CHIEF SCIENTIST OFFICE

CODE: CAF/19/04

RESEARCH PROJECT BRIEFING

Prognostic research in first episode psychosis and in delirium

AIMS

The prognosis of people with first episode psychosis (FEP) is poor in around half of those affected and difficult to predict in individuals. Prognostic prediction models could facilitate early identification of individuals at risk of poor outcome allowing us to intervene to change clinical trajectories and improve prognosis. We aimed:

1. To review the existing evidence for prediction models in FEP.
2. To develop a prediction model for FEP patients and test it in different populations.
3. To test whether the neurotransmitter glutamate and inflammatory blood biomarkers (both relevant to the biology of psychosis) or machine learning methods improve the performance of prediction models in FEP.
4. To test if it is feasible to use routinely collected electronic healthcare record (EHR) data from NHS Greater Glasgow & Clyde (GG&C) for prognostic research (we changed from studying FEP to studying delirium as data collection for FEP was delayed due to COVID).

KEY FINDINGS

- Systematic review of the literature showed that there is a growing body of research into prediction modelling in FEP but most existing studies have methodological flaws.
- Developing on from this literature, we built a prediction model with clinical variables to predict poor outcome (nonremission) in FEP and tested it in different populations. Our model was able to accurately predict which patients would improve and which patients would not. It could allow us to intervene to change trajectories and improve prognosis.
- The addition of glutamate neuroimaging and inflammatory blood biomarkers to the model did not appear to improve the performance of prediction models in FEP.
- Machine learning methods did not improve the overall performance of prediction models in FEP compared to logistic regression (a conventional statistical approach for the prediction of binary outcomes based on prior observations in a dataset).
- Considering a different clinical problem from FEP, we found that high quality prognostic research is possible using routinely collected EHR data from NHS GG&C. Specifically, we showed that an episode of delirium over the age of 65 is associated with a 31% risk of new dementia by five years and an even greater risk of death by five years.

WHAT DID THE STUDY INVOLVE?

The research had four stages.

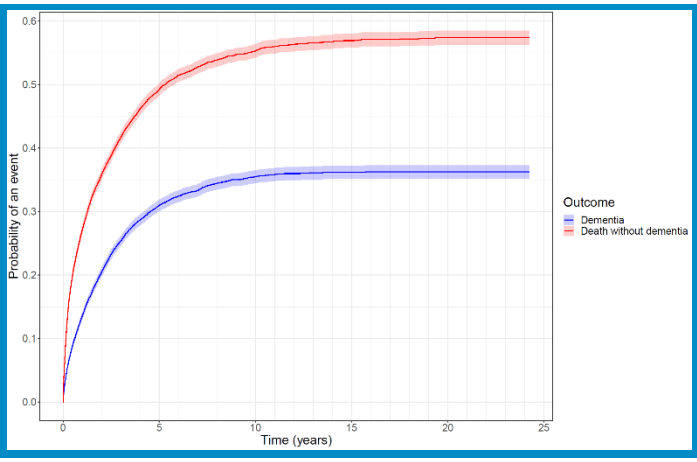
1. We systematically reviewed the literature for evidence of prediction models in FEP.
2. We developed a prediction model to predict poor outcome (nonremission) in 673 patients with FEP and then tested it in another sample of 191 FEP patients from different services. Young people from early psychosis services were consulted on the design and delivery of the data gathering aspect of this work.
3. We tested if glutamate neuroimaging and blood biomarkers or machine learning methods improved prediction model performance in a sample of 168 patients with FEP. This was a secondary analysis of clinical trial data.
4. Finally, considering a different clinical problem, we used routinely collected NHS data from 12949 patients with delirium to determine the risk of developing dementia in the over 65s.

WHAT WERE THE RESULTS AND WHAT DO THEY MEAN?

- Our systematic review identified 13 studies reporting 31 prediction models across a range of clinical outcomes in FEP. Most studies used logistic regression (a conventional statistical approach) rather than machine learning and employed clinical variables (such as age, sex and symptom scores). Further, most studies had methodological limitations such that the potential for prediction modelling in FEP was not been fully realised.
- Developing on from this literature, we built and externally validated a prediction model of symptom nonremission in FEP using a logistic regression and clinical variables. The model showed good discrimination (distinguishing between those with and without the outcome) and was well calibrated (showing agreement between the observed outcomes and their predictions). It demonstrated clinical utility to detect individuals at high risk of nonremission.
- We explored the potential for glutamate neuroimaging and inflammatory blood biomarkers, and machine learning methods for prediction in FEP. The addition of a biomarker did not improve the performance of a model built using solely clinical variables. Machine learning methods were not superior to logistic regression.
- In a separate clinical area, we demonstrated the feasibility of using routinely collected EHR data from NHS GG&C for prognostic research into delirium and the risk of subsequent dementia in the over 65s (**see figure below**).

The estimated cumulative incidences of dementia and for the competing risk of death without a dementia diagnosis after an episode of delirium in the over 65s.

Following an episode of delirium, the risk of dementia was 31% by five years while the risk of death without a dementia diagnosis was 49.2% by five years.



WHAT IMPACT COULD THE FINDINGS HAVE?

- Once our FEP nonremission prediction model has been further tested in new patients in clinical practice, it could facilitate the early identification of patients at high risk of nonremission and prioritise the timely delivery of effective disease phase specific treatments like clozapine for treatment resistance.
- Future FEP prognostic studies will be possible using routinely collected EHR data once data collection for FEP is fully rolled out in NHS GG&C.
- The clinical predictor variables from our study have helped influence the choice of outcome measures chosen by Healthcare Improvement Scotland to be collected by their Early Intervention in Psychosis pathfinder sites.
- Delirium prevention strategies could help reduce the incidence of dementia in the over 65s.

HOW WILL THE OUTCOMES BE DISSEMINATED?

- Findings from this research have been published in peer-reviewed journals including the British Journal of Psychiatry, presented at international conferences and shared on Twitter.
- An important next step will be a prospective validation study of our FEP nonremission prediction model in clinical practice. This will be followed by a feasibility study which will assess if it is possible to collect the clinical and sociodemographic information required for applying the model, the practicality and acceptability of delivering the model in a clinical setting including any barriers to implementation and any unintended negative effects.

CONCLUSION

- Review of the literature shows a growing body of evidence for prediction modelling in FEP but most existing models have methodological flaws.
- We developed and externally validated a FEP nonremission prediction model in two large FEP patient populations. The model performed well and could help facilitate the early identification of FEP patients at high risk of nonremission.
- The potential for glutamate neuroimaging and inflammatory blood biomarkers, and machine learning for outcome prediction in FEP has not been proven.
- It is feasible to use routinely collected EHR data for prognostic research in NHS GG&C.

RESEARCH TEAM & CONTACT

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Additional Information

This project was completed on 1st March 2023. The total funding awarded was £238,177.