University of Glasgow | School of Computing Science

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From Reproducibility to Generalisability

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Problem Definition and Data Inspection

- What is the research question?
- What is known already about the predictors?
- How were patients selected?
- How should we deal with treatment effects in prognostic analyses?
- Were the predictors reliable and completely measured?
- Is the prediction outcome of interest?

Coding of Predictors

- Categorical and continuous variables can be coded in different ways
  - Categories with infrequent occurrence may for instance concatenated with others
  - Continuous variables can be modeled as linear associations in a regression model
  - Continuous variables should not be categorized as below or above a certain threshold

Model specification and Variable Selection

- Stepwise selection method
  - The addition or removal of an explanatory variable is considered in each step along with its statistical significance.
  - The selection process is unstable when the number of events is small
  - Correlated predictors limit the effectiveness of this method
- Occam Razor principle is followed to select the best model.

Model Estimation and Model Performance

- Define a regression model and fit its parameter with cross-validation techniques
- Statistical shrinkage approaches
  - Least absolute shrinkage and selection operator (LASSO)

$$\hat{\beta} = argmin(\|y - X\beta\|^2 + \lambda_1 \|\beta\|_1)$$

  - Elastic net regularization

$$\hat{\beta} = argmin(\|y - X\beta\|^2 + \lambda_2 \|\beta\|^2 + \lambda_1 \|\beta\|_1)$$

- Nested cross-validation to find the optimum parameters of the regularisation

Model Validity

- Internal Validation
  - Evaluate the performance of the model
  - Reproducibility/Generalisability under similar underlying population assumptions
  - Stability of the selection of predictors

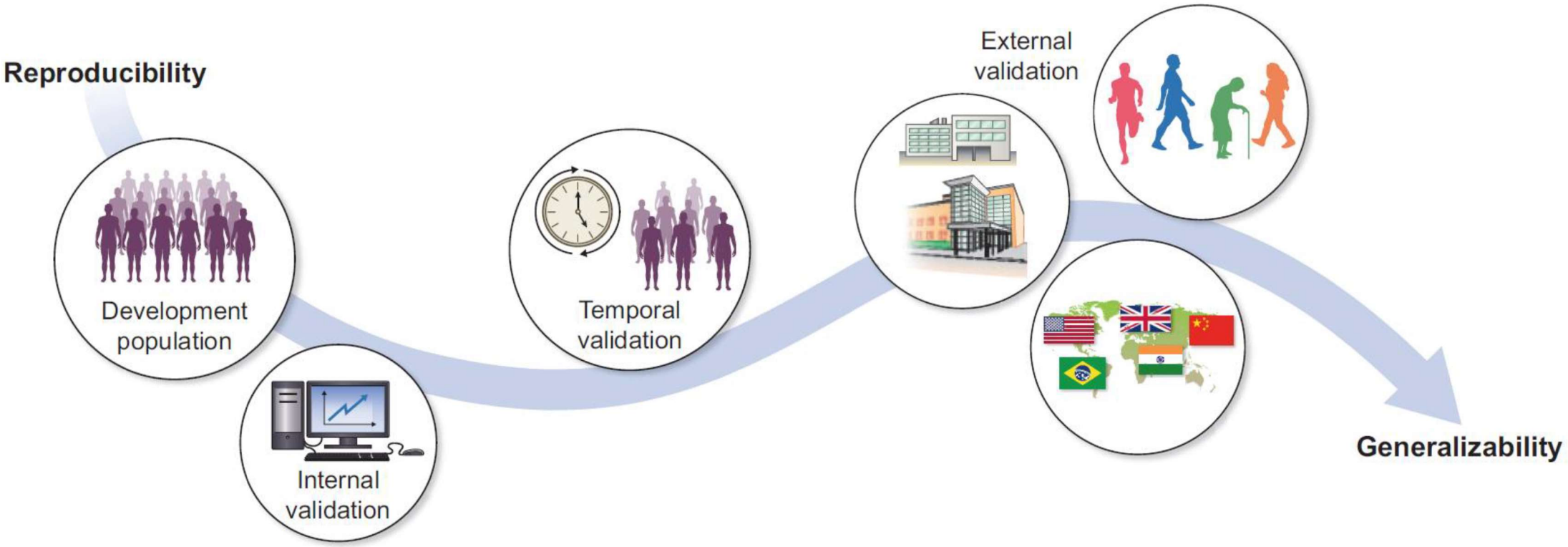
Internal Validation

- Spit-sample validation
  - Training and Validation cohort
- Cross Validation
  - Validation Folds
- Bootstrapping
  - Resampling technique

Model Validity

- Internal Validation
  - Evaluate the performance of the model
  - Reproducibility/Generalisability under similar underlying population assumptions
  - Stability of the selection of predictors
- External Validation
  - Generalisability to ‘plausibly related populations’
  - Patients more recently treated (temporal validation)
  - Patients from other hospitals (geographical validation)
  - Fully different settings (strong external validation)

Reproducibility - Generalizability

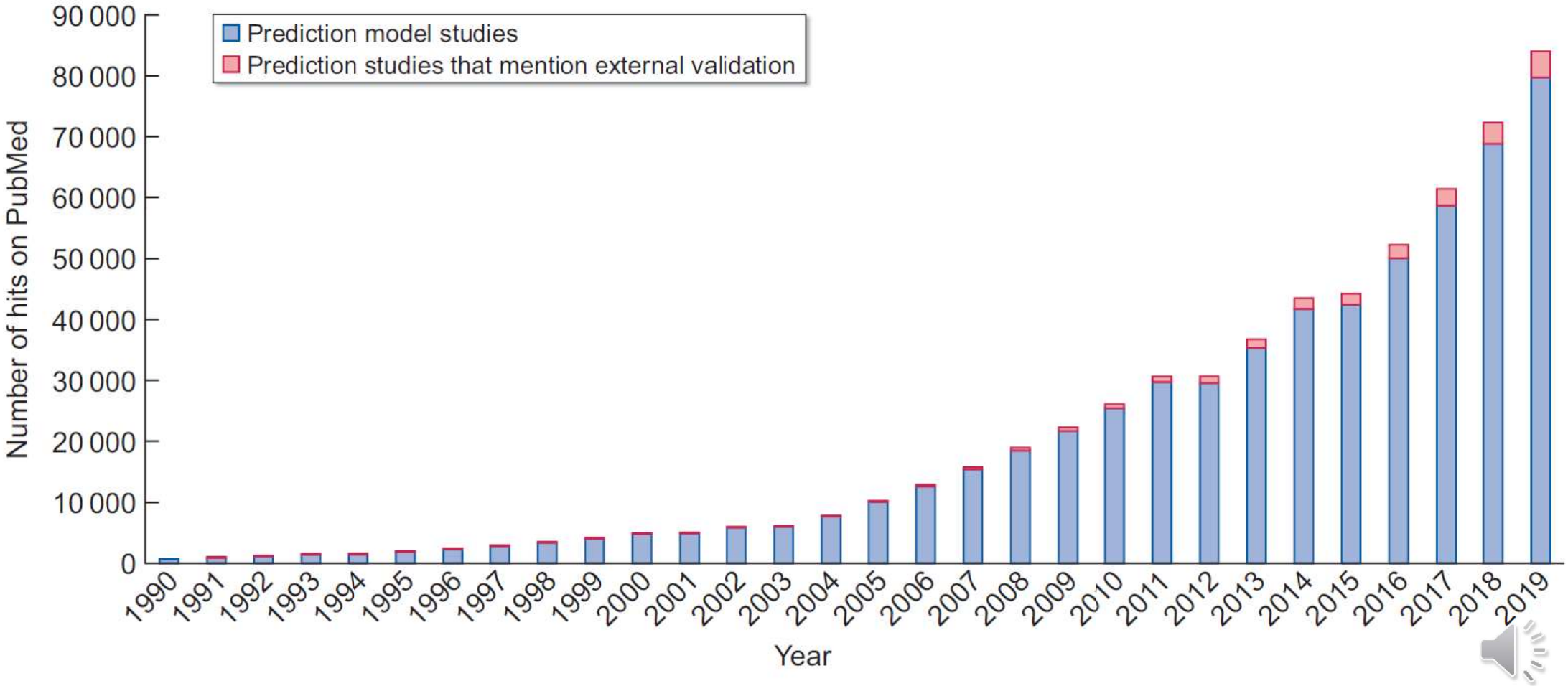


Ramspek et al. ‘External validation of prognostic models: what, why, how, when and where?’, Clinical Kidney Journal, 2021.

External Validation - Generalisability

- External Validation is important to test models generalizability
- External Validation is required to establish a prediction risk model as clinical decision support system
- Generalisability (transportability) involves testing whether a model is transportable to a separate population
- Generalisability should not assessed at the same time as reproducibility

External - Internal Validation



Ramspek et al. 'External validation of prognostic models: what, why, how, when and where?', Clinical Kidney Journal, 2021.

Human Centred Interface

- Model presentation
  - Graphs, charts, model formulas
  - Interactive tools?
- Application type
  - Web-based applications
  - Mobile and table applications
  - Clinical decision-making?

Summary

- Effective clinical decision-making systems require the acceptance of healthcare users
- Traditional clinical systems follow a strict process of development and validation pipeline that fulfills certain requirements
- Understanding clinical needs and designing applications around them are important

References

- Steyerberg et al. ‘Towards better clinical prediction models: seven steps for development and an ABCD for validation’, European Heart Journal, 2014.
- Ramspek et al. ‘External validation of prognostic models: what, why, how, when and where?’, Clinical Kidney Journal, 2021.