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Adherence to Oral Chemotherapy Agents in Oncology Patients: A Scoping Review

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Abstract: *This study aims to conduct a scoping review of research related to oral chemotherapy drug adherence in cancer patients, providing a reference for the development of standardized intervention protocols for cancer patients. Based on the scoping review framework proposed by Arksey and O'Malley, we systematically searched eight databases up to December 1, 2024, according to three research questions, and conducted screening and information extraction. A total of 22 studies were included. Most interventions are based on assessment, education, monitoring, and follow-up, primarily led by nurses, pharmacists, or multidisciplinary teams. Intervention content includes core knowledge such as medication administration methods, identification and management of side effects, and self-management strategies, supplemented by behavioral support and psychological adjustment techniques. Outcome evaluation indicators primarily include questionnaire or self-report tools to assess behavioral changes, supplemented by objective monitoring data on adherence rates. Although there has been an increase in intervention studies on oral chemotherapy medication adherence, few have undergone rigorous validation, and there is a lack of interventions tailored to the needs of different patient populations. It is recommended that future research be based on appropriate theoretical models to develop strategies to improve adherence and explain the underlying mechanisms. Digital interventions offer a new direction for improving oral chemotherapy adherence, particularly for elderly home-dwelling patients. However, their effectiveness depends on technical design and patient acceptance. Therefore, future efforts should focus on developing humanized, elderly-friendly smart care systems, optimizing the specific content of intervention programs, conducting high-quality research, and promoting improved medication adherence to enhance patients' self-management capabilities.*

Keywords: *Cancer Patients; Oral Chemotherapy; Adherence; Interventions; Scoping Review*

1. Introduction

In the field of tumor treatment, oral chemotherapy is widely accepted by patients due to its convenience, low invasiveness, and economy, and adherence to oral chemotherapeutic agents has become an important factor in determining the efficacy of treatment. Some studies have shown [1] that oral chemotherapy can prolong survival, improve quality of life as well as reduce economic burden for patients. However, while ensuring therapeutic efficacy, oral therapies also pose challenges to patient safety and adherence management: some studies have shown that oncology patients' adherence in the face of complex cycle regimens, multi-drug combinations, and long-term toxicity monitoring averaged only 78% [2], which is significantly higher than that of 50% for chronic non-oncology diseases [3-4]. The level of adherence to oral chemotherapy ranges from 46% to 100%, suggesting that there is a wide fluctuation in adherence to treatment regimens among patients receiving oral chemotherapy [5]. Other studies have shown that poor adherence is associated with disease progression, low survival, and healthcare utilization and cost [6-7]. Interventions targeting adherence to oral chemotherapeutic agents in oncology patients have increased in recent years, but as these oral chemotherapeutic agents continue to be a part of a patient's treatment regimen, it is becoming increasingly important to address poor adherence and develop intervention strategies to support the patient's needs. Therefore, the purpose of this scoping review is to summarize published interventions for oral chemotherapy medication adherence, focusing on the scope and type of interventions, measurement indicators, and evaluation of effectiveness, and to analyze the limitations of the studies, with the aim of providing a basis for clinical improvement of oral chemotherapy medication adherence.

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2. Methods

This study used the 5 stages of a scoping review proposed by Arksey and O'Malley as a methodological framework [8]. This design was chosen to assess the breadth of the literature, identify research gaps, and summarize the results of different studies. The five key stages of a scoping review include: stage 1 identifying the research question, stage 2 searching for relevant studies, stage 3 selecting studies, stage 4 extracting relevant data, and stage 5 collating, summarizing, and reporting results.

2.1 Defining the research question

The research questions guiding this scoping review include: Among cancer patients, (1) what are the specific contents and forms of adherence interventions for oral chemotherapy drugs? (2) Which indicators can be used to assess adherence to oral chemotherapy drugs? (3) What are the current shortcomings in existing intervention studies?

2.2 Search and information sources

The search terms were determined based on three research questions. A total of 8 Chinese and English databases were searched, including CNKI, Wanfang Database, VIP Database, Chinese Biomedical Literature Database (CBM), EMBASE, PubMed, Web of Science, and CINAHL, with the search period spanning from the inception of each database to December 1, 2024. The literature search employed a combination of subject headings and free-text terms, supplemented by snowballing search methods when necessary. Search terms are Oral, anticancer, cancer, chemotherap* , agent* , drug* , oral chemotherapy, randomized controlled trial, patient compliance, medication compliance, medication adherence.

2.3 Inclusion and exclusion criteria for the literature

The present study was based on the PICOS principle to develop the nativity criteria. The inclusion criteria were as follows: P (population): oncology patients, including but not limited to research questions on adherence to oral chemotherapy drugs in hospitals, outpatient clinics, communities, homes, and other study sites; I (intervention) interventions for adherence to medication; C (comparison): unqualified; O (outcome): including but not limited to adherence, or reference indicators with objectivity; S (study design): experimental studies. Exclusion criteria: (1) Full text not available. (2) Literature type: review, Meta, systematic evaluation, conference abstract, dissertation.

2.4 Literature screening

The title of the retrieved literature was imported into NoteExpress, duplicates were removed, and initial screening was performed by 2 graduate nursing students by reading the title and abstract, and further screening was performed by reading the full text, with both parties proceeding independently, and if there was disagreement about the content, the content was discussed with the 3rd researcher until there was unity of opinion. Extracts included: general information (e.g., author, year of publication, country, etc.), study population, description of the intervention (e.g., specific intervention content/modality, intervention period/frequency), adherence measures, and conclusions.

3. Results

A total of 1,454 documents were obtained by searching the database, 1,132 documents remained after removing duplicates, 304 documents were initially screened after reading the title and abstract, 9 documents were obtained by snowballing, and 22 documents were finally included by reading the full text for re-screening. To ensure transparency, the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extensions for Scoping Reviews) was used (Figure 1).

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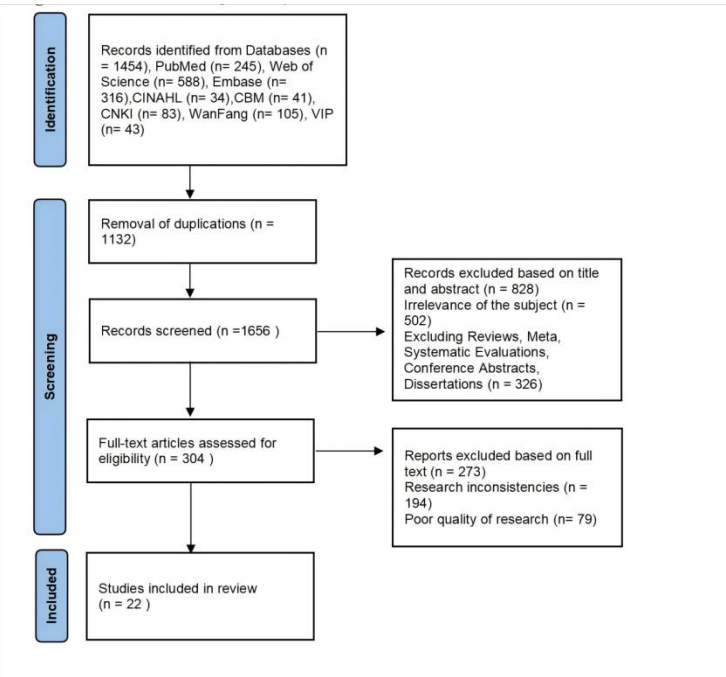

Figure 1 PRISMA 2020 flow diagram for systematic reviews

3.1 Characteristics of selected articles

A total of 22 articles on oral chemotherapy drug intervention strategies for oncology patients were included in this study. The studies were conducted in nine countries, including the United States (n=10)[1-2,9-15], China (n=2)[16-17], Canada (n=2)[4,18], Turkey (n=3)[19-21], France (n=1)[22], Egypt (n=1)[23], Japan (n=1)[24], Germany (n=1)[3], Australia (n=1)[25], and Brazil (n=1)[26]. In terms of study type, 11 randomized controlled trials, 4 prospective cohort studies, 1 mixed study, 1 retrospective study, and 5 pilot studies. The basic characteristics of the included literature are shown in Table 1.

Table 1 Basic characteristics of the included literature (n=22)

Author	Nations	study population	Content of interventions	intervention time	Measurement Methods	Outcomes
Haider I et al.[4]	CA	Multiple Myeloma Patients	Structured Educational Tools (MOATT)	6 months	MEMS Electronic Pill Box + Self-Reporting Scale (BARS)	Adherence in the intervention vs. control group (85.6% vs. 87.9%).
Lau-Min et al.[9]	USA	Gastrointestinal cancer patients	PENNY-GI, a cell phone SMS-based chatbot	not mentioned	Proportion of wrong advice in SMS exchanges	>90% of SMS recommendations are accurate, but there is a risk of technical miscalculation (7.3% incorrect recommendations)
McGrady et al.[10]	USA	Cancer Patients	Individualized Behavioral Interventions (BWSE Tool Based Matching Disorder)	8 weeks	Feasibility (recruitment rate, retention rate)	Recruitment rate 70%
Sümeyye et al.[19]	TUR	Cancer Patients	Educational videos and text messages via WhatsApp followed by phone monitoring	12 weeks	Medication adherence (OCAS scale)	Intervention group vs. control group (87.52% vs. 67.72%)
Dang et al.[25]	AUS	Cancer Patients	Mobile Apps + Online Motivational Interviewing Platform	12 weeks	Technical acceptability + feasibility (recruitment rates, retention rates, intervention adherence)	High acceptance by the intervention group
Akmak HS et al.[20]	TUR	Oral chemotherapy	Motivational interviewing techniques + telephone follow-up	12 weeks	Self-Efficacy Scale (MASES) + Adherence Scale (OCAS)	Significant increase in self-efficacy and adherence in the intervention group
Vacher L et al.[22]	FRA	Oral capecitabine	Pharmacist-led personalized health education	9 weeks	MEMS Electronic Pill Box + Toxicity Classification	Mean adherence scores for non-adherent patients improved by 17.8%

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					(CTCAE)	
Komatsu H et al.[24]	JPN	Breast cancer patients	Nurse-led patient-centered medication self-management support program	3 months	Medication Possession Rate (MPR) + Self-Efficacy Scale (GSE)	MPR was >90% in both groups, with no significant difference, and self-efficacy was significantly higher in the intervention group
Eldeib HK et al.[23]	EGY	Colorectal or gastric cancer patients	telephone follow-up	not mentioned	pill counting + Toxicity Classification (CTCAE)	No significant difference in adherence
Li Yiping et al.[16]	CHN	Gastric cancer patients	Integrated Continuum of Care	not mentioned	self-reporting	Adherence in intervention group vs. control group (95.0% vs. 70.0%)
Jacobs JM et al.[1]	USA	Oral chemotherapy	Electronic pillbox monitoring	12 weeks	Electronic pill box (MEMSCap) + self-report scale (CTSQ)	Average adherence rate 89.3%, with higher adherence among women
Tokdemir G et al.[21]	TUR	Oral capecitabine	Structured Educational Tools (MOATT) + telephone follow-up	2 weeks	Self-Efficacy Scale (MASES) + Journaling	Significant increase in self-efficacy ($p<0.05$)
Sun et al.[17]	CHN	Cancer Patients	Multidisciplinary team interventions	3 months	Self-reporting	Adherence in intervention group vs. control group (90.5% vs. 69.1%)
Figueiredo Junior AG et al.[26]	BRA	Colorectal, breast cancer patients	Multidisciplinary team interventions	not mentioned	Pill counting + Quality of life (EORTC QLQ-C30 Scale)	overall compliance rate: 88.3%-96.2%, dyspnea negatively correlates with adherence ($p=0.042$)
Schneider et al.[11]	USA	Cancer Patients	Nurse-directed individualized interventions	6 months	Pill counting + Pharmacy holding rate	Adherence rate 2 months, 4 months in intervention group (91.3%, 95.1%) vs. control group (80.0%, 82.4%)
Campbell et al.[18]	CA	Cancer Patients	Nurse-directed individualized interventions	3 months	pill counting + Audit of medical records	Significant increase in patient knowledge and confidence
Krolop L et al.[3]	DEU	Colorectal, breast cancer patients	Pharmacist-led modular medication management	6 cycles	MEMS Electronic Pill Box	Non-adherent patients' adherence increased from 85.7% to 97.6%
Spoelstra et al.[12]	USA	Breast, colon, and lung cancer patients	Automated Voice Response (AVR) + Nurse Intervention	8 weeks	Self-reporting + Audit of medical records	Non-adherence rate 42% (associated with program complexity)
Khandelwal N et al.[2]	USA	Cancer Patients	Oral Chemotherapy Cycle Management Program (CMP)	6 months	Medication Possession Rate (MPR)	Persistence in intervention group vs. control group (23.8% vs. 7.8%)
Sommers et al.[13]	USA	Gastrointestinal cancer patients	Nurse phone follow-up + medication diary	1 cycles	Self-reporting	Overall high adherence
Partridge AH et al.[14]	USA	Breast cancer patients	Electronic pillbox monitoring	6 cycles	MEMS Electronic Pill Box	Average compliance rate of 78%
Decker et al.[15]	USA	Breast cancer patients	Automated Voice Response (AVR) + Nurse Intervention	8 weeks	Self-reporting	Symptom management was associated with adherence

3.2 Characteristics of oral chemotherapeutic drug intervention strategies

The specifics of the interventions covered 3 areas: 1) 12 studies[1-4,12,14-15,21-24,27] provided traditional interventions: including written or verbal oral chemotherapy medication instructions, symptom monitoring, telephone follow-up, and medication diary entries; 2) 5 studies[10,13,16,20,26] provided technology tools to assist interventions: including cell phone text message-based chatbots, mobile applications, automated voice response systems AVR, and nurse involvement in supervision or follow-up (e.g., dealing with technological miscues, providing manual support); 3) 5 studies [11,17-19,25] provided comprehensive interventions: primarily clinical nurse or APN-led (including education, follow-up) individualized interventions, followed by the formation of a multidisciplinary team to provide systematic interventions for patients.

Four of the included studies utilized theoretical models: in one study [10], a self-regulation model was used to develop interventions for patients to overcome barriers to adherence to oral chemotherapy medications at the level of knowledge strategies, behavioral skills, and emotional support. two studies used motivational interviewing techniques for educational follow-up, which enhanced patients' self-efficacy and medication adherence[8-9]. One study[11]used the behavioral Intervention Staged Development Model ORBIT (Obesity-Related Behavioral Intervention Trials) as an overall framework, which is a framework for developing and evaluating behavioral interventions, initially used for obesity behavioral interventions, and is now widely used in a wide range of behavioral intervention studies. The ORBIT model is divided into 3 phases, including Problem Definition, Intervention Design, Initial Testing, and Optimization, using the Best-Worst Scale (BWSE) to identify the patient's primary barriers to adherence, using the COM-B model to categorize the obstacles into three dimensions of Capability, Opportunity, and Motivation, and utilizing the theory of Behavior Change Techniques (BCTs)

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Theoretically guiding the intervention in terms of Social Cognition, Motivational Interviewing, and Problem Solving Therapy, respectively, the study developed a personalized adherence intervention and validated its initial feasibility and acceptability.

Measurement tools included 2 categories: 1) self-report was the most common method used in 12 studies. They are the Morisky Medication Adherence Scale[14], the Brief Adherence Rating Scale (BARS)[1,4,23], the Medication Adherence Self-Efficacy Scale (MASES)[3,20-21], Self-report Adherence Scale (ASK-12)[15,25], Self-designed Oral Chemotherapy Adherence Questionnaire[20], and diary[14,22], 2) 4-item use of medical records: medication possession Ratio (MPR) [2][25], and pharmacy dispensing records[12-13]; 3) 2 used pill counting[24,27] 4) 4 used electronic testing: the Medication Event Monitoring System (MEMS)[2-3,14,22].

The outcome metrics consisted of 2 dimensions: 1) primary outcome metrics. 7 studies [14,16-18,20-22] were medication adherence (by questionnaire or self-report), 4 studies[1-4,15,23-25,27] used adherence rate monitoring (MEMS monitoring, pill counting method); 1 study[10]used the proportion of incorrect advice in text message exchanges; and 1 study[26] used technology acceptance (UTAUT scale) and feasibility (recruitment rate, retention rate, intervention adherence) as primary outcome indicators.2) Secondary outcome indicators. These included symptom assessment scale, self-efficacy scale, medication knowledge acquisition, patient-reported side effects, anxiety-depression scale, quality of life (QLQ-C30), satisfaction with cancer treatment, and hospitalization rate.

4. Discussion

4.1 Digital interventions offer new forms of adherence, but technology needs further optimization

Previous studies have shown that electronic monitoring devices, remote follow-up systems, and mobile apps can moderately enhance oral chemotherapy adherence, especially for home-based treatment and long-term medication management[4,23-24]. Standard digital interventions include smart medication dispensers, telehealth calls, and mobile apps. While electronic pillboxes allow objective adherence tracking, their technical complexity and reliance pose usability challenges for older adults [15]. Telephone follow-ups—a "low-tech but high-engagement" approach—have proven adaptable and well-accepted across studies, particularly when incorporating motivational interviewing to boost patient self-efficacy and compliance[21]. However, technological efficacy is often limited by age, health literacy, and cognitive function, with some elderly patients struggling to adopt digital tools even with professional or familial support[25,27]. Despite their promise, current solutions face barriers like steep learning curves, poor user interfaces, and inadequate engagement incentives. To address these gaps, future designs should prioritize intuitive interfaces, streamlined workflows, and training programs to improve patient competency. Incorporating caregiver monitoring modules would further enhance accessibility and broad applicability.

4.2 Multidimensional interventions have positive effects and still require stratified and precise management

Multifaceted intervention strategies have shown promising results in improving adherence to oral chemotherapy. These comprehensive approaches often integrate structured medication education, telephone follow-ups, nursing support, personalized behavioral interventions, and adverse effect monitoring. Studies[3] reveal that such multidimensional programs significantly enhance medication compliance, self-efficacy, and treatment satisfaction among oral chemotherapy patients compared to single-method interventions[22]. Earlier research[4,24] relying solely on isolated measures like telephone reminders or standardized education failed to demonstrate meaningful adherence improvements, likely due to rigid methodologies that overlooked individual patient variability and diverse population needs. Krolop et al[3] studied that by early screening of patients with poor medication habits and providing targeted guidance, their medication adherence rates could be significantly improved. The effectiveness of multidimensional interventions often exhibits heterogeneity across different populations. Among elderly female patients, nurse-led self-management support programs not only improved adherence but also enhanced their quality of life and psychological adjustment capabilities[25]. However, in high-risk non-adherence groups (e.g., those with lower cognitive function or receiving polypharmacy), intervention effects were only significant when combined with personalized follow-up and behavioral incentives[22,23]. Additionally, some studies noted that individual factors such as patients' educational background, cultural acceptance, and disease comprehension level may modulate the final intervention outcomes[28-29]. Therefore, improving oral chemotherapy adherence requires multidimensional

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interventions, as a single educational tool is insufficient to address complex patient needs. Future research should focus on individual characteristic identification and risk-stratified management, using initial screening tools to assess patients' adherence risk levels and subsequently developing stratified intervention plans.

4.3 Challenges and Prospects for Adherence Intervention

Current research on medication adherence interventions shows diverse forms, but there remains a gap in the design of intervention methods across studies. The implementation and sustainability of various programs have not been well described[30]. Most rigorously designed interventions are pilot studies, limiting external validation and generalizability of research findings. The heterogeneity in intervention content and intensity prevents meta-analysis or systematic reviews to confirm effectiveness, necessitating further strictly designed studies. Secondly, many intervention studies lack clear theoretical guidance, which leads to inconsistency in intervention content, making it difficult to replicate and promote[31]. The systematic application of theory in intervention design clarifies intervention mechanisms, enhancing the scientific rigor and replicability of interventions. Furthermore, oral chemotherapy medication adherence programs are rarely standardized, and existing studies exhibit significant differences in intervention content, implementation methods, and evaluation indicators, making cross-sectional comparisons and comprehensive analysis challenging[32]. It is recommended to establish unified intervention content and evaluation standards to facilitate comparisons and comprehensive analysis across different studies.

5. Conclusions

This study is based on the theoretical framework of a scoping review and examines the literature related to oral chemotherapy medication adherence among cancer patients. The findings indicate that adherence interventions utilizing digital technologies have become a trend and are effective. At the same time, cancer patients have diverse needs and preferences regarding digital technologies. When guiding them in using mobile technologies, it is essential to first assess their psychological needs and concerns, then provide personalized recommendations for mobile tools that align with their preferences. This study also has limitations, as the included literature lacks qualitative research, thereby somewhat overlooking the subjective experiences of the study participants and providing an incomplete explanation of influencing factors. Therefore, qualitative research should be appropriately incorporated to enrich perspectives, construct theory, and make the analytical results more practical. Future research should further optimize the specific content of intervention programs, conduct high-quality studies, and promote improved medication adherence among patients to enhance their self-management.

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