

A simulation approach to calculating minimum sample sizes for prediction modelling

The `pmsims` package for R

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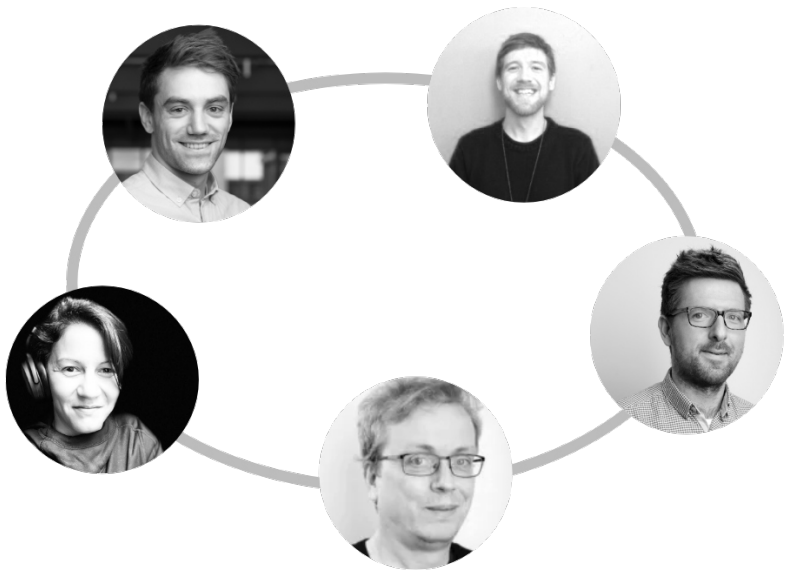
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30-second version

1. Most prediction models use small samples.
2. Small samples cause overfitting and imprecise estimates.
3. Existing tools can estimate minimum samples for continuous, binary, and survival outcomes.
4. Nothing exists for other models or data types.

We're developing a simulation-based approach that works with any outcome or method.



This talk

1. Background
 - What's the problem we're trying to solve?
 - What solutions currently exist?
2. Our simulation-based approach
 - Workflow and user interface
 - How it compares to other packages
3. Demonstration
4. Development status and next steps

We're still developing the package.
Your feedback is welcome.
Please get in touch.



What's the problem?

Hundreds of prediction models are developed each year. Most have inadequate samples.

- Insufficient sample sizes was the most common cause of bias in 731 models for COVID-19.³
- Inadequate samples were found in:

67% models for COVID-19³

56% models using supervised machine learning⁴

73% models in psychiatry⁶

- Just **8%** of machine learning models in oncology reported a sample size justification.⁵

Inadequate samples = research waste

- Inadequate samples lead to overfitting and inaccurate estimates of model parameters.
- This may generate inappropriate decisions about patient care or lead to models not being implemented into clinical practice.
- Data collection can be invasive and inconvenient and diverts resources from other activities that benefit patients.

Ensuring sample sizes are sufficient **before model development** would improve patient outcomes by avoiding models developed with inadequate samples and reducing participant burden.

What tools currently exist?

Most studies ignore sample size.



Or use rules of thumb (e.g., 10 events per variable) that have no rationale in prediction modelling.²

In 2018, Riley et al released `pmsampsize` for R and Stata.

Minimum sample size for developing a multivariable prediction model: PART II - binary and time-to-event outcomes

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When designing a study to develop a new prediction model with binary or time-to-event outcomes, researchers should ensure their sample size is adequate in terms of the number of participants (n) and outcome events (E) relative to the number of predictor parameters (p) considered for inclusion. We propose that the minimum values of n and E (and subsequently the minimum number of events per predictor parameter, EPP) should be calculated to meet the following three criteria: (i) small optimism in predictor effect estimates as defined by a global shrinkage factor of ≥ 0.9 , (ii) small absolute difference of ≤ 0.05 in the model's apparent and adjusted Nagelkerke's R^2 , and (iii) precise estimation of the overall risk in the population. Criteria (i) and (ii) aim to reduce overfitting conditional on a chosen p , and require prespecification of the model's anticipated Cox-Snell R^2 , which we show can be obtained from previous studies. The values of n and E that meet all three criteria provides the minimum sample size required for model development. Upon application of our approach, a new diagnostic model for Chagas disease requires an EPP of at least 4.8 and a new prognostic model for recurrent venous thromboembolism requires an EPP of at least 23. This reinforces why rules of thumb (eg, 10 EPP) should be avoided. Researchers might additionally ensure the sample size gives precise estimates of key predictor effects; this is especially important when key categorical predictors have few events in some categories, as this may substantially increase the numbers required.

KEYWORDS

binary and time-to-event outcomes, logistic and Cox regression, multivariable prediction model, pseudo R -squared, sample size, shrinkage

pmsampsize has methods for simple continuous, binary, and survival outcome.

The package identifies the minimum sample that results in:

Continuous	Binary
i. Small optimism in predictor effect estimates, indicated by a global shrinkage factor of 0.9.	
ii. Small absolute difference of 0.05 in the apparent and adjusted R^2	
iii. Precise estimation of the model's residual standard deviation.	Precise estimation of the overall risk in the population.
iv. Precise estimation of the model intercept.	

We ❤️ pmsampsize, but...

We increasingly need to estimate minimum samples for:

Other models

- Regularised regression (e.g., LASSO, elastic net)
- Machine learning algorithms (e.g., random forests, gradient boosting)

Other types of data

- Longitudinal and repeated measures
- Clustered data

We're creating a simulation-based framework to estimate sample sizes for prediction.

The pmsims package for R

Key features:

- Able to estimate minimum sample sizes for any model or data type;
- Provides defaults for common model and data types;
- Efficient estimation.

This last point is key: most machine learning approaches are too computationally demanding for conventional simulation approaches.

Our approach

Setting

1. A study population represented by outcome-related individual characteristics (i.e., candidate predictors).
2. A chosen statistical or machine learning model.
3. Expected achievable performance (e.g., R^2 , AUC) without sample size constraints, P^* .
4. Minimum acceptable performance of the model, P^{OK} .

Our approach

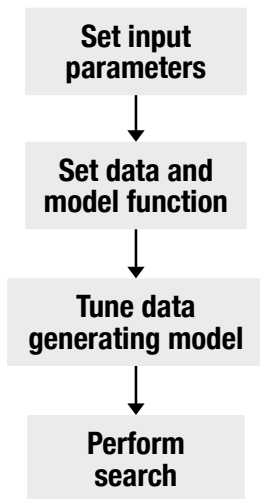
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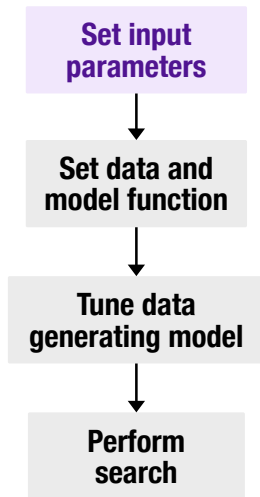


Find the minimum sample that ensures test performance of P^{OK} with probability of 80%, given the population, predictors, and P^* .

How does it work?



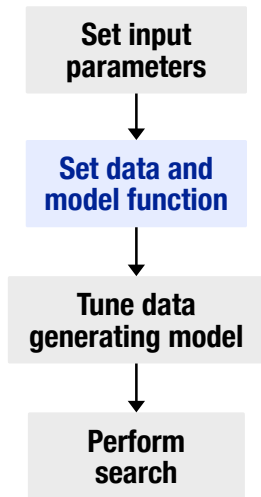
How does it work?



The user specifies:

1. The candidate predictors (number, type)
2. The chosen statistical model
3. The expected large sample performance (P^*)
4. The minimum acceptable performance (P^{OK})

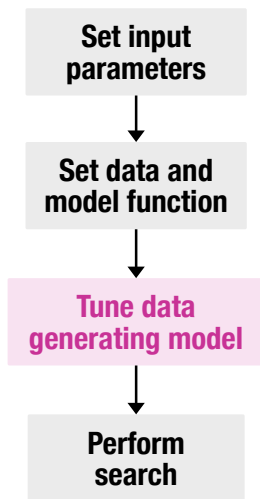
How does it work?



Based on their input, we set:

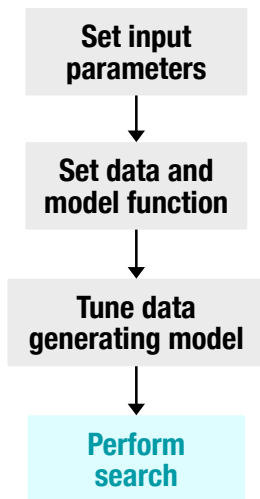
1. A data generating function
2. A model function
3. A metric function

How does it work?



We then tune the data generating model, so the large sample performance is P^* .

How does it work?



Performing the search

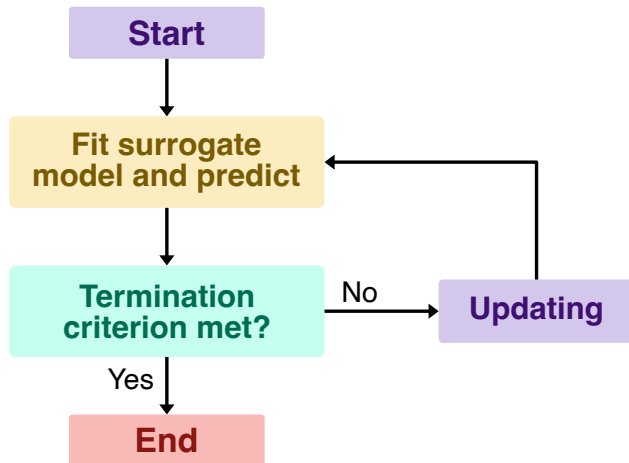
An exhaustive grid search would be too slow for many model types.



Surrogate modelling

- Surrogate modelling approximates the relationship between sample size and P^{OK} .
- Also referred to as 'learning curve fitting'.^{1,7}
- We're building on the mlpwr R package by Felix Zimmer and Rudolf Debelak CITE. *Simulation-based Design Optimization for Statistical Power: Utilizing Machine Learning* (Forthcoming, JOURNAL)
- This uses Gaussian process regression.

Surrogate modelling



Slide with graph showing how surrogate modelling works

Ewan will add.

What is performance?

Diana slide 1 - our criteria, how we assess them.

What is performance?

Diana slide 2 - how our criteria compare to pmsampsize

CRITERIA

We then return the minimum sample that is within 10% of expected large sample performance in 80% of replications.

If we had unlimited data, what's possible? Best case. What is the sample size that is sufficient to be within 10% of this maximum achievable.

How many replications?

The user interface

- `simulate_continuous`
- `simulate_binary`
- `simulate_survival`

Which each call:

- `simulate_custom`

Example 1: Binary outcome, logistic regression

including comparison with `pmsampsize`

Example 2: Binary outcome, LASSO regression

Example 3: Custom model function

`simulate_custom`

XGBoost

Maybe put slide with simulations here?

With our package we can replicate other criteria.

How would it look if we included `pmsampsize` criteria within `pmsims` framework?

For example, shrinkage from `pmsampsize`:

DEMO

We can accomodate any.

Development status

Package in development; functioning, but more testing needed.

- Follow fediscience.org/@ewan for updates.
- Or enter an email address at tinyurl.com/is-it-ready-yet to get one email when a public release is available.

Please come and talk to us.

Criteria/models/etc. all subject to change.

What's next? (1/2)

1. Machine learning

2. Longitudinal data

What's next? (2/2)

3. Common data types

e.g., clinical, NLP, genetic.

4. Performance

Thank you for listening.

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