Predictors of multiple treatment failure of antipsychotics in early-onset psychosis

[1, 3]Pina-Camacho, L., [1]Dean, H., [1]Lechler, S., [1]Sears, N., [1]Patel, R., [1]Kartoglu, I., [1]Shetty, H., [1]Hotopf, M., [2]Ford, T., [1]Kyriakopoulos, M., [3]Arango, C., [1]MacCabe, J., [1]Hayes, R.D., [1]Downs, J.

P.3.d.017

laura.pina@kcl.ac.uk

[1] Institute of Psychiatry Psychology Neuroscience, King's College London & NIHR South London and Maudsley Biomedical Research Centre; [2] University of Exeter Medical School; [3] Child and Adolescent Psychiatry Department, Hospital General Universitario Gregorio Marañón, IiSGM, School of Medicine, Universidad Complutense, CIBERSAM, Madrid, Spain

INTRODUCTION

• In adult-onset psychosis, a number of factors are associated with poor outcomes, including: severity of negative symptoms (NS) at illness onset, presence of premorbid difficulties & family history of psychotic disorder [1]

• If and how these factors effect psychosis prognosis in children and adolescents is unclear [2,3]

• Furthermore, very little is known about the effect of these risk factors on the response to antipsychotic medications in early-onset psychosis (EOP)

OBJECTIVES & HYPOTHESES

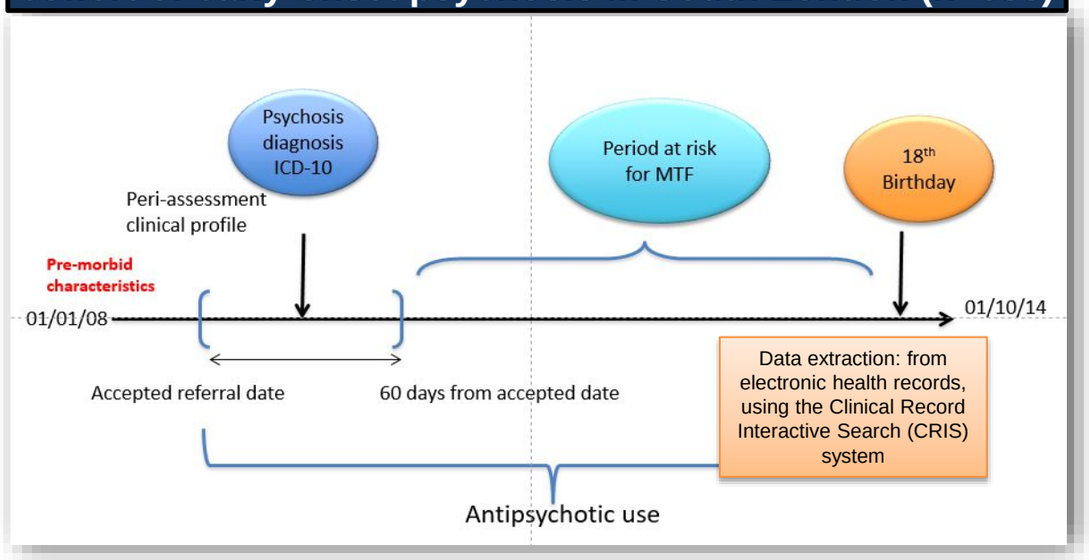
• In a historical cohort of individuals with EOP, to investigate the prospective association of demographic and clinical variables at first presentation to services with the eventual development of multiple treatment failure (MTF)

→ ***MTF = initiation of 3rd trial of novel antipsychotic for psychosis***

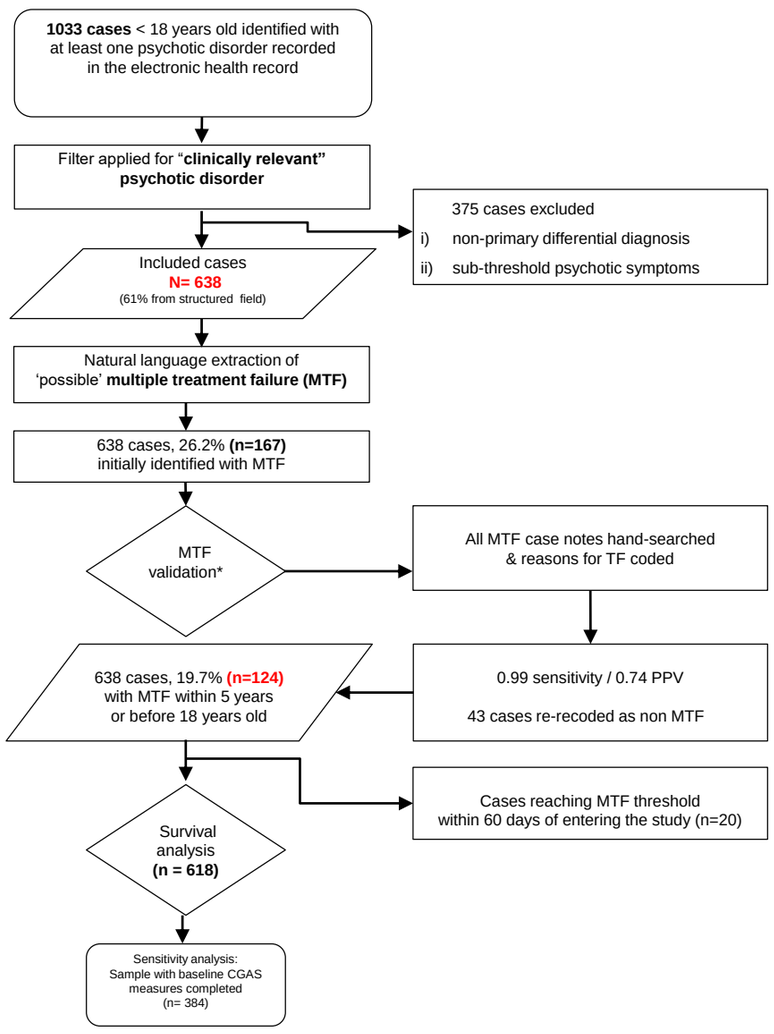
• Hypothesis: the presence of NS at first presentation, of premorbid difficulties (e.g. comorbid ASD), and 1st degree family history of psychosis would be positively associated with MTF

METHODS

Longitudinal naturalistic study of historical clinical cohort of early-onset psychosis in South London (n=638)



Flowchart of study selection, inclusion criteria and data extraction



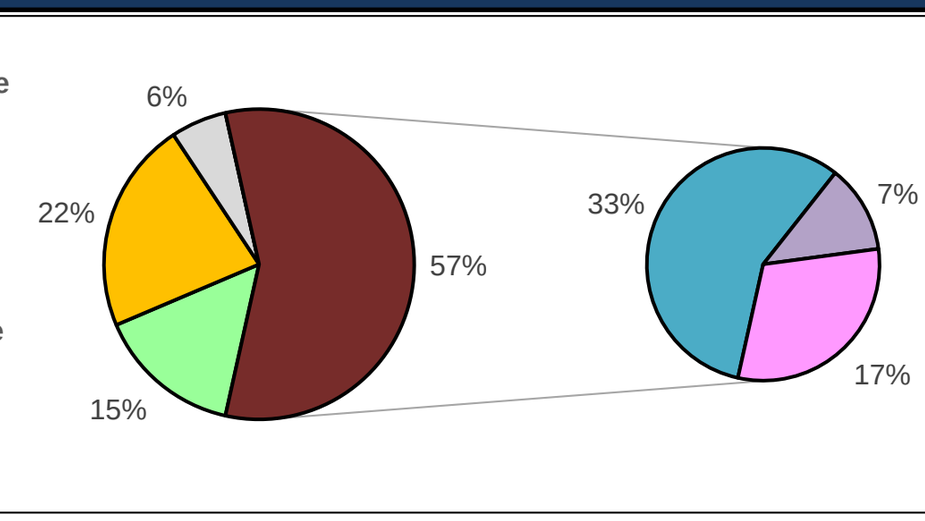
*Three independent raters, hand search of 100 cases each, including all cases where MTF was identified, and a random selection of non-MTF cases

RESULTS

1) Main characteristics of the sample (n=638)

- Mean age at referral **15.6 years** (1.9) **[10-17], 51% male**
- Mean duration of **follow up = 1.79 years** (SD 1.4)
- 40.8% White British, 32.8% Black ethnicity, 26.4% other / not stated
- Mean baseline CGAS score = 38.3 (15.9); Comorbidities: 17.9% ASD, 10.2% LD, 6.3%ADHD
- **124 individuals (19.7%) developed MTF** during the follow-up period, mean age 16.3 y (1.4)

2) Reasons for discontinuing antipsychotics in MTF sample (n=124)



*% refers to percentages of MTF individuals for whom information on main reason of discontinuation was available, i.e. 38 cases excluded due to no reason ' or 'other reason' ascertained in the electronic health record

3) Cox regression analysis of the association between demographic and baseline clinical variables and MTF (n=618)

Risk of MTF within 5 years or before 18y	Fully-adjusted Model H.R. (95% CI)	Complete case analysis (CGAS available, n=384) Fully-adjusted Model H.R. (95% CI)
Presence of ≥2 Marder NS	**1.70 (1.14 – 2.54)****	**2.02 (1.18 – 3.45)***
Comorbid ASD diagnosis	**1.69 (1.04 – 2.74)***	**1.94 (1.05 – 3.59)***
Comorbid hyperkinetic disorder or ID	0.65 (0.36 – 1.18)	0.57 (0.24 – 1.34)
1st degree family history psychosis	**2.07 (1.35 – 3.18)****	**2.29 (1.29 - 4.08)****
Age at referral for FEP	1.29 (1.11 – 1.49)	1.03 (0.85 – 1.24)
Female (vs male)	1.12 (0.75 – 1.69)	1.22 (0.70 – 2.13)
Ethnicity		
White British	Reference	Reference
White Other / Mixed	1.39 (0.76 – 2.53)	1.28 (0.57 – 2.85)
Black	**1.94 (1.21 – 3.09)****	**2.08 (1.16 – 3.74)***
Asian	1.30 (0.53 – 3.19)	0.99 (0.29 – 3.47)
Socioeconomic status		
1st (least deprived)	Reference	Reference
2nd	0.64 (0.37-1.10)	0.79 (0.40-1.55)
3rd	0.57 (0.32-1.00)	0.85 (0.43-1.70)
4th (most deprived)	0.63 (0.36-1.10)	0.58 (0.26-1.28)
Comorbid dx of affective disorder	0.73 (0.46-1.15)	0.68 (0.38-1.23)
CGAS score at baseline	--	0.99 (0.97-1.00)

***p<.05; **p<.01;** ASD: autism spectrum disorder; CGAS: Children's Global Assessment Scale; H.R.: hazard ratio; ID: intellectual disability; MTF: multiple treatment failure; NS: negative symptoms

CONCLUSIONS

Presence of prominent negative symptoms at first presentation to services, co-morbid ASD and first degree family history of psychosis delineate a subset of children and adolescents with psychosis at higher risk of antipsychotic treatment failure

These children may require alternative treatment strategies

References

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Funding Sources: *the Clinical Records Interactive Search (CRIS) system is funded and developed by the National Institute for Health Research (NIHR) Mental Health Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London and a joint infrastructure grant from Guy's and St Thomas' Charity and the Maudsley Charity (grant number BRC-2011-10035).*

Disclosures: *Dr Downs is supported by a Medical Research Council (MRC) Clinical Research Training Fellowship MR/L017105/1. Mr Dean and Lechler received salary support from the Foundation of Professional Services to Adolescents, UK. Dr Hayes is funded by a n MRC Population Health Scientist Fellowship (MR/J01219X/1). Dr Pina-Camacho and Dr Arango have held a grant from Instituto de Salud Carlos III, Spanish Ministry of Economy and Competitiveness, CIBERSAM and the Alicia Koplowitz Foundation. Professors Hotopf, Dr MacCabe and Mr Shetty receive salary support from the National Institute for Health Research (NIHR) Mental Health Biomedical Research Centre*