

Advancements in Pharmaceutical Compounding and Personalized Medicine: A Comprehensive Review on Enhancing Medication Adherence and Patient Engagement

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Abstract

Medication adherence is a critical component of effective healthcare, yet non-adherence poses a significant public health challenge, leading to preventable morbidity and mortality. Factors influencing adherence include socioeconomic conditions, healthcare systems, and medication characteristics. This review explores advances in compounding pharmacy and personalized medicine as strategies to enhance medication adherence. This review synthesizes existing literature on medication adherence, focusing on the role of pharmaceutical compounding and personalized medicine. Key performance indicators (KPIs), 360-degree feedback, self-assessments, and surveys were employed to evaluate patient preferences and adherence rates related to compounded medications. The findings indicate that orodispersible dosage forms significantly improve adherence compared to traditional medications. Additionally, the customization of medications through compounding addresses specific patient needs, particularly in pediatric and geriatric populations, enhancing overall treatment compliance. The review also highlights the necessity of a patient-centric approach in compounding practices to accommodate individual preferences and improve adherence rates. The integration of compounding pharmacy and personalized medicine represents a promising avenue for addressing the multifaceted issue of medication non-adherence. By tailoring medications to meet the unique needs of patients, healthcare providers can enhance patient engagement, satisfaction, and overall health outcomes. Future research should investigate the long-term impacts of these approaches on adherence and health outcomes across diverse patient populations.

Keywords: Medication Adherence, Pharmaceutical Compounding, Personalized Medicine, Patient-Centered Care, Healthcare Outcomes.

Introduction

Medication adherence is characterized as the active, collaborative, and voluntary engagement of the patient in adhering to the dose regimens prescribed by a healthcare professional [1]. This behavior may be

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categorized into three distinct phases: initiation (the patient's first dosage), implementation (adherence to the specified dosing schedule), and persistence (the duration until treatment cessation) [1]. Non-adherence is a progressively significant public health concern. In Europe, it has been shown to cause almost 200,000 premature fatalities, leading to annual expenses of EUR 125 billion in preventable hospitals, emergency services, and outpatient consultations [2]. Various variables may affect drug adherence. The World Health Organization categorizes the reasons of non-adherence into five primary dimensions: socioeconomic factors, healthcare and system-related variables, therapy-related variables, condition-related variables, and factors associated with patients [3].

Numerous studies indicate that adherence to pharmacological therapy is far below expectations, with a non-adherence rate of 50%, which might escalate to 75% among psoriasis patients using topical therapies [4,5]. Various therapy-related variables may affect adherence, including features of the medication product such as swallowability, packaging, dosing routine, container closing mechanism, and dose form type [6]. Orodispersible dose forms have the benefits of being easily ingested without the need for drinking or chewing, and they do not need water for patient administration [7]. Patient adherence is often enhanced relative to traditional solid dose formulations. An example is the delivery of olanzapine in orodispersible tablet form vs traditional tablets [8].

Patient preferences for a certain vehicle may also differ based on the condition [9]. Recent research indicated that individuals with acne preferred tretinoin lotion over cream [10], but for psoriasis, ointments, creams, and foams (especially for the scalp) were identified as the preferred dose forms [9]. The influence of the vehicle on treatment adherence has recently been objectively assessed in a cohort of psoriasis patients [5]. Adherence was much superior among individuals using gels and creams compared to those employing ointments, particularly when lesions included a large body surface area. The findings, influenced by the dose form, underscore the need to meticulously design medication formulations to effectively tackle the public health issue of non-adherence and provide a more significant role for pharmaceutical compounding in enhancing treatment adherence.

Pharmaceutical Formulation and Regulatory Structure

Pharmaceutical compounding is the creation of tailored medications to address the unique requirements of patients that are not fulfilled by commercially accessible pharmaceuticals. This is a longstanding process whereby pharmacists amalgamate, blend, or modify substances to make bespoke compounded medications predicated on the doctor-patient-pharmacist triad connection. Compounding is now a fundamental aspect of the pharmacy profession and is vital to healthcare delivery [10]. The ongoing COVID-19 pandemic has underscored the significance of compounding, as pharmacists globally swiftly formulated hand sanitizers, surface disinfectants, oral liquids, and capsules, including hydroxychloroquine sulfate, dexamethasone, remdesivir, and other potentially efficacious off-label medications [11]. Compounded medications are projected to constitute 1% to 3% of pharmaceutical prescriptions, with their use on the rise [12]. The rising demand for compounded medications is likely attributable to various factors, including restricted dosage forms; limited dosages/strengths; scarcity of orphan drugs; necessity for alternative raw materials and organoleptic properties; requirement for specific combinations of active pharmaceutical ingredients (APIs); and shortages or discontinuation of commercial medications. Compounding is a crucial therapeutic alternative across all medical fields, especially significant in pediatric and geriatric specialties, which are often neglected by the pharmaceutical business.

While compounded medications do not need regulatory clearance, the process of pharmaceutical compounding is governed by national or state pharmacy boards. The regulatory system lacks worldwide harmonization, leading to significant variations in standards of practice, compounding environments, and definitions between the United States of America and European nations [13]. Adherence to the regulatory framework is crucial for ensuring the quality, safety, and effectiveness of compounded medications. Pharmaceutical compounding errors are avoidable; yet there are documented instances of inadvertent mistakes that have resulted in significant damage to people globally. The most significant blunder occurred in 2012 when tainted steroid injections produced by the New England Compounding Center (NECC) were given to 14,000 patients, resulting in a multistate epidemic of fungal meningitis with over 60 reported

fatalities. This specific mistake stemmed from microbial contamination; however, other sorts of errors may also pose significant damage. For example, the administration of compounded medications with erroneous constituents or improper dose strengths [12,14]. Pharmaceutical compounding is both safe and vital, contingent upon the anticipation and prevention of all sorts of mistakes via adherence to the compounding regulations.

Compounding Formulations Tailored to Patient Demands and Requirements

Medications are ineffective in individuals who do not adhere to their regimen. When the factors contributing to pharmaceutical nonadherence are comprehensively identified by the triad of doctor, patient, and pharmacist, the formulation of a patient-specific drug may enhance treatment adherence [15-20]. Numerous factors contribute to individuals, particularly among adolescent and geriatric populations, making the logical choice to forgo adherence to recommended pharmaceutical regimens. Adherence to medication in pediatrics sometimes poses difficulties, since youngsters may either refuse or lack the capacity to ingest solid dose forms such as pills and capsules [21-24]. Moreover, youngsters exhibit heightened sensitivity to the taste and odor of pharmaceuticals; hence, neglecting the patient's preferences significantly increases the likelihood of medication refusal. Parents and caregivers often have difficulties administering medicine to children, resulting in impaired therapy due to missing dosing [25]. Medication adherence in geriatrics is particularly intricate due to the impact of physical, emotional, and social factors on the decision-making of the elderly. Moreover, some senior health issues are chronic rather than acute, necessitating lifelong pharmaceutical use. If patients are not completely content with the recommended drugs, it is quite probable that doses are overlooked, and treatments are undermined. A deficiency in communication may compel clinicians to unnecessarily escalate pharmaceutical dosages to attain the intended effectiveness, leading to significant patient damage and superfluous expenses. Given the expanding aging population and rising life expectancy, addressing pharmaceutical nonadherence is considered a priority in contemporary healthcare.

The pediatric population significantly differs from adults and comprises a varied group, including preterm newborns to teenagers, each with distinct treatment requirements throughout growth and development. In pediatrics, dose strengths are often determined by the child's age, body weight (mg/kg), or surface area (mg/m²) [26]. A 3-year-old kid weighing 15 kg needs a daily dosage of 10 mg of the proton pump inhibitor omeprazole for the management of benign gastric ulcers, whereas a newborn weighing 4 kg requires just 2.8 mg daily (700 micrograms x 4 kg) of oral omeprazole. Considering that most commercial medications are offered in standardized dose strengths designed for adults, access to age-appropriate dosages is essential for ensuring safe and effective pharmacological therapy for children [11,27].

Oral liquids, including emulsions, solutions, and suspensions, are the predominant dose forms used in pediatrics. Nonetheless, the flavor, aroma, visual aspect, texture, and quantity of liquid administered at each dosage may be quite repugnant to some people [28]. An alternative to oral liquids is child-friendly dose forms, such as medicated lollipops and lozenges (troches) [28,29]. The administration of these dosage forms is simplified due to their delayed dissolution in the mouth or their ease of being chewed and swallowed. Soft and chewable lozenges may be novelty-shaped (e.g., gummy bears), enhancing their appeal [30].

The significance of taste masking in pediatrics is unequivocal. Younger patients' aversion to the taste, odor, or look of their oral drugs will certainly jeopardize treatment adherence [31]. Commercial oral liquids are designed with the general population's preferences in mind; yet, 'one size does not fit all'—patients are unique, react individually, and must be treated as such [12]. Pharmaceutical compounding significantly contributes to drug adherence. Pharmacists may formulate alternative compounded drugs by selecting appropriate flavoring agents and sweeteners to align with the patient's preferences. The FLAVORx pediatric system exemplifies the extensive variety of tastes now accessible for children in pharmaceutical compounding. Upon enrollment, pharmacists get access to an extensive online flavoring formulary including hundreds of formulas, including flavors, sweetening agents, and bitterness mitigators [32]. Data from 2011 indicates that the favored tastes among U.S. consumers are grape, bubblegum, strawberry, watermelon, and cherry [33].

Older adults often have many health issues (multimorbidity) that need medicine for each ailment, resulting in a substantial daily consumption of drugs (polypharmacy). The frequency and incidence of polypharmacy, stemming from multimorbidity, is notably high in geriatrics and may lead to medication nonadherence owing to the substantial burden on patients' lives. Pharmaceutical compounding may simplify prescription regimens by creating specialized drug combinations that amalgamate many commercial medications into a single dose form. Oncology and pain management are medical areas that significantly benefit from medication combinations. Compounded mouthwashes for chemotherapy-induced oral mucositis significantly impact the quality of life of cancer patients. These mouthwashes often include diphenhydramine, aluminum-magnesium antacids, and lidocaine, together with antibiotics like nystatin or tetracycline to prevent or cure infections; corticosteroids may moreover be included to alleviate mucosal irritation in immunocompromised people [34].

Transdermal pharmaceuticals provide the simultaneous delivery of several drugs in multiple dose strengths with a single topical application. Furthermore, these permeation-enhancing agents circumvent hepatic first-pass metabolism, resulting in increased bioavailability and reduced dosage requirements to attain therapeutic benefits [35]. This composition has been shown to enhance the efficient transdermal transport of all components and is particularly advantageous in pain treatment due to its ability to concurrently target various receptors and pain pathways [36].

Dysphagia, characterized by physical and/or psychological difficulty in swallowing, is estimated to afflict 1 in 6 persons in the USA. Individuals with the highest risk of developing dysphagia include individuals with degenerative neurological or muscle illnesses, including Alzheimer's and Parkinson's diseases, which are more prevalent in the elderly population [37]. Stroke, oropharyngeal neoplasms, head and neck trauma, or cerebrovascular accidents increase the likelihood of dysphagia in patients. This disease may substantially influence the patient's quality of life by influencing medication, nutrition, and hydration, along with possible psychological and social repercussions [38].

Elderly dysphagic individuals require alternative dose forms to the typically recommended, challenging-to-swallow commercial pills and capsules. Examples include oral disintegrating pills, transdermal systems, rectal and buccal drug administration methods, and modified-thickness oral liquids [38]. Pharmaceutical compounding may provide patients many alternative dose forms to enhance drug compliance and improve treatment adherence. An instance of transdermal medicine has been previously discussed as an alternative to the pill load in pain treatment.

Functional and cognitive impairments in the elderly may hinder their capacity to self-administer medicines. Frequent challenges include opening lidded containers, extracting medicine from blister packs, and dividing pills to get the prescribed dosage. If these compromised patients do not get the necessary assistance during medicine administration, nonadherence is likely to jeopardize the efficacy of their therapies [39].

A variety of compliance packaging solutions have been developed to enhance adherence by facilitating the delivery of medicine to elderly people. Community pharmacists are now permitted to repack commercial pills and capsules into multidose dispensing systems (MDDS). These adaptable customizable packets also facilitate medication management by structuring the pill regimen in monthly or weekly calendar formats [40]. If patients choose compounded prescriptions tailored to their specific requirements, the container should be deliberately designed for user-friendliness. Patients who have difficulty opening containers may receive multidose oral liquids in single-dose oral syringes (Figure 2). When manual tablet division is a challenge, the appropriate dose may be customized in capsules [41].

The need for alternative excipients in pharmaceuticals is increasing due to allergies and intolerances among sensitive patients. Commonly encountered problematic excipients in commercial pharmaceuticals include colors, flavorings, sweeteners, preservatives, gelatin, alcohol, dairy products, and substances containing gluten, maize, soy, or nuts. If a patient poorly tolerates pharmacological therapy, medication adherence is likely to be compromised. The resolution to this issue is the formulation of an alternate compounded drug that omits or replaces the problematic excipient [42]. For example, replacing lactose, a common diluent in commercial tablets, with compounded capsules containing a cellulose derivative, such as methylcellulose,

for individuals with lactose intolerance. Similarly, replacing commercial gelatin capsules with vegetable-based compounded capsules made from starch or polymer is advisable for vegetarian patients or those with religious prohibitions on pig intake [43]. Pharmaceutical compounding is sometimes the only choice for these vulnerable individuals; hence it is crucial in enhancing drug adherence.

Medications designated for the diagnosis, prevention, or treatment of disorders with very low prevalence (rare diseases) are referred to as 'orphan medications'. Presently, more than 200 orphan drugs are registered in Europe, however, it is believed that there exist between 5,000 and 8,000 distinct uncommon illnesses. In the absence of an authorized orphan drug, patients with uncommon diseases depend only on pharmaceutical compounding to meet their treatment requirements [44]. In many instances, orphan 'compounded' medications represent the only therapeutic alternative. Compounded drugs used for unusual illnesses include L-carnitine solution, sodium thiosulphate injection, and chenodesoxycholic acid capsules [45,46]. Moreover, authorized orphan drugs are not universally sufficient for all patients with uncommon diseases. Once again, 'one size does not fit all,' and tailored orphan 'compounded' medications are likely to enhance prescription adherence. For example, the ad hoc formulation of a sildenafil oral solution rather than dispensing the approved tablets (Revatio®) for juvenile patients with pulmonary arterial hypertension [45].

The Influence of Mixing on Pharmaceutical Compliance

The major objective of compounding is to address the unmet needs of patients when the pharmaceutical industry has no therapeutic alternatives. The encouragement of medication adherence serves as a secondary effect of pharmaceutical compounding in this context. Another aspect is the effect of compounding on drug adherence relative to industrial medications, specifically by contrasting adherence rates between patients receiving compounded formulations and those using proprietary pharmaceuticals for the treatment of the same condition. Multiple hypotheses might be suggested about the alleged impact of compounding in enhancing drug adherence. The customisation may serve as a positive reinforcement for the commencement of treatment by allowing patients to participate in medication choices, so enhancing their trust in the effectiveness of such personalized therapy. Patients who participate in the therapy selection process often exhibit greater adherence [47]. Implementation may be advantageous, since teaching about posology and administration, together with the resolution of inquiries, may be effectively conducted in a pharmacy environment. The often brief beyond-use dates of compounded formulations need frequent refills and increased pharmacy visits, hence enhancing the pharmacists' responsibility in teaching patients about the advantages of effective medicine adherence. A significant limitation to the utilization of compound drugs is their expense, which may impede effective adherence [48]. Nonetheless, compounded medications might sometimes be more economical than their commercial counterparts. When patients are unable to purchase commercially accessible medications, compounding may represent the only choice.

In addition to these assumptions, the literature lacks research examining the impact of compounding on adherence promotion. The limited prevalence of compounded drugs likely contributes to methodological challenges and may have restricted research in this area. Compounded drugs may be excluded from e-prescribing software [49], so undermining data gathering and analysis. There is little accurate published data about the prevalence of compounding by community pharmacists and the percentage of patients using compounded drugs. The majority of research indicates that the incidence of compounding practice is minimal (below 5%) [50]. In a 2013 survey done in the USA, the prevalence of compound users was just 1.4% of eligible insured individuals [48]. Various factors may be attributed to the insufficient examination of the significance of pharmaceutical compounding for public health, including concerns around cost, possible dangers, and adherence to appropriate compounding methods. Recent reviews have addressed compounding mistakes. Despite compounding mistakes being detected in about 3% of the evaluated reports, the majority resulted in patient damage [14]. A reduced prescription rate is a significant factor contributing to the low incidence of compounding. In 2006, compounded formulations constituted 2.3% of all prescriptions issued by compounding pharmacies in the USA [50]. This is particularly remarkable given that the chance to get this tailored therapy seems to be accessible to the majority of patients, although perhaps dependent on the nation. In a 2012 study, 85.5% of community pharmacies in the USA said that they offered compounding services [51]. This scenario asserts the engagement of legislators in establishing

a regulatory framework conducive to the compounding activity, advantageous for pharmacies, patients, and public health.

The patient-centric pharmaceuticals drug product development (PCDPD) process identifies all of the requirements and preferences of individuals, utilizing this information to inform the design of pharmaceutical drug products, which can be particularly beneficial for extemporaneously prepared and tailored medications for specific patients. Although PCDPD is beneficial for pharmaceutical businesses, particularly when enough data exists for a target group, it is more efficient when focusing on individual patients. The role of PCDPD in enhancing medication adherence has been recently evaluated [6]. We propose a patient-centric compounding design (PCCD) technique to standardize the formulation of compounded medications with the objective of enhancing medication adherence (Figure 1). The data pertinent to the population, based on clinical conditions and sociodemographic characteristics of patients initiating a therapy regimen with a compounded formulation, should be studied in advance. The patient should thereafter be questioned to evaluate self-reported requirements and preferences. Standardized surveys would be quite beneficial for achieving uniformity. A target product profile (TPP) may then be established, using the information gathered by the pharmacist and the physician. The compounding pharmacist may determine the optimal formulation and packaging by consultation with the prescribing physician, after a review of official formularies and monographs. In all instances, quality and safety must be guaranteed by the execution of risk assessments and the use of sound compounding procedures [16,18]. Patient insights after commencement may aid in the optimization of TPP. The sequential method illustrated in Figure 1 may signify a pertinent pharmaceutical intervention to enhance medication adherence.

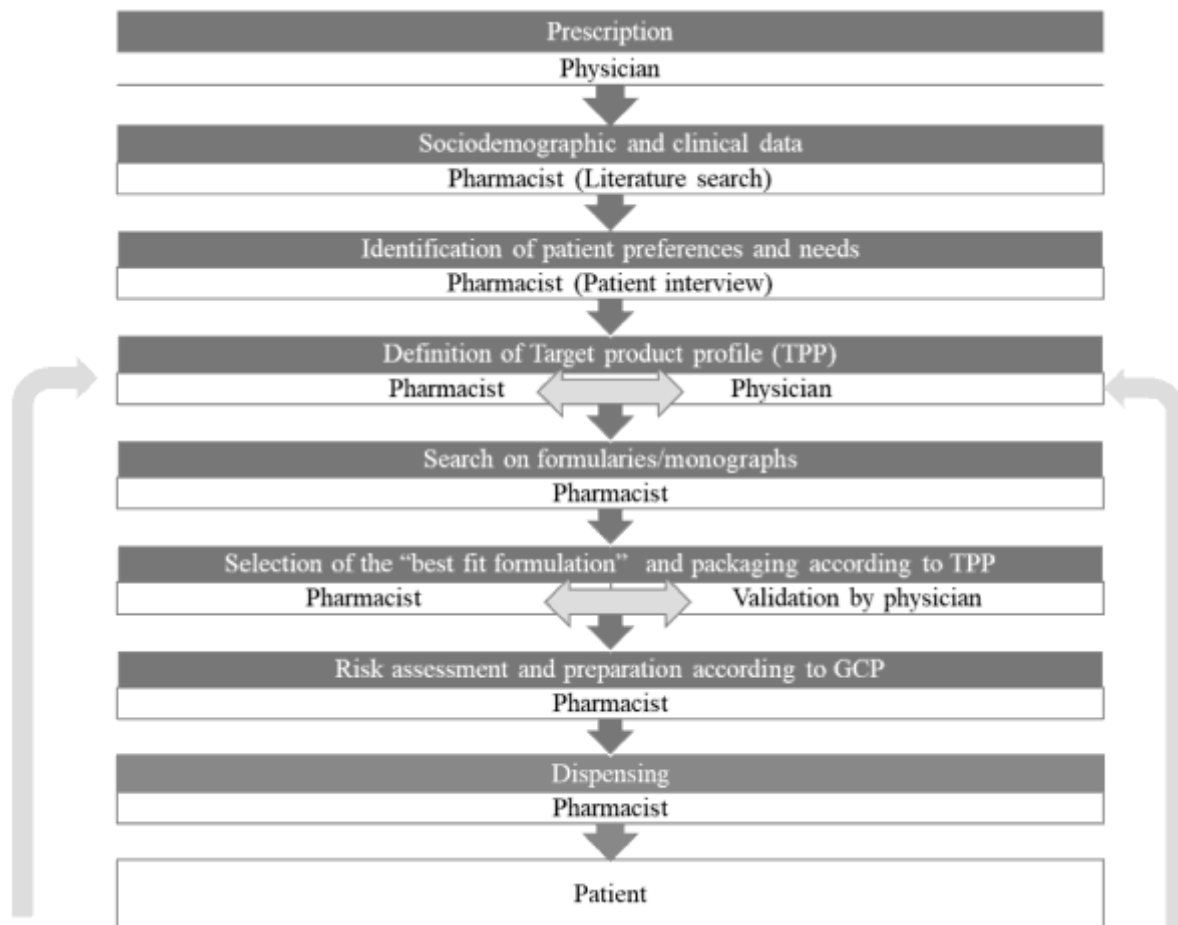


Figure 1. The Application of Patient-Centric Drug Product Development (PCDPD) to Compounding Mixtures: Patient-Centric Compounding Design (PCCD).

Conclusions

Pharmaceutical compounding and personalized medicine are pivotal in addressing the growing challenge of medication non-adherence. As healthcare systems evolve, the need for tailored therapeutic solutions has become increasingly apparent, particularly in the context of chronic diseases and diverse patient populations. This review underscores the significance of customizing medications to improve adherence, highlighting that patient preferences and experiences must guide pharmaceutical practices.

The research indicates that compounded formulations, such as orodispersible tablets, can effectively enhance adherence compared to traditional dosage forms. The ability to modify medication characteristics—including taste, dosing frequency, and delivery mechanisms—enables healthcare providers to cater to individual patient needs, ultimately fostering a more engaging treatment experience. This is especially crucial for vulnerable populations, such as children and the elderly, who may face unique challenges in medication administration.

Moreover, the review emphasizes the importance of a collaborative approach involving physicians, pharmacists, and patients in the compounding process. By engaging patients in discussions about their treatment options and incorporating their feedback into medication design, healthcare providers can enhance trust and satisfaction. This participatory model not only empowers patients but also aligns treatment goals with patients' values and lifestyles.

As the healthcare landscape continues to transform, ongoing research and clinical trials are essential to further understand the efficacy of compounded medications in improving adherence rates. Policymakers should also prioritize the establishment of regulatory frameworks that support innovation in compounding practices, ensuring that pharmacists are equipped with the necessary resources and training to implement patient-centered solutions.

In conclusion, the integration of pharmaceutical compounding and personalized medicine presents a viable strategy for overcoming the barriers to medication adherence. By prioritizing the unique needs of patients and fostering collaborative practice environments, healthcare systems can significantly enhance treatment outcomes and overall public health.

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التطورات في التركيب الصيدلاني والطب الشخصي: مراجعة شاملة حول تعزيز الالتزام الدوائي ومشاركة المرضى

الملخص

الخلفية: يُعدُّ الالتزام الدوائي عنصرًا أساسيًا في الرعاية الصحية الفعالة، ومع ذلك، فإن عدم الالتزام يُشكل تحديًا صحيًا عالميًا كبيرًا، مما يؤدي إلى اعتلالات ووفيات يمكن الوقاية منها. تشمل العوامل التي تؤثر على الالتزام الظروف الاجتماعية والاقتصادية، وأنظمة الرعاية الصحية، وخصائص الأدوية. تستعرض هذه المراجعة التطورات في الصيدلة التركيبية والطب الشخصي كاستراتيجيات لتعزيز الالتزام الدوائي.

المنهجية: تقوم هذه المراجعة بتجميع الأدبيات الحالية حول الالتزام الدوائي، مع التركيز على دور الصيدلة التركيبية والطب الشخصي. تم استخدام مؤشرات الأداء الرئيسية (KPIs)، والتغذية الراجعة الشاملة (360-degree feedback)، والتقييمات الذاتية، والاستبيانات لتقييم تفضيلات المرضى ومعدلات الالتزام المتعلقة بالأدوية المركبة.

النتائج: تشير النتائج إلى أن الأشكال الدوائية المتحللة فمويًا (orodispersible dosage forms) تُحسن بشكل كبير من معدلات الالتزام مقارنة بالأدوية التقليدية. بالإضافة إلى ذلك، فإن تخصيص الأدوية من خلال الصيدلة التركيبية يُلبّي احتياجات المرضى المحددة، لا سيما في الفئات العمرية مثل الأطفال وكبار السن، مما يعزز الامتثال العام للعلاج. كما تُبرز المراجعة أهمية اتباع نهج يركز على المريض في ممارسات الصيدلة التركيبية لاستيعاب التفضيلات الفردية وتحسين معدلات الالتزام.

الاستنتاج: يمثل دمج الصيدلة التركيبية والطب الشخصي نهجًا واعدًا لمعالجة مشكلة عدم الالتزام الدوائي متعددة الأبعاد. ومن خلال تكيف الأدوية لتناسب الاحتياجات الفريدة للمرضى، يمكن لمقدمي الرعاية الصحية تعزيز مشاركة المرضى ورضاهم وتحسين النتائج الصحية العامة. ينبغي أن تركز الأبحاث المستقبلية على دراسة التأثيرات طويلة المدى لهذه الأساليب على معدلات الالتزام والنتائج الصحية عبر مجموعات سكانية متنوعة.

الكلمات المفتاحية: الالتزام الدوائي، الصيدلة التركيبية، الطب الشخصي، رعاية تتمحور حول المريض، نتائج الرعاية الصحية.