

Appendix 2: Pre-rechallenge assessments and recommendations

Study details	Pre-rechallenge details								
Author	Cardiology review for suitability prior to rechallenge	Time from clozapine discontinuation to rechallenge	Collaborative risk benefit analysis	Psychotropic medication suggestions	Cardiac medication suggestions	Baseline CMR	Baseline TTE	Baseline ECG	Baseline bloods
Published case reports - successful									
1. Boscutti et al. 2022	N/R	6 months	N/R	Brexpiprazole ceased, clozapine cross titration from olanzapine	N/R	N/R	+	+	+ BNP, CK, clozapine level, CRP, electrolytes, GPT, troponin
2. Bouhlel et al. 2014	N/R	1 month	N/R	N/R	N/R	N/R	N/R	N/R	N/R
3. Bowers et al. 2022	N/R	10 months	+	Olanzapine continued	N/R	N/R	N/R	+	N/R
4. Bray & Reid 2011	+	"Several" months	+	N/R	N/R	N/R	+	N/R	N/R
5. Carswell et al. 2023 (A)	+	18 months	N/R	Valproate ceased, lamotrigine + lithium commenced instead	N/R	N/R	N/R	N/R	N/R
6. Carswell et al. 2023 (B)	N/R	6 months	N/R	Cross-titrated from olanzapine, continued paliperidone depot	N/R	N/R	N/R	N/R	N/R
7. Chow et al. 2014	N/R	8 months	+	N/R	N/R	+	+	N/R	+ CRP, troponin

8. Danilewitz et al. 2021		+	5 months	+	N/R	N/R	N/R	N/R	N/R	+ CRP, troponin
9. Granja-Ingram et al. 2013		N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R
10. Griffin et al. 2021 (A)		+	10 months	+	N/R	Commenced BB	N/R	+	+	N/R
11. Griffin et al. 2021 (B)		N/R	12 months	N/R	N/R	Commenced ACEi, continued BB	N/R	+	+	+ BNP, CRP, troponin
12. Halawa et al. 2023	1)	N/R	6 months	N/R	Loxapine reduced to 20mg, quetiapine XR reduced to 800mg	N/R	N/R	+	+	+ CRP, troponin
	2)	+	18 months	+	Valproate ceased, quetiapine XR reduced to 600mg	N/R	N/R	+	N/R	+ CRP, FBC, troponin
13. Hassan et al. 2011		+	25 months	+	N/R	N/R	N/R	+	N/R	N/R
14. Holden & Begum 2022		+	0.76 months	+	N/R	N/R	N/R	N/R	N/R	+ Improved CRP, neutrophils, troponin
15. Hosseini et al. 2020		N/R	1.93 months	+	N/R	N/R	N/R	N/R	N/R	N/R
16. Ittasakul et al. 2016		+	0.2 months	+	N/R	Commenced ACEi & BB	N/R	+	N/R	+ Improved CRP, troponin, WCC
17. Koparal et al. 2019		+	7 months	+	N/R	N/R	N/R	+	+	+

									CRP, "cardiac damage profile"
18. Nguyen et al. 2017	+	5 months	+	N/R	N/R	N/R	N/R	N/R	N/R
19. Otsuka et al. 2019	N/R	2.97 months	+	Tapering of olanzapine + flunitrazepam	N/R	N/R	N/R	N/R	N/R
20. Reid et al. 2001	+	>18 months	+	N/R	N/R	N/R	+	+	N/R
21. Reinders et al. 2004	+	10 months	N/R	N/R	N/R	N/R	N/R	N/R	N/R
22. Ronaldson et al. 2012 (A)	N/R	0.3 months	+	N/R	N/R	N/R	N/R	N/R	N/R
23. Ronaldson et al. 2012 (B)	N/R	8 months	+	N/R	N/R	N/R	N/R	N/R	N/R
24. Ronaldson et al. 2012 (C)	N/R	10 months	+	N/R	N/R	N/R	N/R	N/R	N/R
25. Ronaldson et al. 2012 (D)	N/R	19 months	+	N/R	N/R	N/R	N/R	N/R	N/R
26. Rosenfeld et al. 2010	+	0.5 months	+	N/R	N/R	+	+	+	+ BNP, eosinophils, immunoglobulin E, WCC
27. Sarathy &	+	24 months	+	N/R	N/R	N/R	+	+	+

Alexopoulos 2017									BNP, CK, CRP, ESR, FBC, troponin
28. Shivakumar et al. 2020	+	84 months	+	N/R	Commenced ACEi & BB	N/R	N/R	N/R	+ Pharmaco- genetic testing to look at type of clozapine metaboliser
Unsuccessful Rechallenge									
29. Higgins et al. 2019 (A)	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R
30. Higgins et al. 2019 (B)	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R
31. Jayathilake & Singh 2009	+	Unclear	+	N/R	N/R	N/R	N/R	N/R	N/R
32. Masopust et al. 2009	+	4 months	+	N/R	N/R	N/R	N/R	N/R	N/R
33. Mudra et al. et al. 2018	N/R	Unclear	N/R	N/R	N/R	N/R	N/R	N/R	N/R
34. Noel et al. 2019 (A)	N/R	4 months	+	N/R	N/R	N/R	N/R	N/R	N/R
35. Noel et al. 2019 (B)	+	4 months	N/R	N/R	N/R	N/R	N/R	N/R	N/R
36. Noel et al. 2019 (C)	N/R	3.5 months	N/R	N/R	N/R	N/R	N/R	N/R	+ CRP, troponin
37. Ronaldson et al. 2012 (E)	N/R	9 months	+	N/R	N/R	N/R	N/R	N/R	N/R

38. Ronaldson et al. 2012 (F)	N/R	0.37 months	+	N/R	N/R	N/R	N/R	N/R	N/R
39. Ronaldson et al. 2012 (G)	N/R	96 months	+	N/R	N/R	N/R	N/R	N/R	N/R
40. Ronaldson et al. 2012 (H)	N/R	7 months	+	N/R	N/R	N/R	N/R	N/R	N/R
41. Smith et al. 2014	+	0.06 months	N/R	Olanzapine continued	ACEi	N/R	N/R	N/R	+ Non-rising CRP, falling troponin
42. Thanasan 2010	N/R	0.23 months	N/R	N/R	N/R	N/R	N/R	N/R	N/R
Unpublished case Reports – successful									
43. McMahon et al. 2023 – CD (A)	+	3 months	+	N/R	Cardiologist advised no prophylactic medications, commence if cardiac symptoms developed	+	+	+	+ CK, CRP, FBC, LFT, troponin
44. McMahon et al. 2023 – BA (B)	+	120 months	+	Reduce risperidone	Cardiologist advised no prophylactic medications, commence if cardiac symptoms developed	N/R	+	+	+ CK, CRP, FBC, LFT, troponin

45. Qubad et al. 2023	+	2.75 months	+	Tapering of lithium, amisulpride & olanzapine	Unclear if ramipril & ivabradine continued from time of CAM diagnosis	+	+	+	+ BNP, CRP, FBC, troponin
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N/R – not reported in case data; WCC – white cell count; CRP – C-reactive protein; BNP – B-type natriuretic peptide; CK – creatine kinase; FBC – full blood count; CMR – cardiac magnetic resonance imaging; ACEi – Angiotensin converting enzyme inhibitor; BB – beta blocker; TTE – transthoracic echocardiogram; ECG – electrocardiogram; ESR – erythrocyte sedimentation rate; GPT – glutamic-pyruvic transaminase