A systematic review and critical appraisal of risk prediction models for live donor solid organ transplantation: unmasking flawed predictions

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13.11.2019

work in progress

with Aschauer C., Oberbauer R., Heinze G.

Disclosure

- Guideline developer
- Advisory board member European Renal Best Practice
- Cochrane author

- No conflicts

Live donor solid organ transplantation

- live donor = living human individual
- Solid organ transplantation for which living organ donation is possible: kidney and liver

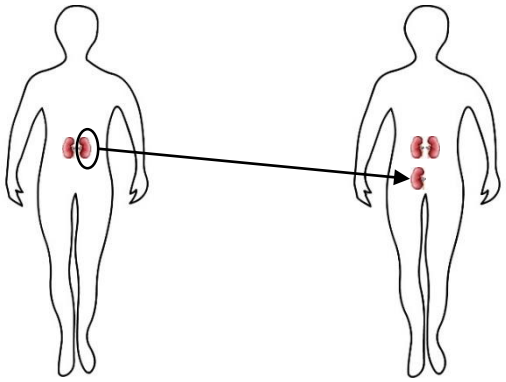
Live donor solid organ transplantation

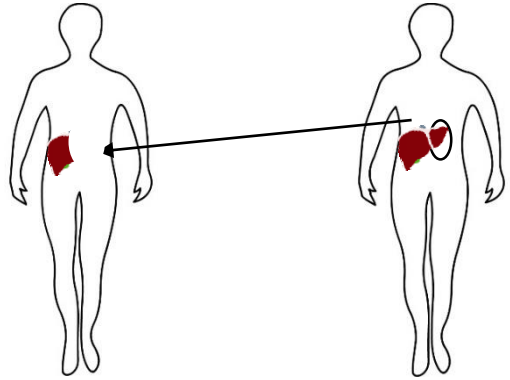
- Why for the world would you take an organ from an healthy individual?
- Because the person in need of that organ is seriously ill

Motivation

- Kidney tx: better outcomes for eligible patients, cost effective
- Liver tx: certain death without tx

<u>BUT living donor = healthy (emotionally) related person</u>





Motivation - PRIMUM NIHIL NOCERE

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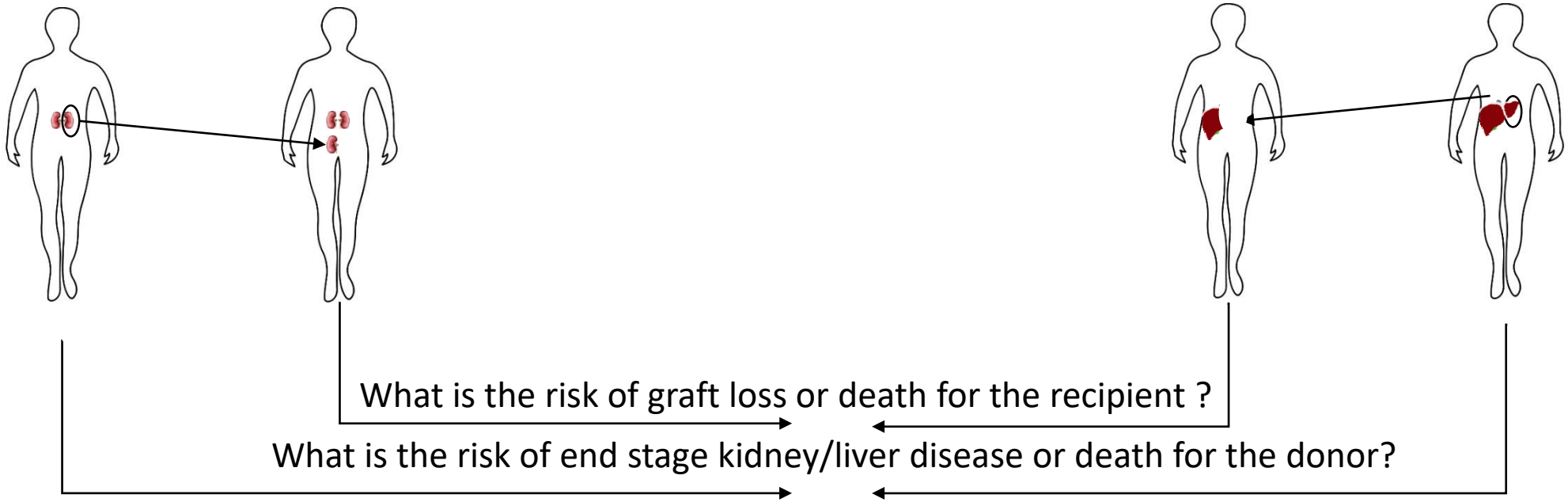

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- Kidney tx: better outcomes for eligible patients, cost effective
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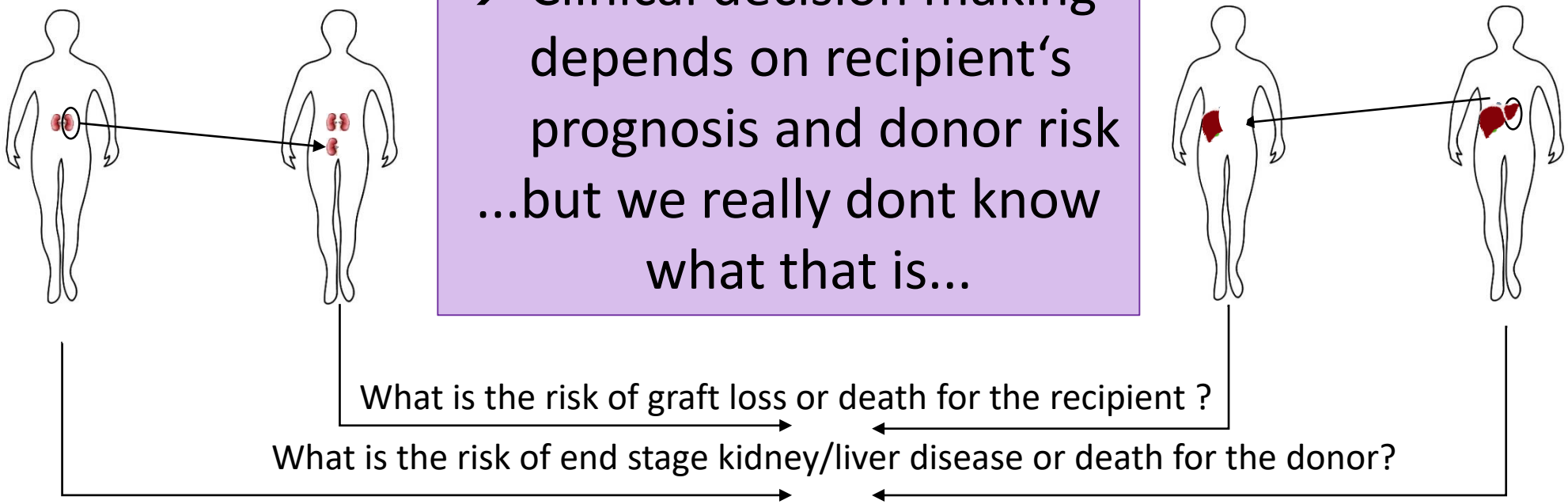
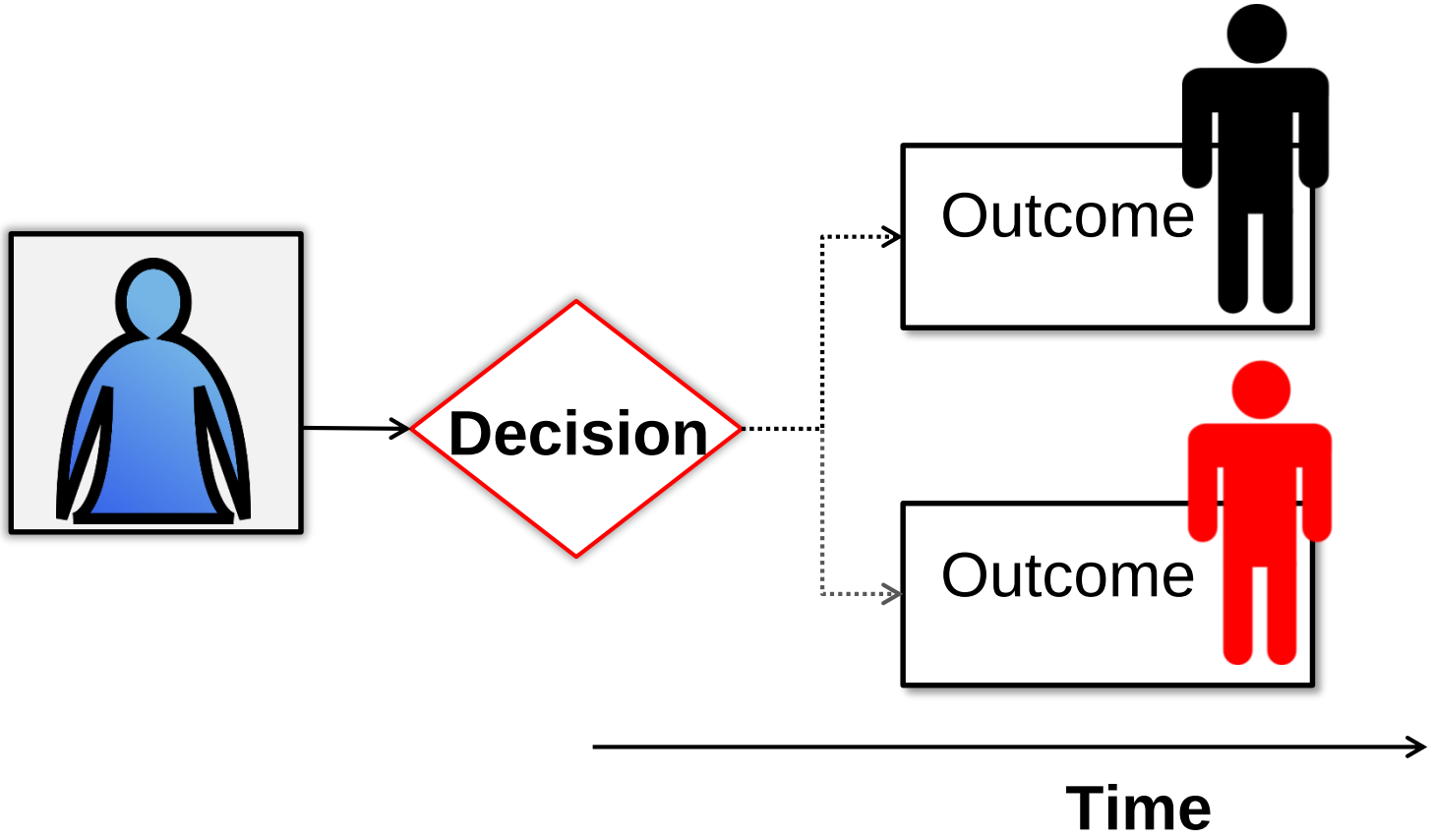
→ Clinical decision making depends on recipient‘s prognosis and donor risk
...but we really dont know what that is...



Risk prediction



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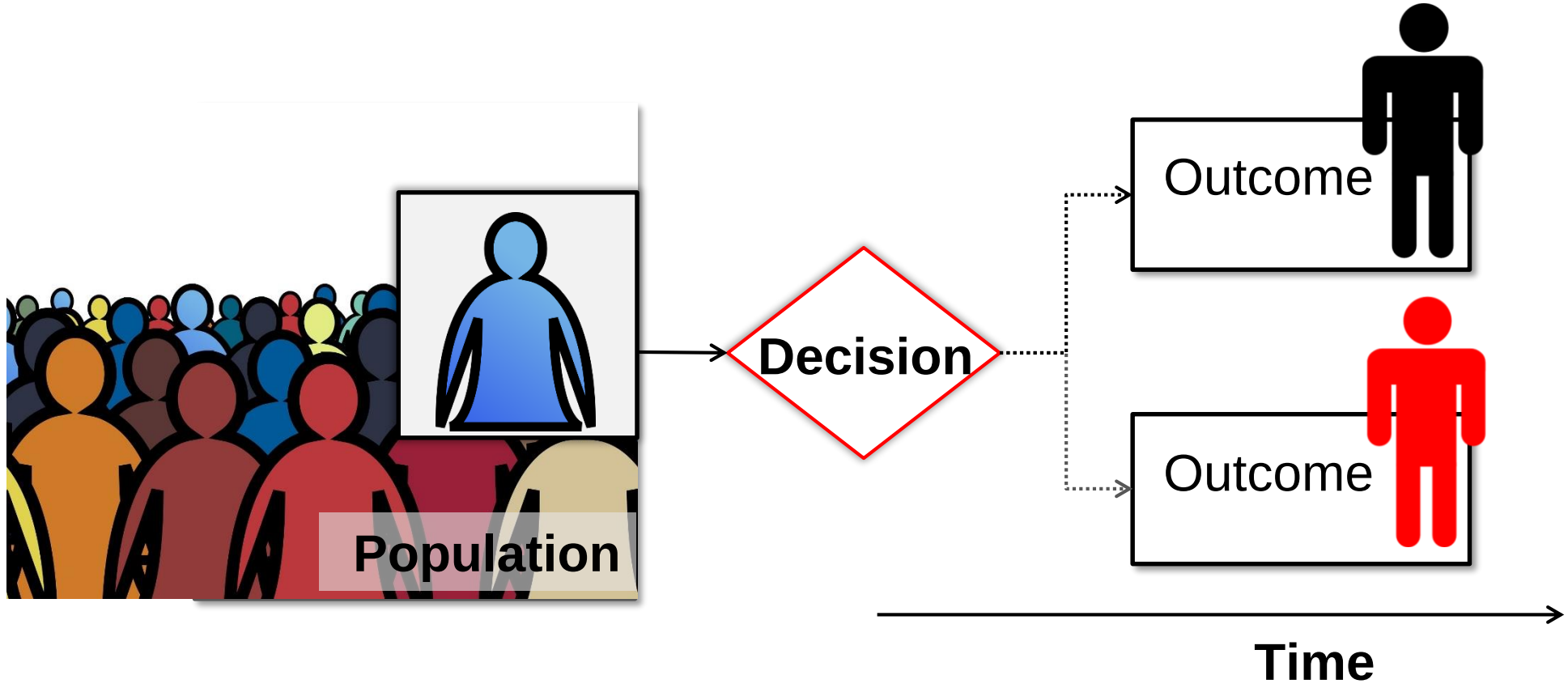
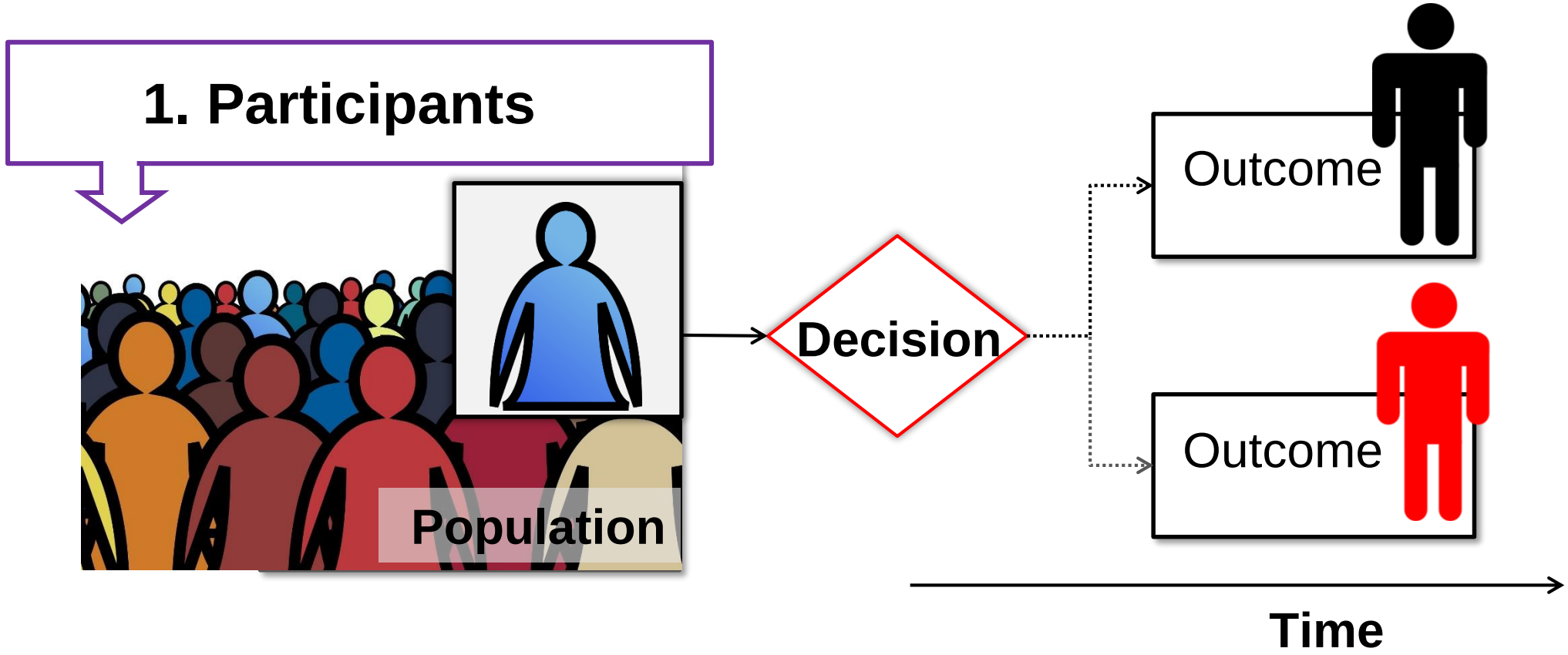


Probability of outcome = f(predictor variables)

Risk prediction - RoB



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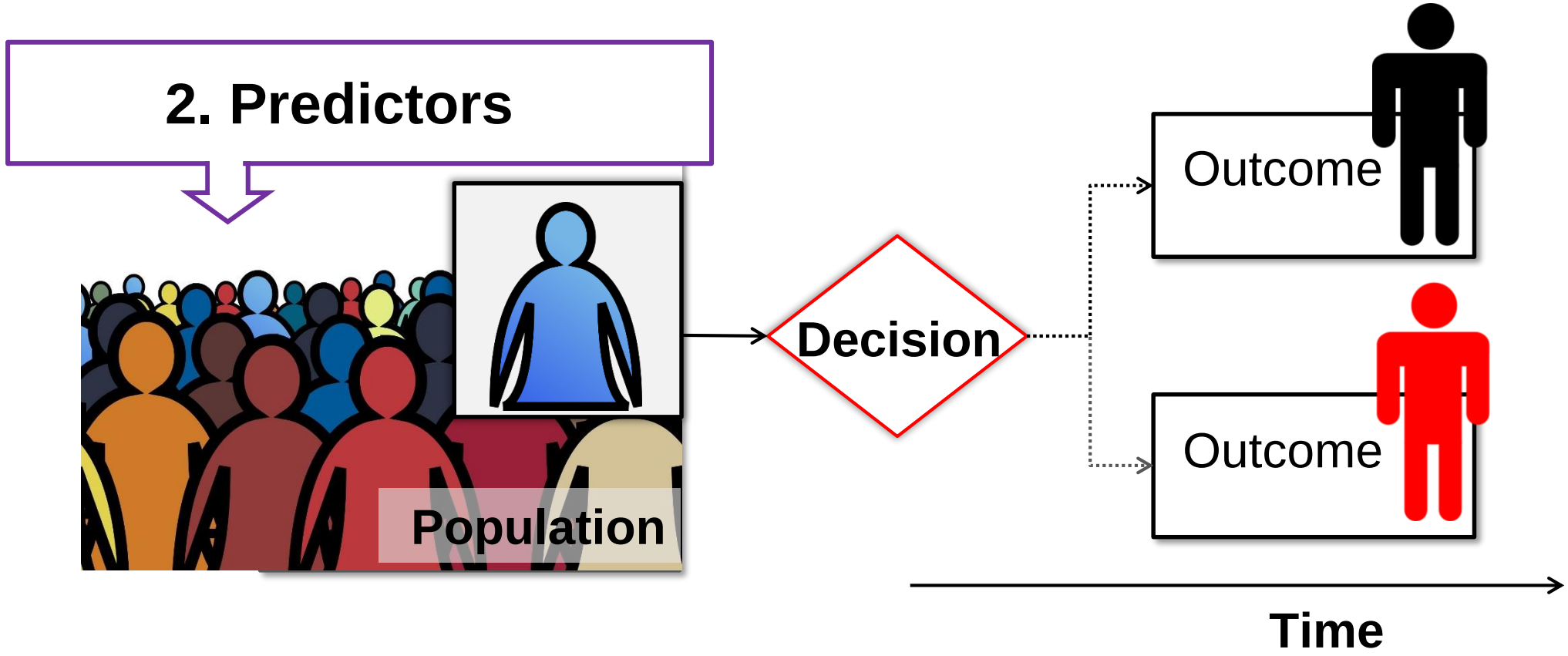

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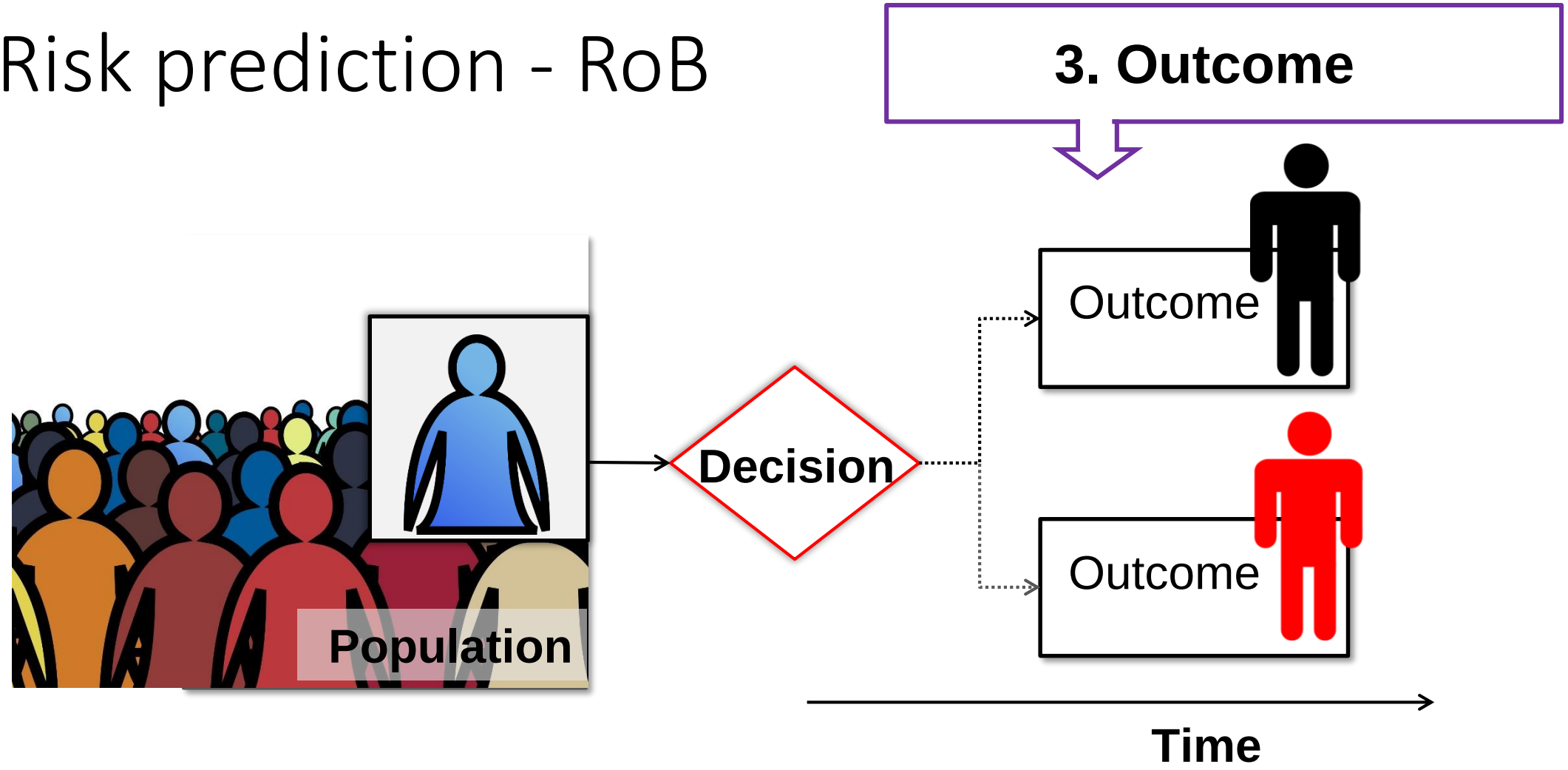

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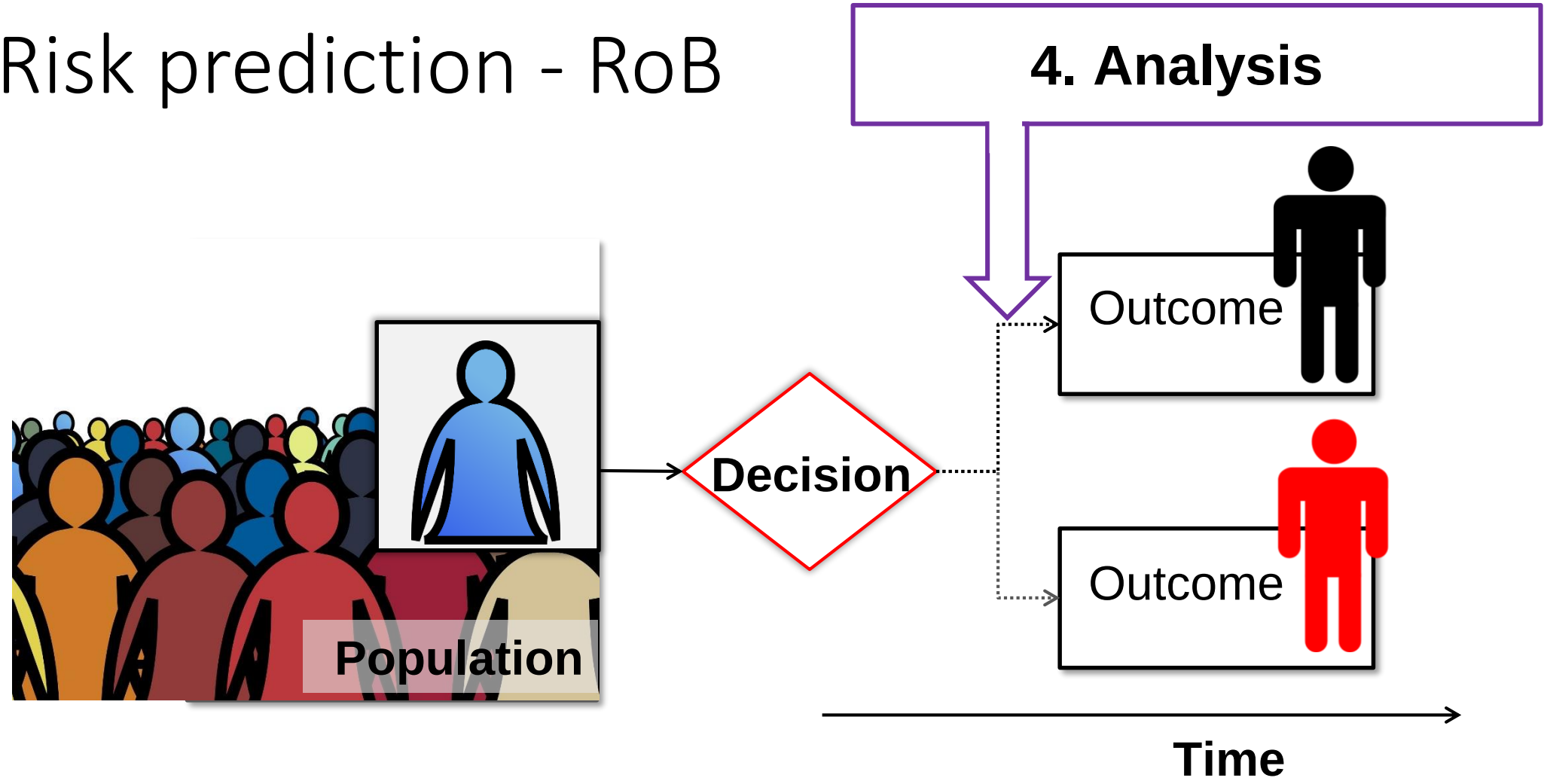

Probability of outcome = f(predictor variables)

Systematic Review Aim

- Identify existing risk prediction models in living donor solid-organ transplantation

→includes kidney and liver

- primary
  - determine the number of risk prediction models published in live donation (quantity)
  - determine what types of outcomes in recipient and donors in live donation are predicted (coverage)
  - determine the quality of reporting and risk of bias of these risk predication models
- secondary
  - identify methodological approaches to including donor information in recipient model building
  - how many studies for what type of live donation, type of risk
  - provide a useful overview and critical appraisal of risk calculators for clinicians

PICOM table using CHARMS

Item 1) Prognostic vs diagnostic prediction

To review prognostic models to predict future events (exclude diagnostic models)

Item 2) Intended scope of review

Models to inform clinicians, patients and their potential living organ donors on outcomes after living donor tx

Item 3) Type of prediction modelling studies

any prediction model, with or without validation

Item 4) Target population

Recipients of and donors for live donation in either kidney or liver transplantation

Item 5) Outcomes to be predicted

Any future events in either donor or recipient after transplantation, most importantly but not limited to graft loss, recipient and donor survival

Item 6) Time span of prediction

No limitation for time span as long as predicted outcomes occur after transplantation but are predicted before tx

Item 7) Intended moment of using the model

Models to be used to inform the decision on whether the transplantation using a kidney or liver from a particular living donor should be performed

http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1001744

Search

- Systematic literature search for publications on live donation in kidney and liver transplantation, filtered for risk prediction in MEDLINE (Ovid) and crosschecking of included studies for relevant citations

- Prognosis Filter published by Geersing (PLoS One 21)

Geersing GJ, Moons KG. Search filters for finding prognostic and diagnostic prediction studies in Medline to enhance systematic reviews. PLoS One. 2012;7(2):e32844.

Data extraction, critical appraisal and quality of reporting

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Guidelines and Guidance

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

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Introduction

Prediction models, both diagnostic and prognostic, are becoming increasingly abundant in the medical literature [1–3]. Diagnostic models are aimed at calculating the probability that an individual has a certain disorder, such as deep vein thrombosis [4,5], ankle fractures [6], or conjunctivitis [7]. Prognostic prediction models concern the prediction of the probability or risk of the future occurrence of a particular outcome or event in individuals at risk of such an event. Prognostic models may involve models for individuals with a particular health condition, such as prediction of recurrence or death after diagnosis of breast cancer [8] or mortality after cardiac surgery [9], but also includes models for predicting the occurrence of future outcomes in apparently healthy individuals such as the risk of developing a coronary event [10] or type 2 diabetes mellitus [11].

There are over 100 models for predicting outcome after brain trauma [12], over 60 models for breast cancer prognosis [13], 45 models for cardiovascular events after being diagnosed with diabetes [14], 43 models for predicting prevalent and incident type 2 diabetes [15], and 20 models for predicting prolonged intensive care stay after cardiac surgery [16]. Furthermore, prediction models are increasingly being appraised and recommended for formal risk assessment in clinical guidelines [17,18].

To evaluate the proliferation of prediction models, systematic

Summary Points

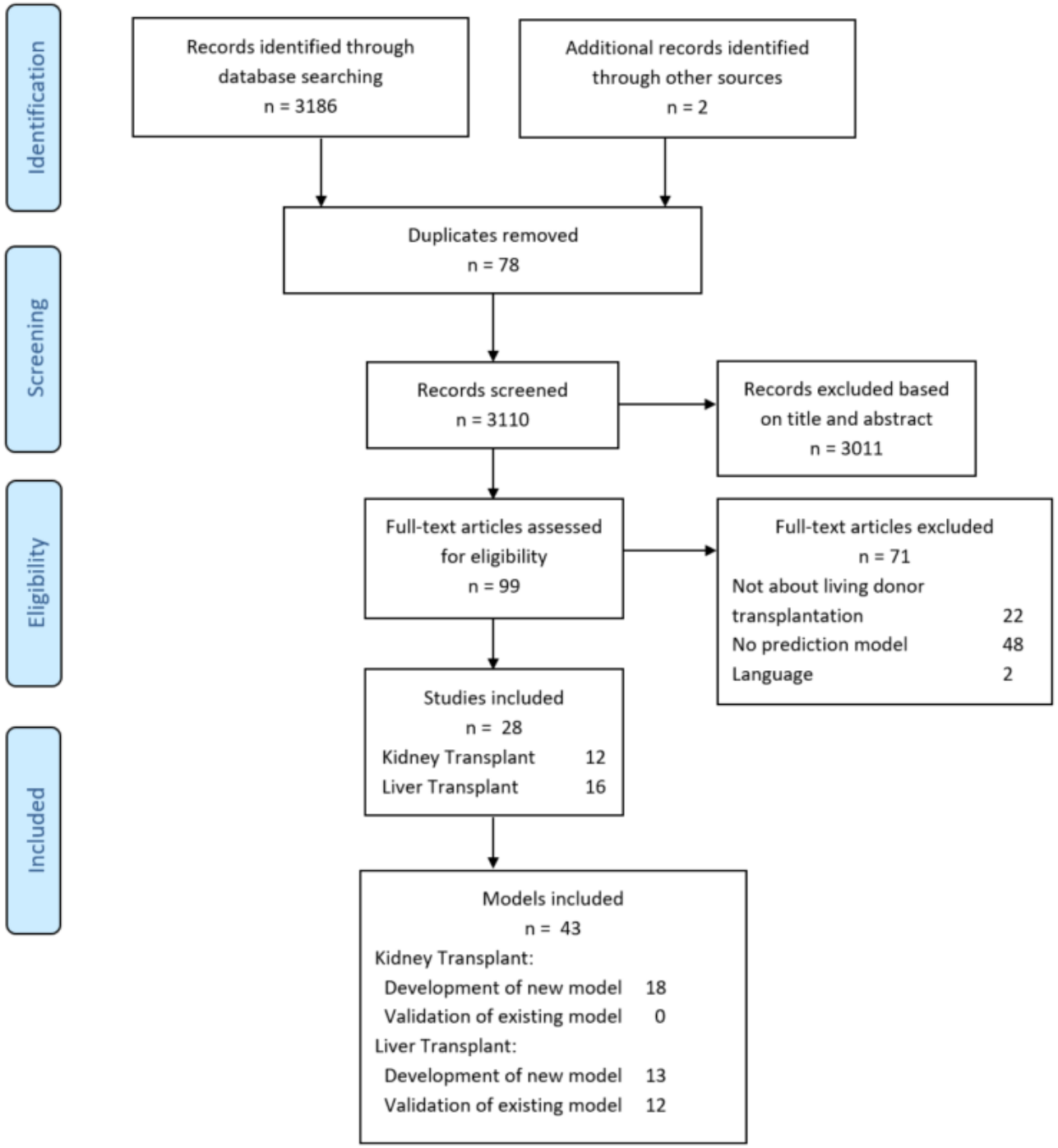
- Publications on clinical prediction models have become abundant for both prognostic and diagnostic purposes. Systematic reviews of these studies are increasingly required to identify and critically appraise existing evidence.
- No specific guidance exists to help frame a well-defined review question and determine which details to extract and critically appraise from primary prediction modelling studies.
- Existing reporting guidelines, quality assessment tools, and key methodological publications were examined to identify seven items important for framing the review question and 11 domains to extract and critically appraise the primary included studies.
- Together these items and domains form the **CH**ecklist for critical **A**ppraisal and data extraction for systematic **R**eviews of prediction **M**odelling **S**tudies (CHARMS).

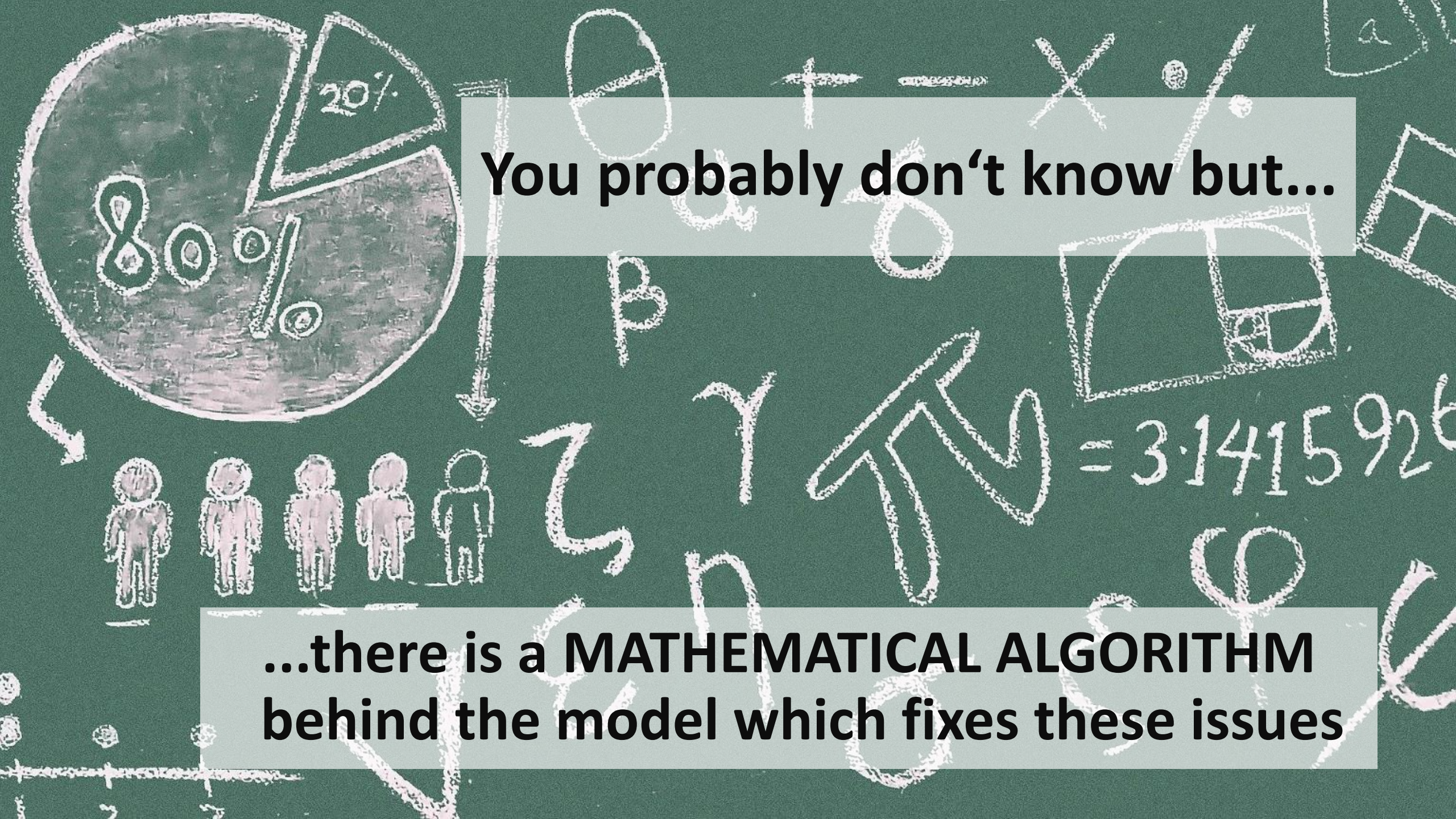
3,12,14,15,27–30]. Some items, such as "selection of predictors during multivariable modelling" and "model presentation", are somewhat more specific to regression approaches. The checklist is not intended for systematic reviews of primary studies of prognostic factors, for which we refer to the QUIPS tool

TRIPOD Checklist: Prediction Model Development and Validation

Section/Topic	Item		Checklist Item	Page
Title and abstract				
Title	1	D;V	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	
Abstract	2	D;V	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	
Introduction				
Background and objectives	3a	D;V	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	
	3b	D;V	Specify the objectives, including whether the study describes the development or validation of the model or both.	
Methods				
Source of data	4a	D;V	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	
	4b	D;V	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	
Participants	5a	D;V	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	
	5b	D;V	Describe eligibility criteria for participants.	
	5c	D;V	Give details of treatments received, if relevant.	
Outcome	6a	D;V	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	
	6b	D;V	Report any actions to blind assessment of the outcome to be predicted.	
Predictors	7a	D;V	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	
	7b	D;V	Report any actions to blind assessment of predictors for the outcome and other predictors.	
Sample size	8	D;V	Explain how the study size was arrived at.	
Missing data	9	D;V	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	
Statistical analysis methods	10a	D	Describe how predictors were handled in the analyses.	
	10b	D	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	
	10c	V	For validation, describe how the predictions were calculated.	
	10d	D;V	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	
	10e	V	Describe any model updating (e.g., recalibration) arising from the validation, if done.	
Risk groups	11	D;V	Provide details on how risk groups were created, if done.	
Development vs. validation	12	V	For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	
Results				
	13a	D;V	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A	

Results: search





You probably don‘t know but...

...there is a MATHEMATICAL ALGORITHM behind the model which fixes these issues

Take Home 1

- Please be very clear about limitations whenever you report magic mathematics!

Take Home 2

- Risk prediction in living donor solid organ transplantation

  → most models poorly done / reported / flawed by high risk of bias and therefore USELESS

  → very important to send this message to clinicians / potential users of the models


THANK YOU