Medication Associated with Delirium Superimposed on Dementia (DSD): A Systematic Review

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Introduction:

Several medications are associated with precipitating and predisposing patients to delirium[1] and therefore to "delirium superimposed on dementia" (DSD). It is not clear whether delirium simply unmasks a previous unrecognized dementia or if it leads to cognitive decline and thereby increases the risk of developing dementia (Figure 1). This systematic review aimed to summarise medication related information associated with the causation, prevention, and treatment of DSD.

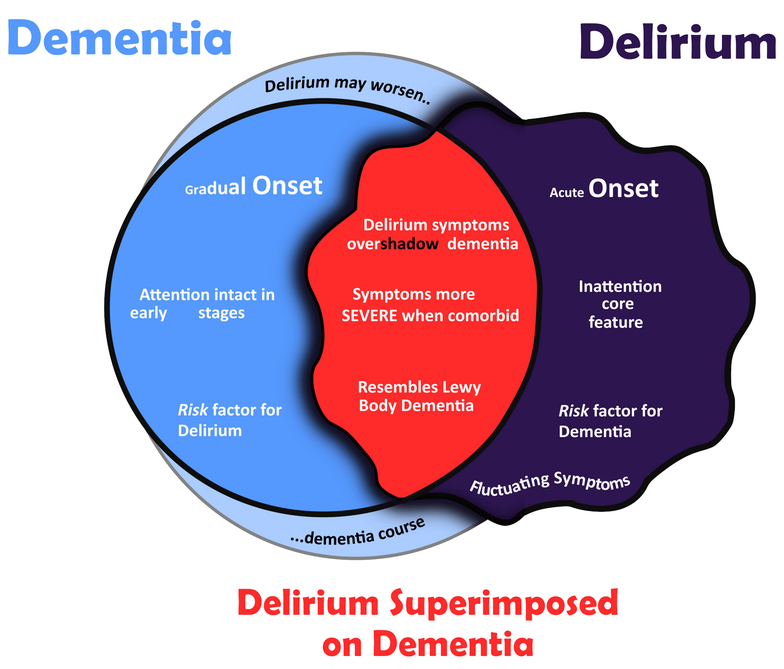

Figure 1: The relationship between delirium and dementia. [Source: Christoper Gabor, www.deliriumday.com/infographics-1]

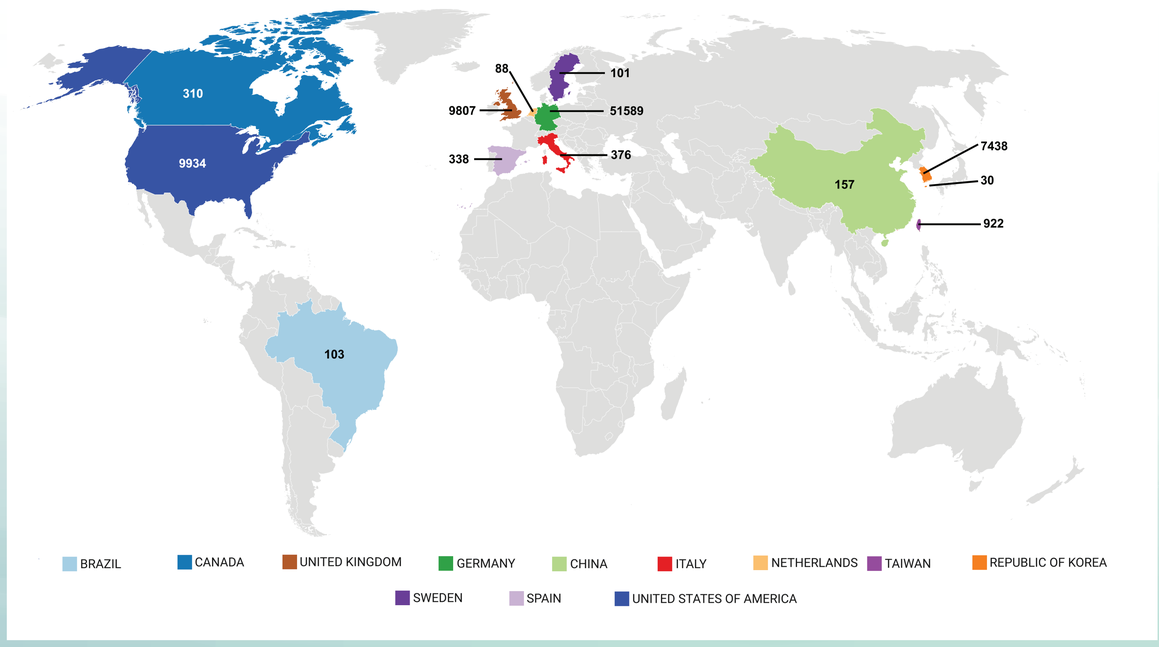

Figure 3: World heat map showing the number of participants included from each of the n=27 original studies.

Methods:

The systematic review across 12 databases was conducted following Joanna-Briggs-Institute (JBI) guidelines [PROSPERO: CRD42024546118]. A search string, based on inclusion criteria was developed with assistance from a scientific librarian. All studies conducted in adult patients 18 years or older, irrespective of dementia disease stage, from all patient care settings form the basis of inclusion criteria. Title and full-text screening was done independently by two reviewers using Covidence.[2] Figure 2 shows the summary of search results. A bespoke data extraction tool was developed and piloted. A narrative analysis of the results was undertaken and the review was reported using PRISMA guidance. The AGREE II and JBI tools were used to assess study quality. [3, 4]

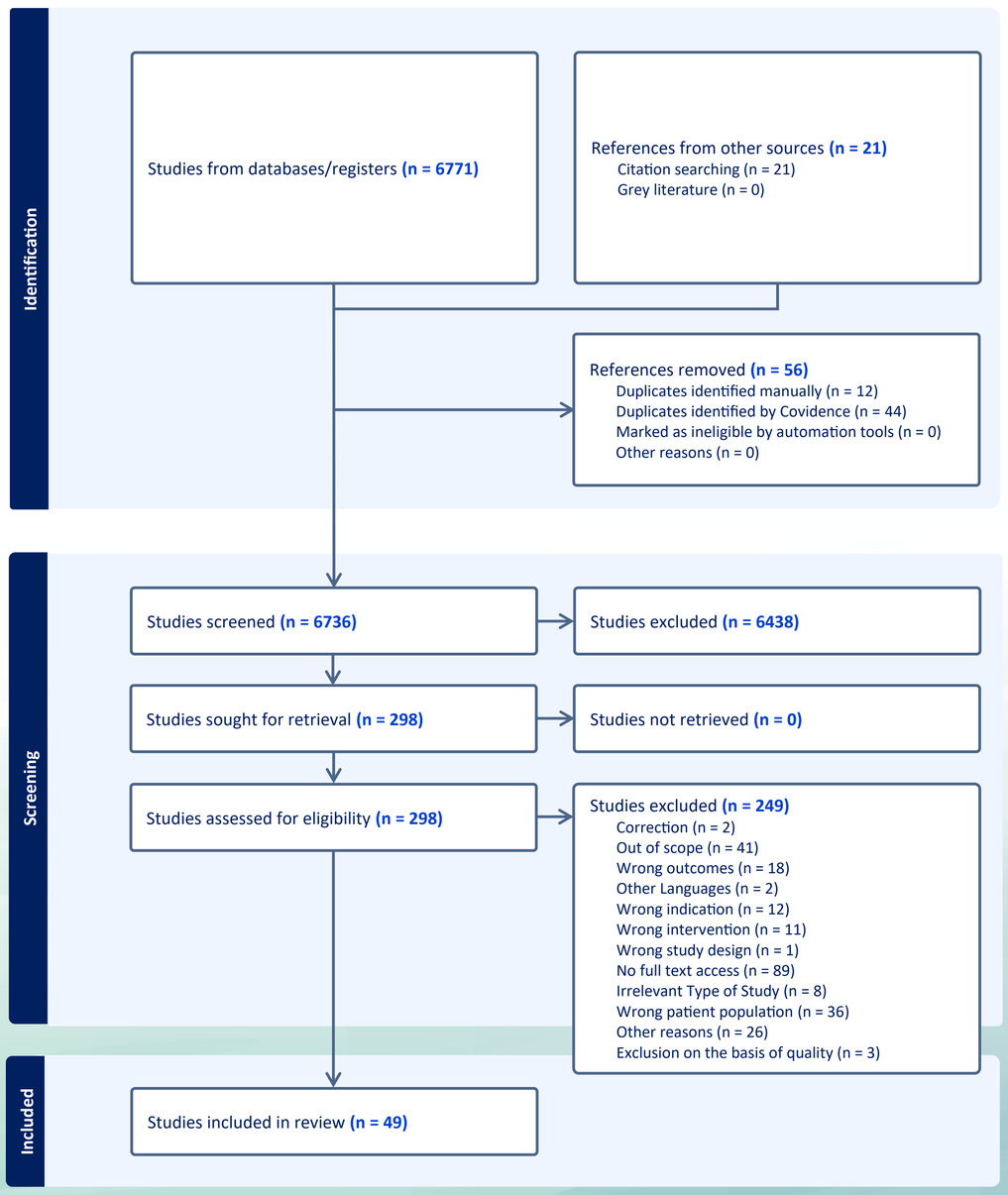

Figure 2: PRISMA chart summarising the detailed database search results, screening process and reasons for exclusion.

Results:

49 out of 6771 studies were included. A total of 81,199 patients with dementia or its subtypes as either a primary diagnosis or as a co-morbidity were included, across n=27 original studies (Figure 3). The medication classes most frequently cited as causing DSD included antipsychotics (n=13), anticholinergics (n=11), and opioids (n=10). No studies focused on pharmacological prevention. While the only high-quality randomised-controlled treatment trial revealed no clinical or statistical effect of antipsychotics (p=0.296, Chi-square test), the moderate to low-quality studies (n=17) recommended their use in treating DSD. Overall quality grading of the evidence was not possible due to paucity and disparity of published studies.

Key conclusions:

Despite brain-health and dementia being a global health priority there is a lack of high-quality evidence of pharmacological contribution to DSD in terms of causation, prevention or treatment to inform clinical practice and patient safety.

References:

1. Ormseth CH, LaHue SC, Oldham MA, Josephson SA, Whitaker E, Douglas VC. Predisposing and Precipitating Factors Associated With Delirium: A Systematic Review. JAMA Netw Open. 2023 Jan 3;6(1):e2249950. doi: 10.1001/jamanetworkopen.2022.49950
2. https://support.covidence.org/help/how-can-i-cite-covidence
3. https://www.agreetrust.org/wp-content/uploads/2017/12/AGREE-II-Users-Manual-and-23-item-Instrument-2009-Update-2017.pdf
4. https://jbi.global/critical-appraisal-tools