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Review Article

Deprescribing: A narrative review of the evidence and practical recommendations for recognizing opportunities and taking action

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ABSTRACT

Deprescribing can be defined as the process of withdrawal or dose reduction of medications which are considered inappropriate in an individual. The aim of this narrative review is to provide an overview of "deprescribing"; firstly discussing the potential benefits and harms followed by the barriers to and enablers of deprescribing. We also provide practical recommendations to recognise opportunities and strategies for deprescribing in practice.
Studies focused on minimizing polypharmacy indicate that deprescribing may be associated with potential benefits including resolution of adverse drug reactions, improved quality of life and medication adherence and a reduction in drug costs. While the data on the benefits is inconsistent, deprescribing appears to be safe. There are, however, potential harms including return of medical conditions or symptoms and adverse drug withdrawal reactions which emphasise the need for the process to be supervised and monitored by a health care professional.
Taking action on deprescribing can be facilitated by knowledge of potential barriers, implementing a deprescribing process (utilising developed tools and resources) and identifying opportunities for deprescribing through engaging with patients and caregivers and other health care professionals and considering deprescribing in a variety of populations.
Important areas for future research include the suitability of deprescribing of 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 positive health and quality of life outcomes.

1. Introduction

Advances in the treatment of medical conditions mean more people are living with multiple co-morbidities for longer, contributing to an ageing population in Western societies [1]. It is imperative that medications are used appropriately in this population to maximise positive health outcomes, while also ensuring the sustainability of government health care programs and minimizing harms to patients. The aim of this narrative review is to provide an overview of "deprescribing"; firstly discussing the potential benefits and harms followed by the barriers to and enablers of deprescribing. We also provide practical recommendations to recognise opportunities and strategies for deprescribing in practice.

This narrative review was informed by a literature search conducted in August 2016. Published systematic reviews into different aspects of deprescribing were utilised with citation and reference checking (Google Scholar). Additional searches were conducted in PubMed and Google Scholar to determine if there were recent studies not included in these reviews (searched after the date of systematic review search). Where systematic reviews were not identified, additional searches were conducted using keyword searches (e.g. 'geriatrician' and 'deprescribing' and appropriate variations). Personal reference libraries were also utilised.

2. What is "deprescribing"?

The word "deprescribing" first appeared in the literature in 2003 [2,3]. With growing concern worldwide about the negative effects of overuse of certain medications, increasing attention is being paid to approaches to minimize harm. The focus is shifting from prescribing, which has traditionally been thought of as starting or

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renewing medications, to that of deprescribing - especially as people age. Deprescribing has been defined as "the process of withdrawal of an inappropriate medication, supervised by a health care professional with the goal of managing polypharmacy and improving outcomes" based on a systematic review of articles using this term between 2003 and 2014 [3]. Dose reduction and switching to safer medications are also considered deprescribing strategies that maintain effectiveness while minimizing harm. The term "inappropriate medication" encompasses medications where the potential risks outweigh the potential benefits in the individual. This includes both medications which are high risk of harm and those which are unnecessary or ineffective. It may also include those that do not fit with the goals of treatment (for example preventative medications in palliative care patients) or align with patient values and preferences and those which are overly burdensome [3,4]. It is important to note that "deprescribing" is very different from non-adherence or non-compliance with medication because it involves health care professional direction and supervision with the same level of expertise and attention that prescribing entails.

3. What are the benefits of deprescribing? Are there any risks?

Polypharmacy and potentially inappropriate medications have been associated in observational studies with a number of negative health outcomes including reduced quality of life, adverse drug reactions (ADRs), falls, non-adherence, hospitalisation and mortality [5–9]. For example, Passarelli et al. [10] found that an older adult prescribed a potentially inappropriate medication had double the chance of experiencing an ADR compared to an older adult not taking a potentially inappropriate medication. In turn, it is assumed that if we reduce doses of or stop inappropriate medications and minimize the number of medications taken then this will amount to reduced harms and/or benefits. However, potential benefit needs to be balanced against any risks that may arise from medication deprescribing.

Recently, Huizer-Pajkos and colleagues developed a mouse model of polypharmacy to try and clarify whether there is harm due to polypharmacy in itself [11]. Both young and old mice were administered a 'polypharmacy diet' which consisted of therapeutic doses of five commonly prescribed medications: simvastatin, metoprolol, omeprazole, acetaminophen and citalopram. They found significant declines in mobility, balance and strength in the older polypharmacy diet group (compared to an older group fed a control diet), but no differences in the younger groups. While further studies are needed to confirm these results, the polypharmacy mouse model provides an opportunity to explore the outcomes and reversibility of polypharmacy and inappropriate medication use in a controlled setting.

3.1. Deprescribing studies

When reviewing the literature on the benefits and harms of deprescribing, the types of studies can be broadly classified into two groups.

The first type are studies which focus on whether or not an intervention (e.g. educational intervention, medication review) is effective, with the main outcome the number of medications or number of inappropriate medications used across the population. They generally target older adults, polypharmacy or specific medication classes. The measurement of the effect on health outcomes of deprescribing in these studies is highly dependent on whether or not the intervention works.

The second type of study targets a specific medication or class of medications in a specific population where use of this medication is considered inappropriate. The target medication is stopped and health outcomes are measured. These types of studies are essential for the development of drug-specific deprescribing guidelines [12] to provide guidance on when it is suitable to withdraw medications. They also have the benefit of measuring drug-specific outcomes including resolution of adverse effects or reduction of risk (e.g. reduced falls and improved cognition following withdrawal of psychotropic medications) [13]. The limitation of this type of study is that only a single medication class can be studied in a specific sub-population at a time which may not cover all situations in which it would be inappropriate.

3.2. Systematic reviews of the health-related outcomes of deprescribing

Several systematic reviews have aimed to synthesise the evidence of the feasibility and outcomes of deprescribing [13–17].

3.2.1. Intervention studies

Gnjidic et al. [14], identified that a variety of interventions successfully reduced the number of medications taken by participants. There was, however, minimal and conflicting data on clinical outcomes. Out of the 30 studies identified, only half measured any type of clinical outcome. Six studies reported some benefit on clinical outcomes (e.g. reduction in serious ADRs), however the remaining nine found no positive effect of the intervention [14]. Similarly, Johansson et al. [16] and Cooper et al. [17] found that interventions to reduce polypharmacy generally lead to a reduction in inappropriate medication use, however, were unable to confirm that this leads to clinically important end-points such as improved mortality or reduced hospital admissions.

3.2.2. Medication-specific studies

Iyer et al. conducted a systematic review of studies examining deprescribing of specific medication classes. They found studies on withdrawal of diuretics, antihypertensives, psychotropics, digoxin and nitrates [13]. Several of the studies on psychotropics indicated a benefit to withdrawal and overall the authors concluded that withdrawal of certain medication classes appeared to be safe, but that there were limitations to the study and their review (including poorly described search strategy, single author screening and no formal quality assessment) [13]. Withdrawal of non-psychotropic drugs could also result in benefits including reduced ankle oedema (nitrates) and nausea and vomiting (digoxin) [13]. Declercq et al. conducted a Cochrane review (9 RCTs, 606 patients) into the withdrawal of antipsychotics in people with dementia [18]. They found that withdrawal does not appear to have a detrimental effect on behavioural symptoms for the majority of participants [18].

Page et al. summarized both types of studies in their systematic review conducted in 2015 [15]. They identified 21 studies which aimed to minimize polypharmacy (i.e. non-medication specific) and a further 111 studies which looked at deprescribing of one or two specific medications, medication classes or therapeutic groups. In their meta-analysis of non-randomised studies, minimizing polypharmacy was associated with a significant reduction in mortality (OR 0.32, 95% CI:0.17–0.60), this effect, however, was not found in the meta-analysis of randomised studies (OR 0.82, 95% CI: 0.61–1.11). This difference may be due to bias in the non-controlled studies ($n = 2$) or large variability in the type of interventions of the randomised studies ($n = 10$). Deprescribing of specific medications was not associated with a significant difference in mortality [15].

3.3. Limitations of deprescribing studies

There are several explanations for the minimal evidence of benefit on clinical outcomes such as mortality or falls [5,14,16]. The sample size and follow-up periods in many studies are too small/short to detect a difference. As previously mentioned, the effect on clinical outcomes is likely dependent on the success of the intervention

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