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Title

Concerns Regarding Strength of Conclusions in Systematic Review and Meta-Analysis of Neuroradiological Abnormalities in First-Episode Psychosis

Permalink

<https://escholarship.org/uc/item/2qj90830>

Journal

JAMA Psychiatry, 81(1)

ISSN

2168-622X

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Publication Date

2024

DOI

10.1001/jamapsychiatry.2023.4396

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Peer reviewed

1 **Routine MRI Imaging Should Not be Routinely Ordered in First-Episode Psychosis**

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11 **Word Count: 394**

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14 I recently cared for a patient with a first-episode of psychosis (FEP) with an otherwise normal neurologic
15 exam. The provocative meta-analysis by Blackman et al. prompted me to reflect upon the role of
16 magnetic resonance image (MRI) in such cases.¹ The authors' analysis suggests that 1 in 18 patients
17 with FEP had a 'clinically relevant abnormality', and advocate for routine MRI imaging in initial
18 assessments. However, the study's findings warrant reversal of the resultant implications for three critical
19 reasons.

20
21 Firstly, the criteria used to define the outcome raises suspicion. The definition of a clinically relevant
22 finding lacked requirement for causality with psychosis. Thus, incidental findings are included.
23 Furthermore, clinical relevance was defined as resulting in a diagnosis or a clinical management change.
24 Thus, this outcome includes diagnostic cascades that may result from clinically *irrelevant* findings. It
25 would be prudent for the authors to distinguish between clinically significant and insignificant findings. If
26 data constraints prevent this disentanglement, the accurate framing would address these findings as
27 abnormalities of *uncertain* clinical relevance.

28
29 Secondly, the three included studies with the highest reported prevalence of "clinically relevant
30 abnormalities" (two of which contributed the most to the pooled estimate) contradict the authors'
31 conclusion. Sommer et al (prevalence of 10.3%) concluded that identified findings were not causative of
32 the psychosis, while Falkenberg et al (9.4% prevalence) emphasized no resultant change in clinical
33 management.^{2,3} Additionally, Borgwardt et al (prevalence of 23.3%) found that further investigation of
34 individuals with a brain abnormality "did not result in a neurologic diagnosis or require medical
35 intervention."⁴ This underscores the necessity of scrutinizing meta-analyses that can obscure the
36 underlying evidence base with the use of ambiguously defined outcome.

37
38 Thirdly, the neuroanatomical classification of detected abnormalities further discounts their clinical
39 relevance. While the authors cite references advocating for the importance of white matter changes, the
40 most common MRI abnormality detected, these studies argue for further mechanistic investigation, but do
41 not address the clinical relevance.

42
43 Should I have ordered an MRI for my patient with FEP? Considering that the ambiguously-defined
44 outcome, contradictory underlying evidence base, and the types of abnormalities detected, the answer is
45 resoundingly no. While critically important to study the implications of white matter changes to advance
46 mechanistic knowledge of psychosis, we must strive for a balance between judicious use of MRIs guided
47 by clinical intuition and the potential for waste and harm of unnecessary diagnostic cascades.