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Deprescribing in psychiatry: challenges and opportunities

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Many recommendations, protocols describe the indications for starting medication, but only some of them indicate when they should be discontinued. An analysis of publications indicates a deficit of research in this area, especially in psychiatry. As part of this review, we tried to provide information that provides valuable information about this procedure, about the experience of other countries. Based on a literature review, it was found that in some countries there is already consensus on how to identify a patient who may be reevaluated, recommendations and algorithms have been developed for this procedure with minimal risk to the patient.

Keywords: deprescribing, treatment, withdrawal of treatment, psychiatry, polypharmacy, review

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Отмена препаратов в психиатрии: проблемы и возможности

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Многие рекомендации, протоколы описывают показания к началу приема лекарств, но только некоторые из них указывают, когда их приём следует прекратить. Анализ публикаций указывает на дефицит исследований в этой области, особенно в психиатрии. В рамках этого обзора мы постарались предоставить информацию, которая предоставляет ценную информацию об этой процедуре, об опыте других стран. На основании обзора литературы было установлено, что в некоторых странах уже существует консенсус в отношении того, как определить пациента, лечение которого может быть отменено, для этой процедуры были разработаны рекомендации и алгоритмы с минимальным риском для пациента.

Ключевые слова: депрескрайбинг, лечение, отмена лечения, психиатрия, полипрагмазия, обзор.

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Deprescribing is the process of reducing or discontinuing medicines that are unnecessary or deemed to be harmful [1,2]. The goal of deprescribing is to reduce medication burden and harm, while maintaining or improving quality of life [3]. Many guidelines describe the indications for treatment initiating, but only some of them give recommendation to stop therapy. The aim of the study was to present up-to-date information on deprescribing, its fields of application, and the experience of other countries.

Deprescribing is a proposed antidote to the harms of polypharmacy and is associated with numerous health benefits including improvement in cognition, a reduction in falls, a decrease in fractures, better medication adherence and improvement in quality of life [1].

Deprescribing is an inherent component of good prescribing practice, but is rarely implemented in routine clinical care, and physician practice or views on deprescribing vary greatly [4-6]. It is important to recognize that deprescribing involves more than just identifying inappropriate medicine use [7]. It

involves reviewing of all medical appointments, identifying un-necessary and potentially harmful drugs, deciding which of them can be stopped and setting the order of cancellation or change of dose, form of drug, with adequate monitoring for this. A deprescribing medication management plan is a final step of this process and should include discussion of changes with the patient and getting patient's consent.

Accordingly, the concept of deprescribing first arose in geriatric medicine. Recently, it has been mentioned that deprescribing is also associated with other medical specialties, including cardiology and psychiatry. The increase in potentially inadequate polypharmacy in child psychiatry (observed in many countries) without a clear improvement in functioning is just one reason to focus and stimulate the practice of a thoughtful withdrawal process [8, 9].

The term deprescribing was used in the English language health literature in 2003 in an Australian hospital pharmacy journal in an article titled, «*De-prescribing: achieving better health outcomes for older people through reducing medications*» [10].

The literature from January 1, 2003 to March 30, 2020, was searched to identify published systematic reviews and meta-analyses that were relevant to the project. Search terms included Deprescribing, polypharmacy, suboptimal drug therapy, Deprescribing in psychiatry. Terms were searched alone and in combination. Search limits included human subjects, English language. Data sources for the initial search included PubMed, and references lists of selected articles that the panel.

The initial search identified 50 citations, of which 30 were selected for preliminary review. 20 were excluded for not meeting the study purpose or not containing primary data. An additional research was conducted with the supplementary terms such as antipsychotics and, geriatrics, and elderly prescribing. Previous searches were used to develop additional terms to be included in subsequent searches, such as a list of authors whose work was relevant to the goals of the project. When evidence was sparse on older medications, searches were conducted on drug class and individual medication names and included older search dates for these drugs. Additional articles were found in a manual search of the identified articles reference lists and the panelist's files, book chapter, and recent articles review.

Deprescribing is necessary in connection with the developing polypharmacy of the medical community, which is associated with the multimorbidity of patients, affecting more than 50% of people in primary care [11]. As a result, patients are often prescribed several drugs. In addition, old age and weakness contribute to a decrease in life expectancy [12]. Therefore, physicians often must balance a variety of factors, including the disease (s) the patient may have, the benefit-risk profile of the prescribed drugs, the personal views of the patients, and the opinions of other prescribers. Patients who visit four or more doctors experience problems, like a conflicting medical advice, because of which the number of drugs taken does not decrease [13].

Due to the stigma associated with mental illness, which is often heightened by news media coverage, and an initial treatment focus on remission, a patient's first impression of the psychiatrist may be that of a «pill pusher». Alternatively, a patient may desire to please the prescriber through continued adherence, which might also generate conflict regarding treatment [14]. Medicaid claims data have shown that psychotropic polypharmacy has risen consistently over the past two decades in various states [15,16]. Although certain combinations of

psychotropics have been shown to be beneficial in «treatment resistant» psychiatric disorders, the stability of the treatment-resistant label over time is unknown. In fact, Stahl and Grady found in their review that most practitioners do not try to discontinue one of the drugs after a combination proves beneficial, even if cancellation is necessary [17].

Biological, psychological, and social factors must align to produce a favorable risk-benefit ratio such that a medication regimen becomes established for a patient. Over time, this risk-benefit ratio can change, providing an indication for deprescribing: certain adverse effects may develop only after longer-term use (for example, tardive dyskinesia with antipsychotics and renal impairment with lithium); normal aging alters both the pharmacodynamics and the kinetics of medications, increasing vulnerability to side effects; pregnancy; development of general medical comorbidities; new medication interactions; substance abuse raise. Psychological factors, such as patients' choice, their understanding of illness and medication, and their coping strategies, may evolve over time, shifting their individual risk-benefit ratio. Social factors, such as geographical relocation, changes in financial and insurance status, and changes in religion, may prompt a reappraisal. The growth of the recovery movement and patient-centered care in psychiatry, including in pharmacological management, further necessitates the development of deprescribing skills [14].

The imperfection of psychiatric classifications leads to the fact that in psychiatry (as in geriatrics) often several diagnoses can coexist in one patient. The practice of prescribing treatment «syndromically» is quite common, although international recommendations advise sticking to monotherapy. There are not so many combinations effectiveness of which would be confirmed by high-level studies. In the same way, the point of recommendations on the use of the lowest possible doses is not always followed: often the patient continues the therapy that was needed during the exacerbation, in spite of the fact that smaller doses are sufficient for maintenance therapy. Firstly, it is obvious, deprescribing is not suitable for all patients. This opportunity should be considered if: the patient is determined to participate in resolving issues about his treatment; the majority of the disorder symptom is currently absent; for this patient, unlikely behavior associated with a danger to themselves and others (auto- and hetero-aggressiveness), at the moment and for a long time there were no facts of drugs abuse; the social environment can support the patient, track changes in his condition; it is possible to turn to psychological therapy [18].

Secondly, to cancel drugs is the same science as to prescribe. There are only few studies that would specifically explore the cancellation process. A review of deprescribing processes in medical practice identified five key components: preparing a comprehensive medication history, identifying potentially inappropriate medications, determining whether a potentially inappropriate medication can be ceased, planning the withdrawal regimen (e.g. tapering where necessary), and provision of monitoring, support and documentation [19]. For use in psychiatry, this five-step process has been expanded to include appropriate timing, inclusion of the patient's family, friends and mental health team in the deprescribing process, and development of a plan for relapse identification, prevention and management (Table 1) [9,14, 18].

Deprescribing hinges on effective relapse prevention. A biopsychosocial perspective on relapse prevention, for example, in schizophrenia highlights the significance of psychosocial

Table 1

Steps of deprescribing in psychiatry

Step	Purpose	Implementation
Assess the timing of the intervention	To avoid initiating deprescribing at a time when the individual may be particularly vulnerable to a relapse, e.g. a period of psychosocial instability and/or heavy substance use, recent hospital admission	Assess housing, employment, financial status, social relationships, impending changes in these, and substance use
Review psychiatric and medication history	To minimise chances of relapse or clinical risk during deprescribing	Review psychiatric records, obtain history from the patient and available collateral sources Assess any previous trials of deprescribing/ attempts at reduction or discontinuation Contact other physicians involved in the patient's care and compile a complete medication list Document the dose, route, duration, indication, perceived benefit and side-effects for each medication
Initiate the discussion about deprescribing	To assess the patient's thoughts and feelings about deprescribing If appropriate (e.g. in antipsychotic polypharmacy) a hierarchy of medications with highest to lowest risk/ benefit ratio could be generated	Assess the patient's learning style and check for understanding Explore preferences and values Explore current knowledge Explain risks and benefits Examine choices
Involve the team and social supports	If the patient agrees, to acknowledge and support them in their decision, help them maintain wellness, monitor for early signs of relapse and notify the care team if signs are noticed. With the patient's consent, all providers involved in care should be aware of the initiation of deprescribing, including visiting nurse services, therapists, case managers and primary care	Consider a meeting with family, friends and other significant individuals Establish reliable means of contact, such as telephone or secure email Invite participation and contact from friends and family as desired by the patient
Develop and initiate psychosocial interventions	To help define, detect, and address any increase in symptoms To add supports to help the patient cope with anxiety, threats and challenges related to deprescribing	Develop a relapse prevention plan such as WRAP Consider additional support through psychotherapy, potentially targeting specific symptoms Consider self-help and mutual support groups
Develop and initiate the antipsychotic taper	To reduce the dose in a controlled and conservative way, to minimize negative impact	Decide which antipsychotic to taper Decide the rate of taper Adjust concomitant medications such as anticholinergics accordingly
Monitor and adjust taper according to response	To prevent, as much as possible, relapse or life disruptions due to the taper	Monitor for early signs of relapse Monitor functioning Monitor metabolic and neurological side-effects Slow the rate of taper if needed Reverse the taper if needed

stressors such as loss of employment or housing, bereavement or disruption of relationships. As well stressors of a biological nature such as substance misuse and, perhaps, precipitous, or ill-timed discontinuation of antipsychotics. They root deprescribing in psychiatry in recovery-oriented practices (Table 2), including shared decision-making, a person-centered approach and the nurturing of empowerment and hope [9, 20-23].

Consider the clinical situations in psychiatry in which deprescription can be used. Maintenance Phase of Treatment of Chronic Psychotic Disorders or Bipolar Disorder - the dose of antipsychotic drugs needed to prevent relapse (maintenance

therapy) can be reduced. Medications prescribed for certain side effects. Anticholinergics used to treat extrapyramidal symptoms may not be needed after a certain period due to the development of tolerance to the parkinsonian effects of antipsychotic drugs. Medications Prescribed for Off-Label Uses. Highly sedating antipsychotic medications such as quetiapine are often prescribed for management of insomnia in patients with psychiatric disorders. Similarly, antipsychotic medications are often prescribed for aggression and other behavioral problems not necessarily caused by psychosis or for the control of transient psychotic symptoms in post-traumatic

Table 2

Recovery-oriented practices in mental healthcare and their application to deprescribing

Practice	Description	Application to deprescribing
Shared decision-making	A process of collaboration to arrive at a mutually acceptable treatment plan. It involves two experts: one who knows the scientific literature and has clinical experience, and one who knows their own preferences and subjective experiences	Collaboration and solicitation of the patient's preferences and values at every step are essential components of deprescribing
Person-centered care	Designed to promote service engagement by increasing patient self-determination during treatment. It is defined as a highly individual comprehensive approach to assessment and services and is more focused on developing customized plans for achieving life goals rather than on symptom relief	Deprescribing aims to increase patient engagement and participation in treatment. Person-centered care offers a framework in which individualized antipsychotic tapering plans as well as psychosocial supports are nested
Hope	Hope is the belief that recovery is possible. It involves the recognition and acceptance of the problem and a commitment to change	With its emphasis on individual goals and preferences, deprescribing is based on hope and, by its nature, instils hope
Empowerment	Empowerment may be viewed as a corrective for the helplessness and lack of control that an individual may face in the mental health system. It includes autonomy, courage and responsibility	Deprescribing empowers the individual by encouraging them to take charge of their treatment and providing the space for them to take risks, should they choose to do so

stress disorder. These off-label uses put the patient at risk for serious side effects when other less risky medications or behavioral interventions such as cognitive behavioral therapy for insomnia may be equally or more effective [18, 24].

Another example is Alzheimer's disease (AD) incidence. AD represents a significant challenge for the aging health of our over the world. Because of medical advances, the life expectancy of our residents is increasing. By the year 2030, it is estimated that more than 20% of the United States residents will be older than 65 yr [25]. Advancing age is related to an increased risk of dementia. AD is the most common cause of dementia, accounting for an estimated 60% to 80% of cases [26]. Review Renn examined published practice recommendations for discontinuation of cholinesterase inhibitors (ChEI) in AD. ChEI are widely used and typically employed as first-line pharmacotherapy for symptomatic treatment of major neurocognitive disorder caused by AD; however, treatment often continues through advanced disease stages [27]. A recent Cochrane Review found that ChEI treatment effects are small and of uncertain clinical importance [28]. The trials reviewed did not elucidate the relationship between duration of treatment and response. Because cognitive and behavioral impairments change during the progressive disease course, the effects of medications may be unpredictable, especially over long durations of treatment. Persons with advanced dementia may receive overly aggressive care that does not align with person-centered care goals, and polypharmacy from medications that are minimally beneficial may place patients at unnecessary risk [29-31]. However, ChEI treatment may contribute to meaningful improvements in noncognitive domains, such as reduction in neuropsychiatric symptoms and behavioral disturbance [32].

Twenty years ago antipsychotic polypharmacy (APP) was criticized as being more expensive, having unproven efficacy, and causing more side effects. However, in recent years, anti-

psychotic polypharmacy has become acceptable in the views of clinical practitioners and academic researchers. In an early 1970s survey of 4 states of the United States, the results revealed that New York psychiatrists most frequently prescribed a combination of 2 drugs, and some even prescribed 6 drugs at a time. Currently, no consensus regarding the definition of APP is available; however, most of the research papers have referred to it as the simultaneous use of 2 or more types of antipsychotic medication [33, 34].

Interesting that Currently, APP has become more acceptable than in previous decades, and more evidence-based studies have proved its benefit. As there is no consensus on the ideal rate of APP and the combined use of other psychotropic drugs, the conception of a Health Care Quality Indicator Project can be utilized [35, 36]. In this project, a set of indicators is developed by comparing data from different resources, and then the exact positions of these indicators can be learned by clinicians and health administrators to obtain consistent results. Thus, according to the 2 compatible results from Asia and Europe and previous reports of APP, they suggest the following approximated ideal rates of maintenance treatments in patients with schizophrenia: APP, 30%; combined mood stabilizer, 15%; combined antidepressant, 10%; combined anxiolytics, 30%; and combined hypnotic, 10%. A large discrepancy in the use of anticholinergics exists between Asia and Europe (45,1% vs 16%). This difference might be because Asian patients have been more susceptible to extrapyramidal side effects [37-41]. Thus, the doctor should constantly review the drugs that are prescribed to the patient, especially at the stage of maintenance therapy.

Other scientists-researchers from the Bruyere Research Institute and the Ontario Pharmacy Research Collaboration developed evidence-based guidelines for deprescribing. Each guideline is summarized in an easy-to-use algorithm and information brochure [42]. Algorithm of this guideline

is shown in Figure 1. These recommendations apply to adult patients who have been prescribed antipsychotics for insomnia or behavioral and psychological symptoms in dementia (BPSD), provided the symptoms of the latter are controlled or the patient is unresponsive to a reasonable trial of therapy.

Combined with clinical judgment and an individualized approach to care, this guideline is intended to support clinicians and patients in successfully deprescribing antipsychotics, ultimately striving for better patient care. They also issued guidelines for the abolition of memantine and agonist benzodiazepine receptor [43, 44].

A few studies have been conducted to study about doctors' opinion of this methodology. Many specialists were inclined to believe that deprescribing as «swimming against the tide» of patient expectations, the medical culture of prescribing, and organizational constraints; deprescribing came with inherent risks for both themselves and patients and conveyed a sense of vulnerability in practice. The only incentive to deprescribing they identified was the duty to do what was right for the patient. Some note that even despite existing drug withdrawal algorithms, specialists ignore them (Australia) or general practitioners refuse to do this, citing the fact that these are the duties of specialists. Very often, doctors simply do not have enough information on how to cancel the medication. Physicians fear that patients may perceive deprescribing as withdrawal of care before their end of life. These misconceptions prevent physicians from implementing deprescribing. For many GPs, «maintaining the status quo» for multimorbid patients with polypharmacy who are stable, is seen as the most reasonable course of action to undertake. In addition, clinicians recognize that clinical guidelines are rarely based on evidence from studies in older populations and rarely address modifying clinical targets with advancing age or care goals [12, 45-48]. Physicians recommended organizational changes to support safer prescribing, including targeted funding for annual medicines reviews, computer prompts, improved information flows between prescribers, improved access to expert advice and user-friendly decision support, increased availability of non-pharmaceutical therapies, and enhanced patient engagement in medicines management.

There is another vulnerable group - adults with intellectual disabilities. There are many complexities in prescribing, dispensing, and administering psychotropic medication for such patients. Two large pharmaco-epidemiological studies in UK and England have indicated a marked disassociation between rates of psychotropic prescription in people with intellectual disabilities and recording of underlying mental illness for which they are indicated [49-51].

Ten principles of good deprescribing during medication review in the population with intellectual disabilities, based on the British Pharmacological Society's Principles for Good Prescribing 2010:

1. Be clear about the reasons for de-prescribing psychotropic medication.
2. Consider the patient's medication history before de-prescribing.
3. Consider other factors that might alter the benefits and risks of deprescribing psychotropic medication.
4. Consider the patient's/carer's/families/advocates ideas, concerns and expectations. Share information about the benefits and harms of different options and allow patients/carers to clarify what is important to them about these options.
5. Ensure all medicines are effective, safe, cost-effective, in appropriate form and individualized for the patient with intellectual disability, behaviors that challenge and other conditions such as dysphagia, autism.
6. Adhere to national guidelines and local formularies where appropriate. Use caution where the population with intellectual disabilities have not been considered in the guideline/formulary development process.
7. Write unambiguous accurate documentation detailing reason for de-prescribing psychotropic medications (or other medications).
8. Monitor and document the beneficial and adverse effects of de-prescribing psychotropic medicines and any effects on behavior.
9. Communicate and document all de-prescribing decisions and the reasons for them and ensure information communicated to appropriate personnel such as GP, pharmacist, psychiatrist, epileptologist, carer and patient.

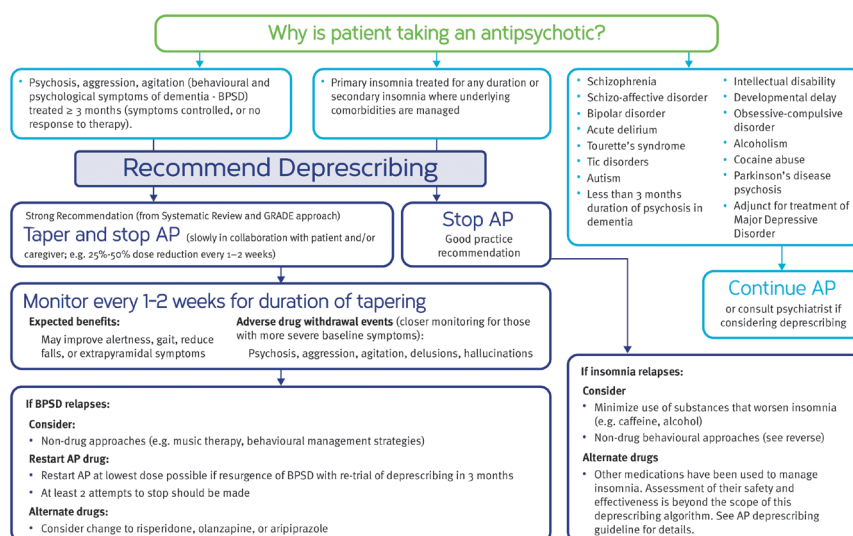


Figure 1. Antipsychotic (AP) Deprescribing Algorithm.

10. Deprescribe psychotropic medications within the limitations of your knowledge, skills and experience of the population with intellectual disabilities and behavior disorders [52].

In conclusion, it should be noted disputes around this topic and researches are only gaining momentum. Even though some data on deprescribing are contradictory, there is security information for this recommendation. Possible negative effects are associated with the return of medical conditions or symptoms and adverse reactions to drug withdrawal, which emphasize necessary control and monitoring of the process by a medical professional. «Deprescribing clinics» are promising the development as a part of a large outpatient psychiatric service or even as a consultation service. Important areas for future researches include the suitability of deprescribing certain medications in specific populations, how to implement deprescribing processes into clinical care in a feasible and cost effective manner, and how to engage consumers throughout the process to achieve health and quality of life positive outcomes. Now, the «ideal» patient for

deprescribing is getting used to living with side symptoms: the «working» scheme often is given to doctors and patients with difficulty, and neither one nor the other is interested in further experiments. Nevertheless, the results of a few studies so far on painless drug withdrawal and numerous ones on their long-term effects make one wonder whether this situation is correct. In the long term, evidence-based deprescribing, like any good practice, could be the final stage of assistance in the chain from the hospital to the outpatient or rehabilitation departments. The concept of deprescribing calls for a shift in focus, a revision of our goals: not to reduce or eliminate symptoms at all costs, but to strive primarily to improve the quality of patients' life.

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