AMBER: Antidepressant Medications: Biology, Exposure and Response

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AMBER

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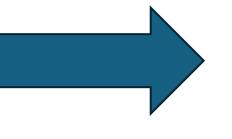




COLLABORATE WITH US

BACKGROUND

- Depression is a highly prevalent global disorder, with both pharmacological and psychological treatments available.
- Substantial progress has been made into how genetics contribute to the risk of developing depression, but this has not translated into treatments.
- Only one-third of patients respond to the first drug prescribed, and our poor mechanistic understanding of antidepressant actions and treatment response has limited personalised treatment¹.



The AMBER project (2023-2028) will use causal inference, electronic health records, and genomic data to advance our understanding of antidepressant mechanisms and individual response variations

PROJECT APPROACH

Patient engagement on ANTIDEPRESSANT TREATMENT

- Convene a Lived Experience Advisory Panel, who will interact regularly with the other work-packages, to guide the entire programme.
- Participatory Research exploring:
- attitudes to personalised medicine in the depression treatment pathway
- the clinical experiences of people with 'difficult-to-treat' depression.
- Community engagement to explore the lack of diversity in mental health research participants.

Sue Fletcher-Watson, Iona Beange, Cristina Douglas & Mark Somerville

Robust and reproducible ANTIDEPRESSANT RESPONSE & EXPOSURE phenotypes

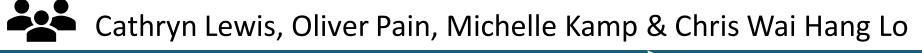


- Use real world data from electronic health care records to inform and derive novel antidepressant exposure and response phenotypes.
- Explore advantages of combining information from structured and unstructured ('free text') clinical data to refine phenotypes.
- Validate, refine and disseminate code for wider use.

Heather Whalley, Matthew Iveson, Arlene Casey & Matúš Falis

Genetic signatures of ANTIDEPRESSANT RESPONSE

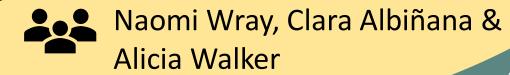
- Establish collaboration and data sharing for clinical studies.
- Define and apply electronic health record algorithms for antidepressant response and resistance.
- Perform genome-wide analysis of antidepressant response to identify genetic associations, polygenic profiles and biological pathways.



Genetic signatures of ANTIDEPRESSANT EXPOSURE

- Identify genomic datasets with antidepressant exposure.
- Conduct genome-wide association studies of antidepressant exposure.
- Conduct DNA methylation, proteomic and metabolomic association studies of antidepressant exposure.
- Apply causal inference methods to identify causal effects of antidepressants on molecular phenotypes.
- Andrew McIntosh, Mark Adams, Amelia Edmondson-Stait & Megan Calnan

Cross-projects



CELLULAR GENOMIC STUDIES on ANTIDEPRESSANT TREATMENT Generate gene expression signatures for antidepressants in human cell lines.

- Use comparative and network-based analyses to understand biological pathways affected by SSRIs
- Analyse SSRI gene signatures in responder and non-responder patient cell lines to assess feasibility of using patient cell line gene expression assays to predict treatment response.

Sonia Shah, Quan Nguyen, Anjali Henders & David Brici

COLLABORATIVE



Conducted in partnership with individuals with lived experience, we aim to foster trust, enhance patient relevance and impactful dissemination of findings.



A core component will be sharing of code, methods for best practice, and guidance for phenotype ascertainment from linked clinical data.

OPEN & TRANSPARENT

SUMMARY

The AMBER project will integrate clinical, genomic, and patient-participatory research to provide insights into antidepressant action and response, enhance understanding of drug mechanisms and biological pathways, and develop predictive models for personalised prescribing to improve patient outcomes.

CONTACT DETAILS

If you are interested in collaborating with us, please contact:

- Prof Cathryn Lewis (PI; cathryn.lewis@kcl.ac.uk)
- Kate Stewart (AMBER Research Project Manager; kate.stewart@kcl.ac.uk)

References: