

## **Review of “Pharmacological and nonpharmacological approaches to reduce disinhibited behaviors in dementia: a systematic review” by Burley, Burns, and Brodaty (2022).**

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### **Key highlights:**

- Among the 30 included studies (9 pharmacological and 21 non-pharmacological), only 14 (7 pharmacological and 7 non-pharmacological) reported significant decreases in disinhibited behaviors. Effective intervention approaches include pain management, antidepressants, models of care, education and/or training, music-based approaches, and physical activity.
- Both pharmacological and non-pharmacological intervention studies have high overall research quality, while the mean effect size of RCT non-pharmacological interventions is larger compared to pharmacological approaches (mean Cohen’s  $d = 0.49$  and  $0.27$ , respectively).
- Some factors that may improve effects of reviewed studies include adopting a consistent and comprehensive definition of disinhibited behaviors, RCT design, larger sample sizes, comprehensive assessment tools with gold standards, and consideration of demographic, health, social and cultural characteristics of PLWD.

Older people living with dementia (PLWD) commonly experience changes in affect, cognition, and behavior. Behavioral and psychological symptoms of dementia (BPSD), which encompass a heterogeneous group of non-cognitive symptoms and behaviors, is the term to describe the multifaceted changes experienced by PLWD (Finkel et al., 1997). Some of the BPSD may cause difficulties for PLWD’s independent living, increase the care burden of families, and may result in more serious social repercussions (Guimet et al., 2021). Therefore, investigating the physiological and phenomenological mechanisms underlying the various BPSD change patterns can help healthcare providers and families better understand the health status of PLWD, and inform the development of interventions aimed at preventing exacerbations of BPSD while also improving the coping capacity of caregivers.

Disinhibited behaviors are one of the behavioral symptoms commonly experienced by PLWD. Specifically, PLWD may exhibit some "socially inappropriate behaviors", such as impulsive aggression, substance abuse, and inappropriate sexual behaviors (Alkhalil et al., 2004; Halloran, 2014; Miller et al., 1997). However, the lack of agreement on the pathological origin and underlying mechanisms in existing research impedes the development of related treatments and interventions. According to Burley et al. (2022), the definitions of disinhibited behaviors are inconsistent on whether to include emotional, psychological, and sexual aspects, which likely explains the variable prevalence rates of disinhibited behaviors reported in the literature. In addition, there is debate regarding the physiological mechanism of disinhibited behaviors, such as "impulse suppression disability" versus "hyperactivity", which largely determines the progress of pharmacological interventions. Furthermore, the appropriateness of PLWD’s behavior may vary in different social, cultural, or religious contexts, which also affects the external validity of behavioral interventions (Guimet et al., 2021). Accordingly, it is necessary to systematically review the existing treatments and interventions for disinhibited behaviors of PLWD, in order to describe their effects and reveal areas for future clinical and research endeavors.

Burley et al. (2022) adopted a rigorous methodology to increase the accuracy and credibility of the review results in light of the aforementioned challenges. To address inconsistencies in the definitions of disinhibited behaviors across studies, they employed a thorough search strategy that included studies on verbal behaviors, sexuality, emotion, and general BPSD. The approach builds on a prior attempt to distinguish between physiological and psycho-behavior-based strategies by categorizing interventions into pharmacological and non-pharmacological categories. To guarantee the statistical and clinical significance of the results, the review also employs structured tools to assess the research quality of included studies based on study design, participant characteristics, outcome measures, and statistical analyses. Standardized effect sizes were also calculated for randomized controlled trials (RCT). The overall methodology satisfies the requirements of the mainstream systematic review quality appraisal framework (i.e., AMSTAR-2) (Shea et al., 2017).

For this systematic review, 30 studies on disinhibited behavior interventions in PLWD were identified, including 9 pharmacological and 21 non-pharmacological interventions. The included studies came from 15 countries, and more than half were conducted in Europe. It is important to note that all these studies treated disinhibited behaviors as secondary outcomes. The Neuropsychiatric Inventory (NPI) disinhibition subscale was used in 26 of the included studies, and other studies used relevant subscales from the Frontal Behavioral Inventory (FBI) and Cohen-Mansfield Agitation Inventory (CMAI). Among the 9 pharmacological interventions, 3 used RCT design, and 7 studies with a total of 2,825 participants reported significant results which indicated that pain management, antidepressants, or traditional herbal medications (e.g., risperidone, citalopram, and yokukansan) can reduce disinhibited behaviors. Although the overall research quality was strong and the 3 RCTs showed small to medium effect sizes (mean Cohen's  $d = 0.27$ ), these studies still have design limitations like small sample sizes, no follow-up, and lack of control/placebo groups.

Among the 21 non-pharmacological interventions, 14 used RCT design, and only 7 had enough data to calculate effect sizes. Seven effective studies (including 4 RCTs) adopted various intervention approaches, including 3 care models, 2 staff education and training programs, 1 music therapy program, and 1 physical activity intervention. Communities, residential care facilities, and dementia-specific care units were among the research settings. Non-pharmacological interventions had comparably strong research quality to pharmacological interventions, but their mean effect size was larger (Cohen's  $d = 0.49$ ). Models of care and educational training programs exhibited the greatest disinhibited behaviors reduction and the largest study effect sizes. These studies share the following three characteristics: First, they are individualized programs that comprehensively assess participants' health status (e.g., BPSD, medications, daily behaviors); Second, they all involve different stakeholders (i.e., family caregivers, nursing staff, psychologists, and physicians) in the development of treatment or training plans; Third, they all have regular effect evaluations to ensure the quality of the interventions. These three characteristics guarantee the effects of interventions and give future interventions a methodological framework.

This systematic review found inconsistent results of existing interventions for reducing PLWD's disinhibited behaviors. Only 14 of the 30 included studies presented statistically significant

findings. Effective studies showed that non-pharmacological interventions have a larger mean effect size than pharmacological interventions, particularly when they employ approaches like models of care and educational training; the person-centered approaches can provide PLWD and their families with creative individualized solutions. Factors dampening the intervention effects include lacking consistent and comprehensive definitions of disinhibited behaviors, RCT design, large samples, comprehensive assessment tools with gold standards, and consideration of the demographic, health, social and cultural characteristics of PLWD.

The results of this systematic review can inform future research. For intervention studies, disinhibited behaviors should be examined specifically and comprehensively as primary outcomes. Although many studies used the disinhibition subscale of NPI as an outcome measure and adapted it for groups of different genders, races, languages, and dementia subtypes, the subscale only assesses hyperactivity rather than the loss of impulse control. Sexual disinhibition was not assessed either. Research should also adopt more rigorous designs, such as using RCT to set control/placebo groups and improve the effectiveness of interventions. For clinical practice, patient-centered non-pharmacological strategies respect the rights of PLWD to the greatest extent, promote communication between healthcare providers and PLWD's families, and caregivers, and avoid /minimize drug toxicity and adverse effects. It is suggested that drug therapy should be reserved for use when nonpharmacological strategies have failed, and then only if necessary in the short term.

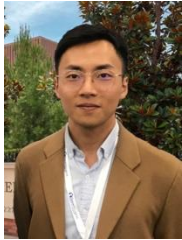
As this systematic review only includes articles published in English, and most of the included studies come from developed regions like Europe and North America, the representativeness of the results for disinhibited behavior interventions in developing countries is questionable. Future research should pay more attention to the implementation of disinhibited behavior interventions in low- and middle-income countries, and present practice solutions to health disparities facing local PLWD populations.

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