Autoimmune Psychosis – The SINAPPS2 Trial

www.sinapps.org.uk

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Neuronal cell surface antibodies – treatable causes of encephalitis

- Voltage Gated Potassium Channel complex (LGI1, CASPR2, contactin-2) 2001, 2010
- N-Methyl-D-aspartate receptor (NMDA) 2008
- GABA-A receptor 2015

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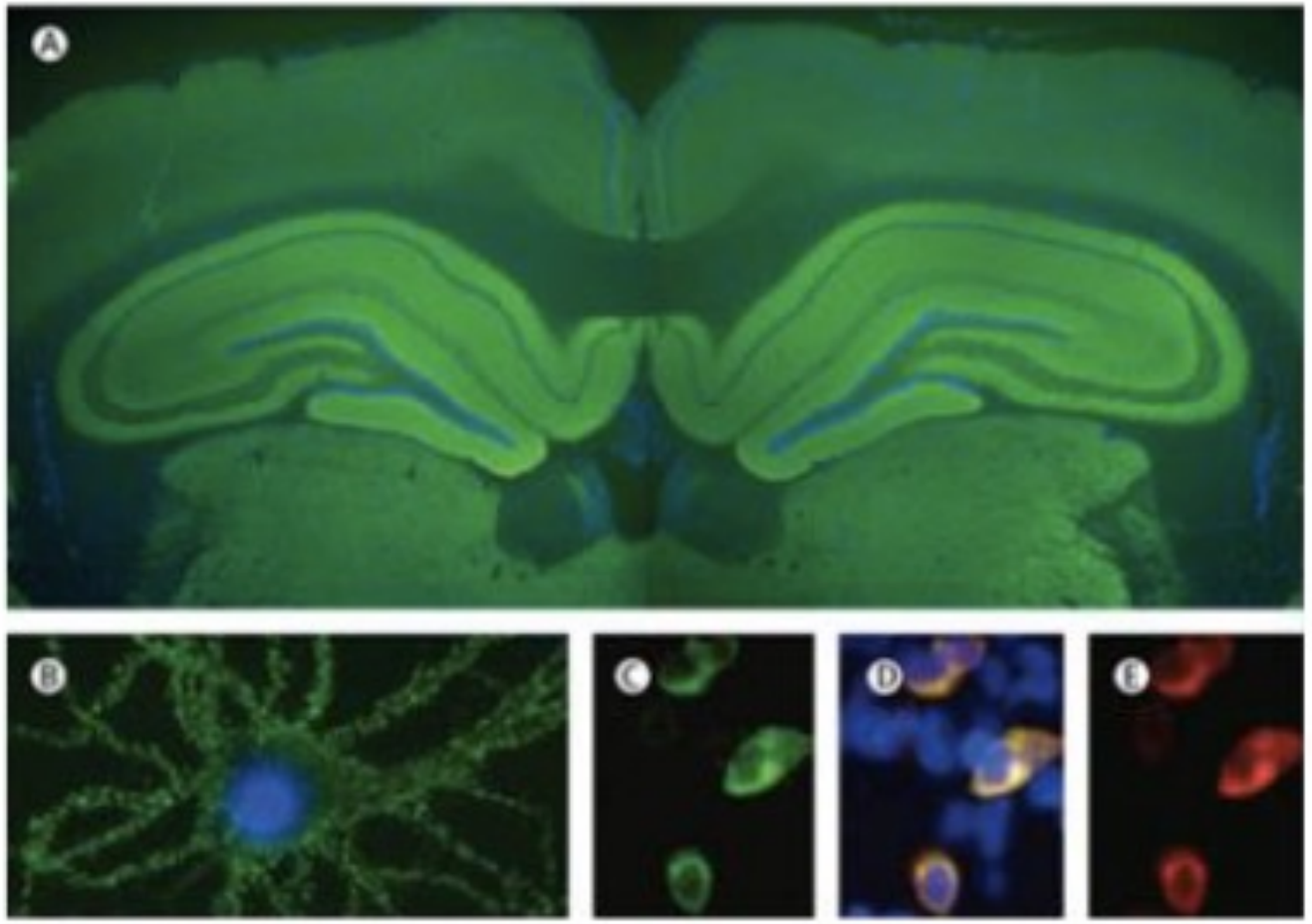
Neuronal cell surface antibodies = pathogenic



Antibody immunolabelling on hippocampal slices, hippocampal neuronal cultures, HEK cell based assays (from Dalmau et al 2011)

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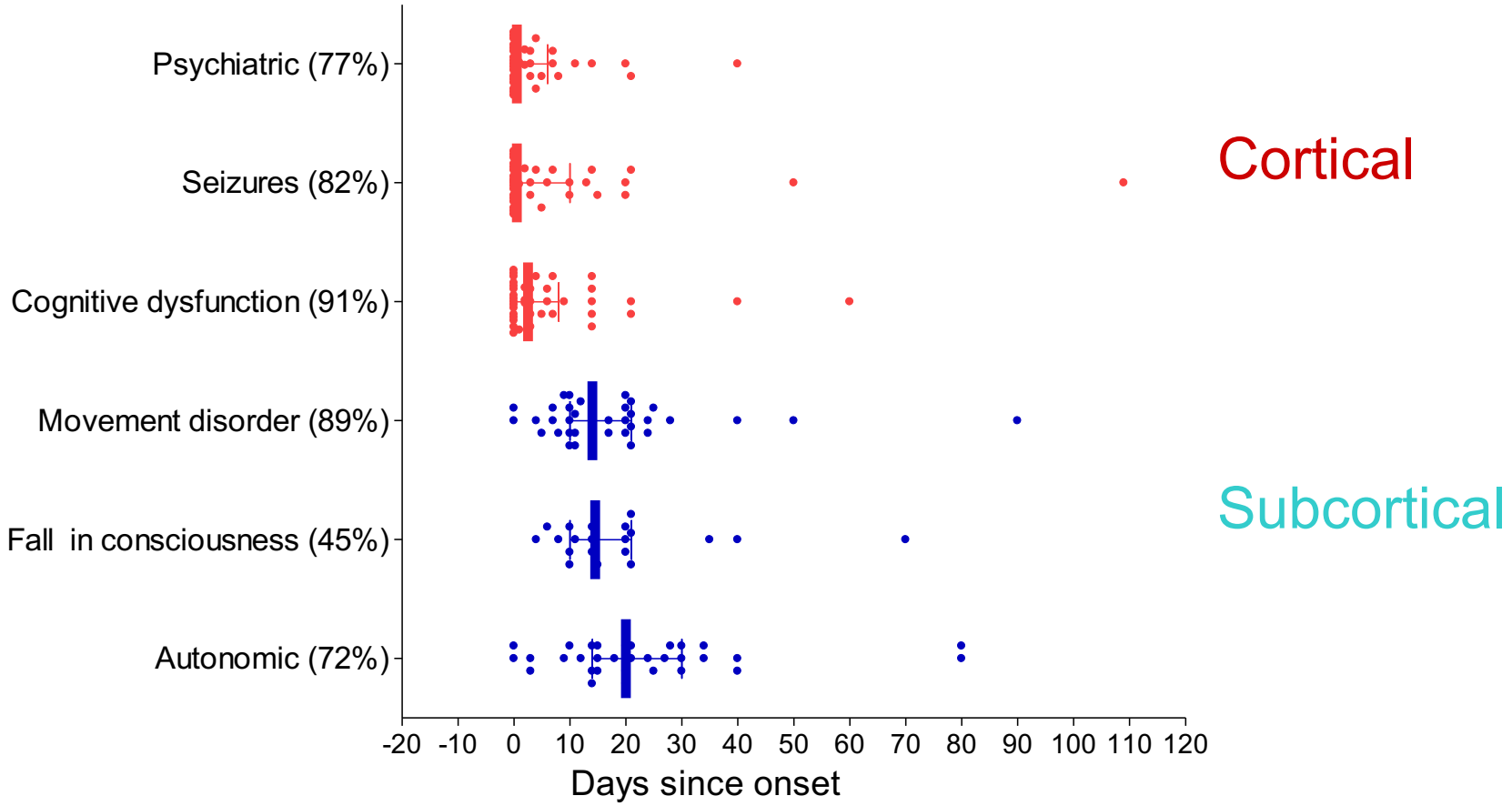
NMDAR encephalitis symptoms and signs



Irani et al *Brain* (2010)

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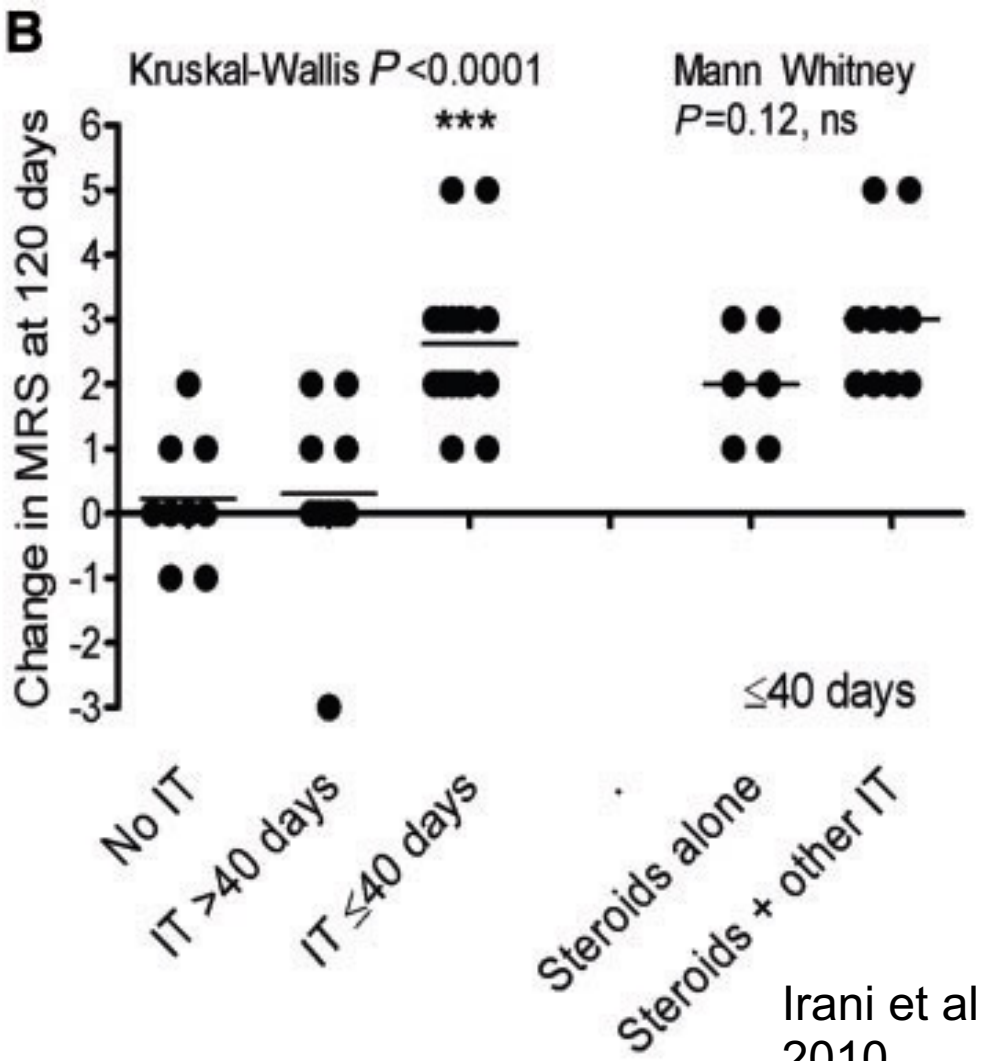
NMDAR encephalitis responsive to early immunotherapy



Irani et al Brain 2010

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Could NMDAR (and other) antibodies be responsible for some cases of psychosis?

Neuronal cell surface antibodies in psychosis

Live cell-based assay	Titres	FEP Patients (n=228)	Controls (n=105)	Odds ratio (95% CI)
NMDAR antibodies	1:30 - 1:150	7 (3·1%)	0	5.4 (p=0.02)*
LGI1 antibodies	1:20 - 1:100	3 (1·3%)	0	2.3 (p=0.13)*
CASPR2 antibodies	1:100 - 1:250	2 (0·9%)	3 (2·9%)	0·3 (0·1 - 1·8)
GABA-AR antibodies	1:50 - 1:100	8 (3·5%)	1 (1%)	3·8 (0·5 - 30·7)
AMPAR antibodies	-	0	0	
Prevalence any neuronal cell surface antibody		20 (8·8%)	4 (3·8%)	2·4 (0·8 - 7·3)

* Likelihood ratio

Lennox et al The Lancet Psychiatry 2016

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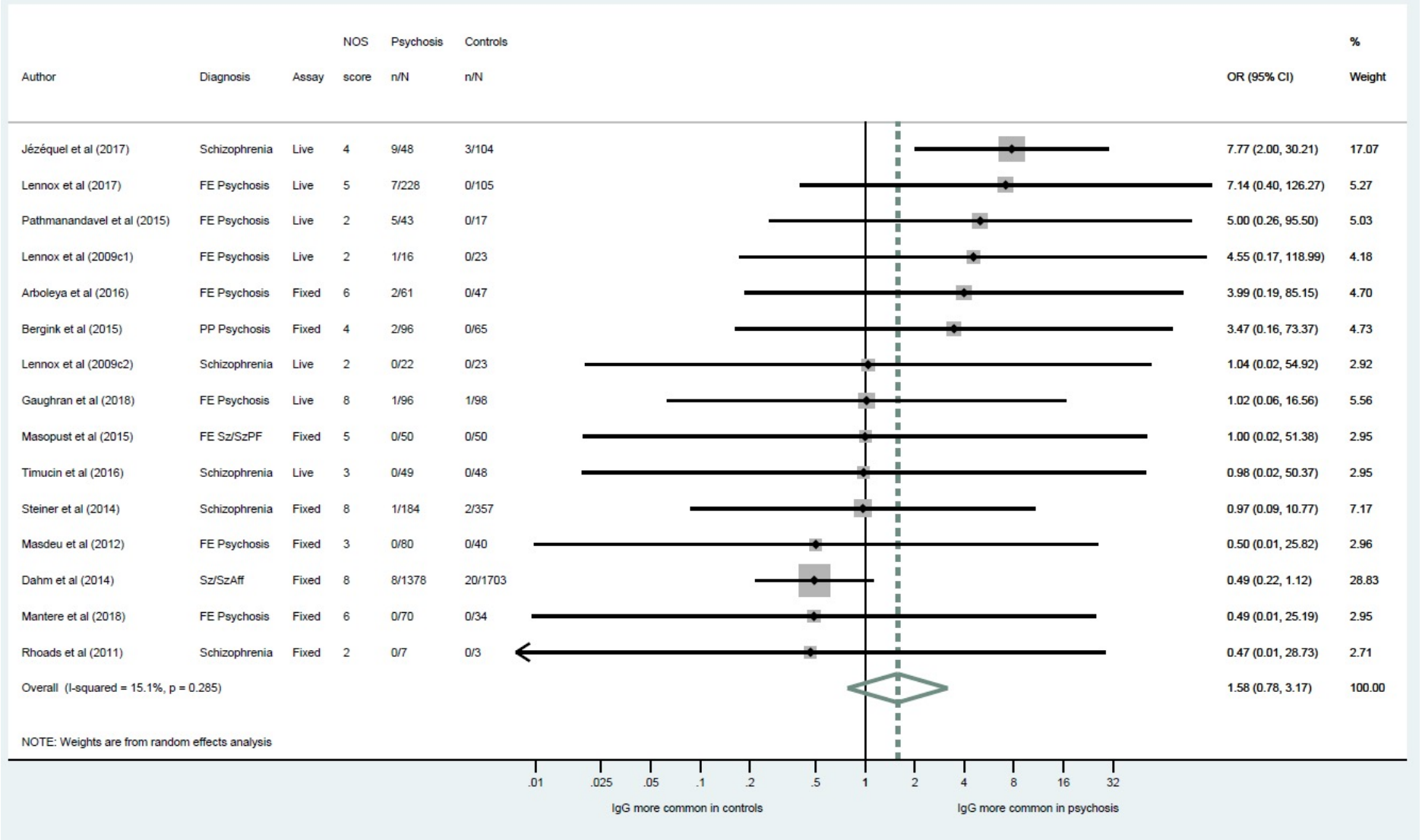
Increased NMDAR antibodies in psychosis?



Cullen et al Lancet Psychiatry 2021

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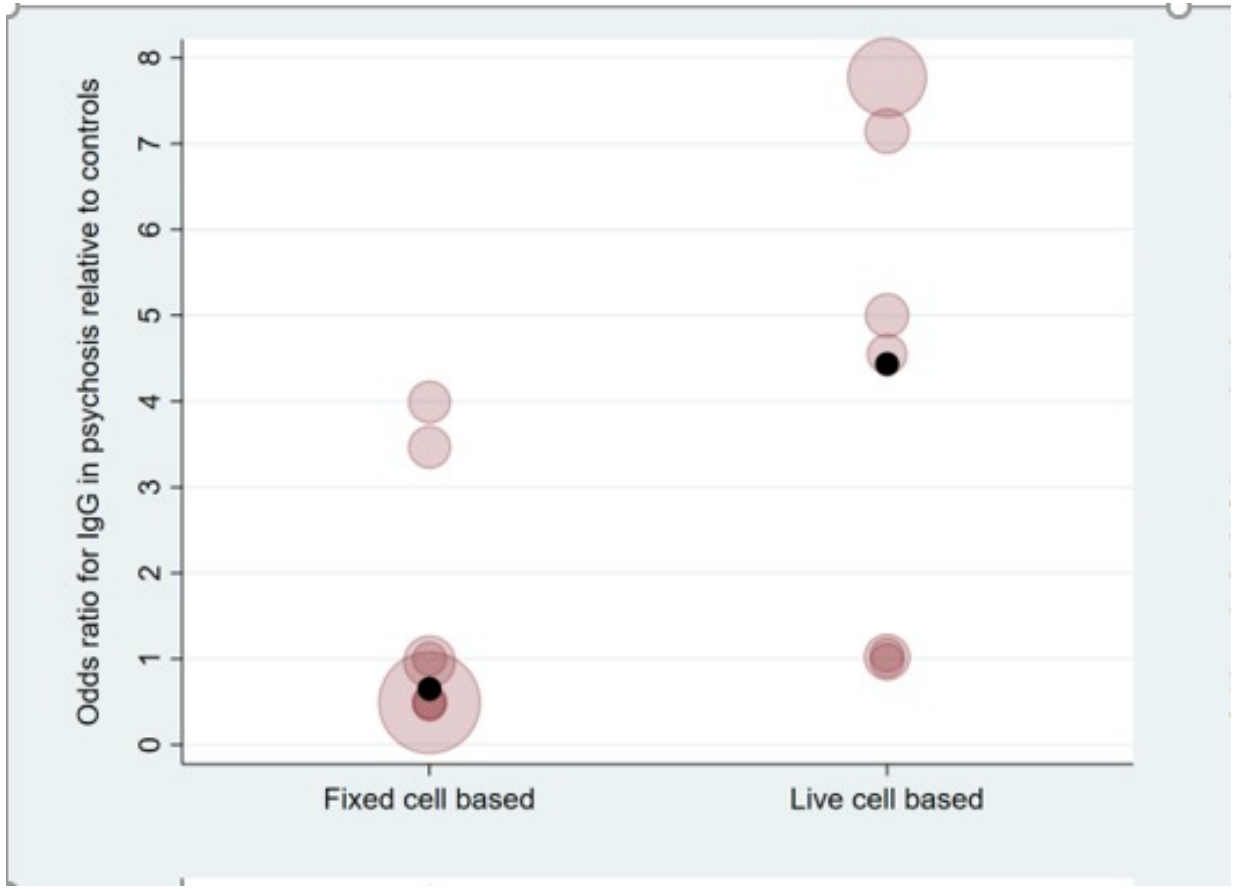
Only with the live Cell Based Assay
Only available through PPiP2



Cullen et al Lancet Psychiatry 2021

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- So what?
- Do patients with psychosis and antibodies get better with immunotherapy in the same way as those with encephalitis?

SINAPPS1 feasibility study

Participant Number	Antibody type	Duration of illness (months)	Treatment given
1	NMDAR	2	PLEX
2	NMDAR	10	PLEX + steroids
3	NMDAR	1	PLEX + steroids
4	NMDAR	2	PLEX
5	NMDAR	5	PLEX+steroids
6	VGKC	60	IVIG
7	VGKC	7	IVIG
8	VGKC	10	PLEX+steroids
9	VGKC	24	IVIG
10	GABAA	11	IVIG

Lennox et al JNNP 2018

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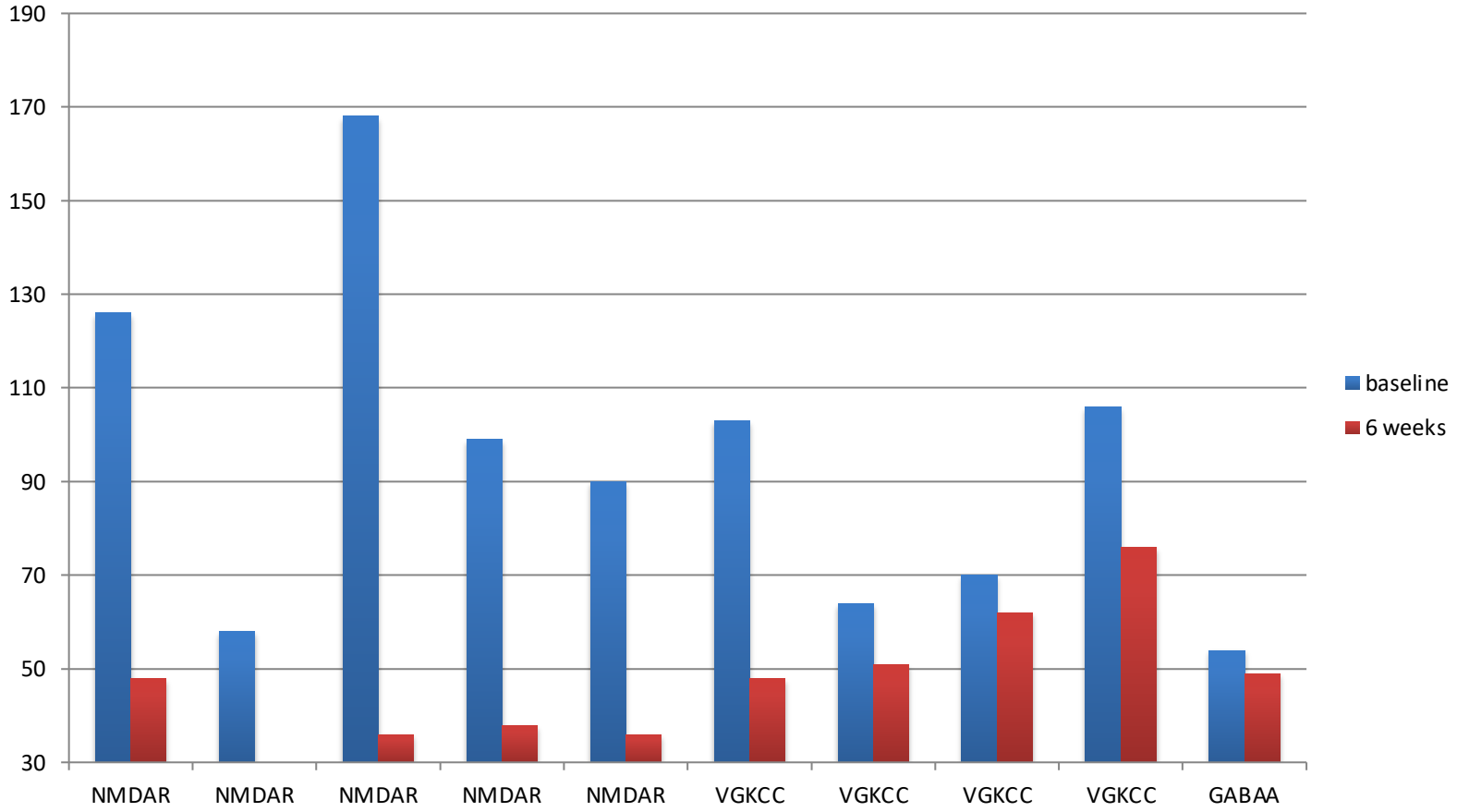
Yes – for psychosis + NMDAR antibodies
PANSS before and after immunotherapy



Lennox et al JNNP 2018

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SINAPPS 2

A randomised, phase II, double-blinded, placebo controlled trial of intravenous immunoglobulins and rituximab in patients with antibody-associated psychosis.

2017-2024

Objectives

To test the **efficacy and safety** of immunotherapy (IVIG and rituximab) in patients with acute psychosis associated with anti-neuronal membrane antibodies.

MRC Medical Research Council

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Methods
Participants

Inclusion Criteria:

1. Age 16-60
2. Acute psychosis symptoms: lasting for **at least the past two weeks** but **no longer than two years** (relapse or first episode of psychosis)
3. Presence of anti-neuronal membrane antibody in serum or CSF

Exclusion criteria:

1. Co-existing severe neurological disease
2. Hepatitis B, C, HIV, previous malignancy, pregnancy, severe infection, severe heart failure and other health safety reasons.

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SINAPPS 2 Treatment

All patients:

Antipsychotic treatment as recommended by treating psychiatrist.

Immunotherapy:

1. Intravenous immunoglobulin given over 2-4 days
2. Intravenous rituximab: 1st infusion between days 28-35, 2nd 14 days later

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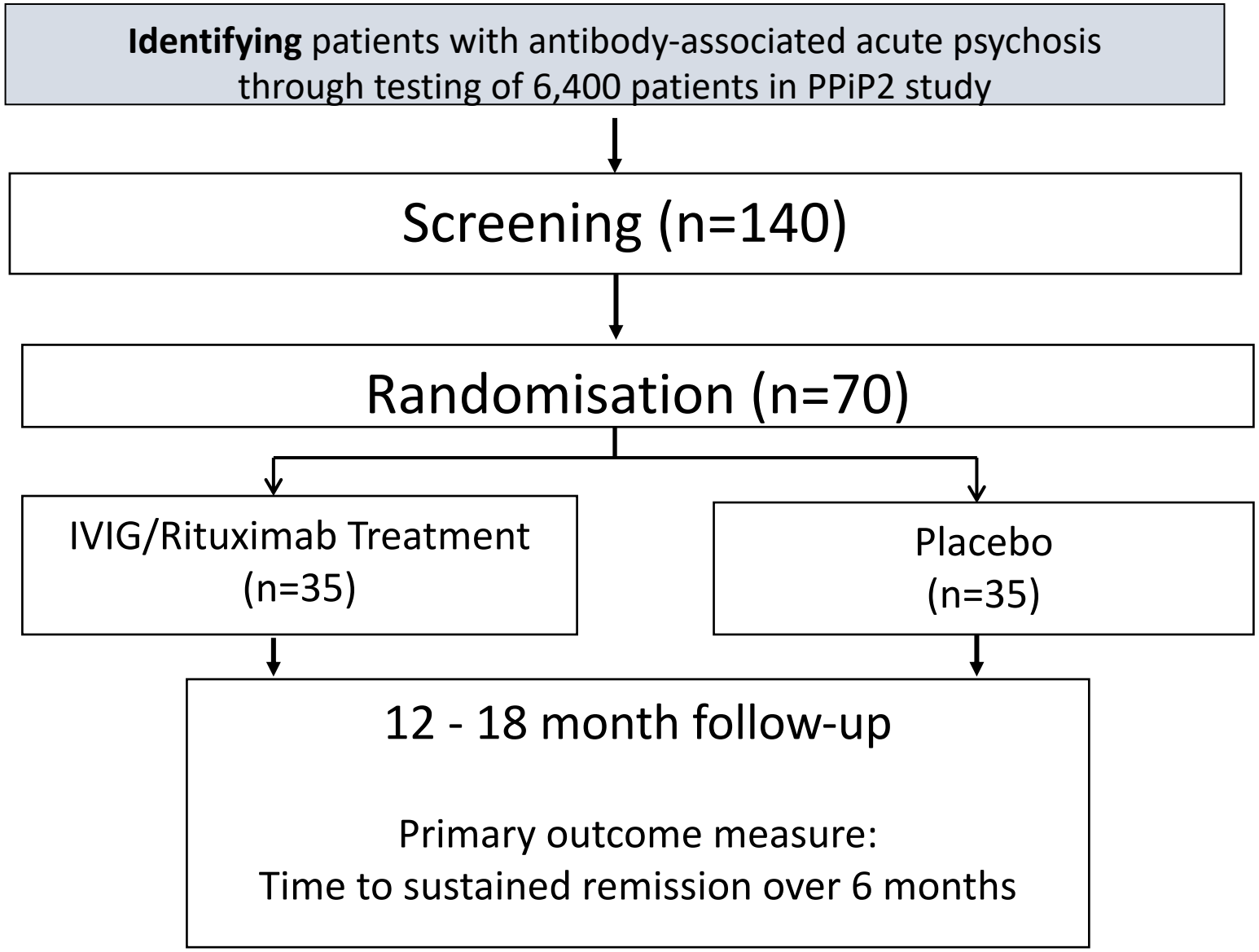
SINAPPS2 Trial



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