

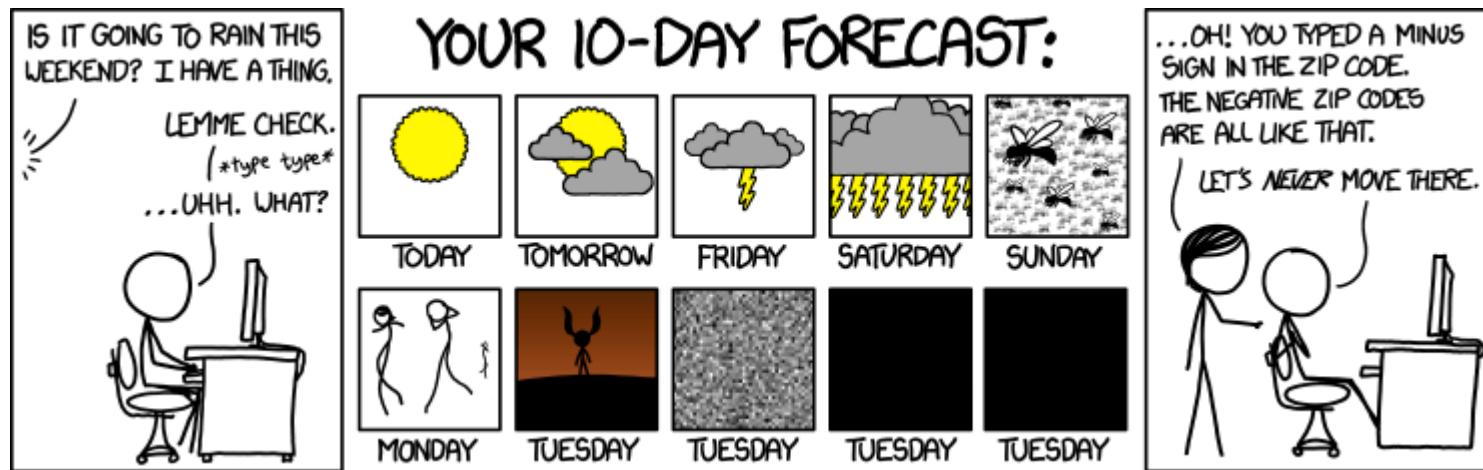


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Statistical methods for IPD-MA of prognosis studies

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What is a good prediction model?



<http://xkcd.com/1245/>



What is a good prediction model?

General requirements

- Generates accurate predictions in individuals from potential population(s) for clinical use
- Ability to discriminate between different risk groups
 - between individuals that will develop or not develop the outcome
- Improves patient outcomes by informing treatment decisions



The reality



The reality

Most prediction models are not as good as we think

bad quality due to

- Quality of many prognostic model studies is poor
 - Absence of a study protocol
 - Exclusion of eligible study participants
 - Poor handling of missing data
 - Complex modelling in small samples
 - Incomplete registrations & reporting

validation especially

- Internal validation too optimistic
- Lack of external validation

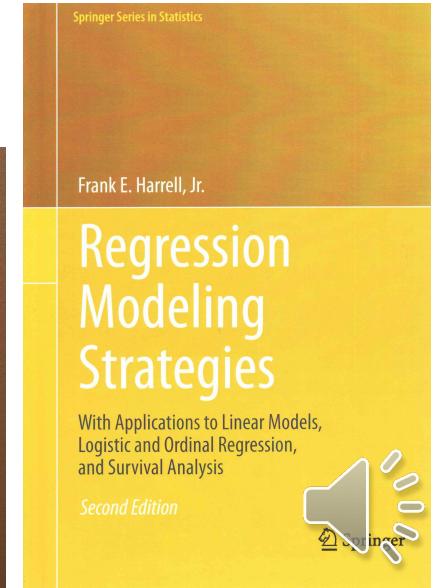


Lack of internal validity

Poor performance in new patients from the development population

- Overfitting
- Inclusion of noise variables (e.g. via stepwise selection)
- Poor handling of missing values

internal: can be assessed easily within the sample (bootstrapping) lack often due to overfitting or if model doesn't account for missing values



Lack of external validity

Poor performance in new patients from different (but related) populations

when population is not exactly the same as the model population - performance not the same



CrossMark

Journal of Clinical Epidemiology 68 (2015) 25–34

**Journal of
Clinical
Epidemiology**

ORIGINAL ARTICLES

External validation of new risk prediction models is infrequent and reveals worse prognostic discrimination

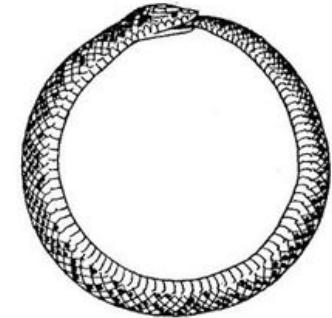
George C.M. Siontis^{a,1}, Ioanna Tzoulaki^{a,b}, Peter J. Castaldi^c, John P.A. Ioannidis^{d,e,f,*}



But wait... this is not the end

developing a new model when researchers don't like the model they had with issue
many models have wrong prediction values - seem too good

There are numerous models for same target population and outcomes



- >500 models alike Framingham, SCORE, QRisk
- >100 models for brain trauma patients
- > 100 diabetes type 2 models
- > 60 models for breast cancer prognosis



Numerous models for same target population + outcomes

RESEARCH

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Prediction models for cardiovascular disease risk in the general population: systematic review

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Numerous models for same target population + outcomes

“Comparing risk prediction models should be routine when deriving a new model for the same purpose” (Collins 2012)



“Substantial work is needed to understand how competing prediction models compare and how they can best be applied to individualize care.” (Wessler 2015)



“There is an excess of models predicting incident CVD in the general population. The usefulness of most of the models remains unclear.” (Damen 2016)

Prediction models for COVID-19

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end of the article.

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Additional material is published
online only. To view please visit
the journal online.

[Cite this as: BMJ 2020; 369:m1272](#)

Prediction models for diagnosis and prognosis of covid-19 infection: systematic review and critical appraisal

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Karel G M Moons,^{4,8} Richard D Riley,¹² Ewoud Schuit,^{4,8} Luc J M Smits,¹ Kym I E Snell,¹²
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ABSTRACT

OBJECTIVE

To review and critically appraise published and preprint reports of prediction models for diagnosing coronavirus disease 2019 (covid-19) in patients with suspected infection, for prognosis of patients with covid-19, and for detecting people in the general population at risk of being admitted to hospital for covid-19 pneumonia.

were identified for predicting hospital admission from pneumonia and other events (as proxy outcomes for covid-19 pneumonia) in the general population; 18 diagnostic models for detecting covid-19 infection (13 were machine learning based on computed tomography scans); and 10 prognostic models for predicting mortality risk, progression to severe disease, or length of hospital stay. Only one study used patient data from outside of China. The most



Prediction models for COVID-19

51 studies included in the review

- **3 models** to identify subjects at risk in the general population
- **47 diagnosis models** for COVID-19 or COVID-19 pneumonia
 - 34 based on medical images (deep learning) to assist diagnosis
- **16 prognosis models** for predicting mortality risk, progression to severe disease, or length of stay



Prediction models for COVID-19

for all identified models - discriminative performance appeared to be very good

- **Hospital admission models:** AUC range 0.73 to 0.81
- **Diagnosis models:** AUC range 0.85 to 0.99
- **Diagnostic imaging models:** AUC range 0.81 to 0.998
- **Prognosis models:** AUC range 0.85 to 0.99



Prediction models for COVID-19

but high risk of bias often non-representative sample, subjective outcomes, and especially analysis domain with small samples and incomplete reporting

- Participants domain: **24/51 at high risk of bias**
 - Non-representative of the target population (e.g., non-consecutive patients)
- Predictors domain: **6/51 at high risk of bias**
 - Predictors not available at time of intended model use
- Outcome domain: **18/51 at high risk of bias**
 - Subjective or proxy outcomes
- Analysis domain: **50/51 at high risk of bias**
 - Small sample size (->overfitting & no adjustment), incomplete reporting of model performance (e.g., no calibration)



Prediction models for COVID-19

poorly reported

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Prediction models for diagnosis and prognosis of covid-19 infection: systematic review and critical appraisal

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- COVID-19 prediction models were poorly reported, at high risk of bias, and their reported performance is probably optimistic
- Application of currently available prediction models not recommended



The rise of big datasets



The rise of big datasets

Data increasingly available for thousands or even millions of patients from multiple practices, hospitals, or countries.

- Meta-analysis of individual participant data (IPD) from multiple studies
 - Observational studies
 - Randomized controlled trials
- Analyses of databases and registry data containing e-health records



The rise of big datasets

The QRESEARCH database

- Anonymised health records of over 25 million people from 1500 general practices spread throughout the UK
- Linkage to Hospital Episode Statistics, Mortality and Cancer Registration data



The rise of big datasets

CALIBER

- EHR data encompassing more than 10 million adults with 400 million person-years of follow-up
- Primary care consultations and hospitalisations
- Clinical examination findings, blood laboratory results, prescriptions and vaccinations
- Diagnoses of diseases and mortality data



The rise of big datasets

main advantages of these huge databases

Why do we need big datasets?

- Development of better prediction models
- More extensive testing of model performance

 OPEN ACCESS

GUIDELINES AND GUIDANCE

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

Thomas P. A. Debray , Richard D. Riley, Maroeska M. Rovers, Johannes B. Reitsma, Karel G. M. Moons,
Cochrane IPD Meta-analysis Methods group 

Published: October 13, 2015 • <https://doi.org/10.1371/journal.pmed.1001886>



The rise of big datasets

