuracy to patient outcome and cost-effectiveness evaluations of diagnostic tests and biomarkers: an exemplary modelling study

Hendrik Koffijberg[1*], Bas van Zaane[2] and Karel GM Moons[1,2]

# 4. Model impact studies

***Moons BMJ 2009 + Heart 2012; Hendriksen JTH 2013***

## 3. Before-After study

- Compare patient outcomes in period before introducing model to the period after introducing

## 4. Geographical comparison or historical control group

- Disadvantages 3+4: both observational
  - Confounding by indication / case mix differences → adjustment in analysis (like all non-randomized intervention studies)

# Take home messages

- **Indeed theoretically 4 consecutive phases of prediction modelling**
  - Development, validation, adjusting (updating), impact assessment
- **But way too much developed models for same outcome or target population**
  - Too much focus on development → 'innovation' / 'own' model
- **If behind your dataset: don't start with phase 1 = developing a model**
  - Do first good systematic review (SR) -- guidance available
  - Then validate these existing models

# Take home messages

- **Validation is not refitting original model or repeat analysis of development study in your data**
  - Testing the model 'as ít is' in your data
  - Requires proper reporting of original developed models, plus how predictors and outcomes defined/measured
  - not reporting of simplified scores only
  - No random-split sample validation
  - Rather by time, geography, setting/clinical domain
  - Validation is not aiming to find same predictive accuracy as in development set → rather: acceptable accuracy

# Take home messages

- **Validation often shows poor accuracy → don't panic → try update first (easy) → suppress your 'development reflex'**

- **If still after updating unsatisfactory performance**
  - Try adjusting original model based on your data

- **If remains unsatisfactory: develop new model + validate**
  - Development No real challenges anymore

# Take home messages

- **Impact assessment – not directly jump to RCT**
  - Use alternative approaches to see whether model may lead to improved decision making + patient outcome
- **No developed model applied or in guideline without at least 1 external validation → preferably with impact assessment**
- **Validation, Updating, Development, Impact → Report your modelling study well**

Annals of Internal Medicine RESEARCH AND REPORTING METHODS

Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD): Explanation and Elaboration

Karel G.M. Moons, PhD; Douglas G. Altman, DSc; Johannes B. Reitsma, MD, PhD; John P.A. Ioannidis, MD, DSc; Petra Macaskill, PhD; Ewout W. Steyerberg, PhD; Andrew J. Vickers, PhD; David F. Ransohoff, MD; and Gary S. Collins, PhD

# Take home messages

## Preffered steps in prediction modelling

- 1. Systematic review existing prediction model for your domain or outcome at interest
- 2. Validate/test the predictive accuracy of these retrieved models in (data of) other subjects
- 3. Adjust/tailor model to local situation using the validation dataset
- 4. Developing prediction model from a particular dataset
- 5. Quantify impact of using a model on decision making and patient outcomes

# Final where to go: Share data for Individual Patient Data (meta-)analyses

*Debray TP et al + Riley et al: 2013, 2014, 2015*

- Many domains limited data (low #events)
  - Problematic for both model development + validation

- Large(r) IPD sets allow for
  - More data – more precision
  - More robust model development – less overfitted models
  - Direct and multiple validation across centers
  - Better testing of model generalisability
  - Better subgroup effects and thus personalized (tailored) care

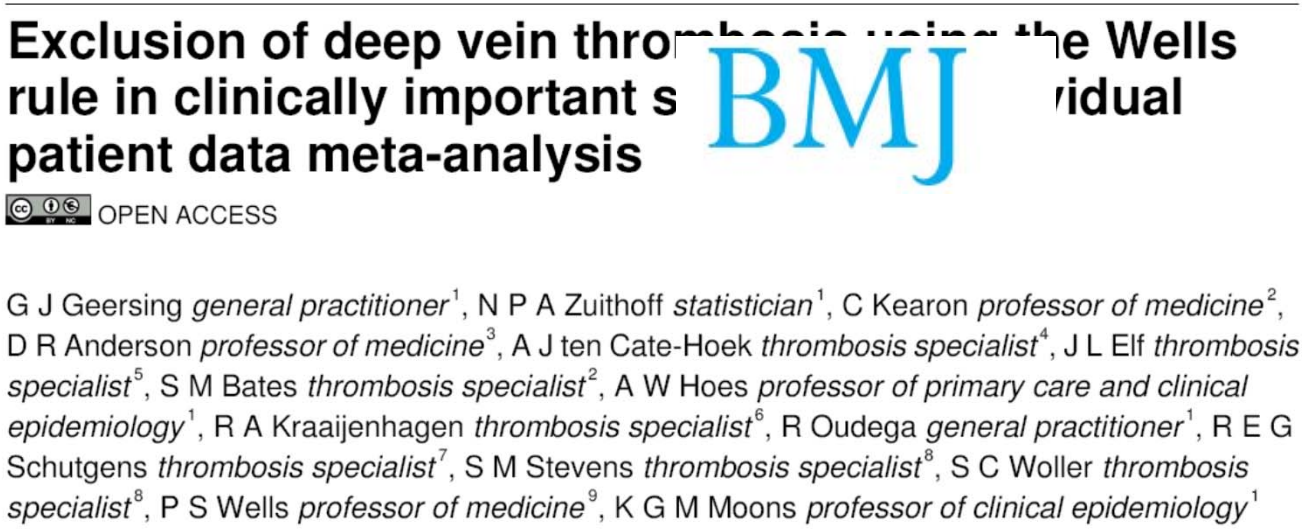
**A framework for developing, implementing, and evaluating clinical prediction models in an individual participant data meta-analysis**

Thomas P. A. Debray,[a*†] Karel G. M. Moons,[a] Ikhlaaq Ahmed,[b] Hendrik Koffijberg[a] and Richard David Riley[b]

# Final Where to go: Share data for Individual Patient Data (meta-)analyses

*Debray TP et al + Riley et al: 2013, 2014, 2015*

- We need to start sharing data – combine datasets
  - Our own (research) world is too small – we not sit on 'our' data
  - Obliged to healthcare and our patients
  - Sharing data doubles our output (win-win)
  - Be aware of IPD MA approaches  based on 'convenient data sets'



**Exclusion of deep vein thro[illegible]he Wells rule in clinically important s[illegible]vidual patient data meta-analysis**

BMJ

OPEN ACCESS

G J Geersing *general practitioner*[1], N P A Zuithoff *statistician*[1], C Kearon *professor of medicine*[2], D R Anderson *professor of medicine*[3], A J ten Cate-Hoek *thrombosis specialist*[4], J L Elf *thrombosis specialist*[5], S M Bates *thrombosis specialist*[2], A W Hoes *professor of primary care and clinical epidemiology*[1], R A Kraaijenhagen *thrombosis specialist*[6], R Oudega *general practitioner*[1], R E G Schutgens *thrombosis specialist*[7], S M Stevens *thrombosis specialist*[8], S C Woller *thrombosis specialist*[8], P S Wells *professor of medicine*[9], K G M Moons *professor of clinical epidemiology*[1]

# Final Where to go: Share data for Individual Patient Data (meta-)analyses

*Debray TP et al + Riley et al: 2013, 2014, 2015*

GUIDELINES AND GUIDANCE

## Individual Participant Data (IPD) Meta-analyses of Diagnostic and Prognostic Modeling Studies: Guidance on Their Use

Thomas P. A. Debray[1,2]*, Richard D. Riley[3], Maroeska M. Rovers[4], Johannes B. Reitsma[1,2], Karel G. M. Moons[1,2], Cochrane IPD Meta-analysis Methods group[¶]

Ahmed et al. BMC Medical Research Methodology 2014, 14:3
http://www.biomedcentral.com/1471-2288/14/3

BMC Medical Research Methodology

RESEARCH ARTICLE Open Access

## Developing and validating risk prediction models in an individual participant data meta-analysis

Ikhlaaq Ahmed[1], Thomas PA Debray[2], Karel GM Moons[2] and Richard D Riley[3*]

## A framework for developing, implementing, and evaluating clinical prediction models in an individual participant data meta-analysis

Thomas P. A. Debray,[a*†] Karel G. M. Moons,[a] Ikhlaaq Ahmed,[b] Hendrik Koffijberg[a] and Richard David Riley[b]



## External validation of clinical prediction models using big datasets from e-health records or IPD meta-analysis: opportunities and challenges

Richard D Riley,[1] Joie Ensor,[1] Kym I E Snell,[2] Thomas P A Debray,[3,4] Doug G Altman,[5] Karel G M Moons,[3,4] Gary S Collins[5]

ELSEVIER

Journal of Clinical Epidemiology 66 (2013) 865–873

ORIGINAL ARTICLES

## Individual participant data meta-analyses should not ignore clustering

Ghada Abo-Zaid[a], Boliang Guo[b], Jonathan J. Deeks[c], Thomas P.A. Debray[d], Ewout W. Steyerberg[e], Karel G.M. Moons[d], Richard David Riley[c,*]

Thank you for your attention