

Deprescription: The prescription metabolism

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ABSTRACT

Deprescribing is a structured approach to drug discontinuation. An alternative suggested term is “prescription metabolism.” The major aim of deprescription is to purge the drug(s) considered unwanted in a given patient, especially in the elderly patients with multiple comorbidities or in those suffering from chronic disease. Like drug metabolism, prescription metabolism is a way of eliminating unwanted, troublesome, or cost-ineffective medications. The removal of such drugs has been found to decrease the incidence of adverse drug reactions and improves the rate of medication adherence, thereby reducing the economic burden on the patient as well as on the health care providers. Certain categories of drugs are to be tapered rather than abruptly stopped. Despite the availability of many tools to minimize drug therapy-related problems, there is little guidance for the process of deprescribing in general clinical practice. Various methods to reduce the risks of polypharmacy include patient education, physician education, and regulatory intervention. The suggested S and S approach (seek and screen, save and severe, sensitize and supervise) may be tried for deprescribing in general practice. More research on deprescribing is the need of the hour in almost all branches of clinical medicine which may pave the way for the betterment of health care.

Key words: Discontinuation, pharmacolysis, prescription pruning, untrials, withdrawal

INTRODUCTION

Deprescribing or deprescription is an emerging topic in the pharmacotherapy of diseases. For the sake of convenience, both terms have been used interchangeably in the following write-up.

What is deprescription or deprescribing? An appropriate shorter definition as implied from a write-up by Scott *et al.* would be, “Deprescribing is a structured approach to drug

discontinuation.”^[1] An elaborate definition shall be, “It is the process of reconstructing multiple medication use by review and analysis and which concludes with dose modification, replacement, or elimination of some drugs or addition of others.”^[2]

The major aim of deprescription is to purge the drug(s) considered unwanted anymore in a given patient, in the course of management of a disease, taking in to account the present condition in relation to the past. In general, deprescription has higher relevance to chronic conditions such as hypertension and psychiatric illness, where polypharmacy is a practice rather than a rule. Other than pruning the unwanted drugs, deprescribing could

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be considered to tackle adverse drug reactions (ADRs), ineffective treatment, or when treatment goals have changed. The other terms used as alternatives to “deprescribing” are “withdrawal,” “discontinuation,” “pharmacolysis,” “untrials,” and “prescription pruning.”^[3]

It is felt that “Prescription metabolism” could be considered as a better alternative phrase to refer the deprescribing process. The process could be equated to drug metabolism (biotransformation). The living organism considers all drugs as foreign and tries to eliminate it through urine (if water-soluble) or transforms it to a more water-soluble metabolite (mainly in the liver) for elimination. In rare instances, certain drugs stay in the body for very long time due to their unique chemical properties. In addition, also, when reviewing a prescription, a drug with more benefit-risk ratio is retained and the one on the opposite side of the spectrum is done away with or replaced with the next among the equals, as the condition warrants. Like drug metabolism, prescription metabolism is a way of elimination of unwanted/troublesome/cost-ineffective medications.

WHY IS THIS DEPRESCRIBING PROCESS GAINING MOMENTUM, ALBEIT AT A SLOWER PACE?

Periodically guidelines are released based on evidences, which serve as framework to manage diseases. However, guidelines generally do not elaborate upon the review, i.e., timing of stoppage of unwanted drug(s) or replacement of drug(s). Guidelines as the name suggests are recommendations for the initiation and continuation of therapy of diseases in general but without much tread on when, which, and why that needs stoppage or replacement nor they take into consideration the patient preference, cost, and other such factors. On the other hand, deprescribing is a process highly suited for individualized management in weaning or pruning drugs, incorporating such factors mentioned earlier, especially in patients with multiple comorbidities, who are shielded under the porous (often) umbrella of polypharmacy.

Yet another reason put forth for the lack of emphasis on deprescription is the absence of incentives for health care personnel to reassess prescriptions and withdraw those with a negative or neutral risk/benefit.^[4]

JUSTIFICATION FOR DEPRESCRIPTION

In elderly as well as terminally ill patients, the efficacy and safety of many drugs is unknown or questionable. In fact, few or more may be the cause for troublesome or severe side effects. The removal of such drugs could be justified. It has been found

that 44% of patients at hospital discharge are prescribed at least one unnecessary drug.^[5] Every third patient receiving five or more drugs suffer an ADR every year, with more than 25% deemed preventable.^[6] Apart from the greater potential for ADR, the rate of compliance is inversely proportional to the number drugs prescribed, and this has been found to be as high as 85%.^[7] A recent study has reinforced that the rate of nonadherence is higher as patients walk in to the geriatric category, when the number of newly prescribed drugs are more than three and also in those hospitalized for diseases of nervous system.^[8]

DEPRESCRIPTION: POINTS TO BE CONSIDERED

As the saying goes *Primum non nocere*, i.e., “first, do no harm” This can be of two-ways. One, by way of not prescribing an unwanted drug and two by discontinuing a drug that is considered unwanted at the time of review (though earlier it would have been necessary).

WHICH ARE THE LIKELY CANDIDATES FOR DEPRESCRIPTION?

Drug candidates for deprescription usually fall under any one or more of the following categories or disease conditions for which they have been prescribed (reproduced with minor modification and additions from a publication by Scott *et al.*).^[1]

- When the efficacy of a drug is nil or of questionable evidence (including nonprescription and complementary agents) and such other factors
 - o Routine prescription of vitamin supplements, irrespective of the disease, is unlikely to be useful.
 - o When a nondrug therapy is likely to have better benefit-risk ratio, such as physiotherapy/heat therapy, for neck, back pain compared to nonsteroidal anti-inflammatory drugs
 - o Prescribing two or more drugs of the same class, where one should suffice - e.g., a cardioselective beta-adrenergic blocker like atenolol in a hypertensive ischemic heart disease patient would suffice than prescribing two different drugs (one for each condition). This also happens when a patient consults different specialists (e.g., a cardiologist and diabetologist) and prescribed two brands of the same drug or class such as statin, antiplatelet agent, and so on
 - o Addition of a second drug to tackle the ADR of an already prescribed drug. In such cases, a simple reduction in dosage or prescribing an alternate drug of the same class or of a different class could avoid the need for a second drug

- o Identifying a drug likely to cause ADR due to drug-drug or drug-food interaction, and substituting the same with a drug lacking such potential
- o Stopping a drug needing cumbersome administration (intravenous) and substituting suitably (with an oral formulation)
- o Taking drug cost into consideration and substituting with low cost/generic but equally effective agent, which would in all probability enhance the compliance
- o Following a wait and watch policy till strong evidence of favorable efficacy/ADR ratio emerge, regarding newer drugs
- When the expected risk is more than the considered benefit, which is more often applicable to high-risk drugs such as antithrombotics, antidiabetics, cardiovascular, and central nervous system (CNS) drugs. With these drug classes, the ADR may be more severe or life threatening or with potential for harm, such as cerebrovascular accidents due to bleeds, hypoglycemia, or fractures due to falls. This is also true with polypharmacy. The incremental risk of ADR is exponential when the number of drugs is more. In general, the risk is more with eight or more drugs, though it is preferable to prescribe five or less number. One has to be doubly vigilant in geriatric population, since they are more often subjected to polypharmacy due to multiple comorbidities. When there is dilemma regarding risk-benefit, it is better to take the patient's preference also into consideration after a thorough discussion
- When a drug is the reason for poor patient compliance which may be due to the patient's belief of no benefit or due to troubling side effect or cost considerations-this calls for a replacement with suitably effective, less costly, less toxic drug
- When the benefit conferred by a drug is likely to take a longer time because of patient's shorter life expectancy-advanced dementia, metastatic cancer, end-stage organ disease whose estimated life span is <1 year, while the estimated time for drug effect is longer
- During a reappraisal of the disease, if the earlier diagnosis happens to be incorrect
- When the disease is no longer active (especially true with treatment involving anticonvulsants, glucocorticoids, etc.)
- When the disease has been corrected by interventions like surgery
- When a subject intends to become pregnant or diagnosed to be pregnant while on therapy for a certain condition, it is well known that any drug unless otherwise is considered absolutely essential, is to be avoided during pregnancy, more so during the first trimester, to prevent teratogenic ADR
- During perioperative periods (for, e.g., antiplatelet agents such as aspirin and ticlopidine may have to be discontinued 1 week prior, ACE inhibitors, and oral antidiabetics 1 day

prior; combined oral contraceptive pill 4–6 weeks prior to surgery, and the list is not complete)

- Not the least but most important, is a tendency to prescribe drugs for each and every symptom the patient catalogs (rather than aiming for the underlying cause of the given condition) or yielding to patients' pressure. Such practice often leads to polypharmacy or prescription of unwanted drugs (e.g., antibiotics being prescribed as antipyretics), with attendant increase in adverse reactions, including morbidity. Elderly people often complain of insomnia, constipation, and such other symptoms, which are more often due to underlying depression, sedentary lifestyle, or when they are on CNS depressants like sedative-hypnotics, and such factors. One often tends or is pressurized, to prescribe a hypnotic, laxative, which adds to the cost, hidden ADR such as falls. Rather, appropriate counseling on healthy lifestyle, sleep hygiene, high fiber diet would not only avoid drugs but also ADR and expenditure.

It has been shown proactive initiatives to deprescribe not only reduced the average number of drugs consumed (by more than 50%), but also reduced mortality (by up to 50%), referrals requiring emergency care (by more than about 50%), and health care cost with improvement in health (by more than 90%).^[9-12]

In a recent Cochrane Review,^[13] it is recommended that programs that aim to withdraw older nursing home residents from long-term antipsychotics should be incorporated into routine clinical practice, especially if the neuropsychiatric symptoms are not severe. For more details, on deprescribing one may take a look at these reviews.^[14,15]

COMMON DRUGS THAT NEED TAPERING RATHER THAN ABRUPT STOPPAGE, WHEN CONSIDERED FOR DEPRESCRIPTION

As a note of caution if a decision is taken to deprescribe, one has to wean rather than abruptly stop certain categories of drugs for fear of worsening the disease or precipitating withdrawal syndrome. Almost all CNS depressants (hypno-sedatives such as benzodiazepines, narcotic analgesics, antidepressants, antipsychotics, as well as anticonvulsants); corticosteroids, especially when patients are on chronic and/or on high dose therapy, beta adrenergic receptor blockers, clonidine, etc., fall under such category.

SOME TOOLS THAT MAY BE USEFUL DURING THE PROCESS OF DEPRESCRIPTION

The following tools would be highly valuable during the process of deprescribing. Some may serve as general guide to predict the magnitude of risk due to drugs.

To identify low-utility drugs (many, not all): Beers criteria^[16] – Note: Many modifications were later made, or the Screening Tool of Older Person’s Prescriptions/Screening Tool to Alert Doctors to the Right Treatment^[17] or the Inappropriate Prescribing in the Elderly Tool.^[18]

Clinical calculators for drugs: mdcalc.com.^[19]

Absolute disease risk: Congestive heart failure, hypertension, age = 75 years, diabetes mellitus, stroke (CHADS) score^[20] for estimating thromboembolic stroke risk and Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile international normalized ratio, Elderly (>65 years), Drugs/alcohol concomitantly (HAS-BLED) score^[21] for estimating risk of major bleeding from anticoagulants.

Despite the availability of many tools to minimize drug therapy-related problems, there is little guidance for the process of deprescribing in general clinical practice. Further to integrate such tools to prescribe drugs may be a difficult task in routine (not to mention busy) practice.

A 10-step conceptual framework has been suggested by Scott *et al.* to minimize the inappropriate medications in the older populations.^[22] The following is a proposed abridged version on the lines of the said framework, which may be applicable for medical practice, in general.

The S and S approach:

- Seek and Screen – Obtain the current prescription(s) along with the drugs currently the patient is on. Screen and segregate them to essential and nonessential ones taking into account the current clinical condition, benefit-harm proportion, patient preference, and cost
- Save and Severe – Save (retain or replace or prune) those that are considered as absolutely essential and severe (delete) those that are duplicated, self-administered over-the-counter products, unwanted vitamins, nutritional products, harmfully interacting drugs
- Sensitize and Supervise – Sensitize the patient on the benefits of deletions of drugs and the benefits they may realize and emphasize on nonpharmacological, quality enhancing lifestyle approaches wherever possible. Finally supervise (monitor) for adherence and implore for further pruning as and when needed.

HOW TO INDOCTRINATE THE EXERCISE OF DEPRESCRIPTION AMONG PRESCRIBERS?

Methods to reduce the risks of polypharmacy include patient education, physician education and regulatory intervention. Constant drug and disease monitoring is essential.^[23]

One of the State Governments in India has initiated recovering the cost of drugs if the prescription is found unjustified^[24] though the bottlenecks of implementation and effectiveness has to be ascertained.

Though many institutes teach to criticize and rewrite prescriptions in practical pharmacology classes, it is prudent that the health care students of medicine, dentistry, nursing, and pharmacy are introduced to the topic of “deprescribing” with pertinent exercises. A humble beginning has been initiated in the 2015 at our Indira Gandhi Medical College and Research Institute, Puducherry, India. Two exercises in practical pharmacology have been introduced. The learners are explained about “therapeutic inertia” and the need for deprescribing. Problem solving exercises to prune unnecessary medications, in clinical scenarios such as hypertension and diabetes mellitus are imparted.

WHAT ELSE TO BE DONE REGARDING DEPRESCRIPTION?

Though earlier it was mentioned that deprescription is an exercise more relevant to chronic diseases, a project in Canada is being experimented in acute care settings. This practice was recognized as an emerging (commendable) practice by the Health Council of Canada.^[25]

More research on deprescribing is the need of the hour, in almost all branches of clinical medicine, which would throw more light on how much mortality, morbidity and cost could be reduced and what quantum of improvement in quality of life could be achieved. It seems to be a fertile field for researchers – potential doctorates and postgraduates included!

CONCLUSION

If appropriate deprescription is not done, whenever obligatory it can be considered as “therapeutic inertia” or “clinical inertia” – an act of omission for not committing oneself when omission is actually required.

With a given prescription if a patient has not much complaints, then the prescriber invariably does a “Repeat all” without a concern to take a closer look on the unnecessary components. The “Repeat all” legacy is so infectious that residents or juniors imbibe and follow the practice meticulously. Let us join hands to break the legacy of prescribing drugs such as a “grocery list” or the so-called “brown paper bag” style.

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