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Early Psychosis: Interventions & Clinical detection

Transdiagnostic risk calculator for automatic detection of individuals at-risk of psychosis

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Early Psychosis:
Interventions &
Clinical detection

1. Issues in detection of individuals at clinical high risk for psychosis
2. Development and validation of transdiagnostic risk calculator for psychosis
3. Implementing the calculator in clinical routine
4. Future work

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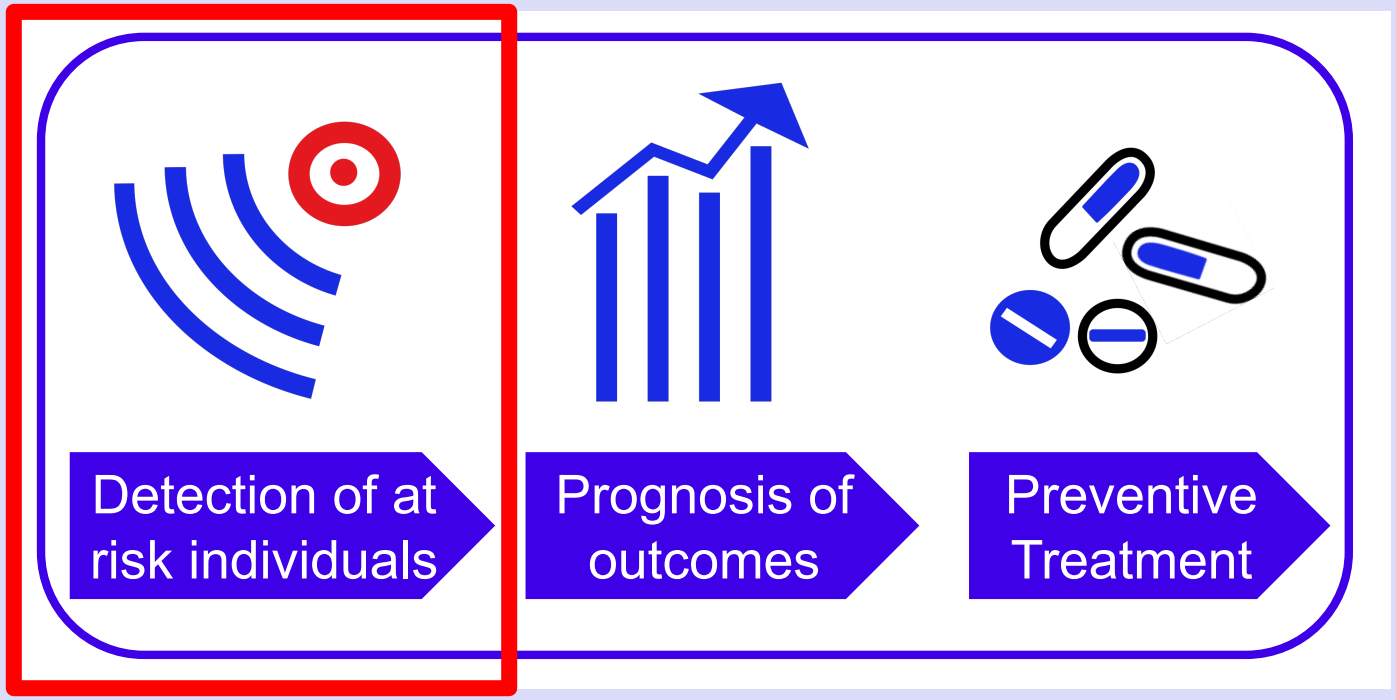
Clinical high risk for psychosis (CHR-P)

- Subtle symptoms and functional impairment
- Identified using CHR-P assessments e.g. CAARMS
- 20% probability of developing psychosis over 2 years
- Potential to alter course of psychosis
- Reduce duration of untreated psychosis

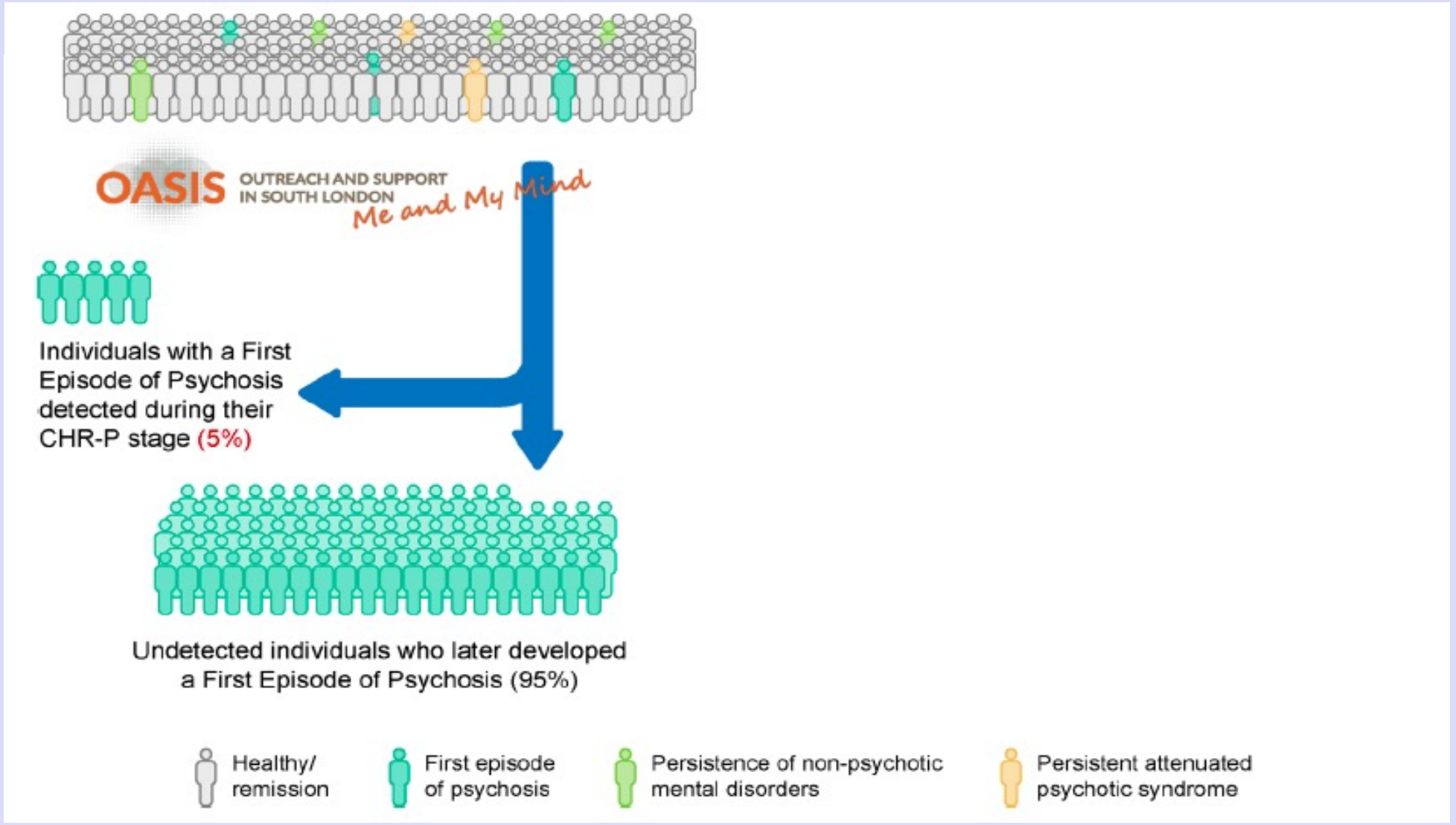
Clinical High Risk for Psychosis CHR-P

- Impact is determined by:



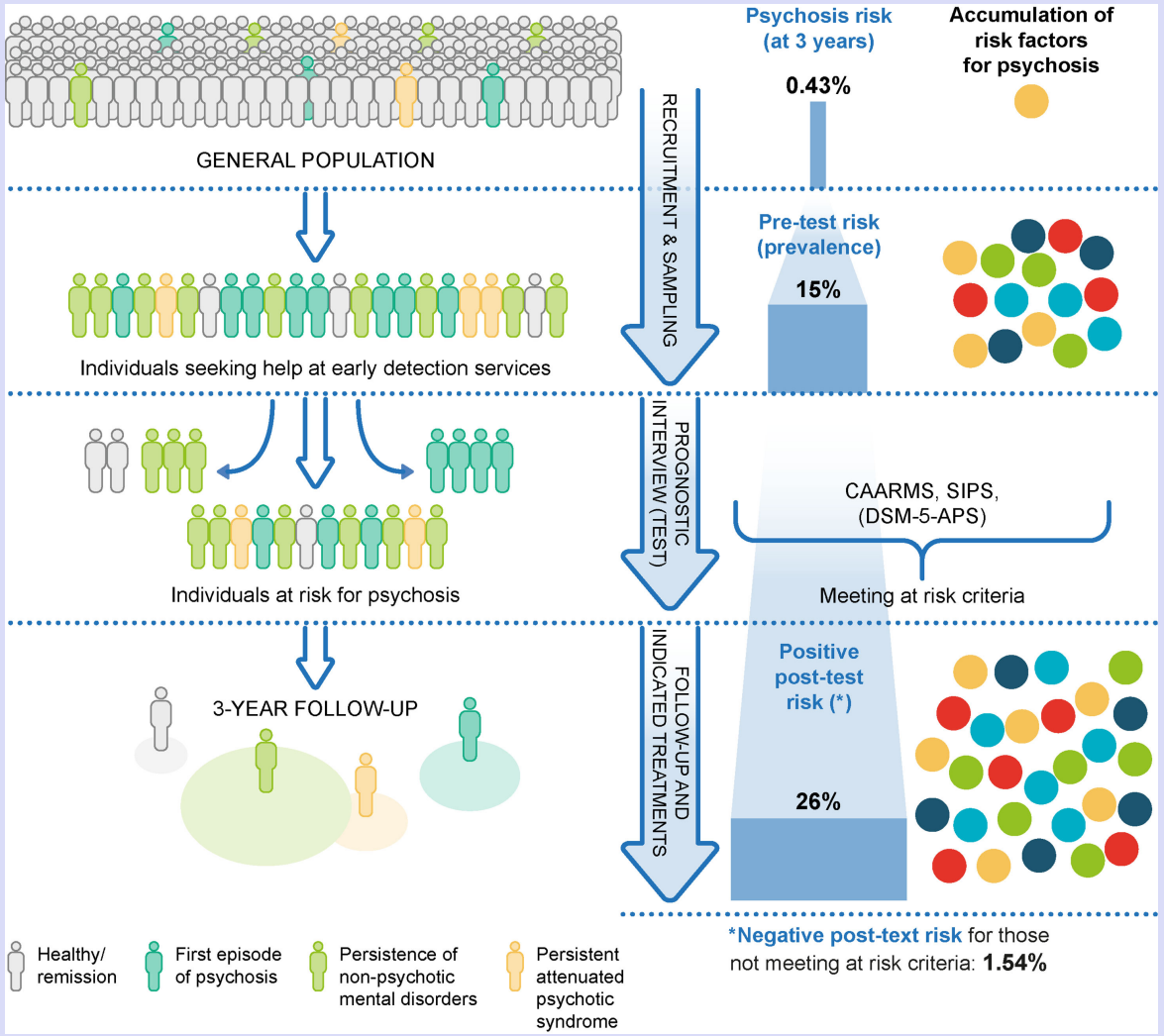
Detection

- First rate-limiting step
- Inefficient detection has big impact
- If you have the most accurate prognostic model and most effective preventive treatment, this would only help a small proportion of people who could benefit



Fusar-Poli et al Front. Psychiatry 2019

Recruitment strategies



- Recruitment affects the level of pre-test risk
- Pre-test risk affects post-test risk
- If CHR-P tools used in general population: 5% CHR-P+ (at 3 years)

Fusar-Poli et al Front. Psychiatry 2019

Improving detection

- Outreach can boost number of people detected[1]
- But also increases number of false positives, diluting risk[2]
- Need solutions that boost our ability to detect people early while maintaining risk enrichment

[1]McGorry et al., 2018
[2]Fusar-Poli et al., 2019

Different, complementary targets

Community

Primary care

Secondary care

Different, complementary targets

Community

- Low psychosis risk
- If everyone assessed, lots of false positives
- Enrich sample with pre-screening tools
- PRIME, PQ-16 etc.

Fusar-Poli et al Front. Psychiatry 2019

Different, complementary targets

Primary care

- 60% young people seen by GPs once a year
- Key referral source (21% at OASIS)
- Higher number of primary care visits result in reduced DUP in FEP
- GPs don’t feel they have the skills to identify CHR-P
- Particularly in areas with limited outreach
- Decision support could be beneficial (e.g. P-risk)

Fusar-Poli et al Front. Psychiatry 2019

Different, complementary targets

Secondary care

- Already help-seeking
- Highest psychosis risk
- Receiving treatment for mental health conditions
- Could be accessing more targeted support through CHR-P services

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Precision psychiatry

Individual prediction of **disease onset**, clinical outcomes or treatment response

Information from genetics, neuroimaging or **electronic health records (EHRs)**

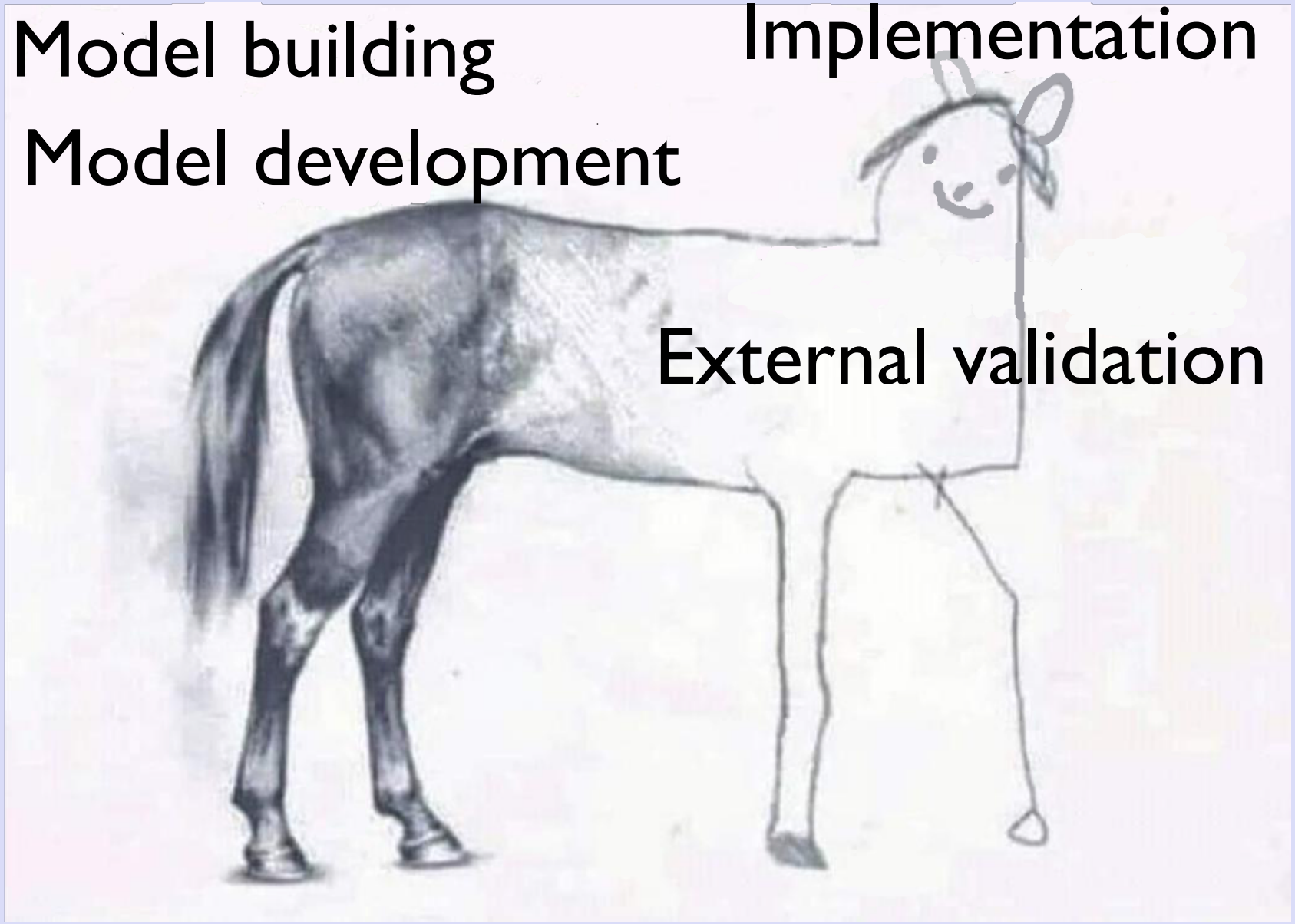
No prediction models have entered clinical practice in psychiatry: a **clear implementation challenge**

Model building

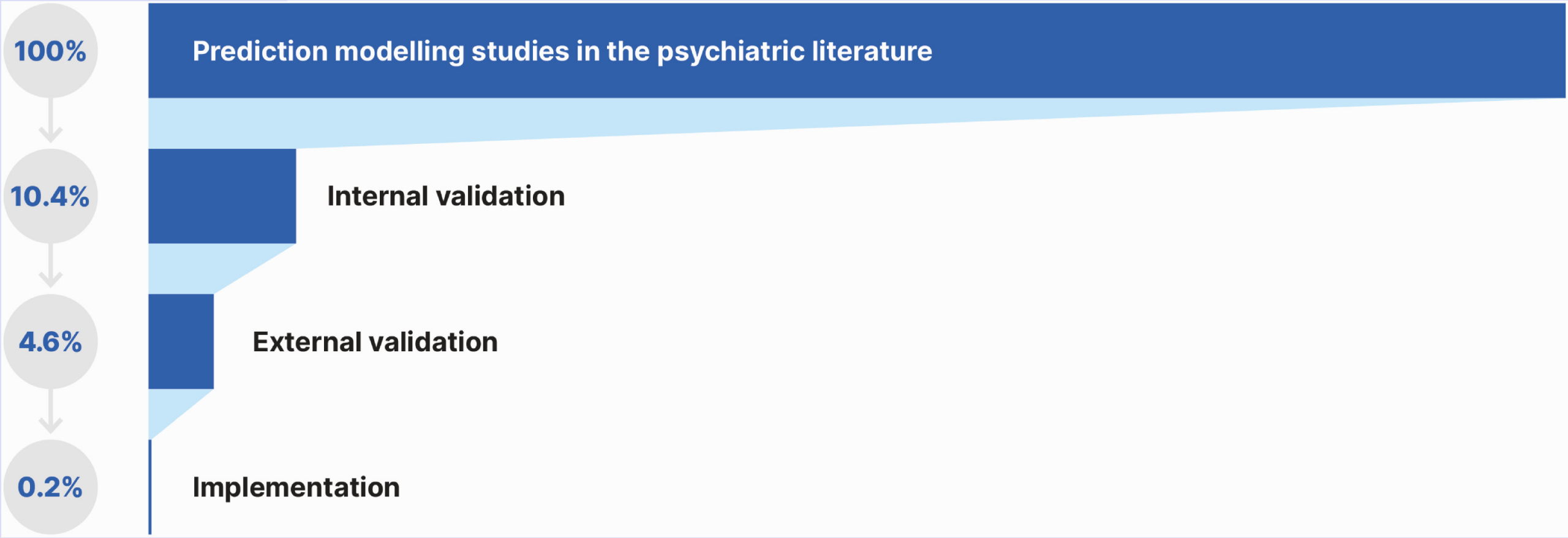
Model development

Implementation

External validation



Salazar de Pablo et al., 2020



Salazar de Pablo et al., 2020

Why EHRs?

- Rich in detail
- No need for additional procedures
- Low additional financial and labour costs
- Large scale

Model development

- Predictors chosen *a priori*:
  - Index diagnosis
  - Age
  - Gender
  - Age*gender
  - Ethnicity
- Kaplan-Meier failure function for incidence of psychosis
- Cox proportional hazards multivariate complete-case analyses
- Outcome: hazard ratio of developing psychotic disorder within 6 years of index diagnosis

Core characteristics

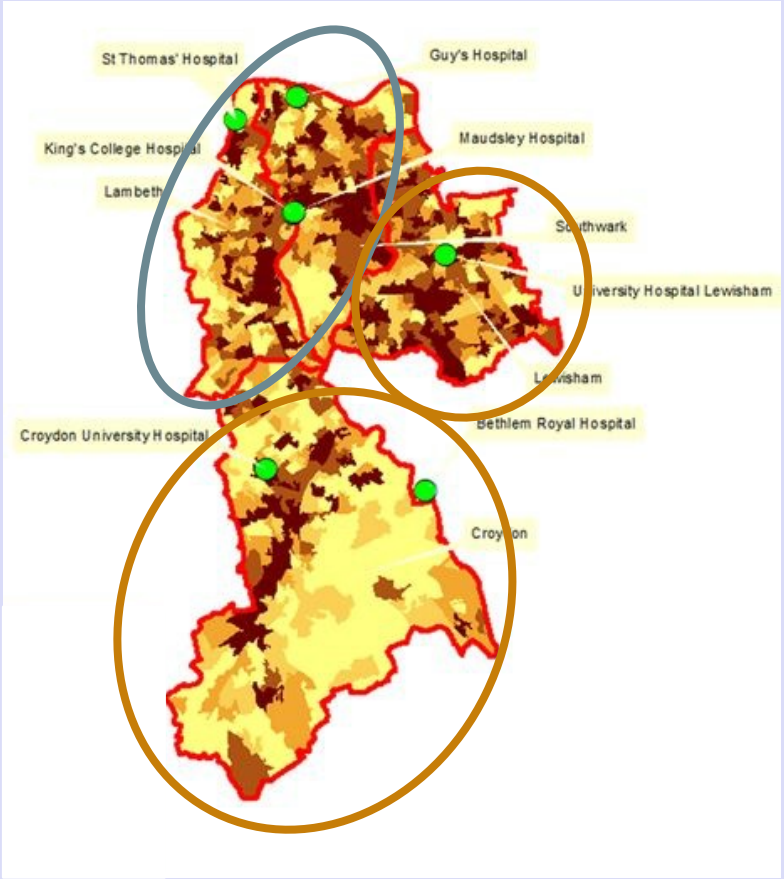
Robust	Predictors selected through *a priori* clinical knowledge
Pragmatic	Not interested in causes of psychosis
Cheap	Predictors routinely collected by clinicians
Automatic	Electronic health records as well as manual entry of predictors
e-Health	Implemented online
Scalable	Screens large electronic health records
Optimisable	Further refined by the inclusion of other predictors

Derivation & validation sets

Data was split by geographical location, not random selection

Better for model generalisability

Derivation
Lambeth & Southwark
N = 33,820



Validation
Croydon & Lewisham
N = 54,716

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TRANSDIAGNOSTIC PREDICTION OF PSYCHOSIS IN SECONDARY MENTAL HEALTH CARE

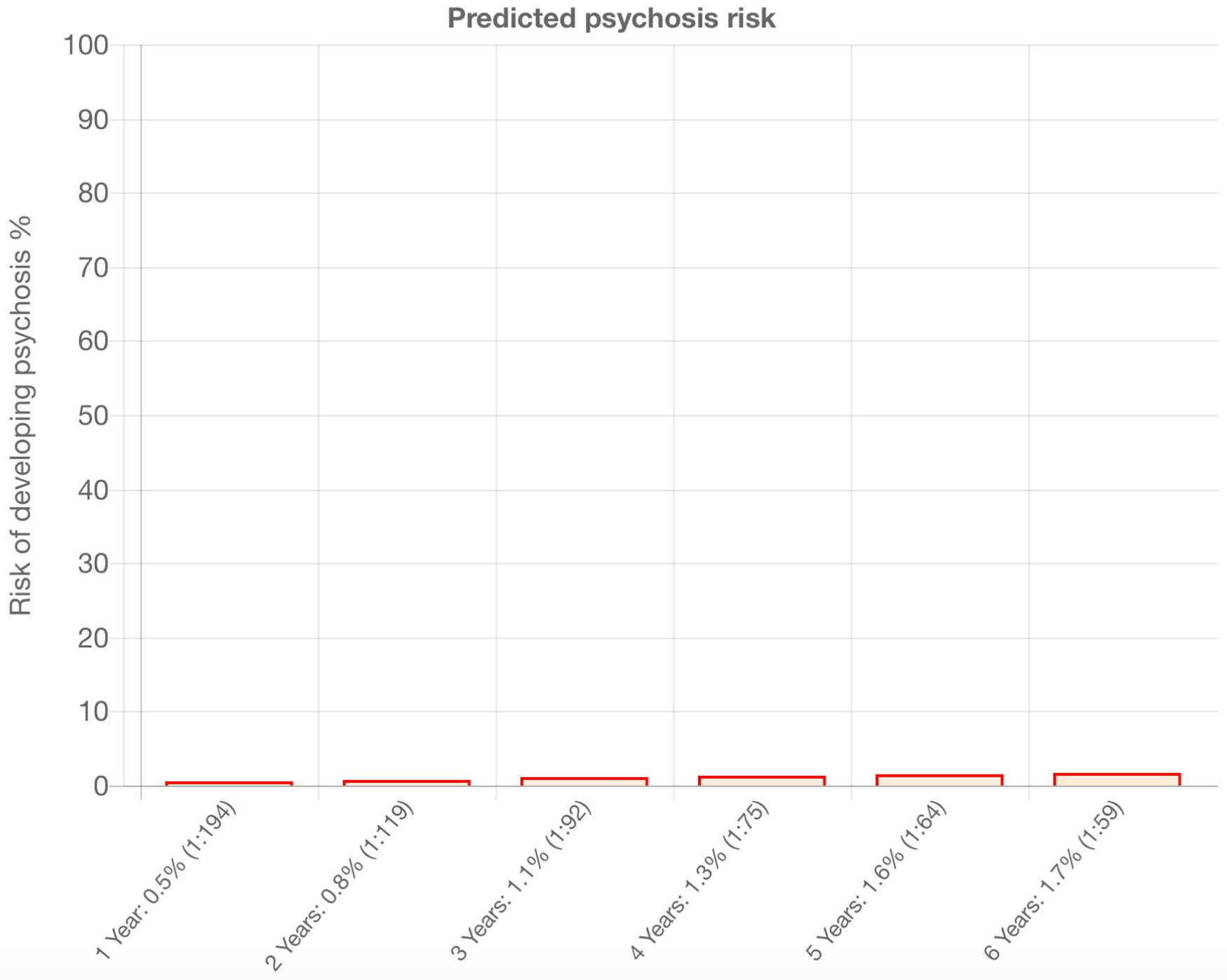
Online Calculator.

PROGRESS

Your entry was;

Age: **14**
Gender: **Female**
Ethnicity: **White**
Diagnosis Category: **Non bipolar mood disorders**
Diagnosis Name: **Mild depressive episode**

www.psychosis-risk.net


Predicted psychosis risk
Risk of developing psychosis %
100
90
80
70
60
50
40
30
20
10
0
1 Year: 0.5% (1:194)
2 Years: 0.8% (1:119)
3 Years: 1.1% (1:92)
4 Years: 1.3% (1:75)
5 Years: 1.6% (1:64)
6 Years: 1.7% (1:59)

TRANSDIAGNOSTIC PREDICTION OF PSYCHOSIS IN SECONDARY MENTAL HEALTH CARE

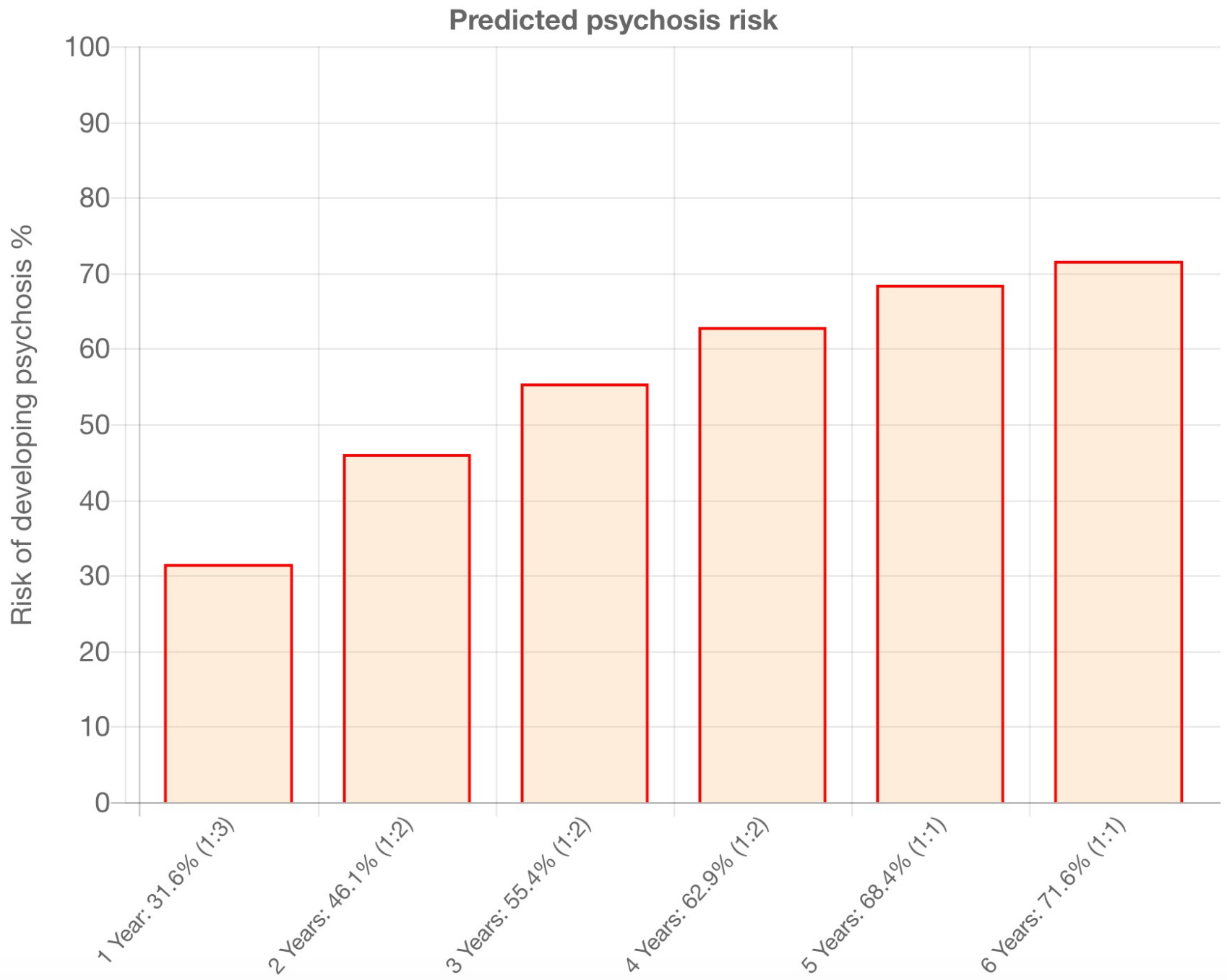
Online Calculator.

PROGRESS

Your entry was;

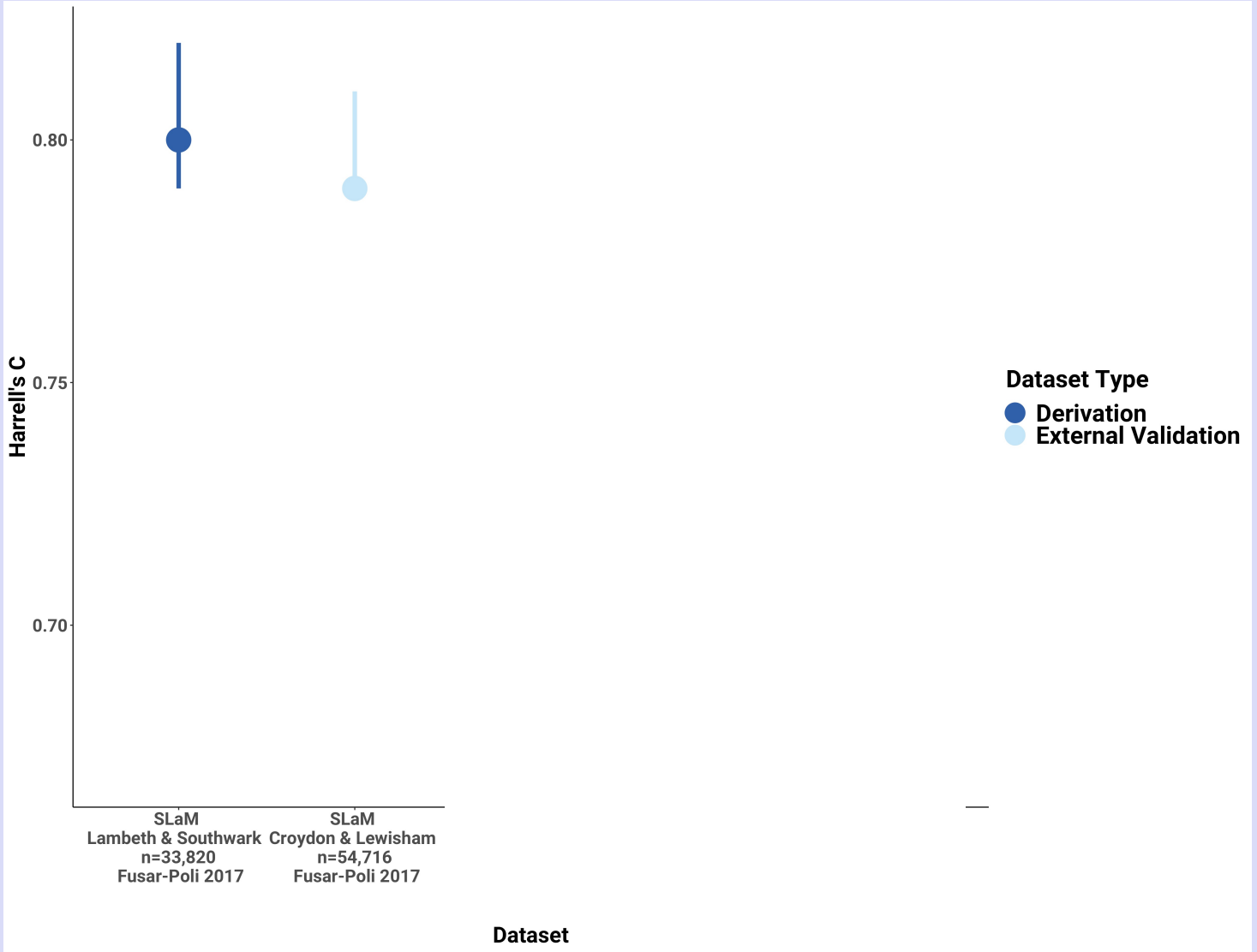
Age: **35**
Gender: **Male**
Ethnicity: **Black**
Diagnosis Category: **Acute and transient psychotic disorders**

www.psychosis-risk.net


Predicted psychosis risk
Risk of developing psychosis %
100
90
80
70
60
50
40
30
20
10
0
1 Year: 31.6% (1:3)
2 Years: 46.1% (1:2)
3 Years: 55.4% (1:2)
4 Years: 62.9% (1:2)
5 Years: 68.4% (1:1)
6 Years: 71.6% (1:1)

Model performance

- Developed and validated on retrospective EHR data
- Harrell's C = 0.80 in derivation set
- Harrell's C = 0.79 in validation set



UK replications

Camden and Islington NHS Foundation Trust

- No CHR-P services
- No CAMHS
- Fewer patients of black ethnicity
- Lower incidence of psychosis (vs SLaM)

Fusar-Poli et al., 2019 Scz Bull

Oxford Health NHS Foundation Trust

- No CHR-P services
- No specialist addiction services
- More patients of white ethnicity
- Lower incidence of psychosis (vs SLaM)
- More rural area

Puntis et al., 2021 Scz Res

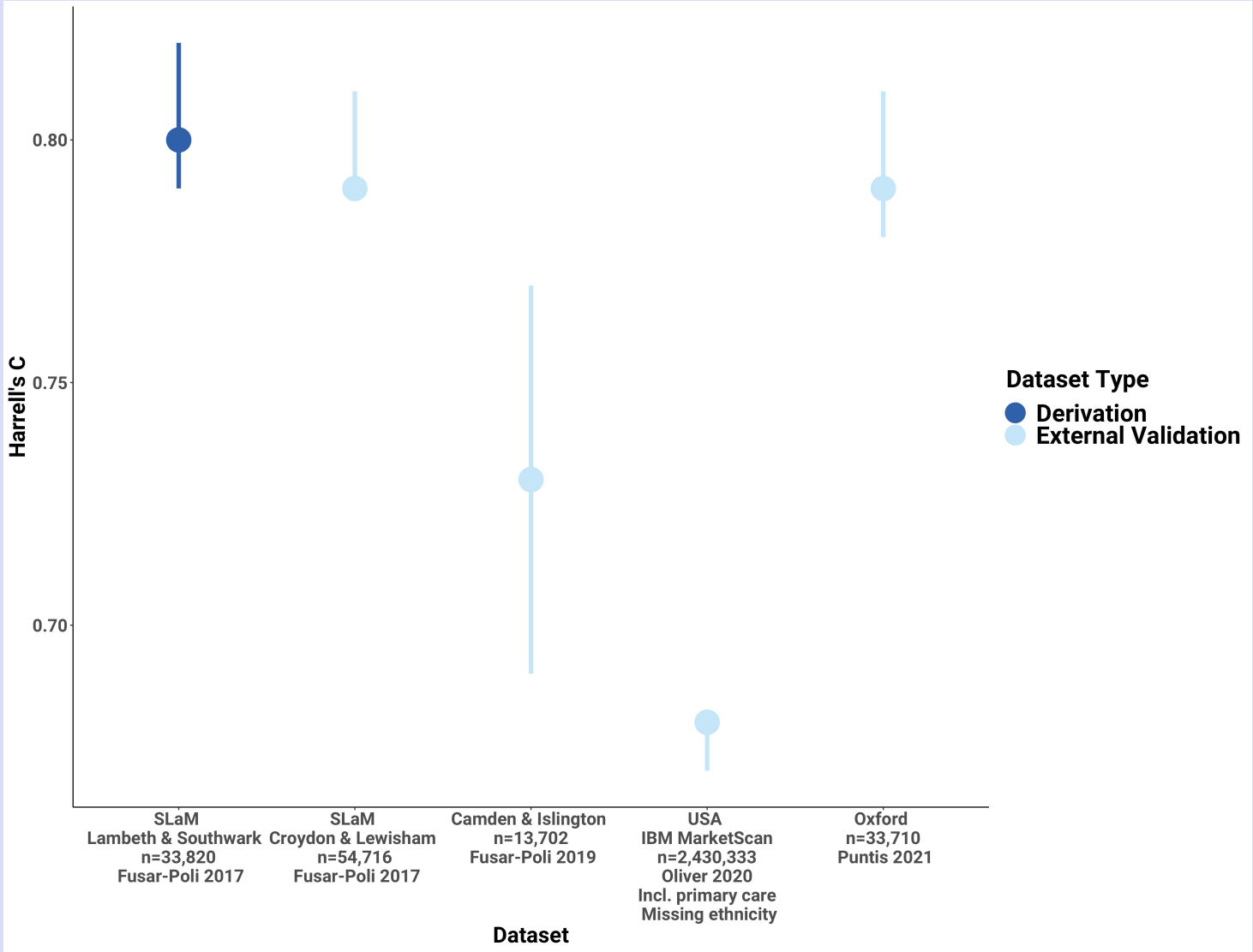
US replication

- Huge sample (2.4m patients)
- No CHR-P services
- No patient-level ethnicity data - imputed based on area-level ethnicity data
- Limited follow-up time (mean = 461 days vs 1560 in SLaM
- Mix of primary and secondary care data

Oliver et al., 2021 Trans. Psych

Model performance

- Harrell's C = 0.80 in derivation set
- Harrell's C = 0.79 in validation set
- Good performance replicated in other settings (0.68-0.79)



Is it feasible to implement the transdiagnostic risk calculator in real-world clinical care?

In-vitro phase

- Integrated risk calculator in local EHR for prospective use
- Consulted with patient support groups
- Consulted with local clinicians

In vivo phase

NHS England

Any new patient accessing secondary mental health care

Clinician-entered variables:

- Age
- Gender
- Age*Gender
- Self-assigned ethnicity
- ICD-10 diagnosis

Automatic risk estimation
Risk >5% at 2 years

Email/phone prompts to clinician

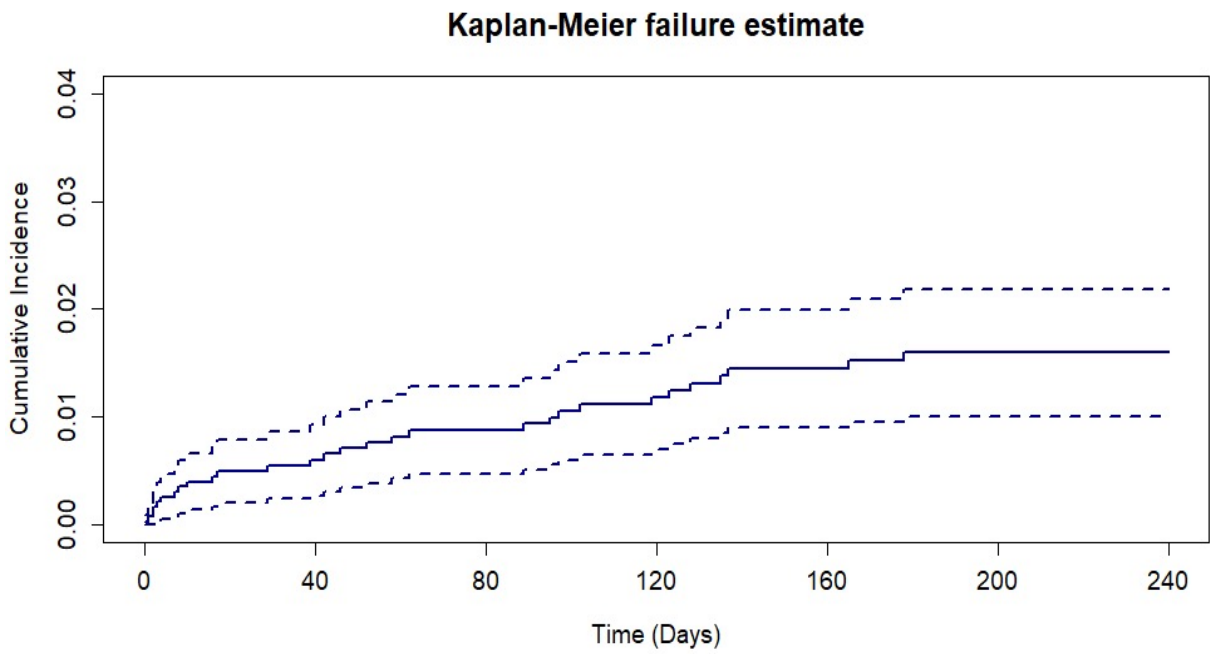
Patient referred to CHR-P service

Treatment as usual

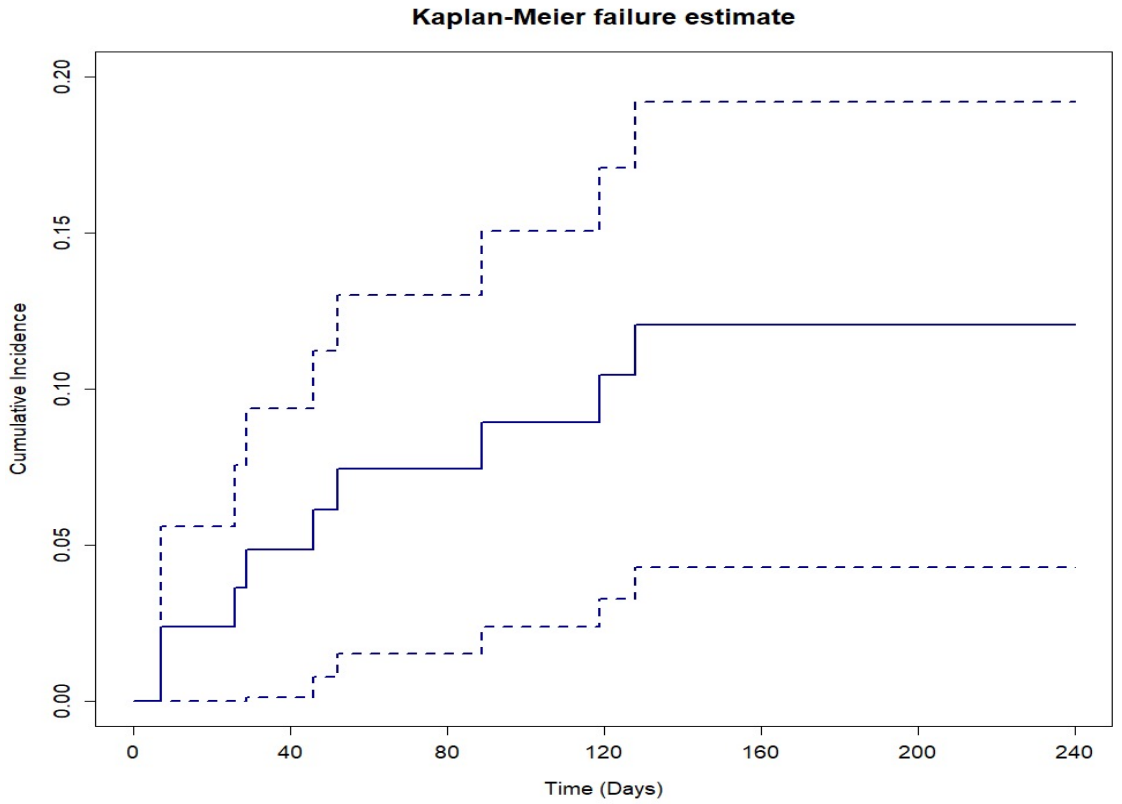
Non-response/non-initiated referral

Higher cumulative incidence of psychosis in those detected

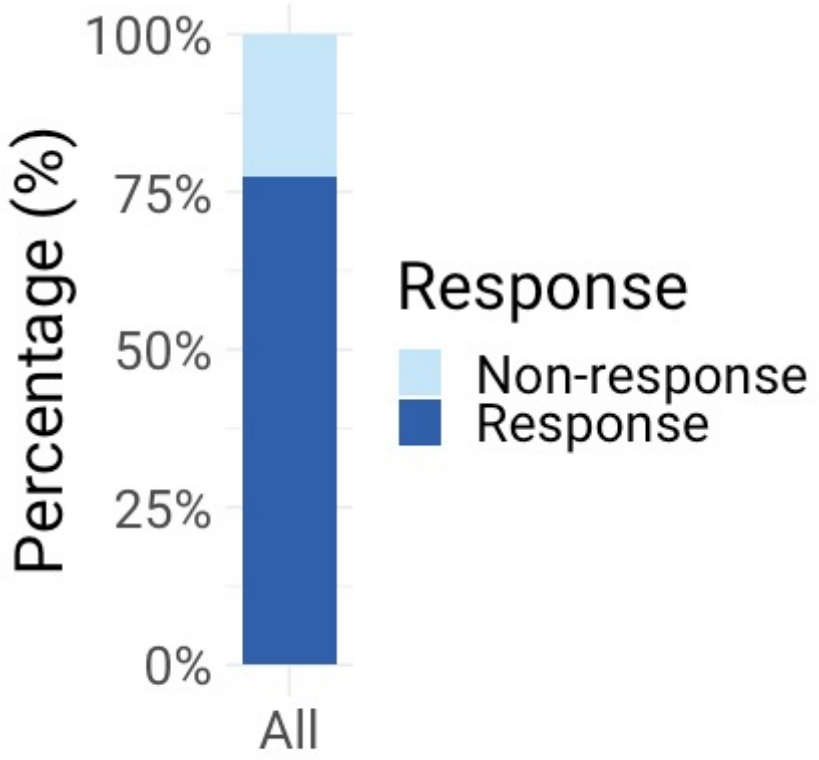
Screened (n=3,640)
Cumulative incidence = 0.016

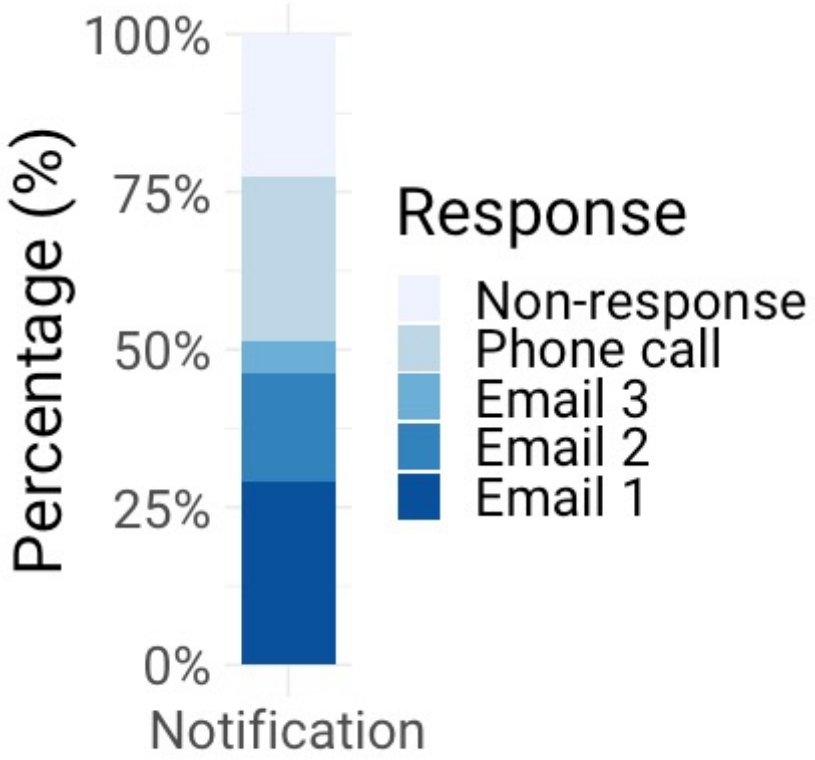


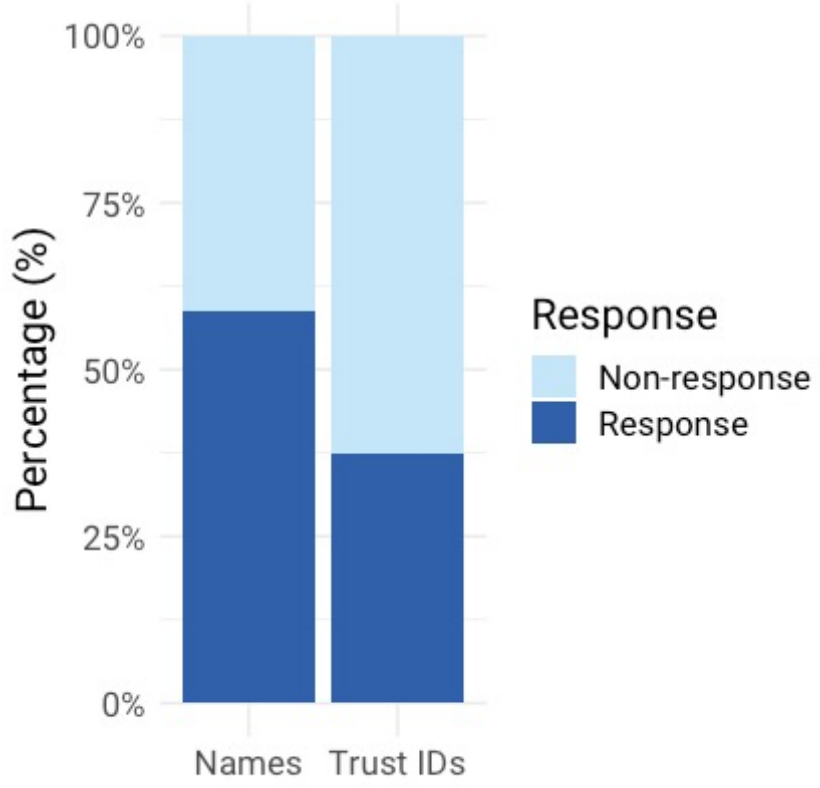
Detected (n=101)
Cumulative incidence = 0.12



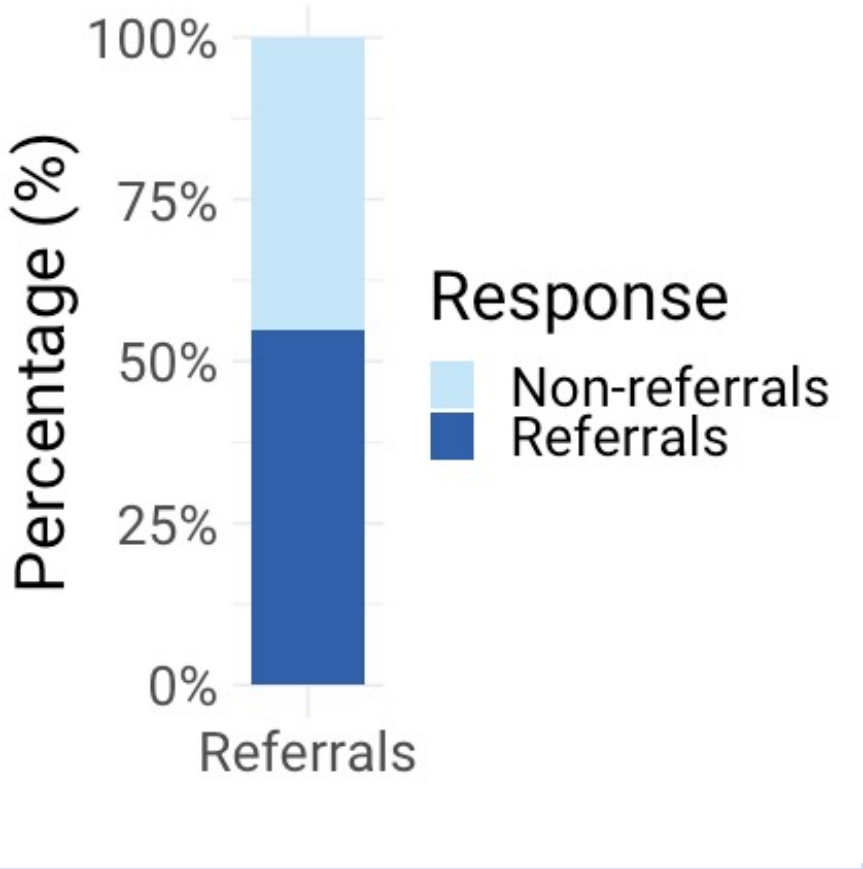
Clinician adherence

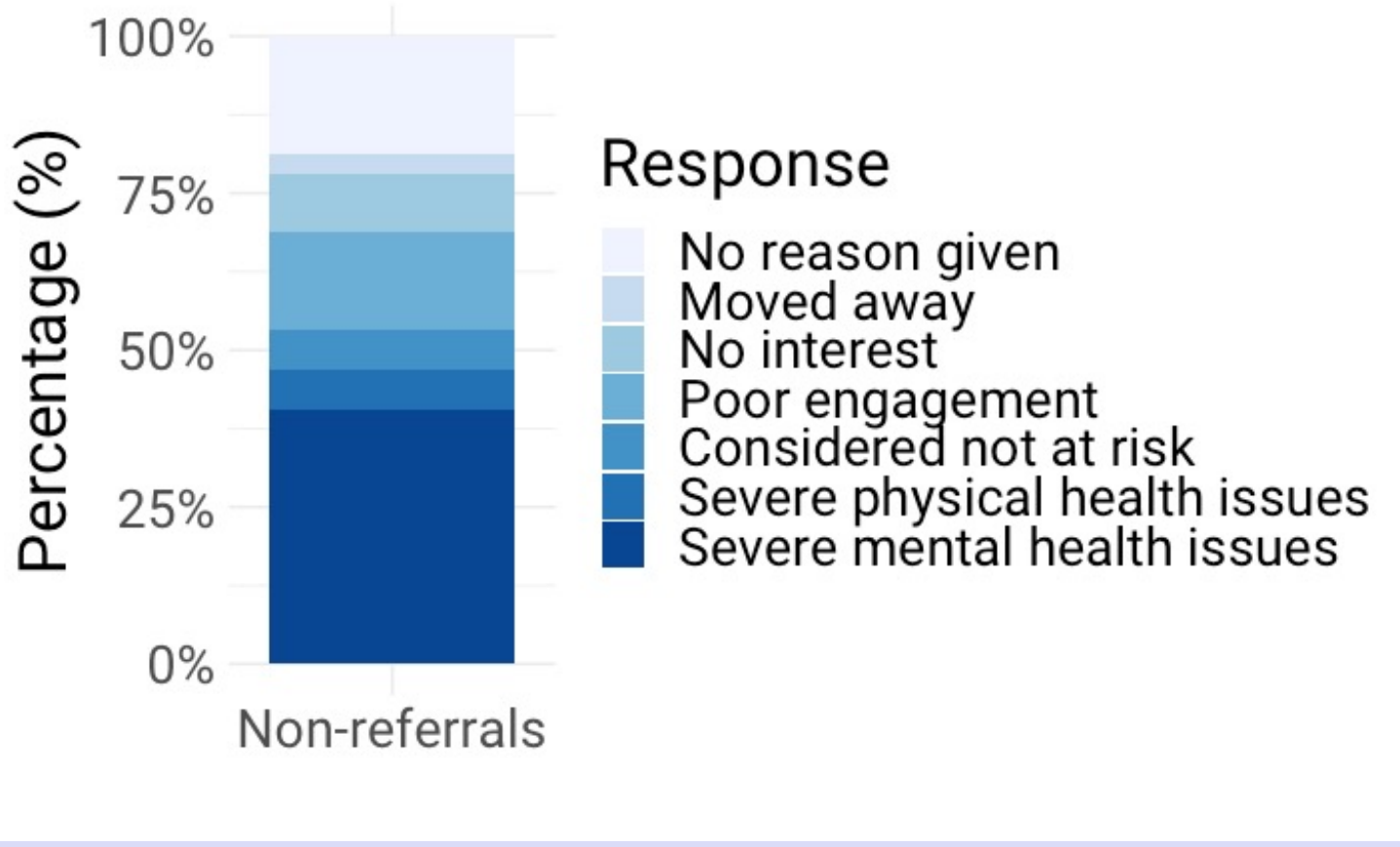




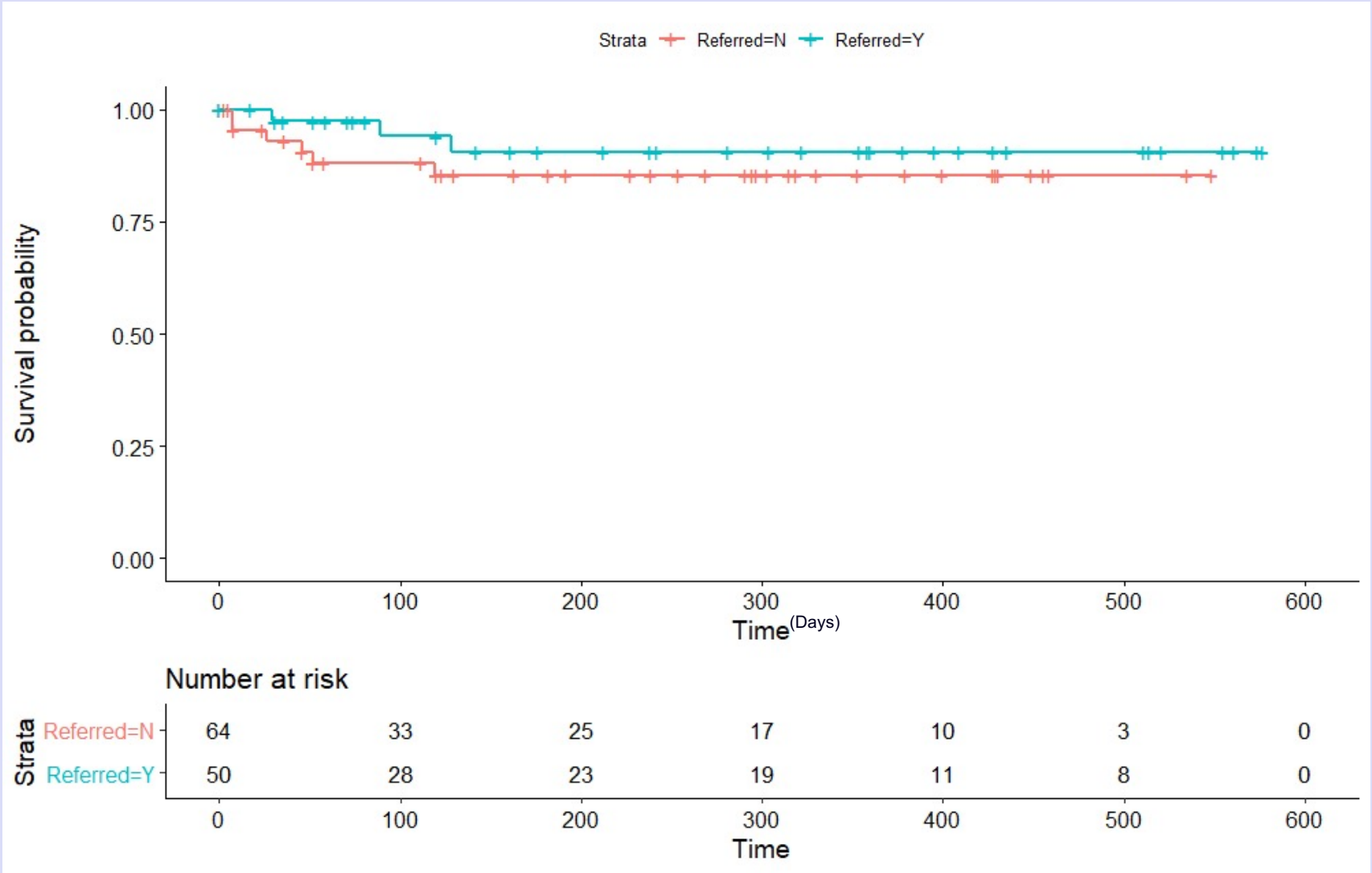


Referrals


100%
75%
50%
25%
0%
Percentage (%)
Referrals
Response
Non-referrals
Referrals


100%
75%
50%
25%
0%
Percentage (%)
Non-referrals
Response
No reason given
Moved away
No interest
Poor engagement
Considered not at risk
Severe physical health issues
Severe mental health issues

No significant differences in incidence of psychosis in those referred/not referred

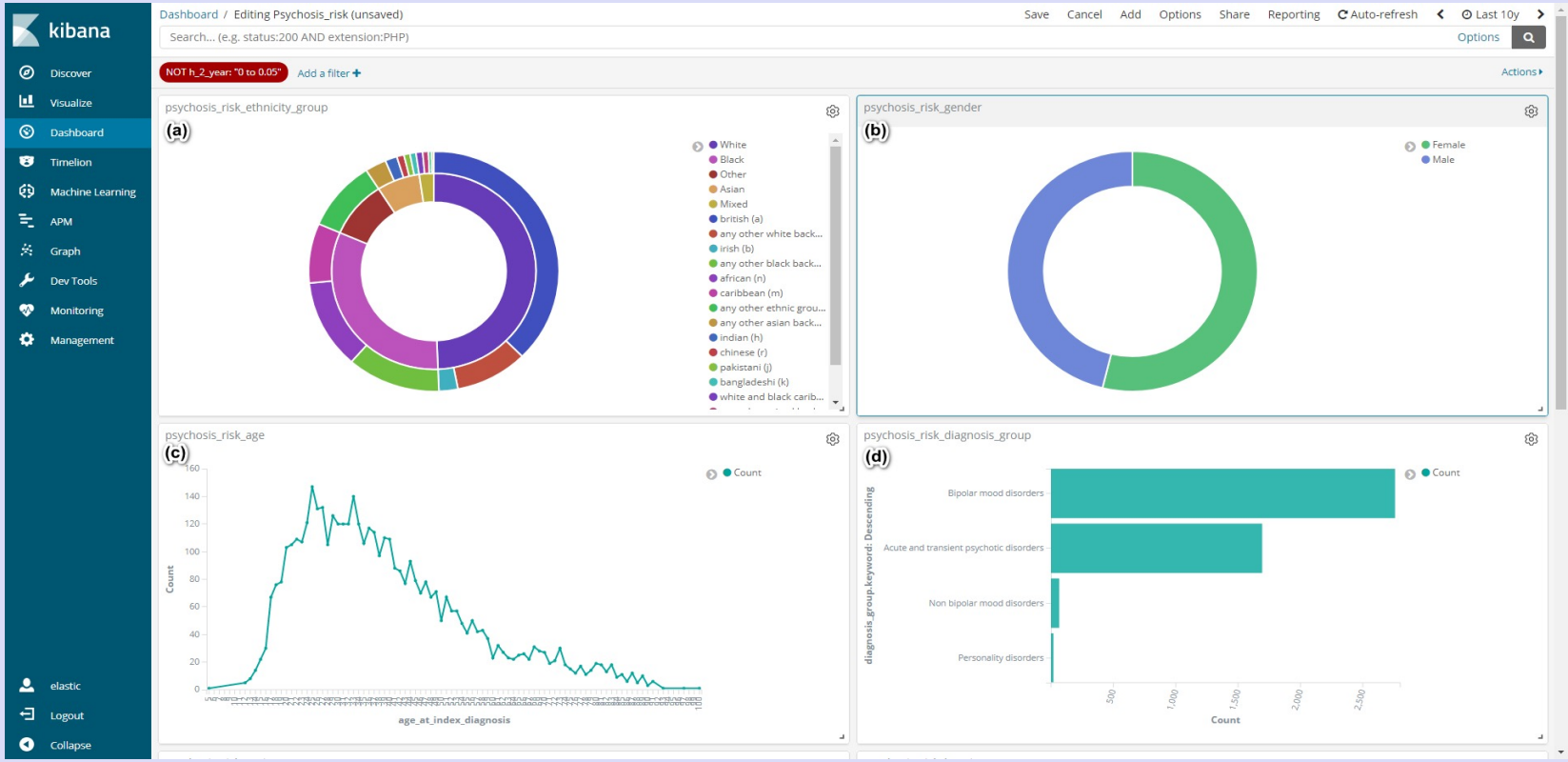


Future work

- Automated alerting/referral pathway (Wang et al., 2020)
- Refining current predictors (e.g. non-linear age, Fusar-Poli et al., 2019)
- Adding new predictors using advanced data mining methods (e.g. NLP symptom data, Irving et al., 2020)
- Further feasibility work
- Dynamic refinement with updating risk estimates as new information is entered

Automated alerting & streamlining referral

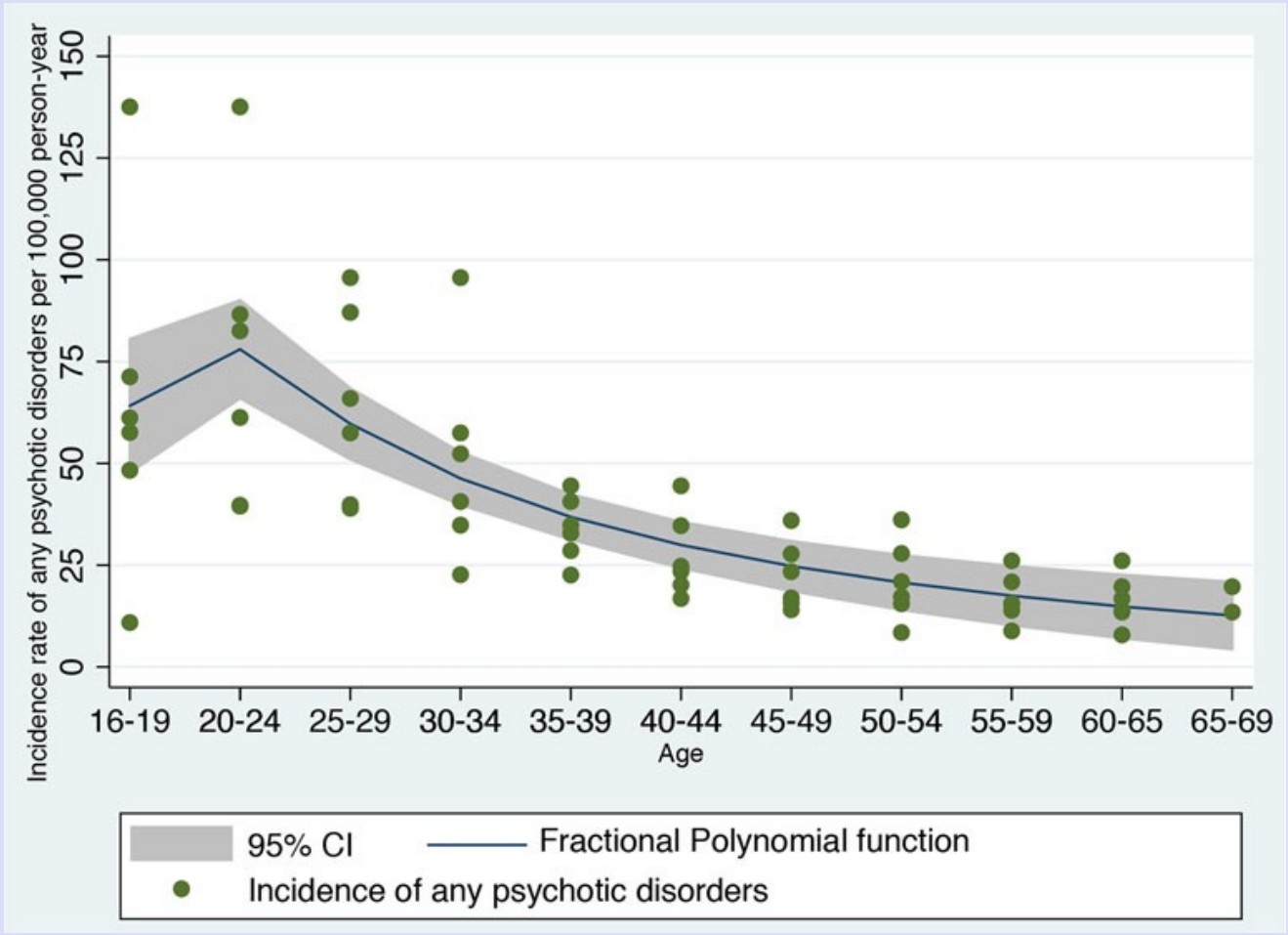
- Real-time updating
- Automated alerting when individual above threshold
- Psychosis VIEWER piloted in SLaM to have interactive dashboard for caseload summaries
- Patient-level alerts with integration with case notes



Wang et al. 2020 Jove

Optimising age

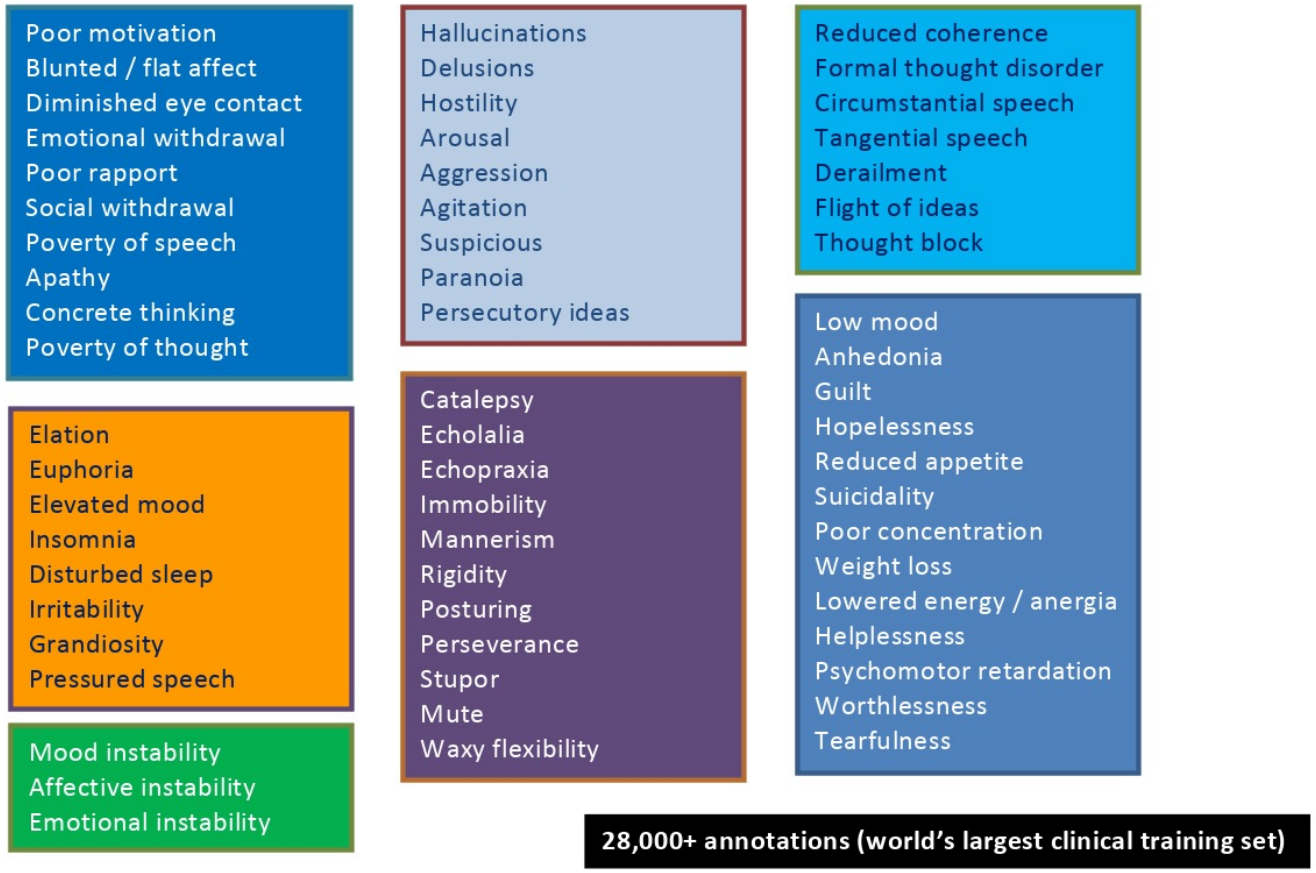
- Non-linear modelling had better fit compared to original model
- Modest but significant improvement in performance
- May have been hampered by lower risk of psychosis and reduced variation in validation dataset



Harrell's C = 0.79 -> 0.81

Fusar-Poli et al. 2019 Front. Psychiatry

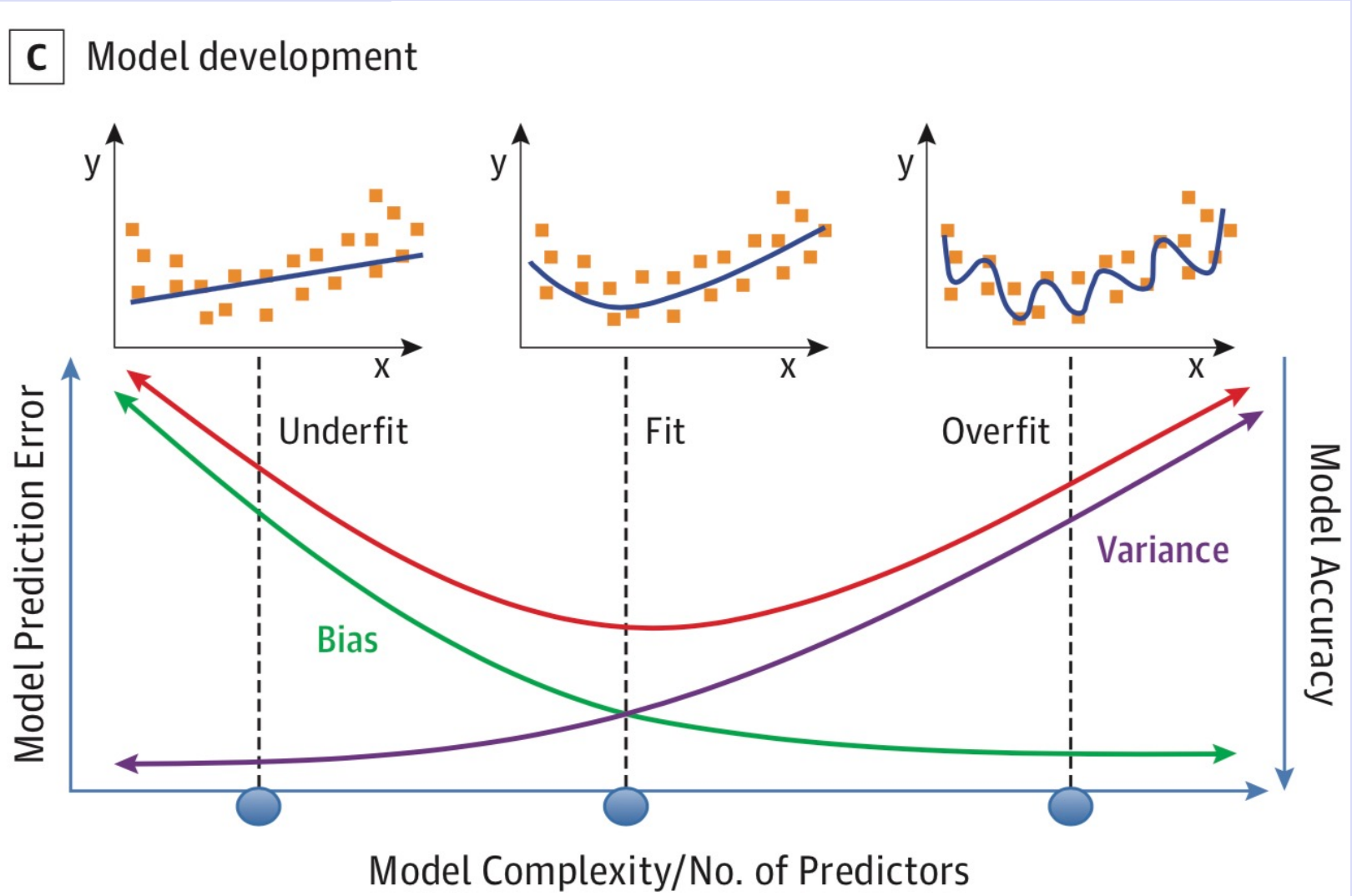
Natural language processing (NLP) apps



- Machine learning applications trained to pick up use of specific words in clinical notes
- Over 50 symptoms shown here grouped by symptom type
- The symptom apps range in precision from 65% - 99%

Irving et al. 2020 Scz Bull

Overfitting



- Key issue in prognostic research is **bias-variance tradeoff**
- Use of 50 NLP apps could lead to overfitting and poor generalisation

Fusar-Poli et al., 2018

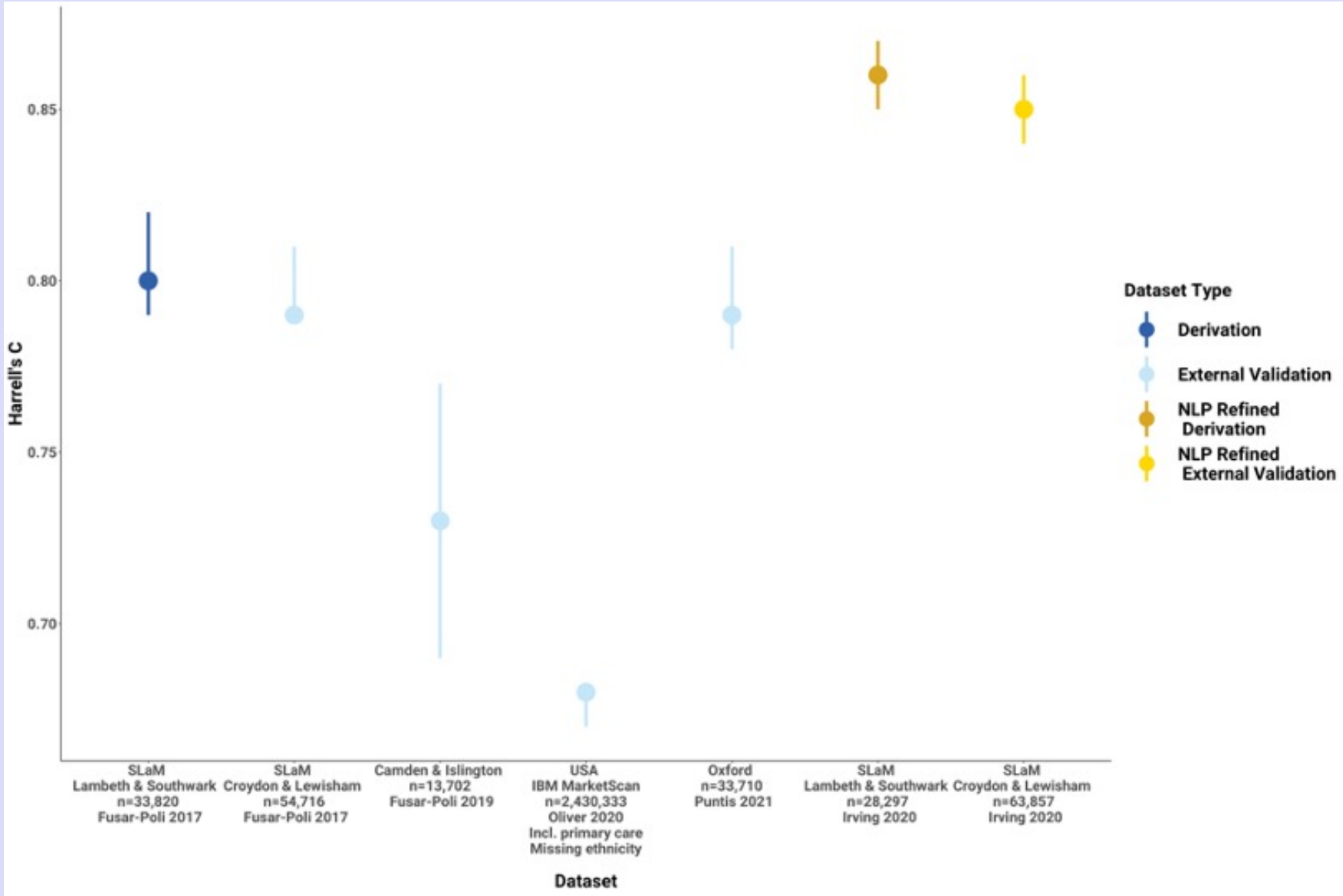
Natural language processing (NLP) apps

Restricted to NLP apps with >80% precision
LASSO used to prevent overfitting
14 NLP predictors retained by model

1. Agitation
2. Appetite loss
3. Cannabis
4. Cocaine
5. Delusions
6. Disturbed sleep
7. Guilt
8. Hopelessness
9. Insomnia
10. Irritability
11. Loss of insight
12. Paranoia
13. Tearfulness
14. Weight loss

Irving et al. 2020 Scz Bull

Better performance with NLP predictors



Sussex feasibility

- NIHR funded grant awarded to Professor Kathryn Greenwood
- NLP-refined model to be replicated in Sussex EHR data
- Prospective feasibility study
- To be completed later this year

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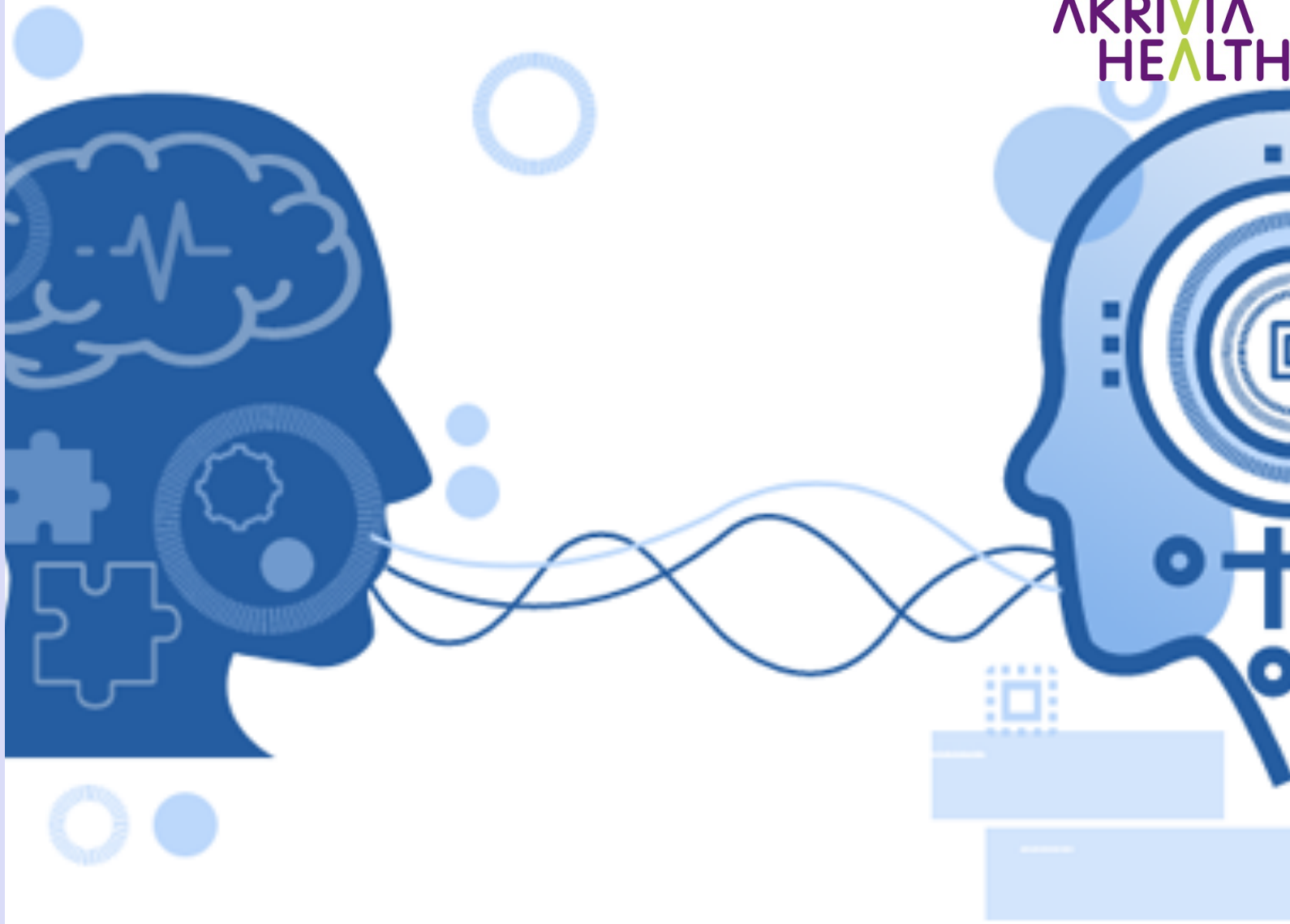
Brighton and Sussex University Hospitals NHS Trust

AKRIVIA HEALTH

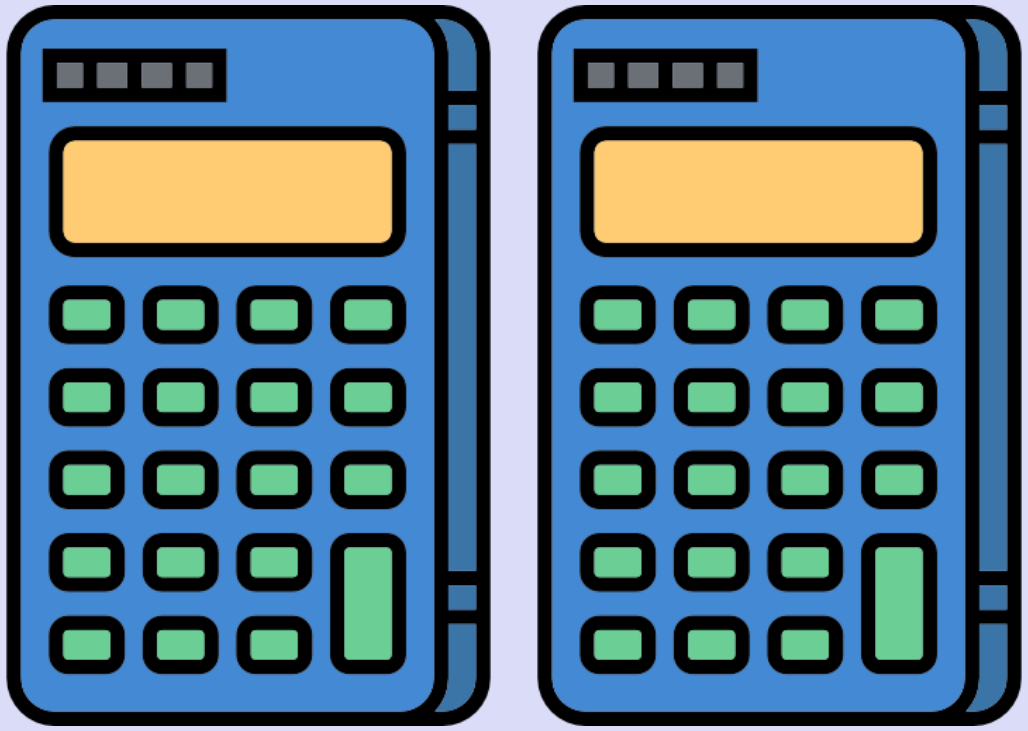
NLP apps

- Akrivia developing NLP library to replicate model performance
- Same constructs as SLaM model, developed using Sussex database



Replication

- Replicating model using SLaM NLP apps
- Replicating model using Akrivia NLP apps
- If performance is similar, model is not reliant on original NLP apps and is more flexible



Feasibility study

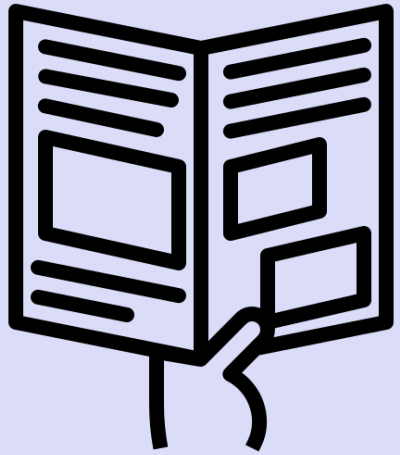
Any new patient accessing secondary mental health care

Clinician-entered variables:

- Age
- Gender
- Age*Gender
- Self-assigned ethnicity
- ICD-10 diagnosis

+ NLP

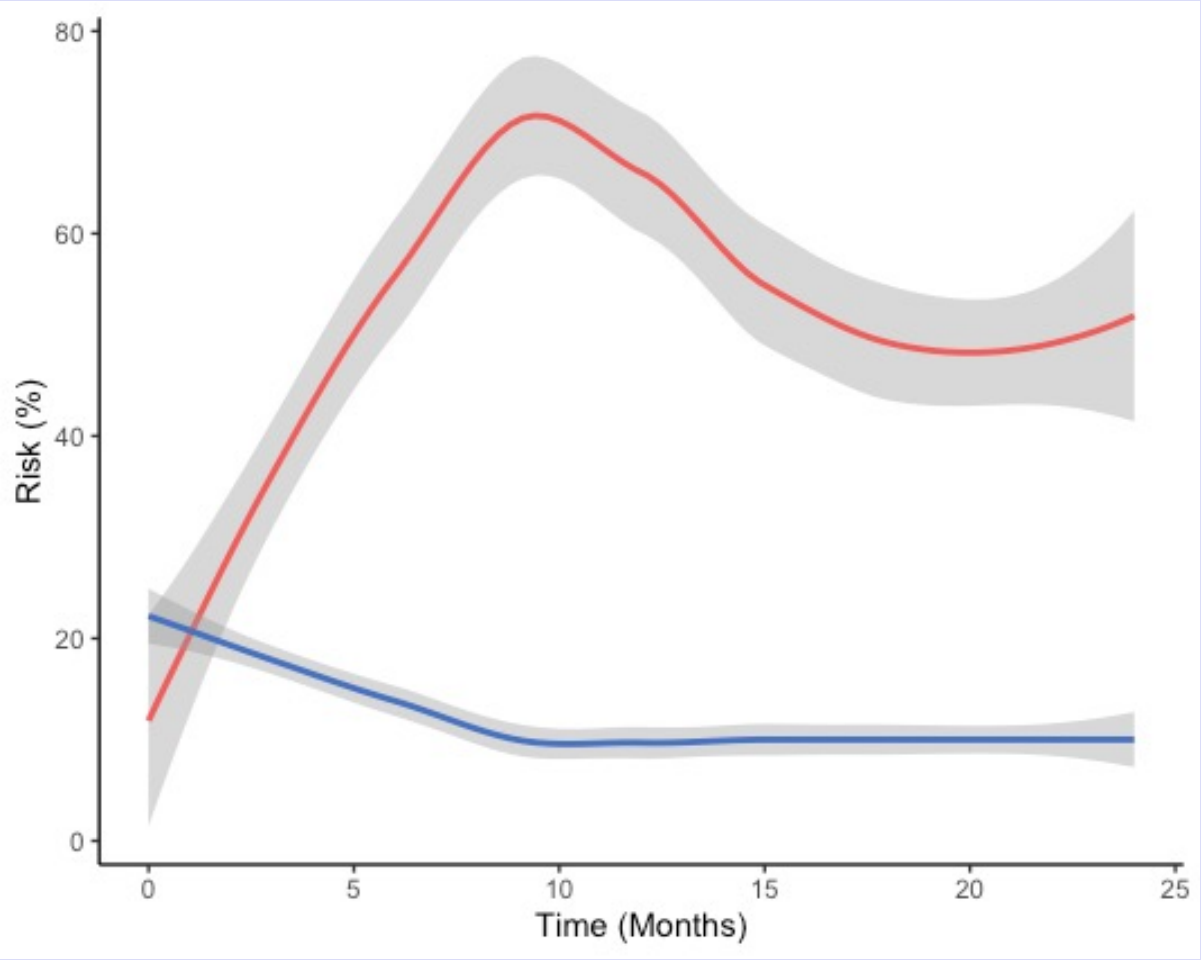
Automatic risk estimation
Risk >5% at 2 years



Evidence-based information posted to patient

Dynamic refinement

- Assumption with original model that psychosis risk is static
- Risk may go up and down as different symptoms are experienced or resolved
- NLP predictors and machine learning to update psychosis risk with new information over time
- New area, need feedback from service users and clinicians for how this would work



Summary

Implementation is under-researched in precision psychiatry

Feasible for implementation in clinical care

The most accurate prediction tool is useless in the real world if clinicians don't use it

Work ongoing to improve clinician experience

Our transdiagnostic risk calculator has performed well in multiple settings

Work ongoing to further refine and implement the model

Acknowledgements

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Matthew Broadbent
Craig Colling
Richard Dobson
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