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Antidepressant Medication Nonadherence in Adult Patients with a Major Depressive Disorder

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This is to certify that the doctoral study by

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has been found to be complete and satisfactory in all respects,
and that any and all revisions required by
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Executive Summary: Clinical Practice Guideline

Antidepressant Medication Nonadherence in Adult Patients with a Major Depressive Disorder

by

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Summary

The chosen approach for the Doctor of Nursing Practice (DNP) project was a clinical practice guideline (CPG) on interventions to improve antidepressant medication adherence in adults diagnosed with depression in an outpatient setting. The consequences of medication nonadherence in patients with depression are devastating for individuals and the healthcare system. Therefore, addressing it within nursing practice is crucial to enhance treatment efficacy and improve patient outcomes. The practice question related to the DNP project was to determine whether the CPG could improve antidepressant medication compliance in adults diagnosed with a depressive disorder in an outpatient setting. I aimed to develop a CPG on evidence-based practice approaches to reduce a gap in practice and improve patient outcomes.

The developed guideline was derived from a literature search that included systematic reviews, meta-analyses, RCTs (randomized control trials), cohort studies, qualitative studies, and literature reviews. Four designated experts used the AGREE II tool to evaluate the developed CPG. All four expert reviewers judged that the developed guideline was of high quality and recommended it for the designated organization and other psychiatric outpatient settings, enabling adults with depression to get equitable, just, and fair healthcare services. By reducing the gap in nursing practice, the CPG could positively affect the organization's standards of care, increase patients' quality of life, reduce healthcare costs, and promote positive social change.

Background

When patients suffering from a major depressive disorder voluntarily discontinue their prescribed medications without the provider's advice, it is referred to as medication nonadherence (Donneyong et al., 2024). The negative impact of medication nonadherence in patients with a major depressive disorder affects individuals, their families, and the whole healthcare system. Despite the available treatment, only 60.0% - 70.0 % of individuals with major depressive disorders take their medications as prescribed (Pitanupong & Sammathit, 2023). The common contributors to antidepressant medication nonadherence are substance use comorbidity, poor treatment alliance with providers, false beliefs and myths about treatment, and the severity of the course of illness (García-Pérez et al., 2023). My purpose with this DNP project was to identify factors contributing to nonadherence to medications in patients struggling with depression and find evidence-based recommendations to develop a CPG that would improve adherence to antidepressant medications.

The selected organization did not have a standard treatment guideline to enhance compliance with antidepressant medications in adults with a major depressive disorder, and providers used a non-standardized treatment process to treat this patient population. The organization has noted over the years that most adult patients taking antidepressants discontinue their medications within the first month of treatment, with approximately one out of five patients taking antidepressant medications as prescribed over 4 months only. Antidepressant medication nonadherence in the organization was strongly evidenced by a significant and continuous increase in patients self-reporting not taking antidepressant

medications as prescribed, a considerable drop in antidepressant medication refills obtained through pharmacy dispensing databases, and a consistent rise in follow-up cancellations for patients with depression taking antidepressant medications. Thus, there was substantial evidence for a change in practice in the organization. The organization firmly acknowledged that enhancing adherence to antidepressant medications was a critical aspect of major depressive disorder treatment management that could significantly improve clinical outcomes and positively impact social change, diversity, equity, and inclusion.

The developed guideline was derived from a literature search that included systematic reviews, meta-analyses, randomized control trials (RCTs), cohort studies, qualitative studies, and literature reviews. Primary databases used for the literature search included CINAHL, PSYINFO, MEDLINE, PubMed, and Cochran. Eight studies were retained from the literature search, and their strength ranged from Level I to V, with an overall quality rating of robust, exemplary, or low. The appraisal process began with the selection of articles whose evidence answered the evidence-based practice (EBP) question. The Hierarchy of Evidence Guide and the Research Evidence Appraisal tools from the Johns Hopkins Evidence-based Practice Model for Nursing and Healthcare Professionals were used to determine study levels and the quality of evidence. Level I evidence included a meta-analysis, a systematic review, and a cluster RCT with a solid overall quality rating. Level II evidence included a quasi-experimental study with an excellent overall rating quality. Level III evidence consisted of a controlled trial and a cohort study with a good overall quality. The two last articles were literature reviews

representing Level V evidence with an excellent overall rating quality. Summarizing and synthesizing findings that helped answer the EBP question were the last steps in the appraisal process, and the best evidence recommendations were synthesized using critical thinking. The recommendations from the eight studies revealed strong and compelling evidence with consistent results justifying a change in practice. The research findings were focused on clinical interventions that providers must initiate on the first encounter with patients and steps to implement during the treatment phase to ensure adherence to treatment with antidepressant medications. Significant findings of the literature search supporting the change in practice included the positive impact of collaborative care, patient-provider communication, brief psychoeducation, and routine assessment of adherence on antidepressant medication adherence. Also, nurturing a therapeutic bond before initiating psychopharmacology interventions and providing clear instructions to patients have been shown to assist adult patients with depression to better comply with their medications (Solmi et al., 2021). Chi et al., (2019), using a controlled study to investigate the importance of the Smart-Phone Application Follow-up System (SPAFS) on antidepressant medications compliance, found that after 6 months of follow-up and management using the system, the intervention group had a significantly lower rate of medication discontinuation of 26.6% versus 7.0% in the control group. I focused my project question on whether the experts would approve and recommend the CPG, which was developed to enhance antidepressant medication adherence in adult patients with a major depressive disorder in an outpatient setting.

Clinical Practice Guideline (CPG) Development

The literature search for this project provided accurate, objective, and authoritative evidence supporting a change in practice in the organization. Significant findings from the literature search answered the EBP question and were included in the CPG. The final CPG represented a table with evidenced-based treatment steps for improving compliance with antidepressant medications in adult patients with a major depressive disorder. The interventions included in the CPG were organized into three phases: screening, treatment, and follow-up (Appendix A). During the screening phase, providers are instructed to use the first encounter with patients to establish a treatment alliance. Next, providers must adopt an interdisciplinary approach to patient care and provide scientific explanations to rectify the myths and beliefs held by patients. Also, in the screening phase, providers must assess factors causing nonadherence to treatment and suicidal ideations while continuing to adopt collaborative care management. In the second phase of treatment, providers are instructed to choose the antidepressant based on each patient's tolerability profile and assess antidepressant adherence at each follow-up visit. The last treatment phase is the follow-up, where providers are instructed to boost patients' confidence in treatment and improve patient satisfaction ratings, as it has been shown to strongly predict antidepressant adherence (Donneyong et al., 2024). Additionally, in the follow-up section, providers are encouraged to consider using the SPAFS as Chi et al., (2019) reported that it has been shown to lower the rate of medication discontinuation by 26.6%.

After developing the CPG, four psychiatric mental health nurse practitioners were selected as experts to evaluate it. The four experts who assessed the CPG included my mentor, who holds DNP degree and provides preceptorship to nurses in master programs. The three other experts have master's degrees in psychiatry, work in adult outpatient clinics, and are completing their doctorates. Each member of the expert panel was selected based on extended experience in treating adult patients with depression and taking antidepressant medications. The chosen expert's clinical expertise ranged from 3-8 years. Each expert was provided with the AGREE II manual through email. Then, a virtual meeting was held with the selected experts to review the grading instrument and the evaluation process and answer questions.

Appraisers used the AGREE II (Appendix B) instrument, a widely recognized tool for evaluating clinical practice guidelines, organized within six domains, and including 23 appraisal criteria. The four selected experts used personal judgment and clinical experience to evaluate each of the seven domains of the grading tool. The six domains include scope and purpose, stakeholder involvement, rigor of development, clarity of presentation, applicability, and editorial independence. A 7-point Likert scale for agreement is available for each item of the grading instrument and includes two global rating items (Hoffmann-Eßer et al., 2018). A calculated quality score for each of the six domains is obtained and can be used to identify high-quality guidelines and their strengths and limitations. Domain scores are obtained by adding up all the scores of the individual items in a domain and by scaling the total as a percentage of the maximum possible score for that domain (Hoffmann-Eßer et al., 2018). Furthermore, it is crucial not

to aggregate all six domain scores into a single quality score as they must remain independent. Interpretation of the results of the domains depends on the importance that organizations put on different domains and items in that context. Therefore, if an organization's leadership prioritizes some quality domains over others, essential stakeholders can create thresholds reflecting the prioritized domain scores before beginning the guideline appraisal. An example of a threshold can be to decide that guidelines with a Domain 2 score greater than 90% are of high quality. AGREE II users appraise the other five domains only when the guideline meets the created quality threshold for the preferred domain (score above 90%). Another component of the domain's results interpretation is when an organization's leadership equally considers all domains. In this case, relevant stakeholders can create an outset across all six domain scores. After obtaining all domain scores, the evaluators are expected to provide two overall assessments of the guideline to judge the quality and recommendation for use in clinical practice (Hoffmann-Eßer et al., 2018)

Results

Before submitting the developed clinical guideline for evaluation, the targeted organization’s administrators reported their preference for Domains 1, 2, and 4, as these domains represented crucial interventions aimed at improving adherence to treatment with antidepressant medications. Therefore, thresholds for Domains 1, 2, and 4 of 90% or above were established for these domains. The expert panel evaluated those three domains first. Next, the scores of the other three domains were calculated, as the three preferred domains scored 90% and above. The results of each domain were as follows:

Domain 1 obtained a total of 100%, Domain 2 scored 97%, Domain 3 scored 90%, Domain 4 scored 93%, Domain 5 scored 98%, and Domain 6 scored 81%. Domain 6 score of 81% did not impact the CPG relevance as a threshold was previously established. The methods used to obtain the scores are illustrated in Appendix C. All four reviewers judged that the developed guideline was of high quality and recommended it to this organization and other psychiatric outpatient settings. The only suggestion the experts made was to clarify how to use the SPAFS in the follow-up phase of treatment, and this was to be done. Effectively, the SPFAS had been used to monitor medication compliance in patients with depression and was shown to lower the rate of medication discontinuation by 26.6% (Chi et al., 2019**).** This guideline will be reviewed and evaluated every 3-5 years, following the organizational policy, and using the best available evidence. A reasonable time limit to update the guidelines is three years, a recommendation by most methodological handbooks (Hoffmann-Eßeret al., 2018). The content review of the developed CPG guideline will be due in 2027 or 2029.

Overall, end users (the organization's nurse practitioners) reported that the CPG represents an excellent opportunity to solve the chronic issue of antidepressant medication nonadherence and that it will be easy to implement. This CPG was developed using EBP recommendations from a comprehensive literature search where study results revealed an enhancement in antidepressant medication compliance in adults with depression. Therefore, the CPG can provide the organization with an evidence-based foundation for ameliorating medication compliance in adult patients with depression. Moreover, using the CPG for medication compliance in patients with depression should

lead to better treatment efficacy and quality of care and increase patient outcomes. Furthermore, the satisfactory results of the CPG evaluation provide a solid foundation for enhancing antidepressant medication compliance beyond the organization. The only potential limitation in developing the CPG was that two of the studies from the body of evidence were literature reviews, representing a lower evidence level in the evidence pyramid. Nevertheless, the findings of the literature reviews were congruent with those of studies with higher levels of evidence.

Conclusion

Medication nonadherence is among the most critical problems in mental health as González de León et al. (2022) reported. Antidepressant medication nonadherence in adults diagnosed with depression represents a significant burden on individuals, their families, and the healthcare system (González de León et al., 2022). The developed CPG for the DNP project is based on EBP interventions to improve antidepressant medication adherence in adults diagnosed with depression in an outpatient setting. Four selected experts evaluated the developed clinical guideline via the AGREE II tool, organized within six domains and including 23 appraisal criteria. Domain scores were obtained as required by the evaluation tool (Appendix B). After obtaining all domain scores, the evaluators provided two overall assessments of the guideline, judging its quality, and recommending it to clinical practice.

The CPG can provide the organization with an evidence-based foundation for enhancing antidepressant medication compliance in adult patients with a major depressive disorder. Also, implementing the CPG in the organization should allow nurse

practitioners to positively impact nursing practice by initiating EBP interventions that benefit patients and reduce the risk of potentially unsafe practices. Furthermore, using the CPG to improve medication adherence in depressive patients will improve treatment efficiency, healthcare safety, and quality of care, positively impacting social change. Moreover, the recommendations of the CPG for mental health settings can promote diversity, equity, and inclusion, as they will reduce irrelevant variations in practice. This CPG will require collaborative care, a solid therapeutic alliance, and continuous monitoring, representing essential nursing values, as several studies showed the positive impact of these nursing interventions on patient adherence to medication.

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Appendix A: Clinical Practice Guideline to Improve Antidepressant Medication Adherence in Adult Patients with Major Depressive Disorder (MDD) in an Outpatient Setting

PART I – Screening	Recommendation/Limitations	Level of Evidence/Quality ratings	Comments	Source of Evidence
Before prescribing Antidepressants				
• Identify the causes of antidepressant medication nonadherence and explore antidepressant side effects.	**Recommended: Strong, compelling evidence, consistent results** - potential publication bias as grey literature (unpublished research articles) was not included	Level 3(systematic review of nonexperimental studies)	There is a negative relationship between Somnolence, sexual dysfunction, gastrointestinal and headaches, and the dropout rates of antidepressant medications.	Niarchou, E., Roberts, L. H., & Naughton, B. D. (2024)
• Establish a treatment alliance with patients and loved ones at the first encounter, if possible.	**Recommended: Strong, compelling evidence**, **consistent results.**	Level 5 (literature review)	-Choosing a one-size-fits-all approach, although recommended by most international clinical guidelines, might work worse than personalized approaches	Solmi et al., *2021*
• Adopt an interdisciplinary approach to patient care that includes collaborative decision-making and mobile applications to remind patients when it is time to take their medication	**Recommended: Strong, compelling evidence, consistent results** **Recommended** **No study limitation**	Level I (metanalysis)	-The treatment team should be cross-functional.	González de León et al., 2022

• Provide scientific explanations to rectify the myths and beliefs held by patients.		Level 5(Literature review)	When most patients start feeling better, they misbelieve that they can interrupt treatment or take less medication. - Some people perceive depression as a normal stage of the aging process, and others believe that they experience depression symptoms because of bad fortune or a weak personality. -It is predicted that low socioeconomic status is positively correlated to less adherence to antidepressants	Marasine et al., 2021
Assessment: • Assess sociocultural, sociodemographic, logistical, patient-related, and medication-related factors.	**Recommended** No limitation **Strongly recommended**	Level 5(Literature review)	-Symptoms improvement relative to antidepressants can be four to six weeks delayed. - Patients younger than 40 are in the majority non-adherent to their prescribed antidepressants.	Marasine et al., 2021

• Assess and address suicidal Ideations at each visit: • Adopt a Collaborative care management model that emphasizes interpersonal psychotherapy, psychoeducation, and antidepressant adherence.	**Recommended**	Level 2(Quasi-experimental study). Level I (Custer RCT)	- Compared to those not experiencing suicide ideations, antidepressant treatment is subsequently less effective in people with suicidal thoughts. -Antidepressant adherence was significantly better among patients attending a CSC (Collaborative Step Care) clinic.	Baeza-Velasco et al., 2018 Pillai et al., 2021
PART II – Treatment Phase				
PRESCRIPTION • Develop an individualized treatment plan based on symptom patterns, history, and adverse events. • Explain the rationale for medications through psychoeducation regarding biological and psychological mechanisms underlying depression.	**Recommended, Robust and compelling evidence, consistent results.** **Recommended, Robust and compelling evidence** **Recommended, Robust and compelling evidence** **Recommended,**	Level 5(literature review) Level 5(literature review Level 5(literature review		Solmi et al., *2021* Solmi et al., *2021* Solmi et al., *2021*

• Select the antidepressant with the best individually tailored tolerability profile in collaboration with the Patient and significant others. • Whenever possible, it is preferable to slowly titrate the drug, simplify the drug regimen, and tailor treatment to the routine. • Use validated scales to assess antidepressant adherence at each follow-up visit. • Provide **brief** psychoeducation emphasizing the consequences of nonadherence**,** lag time before relief of symptoms, possible side effects, the onset of treatment, the drug, dosage, and duration,	**Robust and compelling evidence** **Recommended** **No limitation**	Level 5(literature review. Level 5(literature review Level 5(Literature review)	BMQ and MMAS are examples of validated scales. TDM can be used to assess antidepressant serum levels, and regular TDM can promote adhesion to antidepressants. Antidepressants can take four to six weeks before patients start feeling symptom improvement.	Solmi et al., *2021* Solmi et al., *2021* Marasine et al., 2021
PART III – Treatment Access and Follow-Up				
• Improve Patient satisfaction rating as it strongly predicts antidepressant adherence therapy**.**	**Recommended** . **Good and consistent evidence** -A limited number of participants.	Level 4 (Cohort) Level 1 (Controlled Trial)	The study shows that adherence to antidepressants is positively correlated to Patient's satisfaction with healthcare as `confident patients were more likely to adhere to antidepressants as compared to those not satisfied.	Donneyong et al., 2024 CHI et al., 2019

• Consider using the SPAFS (Smartphone Application Follow-up System)	The intervention group participated in follow-up with the SPAFS, while the subjects in the control group participated in traditional psychological follow-up procedures.		Using the SPAFS (Smartphone et al.) for follow-up significantly lowers the rate of medication discontinuation by 26.6% (CHI et al., 2019).	
BMQ = Brief Medication Questionnaire; MMAS = Morisky Medication Adherence Scale; QIDS = Quick Inventory of Depressive Symptomatology; TDM = Therapeutic Drug Monitoring.				

Appendix B: AGREE II Score Sheet

Domain	ITEMS	AGREE II Rating						
		1 *Strongly Disagree*	**2**	**3**	**4**	**5**	**6**	**7** *Strongly Agree*
1 Scope and Purpose	1. The guideline's overall objective(s) is (are) specifically described.							
	2. The health question(s) covered by the guideline is (are) specifically described.							
	3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.							
2 Stakeholder Involvement	4. The guideline development group includes individuals from all the relevant professional groups.							
	5. The views and preferences of the target population (patients, public, etc.) have been sought.							
	6. The target users of the guideline are clearly defined.							
3 Rigor of Development	7. Systematic methods were used to search for evidence.							
	8. The criteria for selecting the evidence are clearly described.							

Domain	ITEMS	AGREE II Rating						
		1 *Strongly Disagree*	**2**	**3**	**4**	**5**	**6**	**7** *Strongly Agree*
	9. The strengths and limitations of the body of evidence are clearly described.							
	10. The methods for formulating the recommendations are clearly described.							
	11. The health benefits, side effects, and risks have been considered in the recommendations.							
	12. There is an explicit link between the recommendations and the supporting evidence.							
	13. The guideline has been externally reviewed by experts before publication.							
	14. A procedure for updating the guideline is provided.							
4 Clarity of Presentation	15. The recommendations are specific and unambiguous.							
	16. The different options for management of the condition or health issue are clearly presented.							
	17. Key recommendations are easily identifiable.							

Domain	ITEMS	AGREE II Rating						
		1 *Strongly Disagree*	**2**	**3**	**4**	**5**	**6**	**7** *Strongly Agree*
5 Applicability	18. The guideline describes the facilitators and barriers to its application.							
	19. The guideline provides advice and/or tools on how the recommendations can be put into practice.							
	20. The potential resource implications of applying the recommendations have been considered.							
	21. The guideline presents monitoring and/ or auditing criteria.							
6. Editorial Independence	22. The views of the funding body have not influenced the content of the guideline.							
	23. Competing interests of guideline development group members have been recorded and addressed.							

Appendix C: Domain 2 Evaluation: Stakeholder Involvement

	Item I	Item 2	Item 3	TOTAL
Appraiser 1	7	7	7	21
Appraiser 2	6	7	7	20
Appraiser 3	7	7	7	21
Appraiser 4	6	7	7	20
TOTAL	26	28	28	82

Maximum possible score = 7 (strongly agree) x 3 (items) x 4 (appraisers) = 84 Minimum possible score = 1 (strongly disagree) x 3 (items) x 4 (appraisers) = 12

The scaled domain score will be:

$$\frac{\text{Obtained score} - \text{Minimum possible score}}{\text{Maximum possible score} - \text{Minimum possible score}}$$

(82-12/84-12) *100=70/72*100=97%

***Score=97%**