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Measurement and Determinant Factors of Medication Adherence in Hemodialysis Patients: A Prisma-based Review

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Abstract

Adherence to medication is one of the essential determinants of outcomes in patients on maintenance hemodialysis, but there is considerable variability in the rates of medication adherence and the determinants of adherence in different studies. The objective of this review was to summarize the evidence on medication adherence in adult patients on hemodialysis and to identify the determinants that have been most consistently related to medication adherence behavior. A systematic literature search was conducted in PubMed, Scopus, Google Scholar, and Web of Science for studies published in English between January 2005 and January 2024, in accordance with PRISMA 2021 guidelines. Study quality was evaluated using the Newcastle–Ottawa Scale. Fourteen studies met the inclusion criteria, most of which were cross-sectional in design. Medication adherence rates varied widely, ranging from 10% to 94%, largely due to heterogeneity in assessment tools, study populations, and methodological quality. Across studies, psychosocial and cognitive factors emerged as the most consistent predictors of adherence. Motivation and perception of hemodialysis, as well as the level of medical knowledge, were significantly associated with adherence in all studies assessing these variables. Depression, forgetfulness, and economic status were also frequently significant, whereas demographic variables and clinical factors showed inconsistent or weak associations. This review highlights that medication adherence in hemodialysis patients is driven predominantly by psychosocial and knowledge-based determinants rather than by clinical characteristics alone. These findings support a biopsychosocial, patient-centered approach to care and underscore the need for standardized adherence measurement and targeted interventions addressing motivation, health literacy, and mental health to improve outcomes in this vulnerable population.

Keywords: Determinants, Hemodialysis, Medication Adherence, Psychosocial Factors.

Introduction

The World Health Organization defines the World Health Organization adherence as the extent to which a patient's action, such as taking medications following a diet and making lifestyle changes match the recommendations developed with a healthcare provider. This definition of the World Health Organization adherence is now the widely cited in adherence research. It replaces ideas of compliance and highlights the collaborative nature of the relationship between the patient and the healthcare provider. The emphasis on partnership between the patient and the healthcare provider has clinical implications. It shifts the responsibility from the patient to the relationship between the patient and the healthcare provider. Poor adherence to medications is associated with treatment regimens in almost all chronic diseases. This causes the disease to progress leads to hospital admissions and results in unnecessary health expenditures and avoidable deaths (1). The World Health Organization differentiates between indirect techniques for assessing medication adherence. Direct measures, such as observed therapy and therapeutic drug monitoring provide objective evidence of medication adherence. Yet their implementation is limited due to challenges. These challenges include differences in drug metabolism short half-life periods of most medication high costs of analysis and the invasiveness of the testing process (2, 3). In contrast indirect measurements of adherence are more common. Self-report instruments, pill counts, prescription refills and electronic monitoring systems offer compromises between simplicity and validity (4). Despite that every indirect method has limitations.

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Self-reports may be affected by recall and socially desirable answers. Pill counts do not ensure medication intake. Pharmacy records only indicate that a prescription was filled, but not taken (5, 6). The choice of an adherence instrument greatly relies on the clinical situation the behavior being assessed and the available resources (6). Adherence failure is not just a problem. Its causes may range from decisions to take drugs inconsistently to unintentional behaviors driven by forgetfulness, confusion and disruption of habitual routines. Distinguishing between these subtypes has implications for intervention design (7).

Non-adherence to medication is a major problem for healthcare systems globally, imposing substantial clinical and economic burdens. These costs arise from avoidable hospital admissions, emergency department visits, disease progression requiring treatment escalation, and loss of productivity. The impact of non-adherence is especially pronounced among patients with chronic health conditions. Unlike acute illness, where short courses of treatment are the norm, chronic conditions require sustained adherence over years or decades, making the cumulative consequences of non-adherence particularly severe in this population (8).

Patients undergoing hemodialysis are considered one of the vulnerable groups. This is due to the complexity and intensity of their treatment regimens (9). Unlike chronic disease populations adherence in hemodialysis extends beyond taking medications to include dietary restrictions, fluid intake limits and attendance at thrice-weekly dialysis sessions. Each of these represents a behavioral challenge that must be maintained simultaneously and indefinitely. The burden of disease in this population is significant. 70.8% Of hemodialysis patients have at least one comorbidity, most commonly hypertension diabetes mellitus, cardiovascular disease and secondary anemia (9, 10).

These comorbidities complex polypharmacy regimens that often exceed five medications per patient. Some regimens involve ten or more doses. The resulting pill burden, combined with dietary and fluid restrictions, frequent dialysis sessions, fatigue that accompanies end-stage renal disease and the financial strain of ongoing treatment creates a context in which adherence becomes unusually difficult to maintain. Furthermore, many hemodialysis patients are older adults who may also contend with cognitive decline, reduced manual dexterity affecting their ability to handle multiple pill bottles and limited social support (9). All of these factors further compound the challenge of adherence. Reported -adherence rates in this population range from 30% to 80% depending on the measurement method used. This underscores both the magnitude of the problem and the methodological uncertainty that surrounds it. Poor adherence in this group has been linked to increased hospitalization rates accelerated loss of renal function higher cardiovascular morbidity and elevated mortality risk. These downstream consequences create a cycle. Deteriorating health from non-adherence often leads to treatment intensification, which increases regimen complexity and makes sustained adherence even more difficult to achieve (9, 11).

Although medication adherence among patients undergoing hemodialysis has been widely studied the existing literature remains fragmented. Most prior studies have examined adherence rates. Focused on demographic and clinical variables such as age, gender or duration of dialysis. Few reviews have brought together the cognitive influences, like motivation and health beliefs.

Because of these gaps the literature lacks a picture of which determinants are truly the strongest predictors of medication adherence in hemodialysis patients. It also lacks understanding of how the choice of measurement instrument affects reported adherence rates. In addition, there is a need for a biopsychosocial framework that can guide future research and interventions.

This review is designed to fill that void by systematically gathering adherence data, identifying the most robust predictors across studies, and highlighting methodological shortcomings that have prevented consensus so far.

Methodology

This systematic literature review study was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2021 guidelines (12).

Search Strategy and Information Sources

A systematic and extensive search strategy was adopted across various databases such as PubMed, Scopus, Google Scholar, and Web of Science to

obtain relevant literature from January 2005 to January 2024. The search strategy includes a combination of keywords such as hemodialysis, end-stage renal disease, medication adherence, patient compliance, treatment adherence, non-adherence, correlated factors, and contributors.

Eligibility Criteria

For the current systematic review, studies were eligible for inclusion if they had appeared as original research, including both observational as well as interventional research methodologies. Population of interest was clearly defined as adult patients who were 18 years or older, diagnosed with end-stage renal disease, undergoing maintenance hemodialysis. The primary outcome of the short-listed articles had to be an assessment of medication adherence and/or an analysis of factors significantly or otherwise related to it. To ensure the recency and availability of the data, the short-listing was restricted to articles appearing in the English language between January 2005 and January 2024. Numerous criteria were set up for excluding articles from the final listing. Studies were excluded if they only evaluated the adherence to hemodialysis sessions, diet regimens, or fluid intake without specifically examining medication adherence. Moreover, articles were excluded if the full text version was unavailable. Non-original research studies, such as editorials, comments, and case reports, were also excluded.

To select the studies, a two-step process was used. In the first step, all the studies' titles and abstracts were examined in relation to their suitability, and studies found to be unsuitable were excluded. In the second step, the full texts of the remaining studies were used to select the studies based on the inclusion and exclusion criteria. The process of the study selection is shown in the PRISMA flow diagram shown in Figure 1.

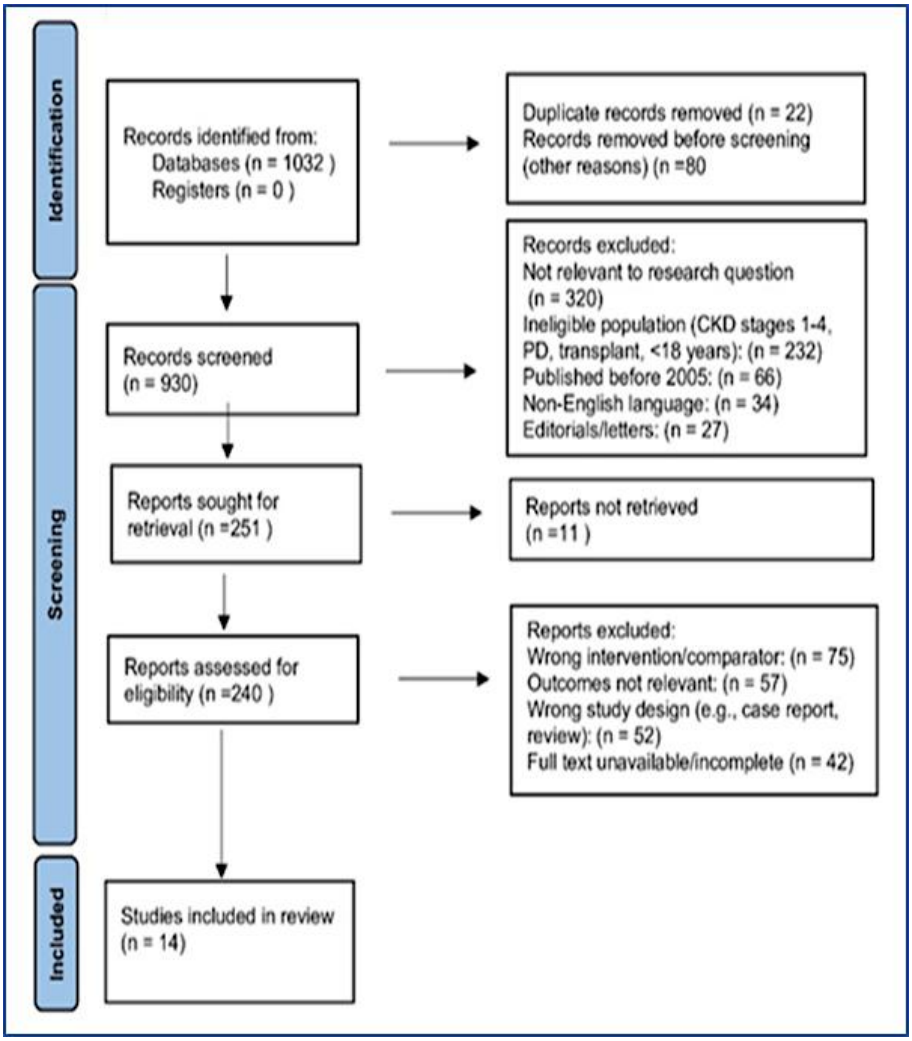

Figure 1: Prisma Flow Diagram; Identification of Studies via Databases and Registers

Data Synthesis and Extraction

To ensure the extraction of the required data, a single data extraction form was used. Three researchers used a standardized form to collect the required data. The collected data include the following:

a) Principal author, year of publication, study design, geographical origin, sample size, mean age, and gender distribution of the studies.
b) Methods used to measure adherence and biochemical markers (serum potassium, phosphorus, hemoglobin), body mass index, self-reported percentage of medication taking, correlates of adherence, and methods used to measure the influencing factors.

Quality Assessment (Risk of Bias)

The quality of the nonrandomized studies included in this systematic review was judged by two authors individually using the Newcastle-Ottawa Quality Assessment Scale (NOS) (13). This tool for quality assessment has already been validated and allows for the evaluation of the quality of studies based on three main aspects: the selection of the study groups, the comparability of the groups, and the ascertainment of either the outcomes or the exposures. The studies are graded based on the number of stars assigned to each study. The maximum number of stars for a single study was nine. Subsequently, the studies are classified into high, moderate, and low quality based on the total number of stars. NOS recognizes the existence of bias in nonrandomized studies and provides a framework for its evaluation.

Results

Fourteen studies were included after the application of the inclusion criteria for this systematic review. The majority were cross-sectional (10 studies, 71.4%), followed by descriptive cross-sectional designs (2 studies, 14.3%), with one descriptive correlational study (7.1%) and one qualitative study (7.1%), as discussed in Supplementary Table 1.

Demographic Information

Across the included studies, sample sizes ranged from 30 to 358 participants, with most studies enrolling between 70 and 230 individuals, as discussed in Supplementary Table 2. Participants were predominantly middle-aged and older adults, with mean ages generally falling between the early 50s and late 60s, although one study included a notably younger mean age and another focused on an older cohort. Across studies reporting gender distribution, males were slightly overrepresented, typically comprising 52-60% of samples, though several studies showed a more balanced distribution. The majority of participants were married, with proportions commonly exceeding 60%, while single, widowed, or divorced individuals constituted smaller subgroups. Employment status, when reported, indicated high levels of unemployment or retirement, particularly among older populations, with several studies reporting unemployment rates above 70%. Economic status was variably reported but often reflected low to moderate income levels, with a substantial proportion of participants categorized as having poor or moderate economic conditions. Educational attainment tended to be low to moderate across studies, with many participants having primary or secondary education; fewer participants had completed higher education, although some studies reported mixed or broadly distributed educational levels. Overall, the demographic profile across studies reflects predominantly middle-aged to elderly populations with relatively low socioeconomic and educational attainment.

Level of Medication Adherence

Medication adherence was assessed using a variety of validated and non-validated tools, shown in Supplementary Table 3. The End-Stage Renal Disease Adherence Questionnaire (ESRD-AQ) was used in four studies, while Morisky-based adherence scales (MMAS or MGL) were applied in three studies. Additional validated instruments, including the Medication Therapy Adherence Scale (MTAS), the Medication Adherence Report Scale (MARS), and the Questionnaire for Adherence in Chronic Kidney Disease (QA-DRC HD), were used in three studies. Four studies employed study-specific or self-developed questionnaires to assess adherence.

Across the included studies, medication adherence among patients on hemodialysis varied widely, ranging from as low as 10% in Indonesia (14) and 28.1% in Saudi Arabia (15) to over 90% in Iran and Brazil (16, 17). Moderate adherence levels were reported in several countries, including Iran, Palestine, Turkey, Japan, and the United States, with rates generally between 60% and 80%, as shown in Supplementary Table 1.

Factors Associated with Medication Adherence

Various validated instruments were used to measure factors affecting medication adherence, such as psychosocial constructs (e.g., depression, anxiety, social support), illness perception, and health-related behaviors. For analysis purposes, determinants were grouped into the following four domains: demographic and socio-economic, patient-related, healthcare system-related, and hemodialysis-related, as discussed in Supplementary Table 4.

A summary of the findings highlights the strong influence of psychosocial and knowledge-based factors as predictors of adherence. In the studies included, a predictor was reported as “significant” when the authors identified a statistically significant association with medication adherence, typically based on their stated thresholds ($p < 0.05$). Interestingly, "Motivation and perception of HD" and "Level of medical knowledge" were significantly associated with adherence in each of the seven studies that included them. Other consistently significant predictors included depression level (significant in 4/4 studies), marital status (4/6 studies), forgetfulness (3/3 studies), and economic status (2/2 studies). However, demographic factors like age (4/6 studies) and gender (4/8 studies) yielded inconsistent results. Clinical measures were also less significant; e.g., "Dialysis vintage" was significant only in one of the four studies that included it. Similarly, factors such as "Frequent modifications to therapeutic regimens" and "Phosphorus, Potassium, Body Mass Index measurements" were exclusively reported as non-significant. This suggests that psychosocial factors, such as motivation, health literacy, and mental health, are stronger predictors than demographic or clinical factors shown in Table 1.

Table 1: Summary of Predictors of Medication Adherence Across Included Studies

Factor/Variable	Number of Studies Where this Factor was Significant	Number of Studies Where this Factor was non-significant
Age	4	2
Gender	4	4
Nationality	1	1
Marital status	4	2
Employment status	2	1
Economic status	2	0
Supportive status	1	1
Forgetfulness	3	0
Motivation and perception of HD	7	0
The level of medical knowledge	7	0
Depression level	4	0
The quality of sleep	1	0
High medication cost	2	0
Complex medications	1	0
Frequent modifications to therapeutic regimens	0	1
Fear of Hospitals and medical staff Care	2	0
Regularity of treatment sessions	2	0
Central Venous Catheter	2	0
Dialysis vintage	1	3
HGB levels	1	0
Phosphorus, Potassium, Body Mass Index measurements	0	1

NOS Results and Sensitivity Analyses

The quality and bias risk of the included fourteen studies were assessed using the Newcastle-Ottawa Scale, and the results are shown in Table 2. The Newcastle-Ottawa Scale is a reliable method of evaluating the quality and bias risk of observational studies, and it consists of three aspects, namely, the selection of study groups, the comparability of study groups, and the ascertainment of outcomes or exposure. Each study was given a score of up to a maximum of nine stars, and the quality of the included studies was divided into

high, moderate, and low quality according to the score. The quality of the included studies varied from low to high, and the scores ranged from 4 to 8. One study obtained the highest score, reaching 8 stars, demonstrating strong methods, notably regarding the representative nature of the sample, the similarity of the groups, and measurement of outcomes (18). Three other studies, also performed very well, achieving scores of 7 stars, demonstrating high quality (19–21). Conversely, two studies, achieved scores of only 4 (22, 23).

Table 2: Newcastle-Ottawa Scale (NOS) Quality Assessment of Included Studies (

Representativeness of the Cases	Sample Size	Non-Response Rate	Ascertainment of the Surveillance Tool	Comparability	Assessment of the Outcome	Statistical test	Total	Study
*			**	*	**	*	7 *	(19)
*		*	**	*	*	*	7 *	(20)
*			**	*	*	*	6*	(16)
*		*	**		*	*	6*	(24)
*		*	**	*	**	*	8*	(18)
*			**	*	**	*	7*	(21)
*		*	*	*	*	*	6*	(25)
			*	*	*	*	4*	(22)
*			*	*	**	*	6*	(17)
*			**	*	*	*	6*	(26)
			**		*	*	4*	(23)
*			*	*	*	*	5*	(14)
*			*	*	*	*	5*	(15)
*		*	*	*	*	*	6*	(27)

Note: * = star(s)

Sensitivity analyses based on study quality demonstrated that adherence estimates were influenced by methodological rigor. When restricted to high-quality studies (NOS≥7), adherence rates ranged from 59.7% to 82.3%, showing reduced variability compared with analyses including all studies (10%–94%). Studies rated as low quality contributed disproportionately to extreme adherence values, indicating potential bias related to small sample sizes, limited reporting, or non-validated measurement tools as shown in Table 3.

Table 3: Sensitivity Analysis of Medication Adherence by Study Quality (NOS)

Quality Category	NOS Range	Adherence Range (%)	Approximate Central Tendency	Interpretation	Number of Studies Included
All studies	4-8	10 - 94	Highly variable	Wide heterogeneity due to methodological differences	14: (14–27)
High quality	7-8	59.7 - 82.3	Moderate–high adherence	Most reliable estimates with validated tools and adequate sampling	4:(18–21)
Moderate quality	5-6	28 -94	Wider dispersion	Some methodological limitations affecting precision	8: (14–17,24–27)
Low quality	≤4	43.3 - 66.2	Least reliable	Small samples, incomplete reporting, non-standardized tools	2: (22,23)

Discussion

This systematic review synthesizes evidence on medication adherence among hemodialysis patients and demonstrates substantial variability across studies. Reported adherence rates ranged widely, from as low as 10% to as high as 94%, reflecting marked heterogeneity in study populations, assessment tools, and healthcare contexts. Given this variability, calculating a pooled mean adherence was not appropriate. Instead, the findings highlight that non-adherence is predominantly influenced by psychosocial and cognitive factors rather than by clinical or demographic characteristics alone.

The Primacy of Psychosocial and Cognitive Factors

The most notable result was the correlation between drug adherence and the two domains:

"Motivation and perception of HD" and "The level of medical knowledge." These determinants were statistically significant in all seven studies that examined them, underscoring that an individual's internal beliefs, health literacy, and perception of the significance of the treatment play an essential role in securing successful adherence. Furthermore, depression emerged as a notable barrier, revealing an appreciable association with non-adherence in four individual studies. This finding is of particular concern given the high incidence of depression in patients with a chronic condition and in the general population (28, 29). When combined with a difficult illness such as end-stage renal disease, depression is capable of drastically impairing the cognitive and motivational functions necessary to cope with demanding medication regimens to produce unintentional non-adherence through forgetting or intentional non-adherence through a perception of hopelessness or exhaustion (30). Poor sleep has emerged as an important correlate of medication non-adherence in hemodialysis patients, although it has been reported in only a single study. Sleep disturbances, including insomnia and obstructive sleep apnea, are markedly more prevalent in this population than in the general public, yet they are frequently overlooked in routine care (31). When ranked by consistency of association across studies, motivation and perception of HD and level of medical knowledge emerged as the most robust determinants, each significant in all seven studies that assessed them, a consistency unmatched by any clinical or demographic variable. This positions these modifiable cognitive factors as the most promising targets for intervention.

The complexity of the treatment regimen and patient burden

The complexity of the hemodialysis treatment schedule is further aggravated by the coexisting comorbidities and related polypharmacy, requiring complex supplements. Adherence to the medication schedule is essential for the successful outcome of dialysis therapy in ESRD, although adherence has remained a complex and rather widespread issue (32). HD patients can readily understand the burden related to managing a multitude of pills related to coexisting problems and the related need for supplementary remedies for coping with the nutritional deficits that remain innate during renal failure and during dialysis therapy. For example, in a study, patients on dialysis were found to average 5.63±2.22 different medications, with more than three-fourths (78.3%) using more than five medications each time a medication refill was obtained (11). This complex medication routine, combined with strict dietary and fluid restrictions and the essential Hemodialysis schedule, significantly contributes to the medication burden and poor HD medication therapy compliance (33). The supplements are also essential since various micronutrients related to HD lead to deficits that necessitate replacement therapy (34). The need for supplementary medications, such as levocarnitine for carnitine deficiency, that is rather highly prevalent, and cholecalciferol for Vitamin D deficiency, is also absolutely necessary for reducing complications related to Erythropoietin-Stimulating Agent resistant Anemia, muscle weakness, and Cardiovascular problems. Disparities related to essential medications, whether related to intention or unintentional, pose absolutely measurable negative implications (35).

Beyond the pill burden itself, several additional pharmaceutical factors merit consideration (36). First, intricate dosage regimens are common in this population, many medications require administration at specific times relative to dialysis sessions, and phosphate binders must be taken with meals, creating a daily schedule that is difficult to sustain. Second, negative side effects of medications, such as gastrointestinal intolerance to phosphate binders or hypotension from antihypertensives, can directly reduce patients' willingness to adhere. Third, financial problems related to medication costs were identified as a significant determinant in two studies in this review, and the cumulative cost of multiple medications and supplements imposes a substantial economic burden, particularly in settings with limited insurance coverage (37). Finally, addressing these interconnected barriers requires active collaboration among healthcare practitioners, including nephrologists, pharmacists, nurses, and dietitians to simplify regimens where clinically possible, identify cost-saving alternatives, monitor side effects, and provide coordinated patient support.

The role of clinical and physical factors

While it was found that the role of psychosocial issues is more significant in non-adherence, this

review showed less consistency in the role of clinical/demographic variables. Age was significant in four of six studies but non-significant in the remaining two, and gender was significant in only half of the eight studies that examined it, with no consistent direction of effect. This degree of contradiction suggests that non-modifiable demographic variables have limited standalone predictive value and likely serve as proxies for underlying psychosocial mechanisms, such as health literacy or motivation, which future studies should measure directly (38). However, it was seen that clinical variables like "Dialysis Vintage" remained mostly non-significant, which implies that the length of treatment does not act as an individual predictor of non-adherence. However, physical experiences of HD, mainly vascular access, retain immense importance. Frequent cannulation difficulties of arteriovenous fistula, which is a common issue, can result in fear, pain, or anxiety (39), which was identified as "significant" in this review ("Fear of Hospitals and Medical Staff Care"). Hematoma or thrombus development owing to frequent cannulation difficulties, or arteriovenous fistula issues like steal syndrome or infection, can generate absenteeism or reinforce adverse attitudes towards the treatment, thus reducing motivation and increasing non-adherence (40).

Findings also highlight the absence of formal interaction analyses across the reviewed literature. Psychological factors such as depression and health literacy are likely interrelated with clinical factors such as polypharmacy burden and vascular access difficulties, yet no study tested these pathways. For example, patients with frequent cannulation difficulties may develop avoidance behaviours that compound depressive symptoms, and those with limited health literacy may struggle more with complex medication regimens (41). The predominantly cross-sectional design prevented mediation or moderation testing, limiting the current evidence to isolated associations rather than integrated models.

Sensitivity analysis of study quality

A sensitivity analysis restricted to higher-quality studies (NOS ≥7) confirmed the robustness of the main findings, narrowing the adherence range to 60–82% with greater internal consistency and reduced variability compared with lower-quality studies, which contributed more extreme estimates. The exclusion of studies with lower NOS scores did not materially alter the overarching conclusion that medication adherence among hemodialysis patients remains suboptimal and is strongly influenced by psychosocial rather than clinical factors. This finding strengthens confidence in the validity of the review's conclusions and suggests that the observed trends are not driven by lower-quality evidence.

Reliability, validity, feasibility, and constraints of the adherence measurement approach

The self-report instruments used across the included studies offer different trade-offs. The ESRD-AQ and Morisky-based scales (MMAS, MGL) have established test-retest reliability in hemodialysis populations (Cronbach's alpha typically exceeding 0.70) and moderate concurrent validity against pill counts and pharmacy refill data. Their feasibility is high and they are brief, inexpensive, and can be administered during dialysis sessions, which explains their frequent use (42, 43). However, their validity is constrained by recall bias and social desirability bias, which likely inflate reported adherence rates (44, 45). The MTAS and MARS share similar feasibility advantages but have been validated in fewer hemodialysis-specific samples, limiting confidence in their construct validity for this population (46). Self-developed questionnaires, used in four studies, offer flexibility to capture context-specific factors but have unknown psychometric properties, making their reliability and validity essentially unreported. This creates a fundamental constraint: comparisons across studies using different instruments may reflect measurement artefact rather than true differences in adherence.

Biochemical markers such as serum potassium, phosphorus, and hemoglobin offer an ostensibly objective alternative but carry their own limitations. Their reliability depends on laboratory standards that vary across centres, and their validity as proxies for medication adherence is indirect; elevated phosphorus may reflect dietary non-adherence as much as phosphate-binder non-adherence. Feasibility is moderate: these markers are routinely collected in clinical care, so no additional burden is placed on patients, but they are not available for all medication classes and cannot capture adherence to non-laboratory-monitored drugs (47). A key constraint is that biochemical markers reflect only recent behaviour

and are influenced by pharmacokinetic factors unrelated to adherence (48). To facilitate comparison of these instruments, Table 4 summarizes their psychometric properties and clinical relevance in hemodialysis populations.

Table 4: Measurement Instruments Used in the Included Studies: Psychometric Properties and Clinical Relevance

Instrument	Type	Psychometric attributes	Clinical relevance in HD	Key constraints
ESRD-AQ	Disease-specific self-report	Content validity established for ESRD; test-retest reliability reported (Cronbach's alpha typically >0.70); moderate concurrent validity against biochemical markers and IDWG	Directly captures HD-specific adherence behaviours (medication, dialysis, diet, fluid); most clinically relevant for this population	Self-report bias; ceiling effects in highly adherent patients; limited use outside its validation populations
MMAS-8 / MGL	Generic self-report	Well-validated in multiple chronic diseases (Cronbach's alpha 0.61-0.83); sensitivity and specificity for low adherence established; cut-off scores available	Widely recognised, allows cross-disease comparison; brief (4-8 items), feasible in busy HD clinics	Not HD-specific; may miss dimensions unique to dialysis care (fluid/diet adherence); social desirability bias
MTAS	Generic self-report	Moderate internal consistency reported; fewer validation studies in HD populations	Clinically practical but limited evidence base specific to HD	Insufficient HD-specific psychometric data to recommend as a sole measure
MARS	Generic self-report	Good test-retest reliability in chronic disease; validated against pharmacy refill data	Captures intentional and unintentional non-adherence; useful in research settings	Limited validation in HD; 5-item version may miss domain-specific adherence behaviours
QA-DRC HD	Disease-specific self-report	Developed and validated specifically for HD patients in Brazil; internal consistency reported	Highly relevant to HD context; items tailored to dialysis-related adherence	Culture- and language-specific validation (Brazilian Portuguese); generalizability to other populations uncertain
Self-developed questionnaires	Study-specific	No standardised psychometric data; reliability and validity unreported	Flexible and context-specific, allowing exploration of novel determinants	Cannot compare across studies; unknown measurement properties; high risk of information bias
Biochemical markers (K+, PO4, Hb, IDWG)	Objective/laboratory	No psychometric properties as adherence measures; reliability depends on laboratory standards	Objectivity is a strength; routinely collected in clinical care; no additional patient burden	Indirect proxy influenced by diet, pharmacokinetics, and timing; reflects only recent behaviour; not available for all drug classes

Reliability, Validity, Feasibility, and Constraints of the Analytical Approaches

The domain-based grouping of determinants (psychosocial, clinical, demographic, healthcare system) improved the interpretability of heterogeneous data and allowed cross-study pattern detection. Its reliability was strengthened by having two independent reviewers extract and classify determinants, and the consistency of findings across the four domains supports face validity. However, the feasibility of this approach depends on the completeness of reporting in primary studies, which was uneven; several studies omitted effect sizes or confidence intervals, precluding meta-analytic synthesis. A major constraint is that domain boundaries are not always distinct: a variable such as "fear of hospitalization" straddles psychosocial and healthcare-system domains, and its classification can influence which domain appears most predictive. The NOS-based sensitivity analysis added methodological rigour and demonstrated that restricting analyses to higher-quality studies (NOS ≥7) narrowed the adherence range from 10-94% to 60-82%, confirming that lower-quality studies contributed extreme values. The NOS itself has acceptable inter-rater reliability when used by trained reviewers, and its content validity for observational studies is well established (49). Feasibility is good, but it requires no specialised equipment and can be applied to any cross-sectional or cohort design. A recognized constraint is that the NOS does not capture all sources of bias relevant to adherence research, particularly those arising from self-report measurement tools themselves, which may lead to an overestimation of study quality in this specific field (50).

Implications for Clinical Practice

The results reflect a shift toward a biopsychosocial model of care for individuals undergoing hemodialysis, moving beyond a purely biomedical approach (51). Based on our findings, we propose the following concrete recommendations. Nephrology specialists should integrate brief psychosocial screening for depression, health literacy, and motivation into routine evaluations, as these factors were more consistently associated with adherence than clinical or demographic variables. Dialysis facilities should establish a structured adherence monitoring protocol combining a validated self-report instrument such as the ESRD-AQ or MMAS-8 with regular biochemical marker review, and designate a staff member to track trends and flag declining adherence. The adoption of digital adherence monitoring systems, such as electronic medication monitors, mobile health applications, and platform-based tools that share real-time data across the care team could further enhance early detection of non-adherence and enable timely, tailored interventions in this population (52). Pharmacotherapy counselling programmes should include medication reconciliation at dialysis initiation and after regimen changes, prioritizing pill organisers, synchronised refills, and simplified dosing schedules. Patient education should replace didactic delivery with interactive approaches incorporating motivational interviewing, focusing on misconceptions identified in this review such as the rationale for phosphate binders.

The psychosocial determinants identified in this review such as motivation, health literacy, depression, and sleep quality align closely with targets addressed by established behavioral health approaches. Integrating cognitive-behavioral therapy for depression, motivational interviewing to address low motivation and negative treatment perceptions, and behavioral activation to improve self-regulation could directly target the most consistent predictors of non-adherence (53). These efforts are best delivered through interdisciplinary care models that actively involve nephrologists, pharmacists, nurses, dietitians, and mental-health professionals working within coordinated pathways rather than in isolated discipline-specific silos (54).

Finally, healthcare policy measures should promote standardized adherence indicators across renal registries and direct funding toward intervention studies targeting the psychosocial determinants highlighted here. However, the present study is limited by the absence of a fully operationalized biopsychosocial mechanism, and the specific pathways through which these domains interact were not empirically tested.

Conclusion

Adherence to medication remains a complex issue for patients undergoing hemodialysis. This review underscores evidence suggesting that medication non-adherence is less influenced by individual

patient characteristics or dialysis vintage and more by patients' knowledge, beliefs, and attitudes. This environment of patient knowledge and attitudes is further challenged by the high treatment burden and physically demanding hemodialysis regimen. A multidisciplinary approach that enhances patient knowledge, addresses motivational deficiencies, and treats coexisting depression or sleep problems can better empower patients struggling with medication non-adherence.

Several limitations of this review should be acknowledged. First, substantial heterogeneity across studies in patient demographics (age, education, economic status), definitions of adherence (dichotomous vs. continuous), research environments (high- to middle-income countries), assessment methodologies (validated instruments, self-developed questionnaires, and biochemical proxies), and statistical techniques (descriptive to multivariate, with many studies omitting effect sizes), meant that a meta-analysis could not be performed and limits direct comparability of the reported adherence rates. Second, the quality of the included studies in this review was variable, with Newcastle-Ottawa Scale scores varying between 4 and 8, which indicates a high level of bias in the studies included in the review. Third, the majority of the studies included in the review were cross-sectional in design, which limits the ability to establish causality between the variables of interest in the review. Fourth, the geographical distribution of the included studies indicates a limitation in the review, with most of the included studies coming from Asia, and little information available from European countries on medication adherence in patients with hemodialysis.

Future research should prioritise intervention studies targeting the modifiable psychosocial determinants identified here, particularly motivation, health literacy, and depression. Achieving consensus on standardised definitions and measurement of adherence is essential to enable meaningful cross-study comparisons. Conceptual models that specify the pathways through which biological, psychological, and social factors interact should be developed and empirically tested. Finally, the feasibility and effectiveness of behavioral health approaches and digital adherence monitoring tools in hemodialysis populations warrant rigorous evaluation.

Abbreviations

ESRD: End-Stage Renal Disease, ESRD-AQ: End-Stage Renal Disease Adherence Questionnaire, HD: Hemodialysis, HGB: Hemoglobin, MARS: Medication Adherence Report Scale, MGL: Morisky-Green-Levine scale, MMAS: Morisky Medication Adherence Scale, MTAS: Medication Therapy Adherence Scale, NOS: Newcastle–Ottawa Scale, QA-DRC HD: Questionnaire for Adherence in Chronic Kidney Disease.

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Author Contributions

Paola Pina: Conceptualization, Study Design, Writing, Literature Review, Elona Prifti: Conceptualization, Study Design, Writing, Literature Review, Argenta Kuburi: Materials, Data Collection, Data Processing, Miranda Konica: Critical Review, Klodiana Gjergji: Materials, Data Collection, Data Processing. All authors have read and approved the final manuscript and agree to be accountable for all aspects of this work.

Conflict of Interest

The authors declare no conflict of interest

Data Availability

The data supporting this review were derived from previously published studies cited in References. The extracted datasets are available from the corresponding authors upon request.

Declaration of Artificial Intelligence (AI) Assistance

AI tool Paper pal is used for grammar correction. The authors take full responsibility for the content's originality, interpretation and accuracy.

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Supplementary Data

Supplementary Table 1: Treatment-Related Characteristics and Adherence

Dialysis Vintage	Country	Study Design	Adherence	Study
Not reported	Iran	Cross-sectional	59.7	(19)
48.16 ± 44.41 months	Palestine	Cross-sectional	81	(20)
36.56 ± 43.34 months	Iran	Cross-sectional	94	(16)
≥60 mo: 50.28%; <60 mo: 49.72%	Saudi	Cross-sectional	54.75	(24)
Full distribution provided	Iran	Descriptive	82.3	(18)
67.54 ± 54.98 months	Turkey	Descriptive cross-	79.9	(21)
Median 81.5 months	Japan	Cross-sectional	68	(25)
Not reported	USA	Cross-sectional	66.2	(22)
Mean 86.11 months	Brazil	Descriptive cross-	93.6	(17)
Not reported	USA	Cross-sectional	39	(26)
4.1 ± 4.1 years	Australia	Qualitative	43.3	(23)
Not reported	Indonesia	Cross-sectional	10	(14)
37.27 ± 48.91 months	Saudi	Cross-sectional	28.09	(15)
6.38 ± 5.41 years	Greece	Cross-sectional	75	(27)

Supplementary Table 2: Demographic characteristics

Sample Size	Mean Age (±SD)	Gender (%F/ %M)	Marital Status	Employment Status	Economic Status	Education Level	Study
229 (88% response)	50.52 (95% CI 48.71–52.33)	42.8 / 57.2	28.8% single / 71.2% married	71.2% unemployed	Not categorically reported	Primary 46.3%, Secondary 21.8%, Diploma 31.9%	(19)
220	56.82 ± 14.51	41.8 / 58.2	14.1% single / 85.9% married	Not reported	Not reported	≤High school 94.5%; ≥College 5.5%	(20)
191	62.49 ± 10.66	47.8 / 52.2	7.9% single / 69.6% married	No job 13.6%; others listed	Poor 45.5%, Medium 49.2%, Good 5.2%	Illiterate 37.7%, Elementary 21.5%, Secondary 12.6%, Diploma 13.1%, University 15.2%	(16)
358	50.0 ± 0.84	52.23 / 47.77	37.99% unmarried / 62.01% married	Not reported	Not reported	Illiterate 31.28%, Educated 68.72%	(24)
218	54.11 ± 14.78	39.6 / 60.4	25.7% single/divorced/widowed	Unemployed 19.2%	Poor 43.3%, Moderate 40.6%, Good 16.1%	Middle/High school 66.8%, Diploma 21%, Academic 12.2%	(18)
274	62.57 ± 13.24	45.6 / 54.4	9.5% single / 79.9% married	98.2% unemployed	Income < expenses 6.6%; = expenses 93.4%	Illiterate 9.9%, Primary 52.6%, High school 16.8%, University 5.8%	(21)
92	67.0 ± 11.6	22.8 / 77.2	20.7% single / 79.3% married	71.7% unemployed	Not reported	Mixed levels; full distribution preserved	(25)
77	Not reported	53.2 / 46.8	Not reported	Not reported	Not reported	≥12th grade vs. <12th grade	(22)
78	51.10 (range	38.5 / 61.5	Not reported	Not reported	Not reported	Not reported	(17)

	22.7–84.3)						
65	51.1 ± 13.0	54 / 46	Not reported	79% unemployed	Not reported	Years of education: 12.1 ± 3.0	(26)
30	69.6 ± 11.0	23.3 / 76.7	56.7% married	Not reported	Not reported	80% ≥ high school	(23)
130	Not reported	60 / 40	6.2% single; 85.4% married; 8.5% widowed	39.3% unemployed	52.3% ≤ minimum wage	Basic 11.5%; Middle 71.5%; Higher 16.9%	(14)
89	5.79 ± 17.69 years	47.2 / 52.8	Not fully reported	Not quantified	Not reported	Three education groups; no percentages	(15)
168	62 (SD not reported)	37.5 / 62.5	20.8% single; 66.7% married	Mostly retired/housewives (75%)	Not reported	Not reported	(27)

Supplementary Table 3: Assessment Instruments for Medication Adherence and Determinants

Assessment tools used to measure medication adherence	**Assessment tools used to measure factor related to adherence**	**Study**
Original self-reported questionnaire	Capability-Opportunity-Motivation-Behavior model (COM-B) Theoretical Domains Framework (TDF) Behavior Change Wheel (BCW)	(19)
End-Stage Renal Disease Adherence Questionnaire (ESRD-AQ)	End-Stage Renal Disease Adherence Questionnaire (ESRD-AQ); Biochemical Markers and Interdialytic Weight Gain (IDW)	(20)
ESRD-Adher ence Questionnaire (ESRD-AQ)	ETPB constructs scale	(16)
ESRD Adherence Questionnaire	Original self-reported questionnaire	(24)
Demographic characteristics questionnaire End-stage renal disease adherence questionnaire	General procrastination scale Decisional procrastination scale Difficulty in emotion regulation scale	(18)
Morisky Green Levine Medication Adherence Scale	Hospital Anxiety and Depression Scale Multidimensional Scale of Perceived Social Support	(21)
Original self-reported questionnaire, "Medication Administration Situation"	EuroQol 5-dimension questionnaire (EQ-5D) KDQOL-SF	(25)
Original self-reported questionnaire	Original self-reported questionnaire	(22)
Questionnaire for Adherence in Chronic Kidney Disease (QA-DRC HD)	QA-DRC HD Biochemical markers	(17)
Medication Therapy Adherence Scale.	Beck Depression Inventory score	(26)
Morisky Green Levine scale	World Health Organization (WHO) determinants of medication adherence	(23)
Original self-reported questionnaire	Original self-reported questionnaire	(14)
Morisky Medication Adherence Scale (MASS-8)	Morisky Medication Adherence Scale (MASS-8) The Center for Epidemiologic Studies Depression Scale (CES-D)	(15)
The Medication Adherence Report Scale (MARS)	The Multidimensional Health Locus of Control (MHLC)	(27)

Supplementary Table 4: Categorization of Variables Reported in the Reviewed Studies

Category	Variables
Demographic and socio-economic factors	Age, gender, ethnicity, educational attainment, marital status, economic status, employment status, and perceived social support.
Patient-related factors	Forgetfulness, motivation, perceived importance of hemodialysis, medical knowledge, levels of stress and depression, and sleep quality.
Healthcare system-related factors	High medication costs, treatment regimen complexity, frequent regimen modifications, fear of hospitalization, and support provided by healthcare professionals.
Hemodialysis-related factors	Session regularity, presence of a central venous catheter, and length of time on hemodialysis.