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Deprescribing in Advanced Illness

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Abstract

Patients with advanced illness such as cancer, Chronic Obstructive Pulmonary Disease (COPD) and Parkinson’s disease experience acute symptoms and are usually prescribed medications to manage these, alongside drugs to treat other co-morbid, long-term conditions. As such, the pharmacotherapeutic burden for these patients is high and polypharmacy is common. Previous studies have revealed the prevalence of potentially inappropriate prescribing within this group of patients, and identified the need for attention to ‘deprescribing’. Deprescribing can be defined as a process of optimization of medication regimens through cessation of potentially inappropriate or unnecessary medications. Patients usually have reservations about taking medications and may be willing to discontinue one or more medications considered ‘inappropriate’. Similarly, healthcare professionals experience some challenges discussing deprescribing with patients with advanced illness. This article reviews research on prescribing medicines to patients with advanced illness, focusing on the identification of the prevalence of inappropriate or unnecessary medicines to the initiation of the deprescribing process. The review demonstrates the paramount importance of further research exploring the perspective of healthcare professionals and patients on the subject of deprescribing to facilitate its further acceptance in practice.
Healthcare systems across the world care for a large number of people with advanced illness, some of who will die from their condition(s). Illnesses termed as advanced are those occurring when one or more conditions become serious enough that general health and functioning decline, and treatments begin to lose their impact.[1] In 2012, out of 56 million deaths across the World, approximately 38 million (68%) were due to advanced non-communicable illnesses, including cancer, cardiovascular disease, Parkinson's disease, Chronic Obstructive Pulmonary Disease (COPD)[2]. These advanced illnesses, which are usually life limiting, are accompanied with acute symptoms, such as pain, breathlessness and fatigue. As a consequence, many of patients with advanced illness are prescribed medication to manage these symptoms.[3] In addition, it is also common for such patients to have multiple co-morbidities – many of which require the use of chronic medication to treat, maintain, or reduce the probability of developing associated complications.[4] As such, polypharmacy is commonly observed in patients with advanced illness.[5] Indeed, it has been shown that in the last year of life, the number of medications a patient uses significantly increases.[6] The increased pharmacotherapeutic burden associated with polypharmacy can result in non-adherence to prescribed treatment [7], as well as increased risk of developing drug-related toxicities through drug-drug interactions. Furthermore, as patients approach the end of their life, the way in which they respond to medications changes – this is mainly due to altering pharmacokinetic parameters of such patients (e.g. declining renal function)[14]. These changes can further increase the probability of developing a drug-related toxicity. [15]

In view of these challenges, it has been recommended that medication use in patients with life-limiting illness should be regularly evaluated to identify potentially inappropriate or unnecessary medications, to reduce polypharmacy and the risks and challenges associated with it. Tools such as the Beers criteria,[8] the Medication Appropriateness Index[9] and the Screening Tool of Older Person's Prescriptions (STOPP) criteria have been developed to
assist healthcare professionals in their decision-making with regards to prescribing medication[10]. The utility of these approaches has been demonstrated in research focusing on reducing inappropriate medication in an elderly population (>65 years of age).[11] Another, perhaps more conceptual approach, has been the development of a framework for medication appropriateness specific to patients late in life. This approach provides the health professional with a number of factors – such as remaining life expectancy and goals of care – that should be considered when prescribing medication to patients with diminished life expectancy.[12]

Another consideration of appropriate medication use in patients with life limiting illness is the ‘time to benefit’ – a term used within the framework proposed by Holmes and colleagues [5] and defined as the time for a population to realise the intended effect of the medication. The ‘time to benefit’ of some medications commonly prescribed to manage co-morbid illness ranges from several months to years. For example, statins for are often prescribed for the primary prevention of cardiovascular disease and have no specific benefit from a symptom point of view for patients. The estimated time to benefit of statins is more than 2 years, depending on indication and outcome. In many cases, this may extend beyond the patient's life expectancy, which raises questions over the risk: benefit ratio of treatment. [4] Indeed, and in view of this, several studies have shown that statins are inappropriately prescribed to patients who have life limiting illness.[13] Other inappropriately prescribed medications reported in the literature include: mineral and vitamin supplements; anti-platelets; anti-hypertensive; and, anti-diabetic agents. [4, 14] Discontinuation of these medications on the basis of remaining patient life expectancy will help minimise polypharmacy as well as potential drug interactions and hence may have positive implications for patient safety and quality of life. How these medicines are discontinued is important, as,
abrupt discontinuation in certain circumstances can result in symptom recurrence or adverse
drug withdrawal events. [14]

One approach to reducing inappropriate medication use among patients with advanced illness
is to decide initially not to prescribe medication for the treatment of co-morbidities. Another
approach is the process of ‘deprescribing’, which is a way of rationalising medications that
provide limited benefit to patients.[15, 16] Medications may be deprescribed for reasons of
non-adherence, lack of efficacy, actual or potential adverse drug reactions, or development of
a contraindication – all of which are circumstances that may arise in the management of older
patients,[14] as well as patients with life-limiting illness.[4] To support the deprescribing
approach, Woodward et al (2003) have developed a 5-step patient-centred deprescribing
process, which engages patients throughout the process with the aim of improving health
outcomes. A study evaluating this process identifies the deprescribing process as including
elicitation of a comprehensive medication history; identifying potentially inappropriate
medications (PIMs); determining whether the potentially inappropriate medication can be
ceased; planning the withdrawal regimen with patients and carers; and, providing monitoring,
support and documentation.[16] A more recent article by Scott and colleagues, describe the
development of a 5-step protocol to deprescribing.[17] This protocol, in contrast to the work
of Woodward, involves an assessment of all drugs the patient is currently taking including
prescribed, over the counter and alternative medicines. The 5-step protocol also involves
prioritisation of drugs for discontinuation by integrating 3 criteria: those with the greatest
harm and least benefit; those easiest to discontinue on the basis of lowest likelihood of
withdrawal reactions or disease rebound; and, those that the patient is most willing to
discontinue first. These criteria rank the drugs to be discontinued from high harm/low benefit
to low harm/high benefit, with priority given to the former. [17]
Despite these advances, there is at present, a lack of published empirical research that explores how deprescribing approaches affect the outcome for patients with advanced illness. One such study by Garfinkel & Mangin (2010) tested the feasibility of applying the Good Palliative – Geriatric Practice algorithm which consists of a number of questions to discuss with patients/guardians in relation to the indication of the drug or possible adverse reactions experienced. The algorithm was applied by discontinuing medications not immediately essential for life in relation to the time until benefit of such medications over a mean follow up of 19 months. The study excluded patients whose life expectancy was less than 3 months.[18] In total, 252 medications were discontinued with consent from the patients, guardians and physicians. The study reported improved quality of life in 88% of 70 patients (by assessing improvements in cognitive impairment), as well as absence of significant deaths or adverse events resulting from the discontinuation of the different medications. The discontinued medicines included anti-hypertensives, aspirin, statins, benzodiazepines, and metformin; importantly, only 2% of the discontinued medicines were re-prescribed due to symptom recurrence.[18] A similar study by the same authors, involving elderly people in nursing departments, resulted in discontinuation of 332 medicines (including nitrates, antihypertensives, potassium supplements and statins). In this study 10% of the medications were readministered due to relapse.[19] The class of medication to be deprescribed is essential as some classes of medication should not be discontinued abruptly, but tapered to prevent drug withdrawal events or recurrence of disease.[14] Focusing on the discontinuation of statins with patients in a palliative care setting, Kutner and colleagues have shown that continuing treatment in patients at the end-of-life does not provide clinically significant positive outcomes compared to patients who have their statin treatment stopped.[13] In addition, the patients who discontinued statins benefited from improved quality of life scores, used fewer medicines, which subsequently contributed to a reduction in medication costs.[13,
Though the findings of this study suggest that discontinuation of statins prescribed for primary or secondary prevention of cardiovascular diseases in advanced illness is safe, it is reasonable for healthcare professionals to discuss with patients and their caregivers around their willingness to discontinue.[13]

For the deprescribing process to be successful, both healthcare professionals and patients should be willing to take part. However, qualitative work has shown that some general practitioners (GPs) have difficulty deprescribing medications during regular clinical practice due to time constraints within consultations and the need for a systematic process to follow to enable successful medication cessation. [21] Schuling et al (2012), who explored the views of GPs in The Netherlands on discontinuation of medications in elderly patients with multimorbidity, showed that GPs find it challenging to discuss life expectancy and deprescribing medication, as they believe patients could perceive it as a sign of being given up on.[22] A systematic review by Anderson et al (2014) highlighted barriers faced by primary care physicians such as: having a poor awareness of the appropriateness of their prescribing; inertia despite awareness that the prescription is potentially inappropriate; lack of self-efficacy with regards to personal ability to alter prescribing pattern; and, feasibility of altering prescribing in the presence of medical and societal health beliefs and culture, work regulations, limited resources (such as time constraints and reimbursement), as well as patient characteristics.[23] Prescribers usually have to consider a lot of factors before embarking on deprescribing, as well as being mindful of risks of harm, blame and litigation.[24] Considering all of these issues, the discussion of deprescribing by healthcare professionals for patients with advanced illness is clearly a sensitive and challenging issue.

Patient perspectives are also important in this process: it has been shown that patients have reservations about taking medications and usually balance these with the perceived benefits they obtain from them.[25] Some of the challenges identified by patients and related
to deprescribing were resistance to change and poor acceptability or trust in alternative options. [23] The work of Reeve and colleagues, revealed patients’ disagreement with the appropriateness of medication cessation, the absence of a comprehensive process for discontinuation, negative influences to cease medications as well as fear of discontinuation. [26] From this, it is evidently critical that patients are included in decisions around deprescribing and, while they may have concerns about the number of prescription medicines they use, they may be unwilling to discontinue some of them, even when recommended by their healthcare professional. [15]. The unwillingness of patients to embrace a change in their medication regimen will make it challenging for healthcare professionals to fully engage in deprescribing process.

One factor that appears to be important in terms of patients engaging in deprescribing is the level of trust they have with their healthcare professionals. Other enablers may include: patients’ experiences/concerns/beliefs concerning adverse effects; dislike of using multiple medications; and, being assured that a ceased medication can be restarted, if required. [26] Mindful of these factors, Reeve et al (2013) developed a Patients’ Attitude Towards Deprescribing (PATD) questionnaire to capture the views of patients regarding the number of medications they were taking and their willingness to discontinue some of them. [15] They found that the readiness of patients to cease medications does not correlate with the age, number of concomitant medications or number of medical conditions. [15, 27] From the PATD study, of the vast majority of participants, ninety two per cent were willing to stop one or more of their medications. The majority of participants in that study believed they were taking too many medications, some of which they considered unnecessary. Though sixty nine per cent of patients were comfortable with the number of medications they were taking, they were still willing to reduce this number. From the literature, it is clear that an individual patient approach to deprescribing should be at the centre of any deprescribing decision. [19]
Sand and colleagues revealed that with respect to taking medications, patients with advanced illness feared losing control, becoming addicted or suffering harmful effects, and as such they were mostly non-adherent either skipping doses or extending dosage intervals. This makes it clear that patients need to discuss their medication practice with healthcare professionals as expected health outcomes can only be achieved by employing a patient-centred approach to prescribing.[28]

In conclusion, this review has identified advances in understanding the prevalence of inappropriate medication used by patients with advanced illness to the processes and issues involved in discontinuation or deprescribing of such medication. The consideration of discontinuation for inappropriate medicines in such patients is important when there is evidence of non-adherence, lack of efficacy, actual or potential adverse drug reactions, or development of a contraindication. Qualitative research involving healthcare professionals and patients has also revealed the challenges around the acceptance of deprescribing. Some healthcare professionals find it difficult to deprescribe due to time constraints and the sensitivity of the subject while discussing with patients who have advanced illnesses. Patients, who may have concerns about the number of medicines they are prescribed, may be unwilling to discontinue some of them even when suggested by their healthcare professional. The benefits of deprescribing some medicines may outweigh the risk; nonetheless patients must be willing to accept, as they are at the centre of every deprescribing decision. The subject of deprescribing can become more practicable when all these challenges are carefully managed as well as the views of all concerned are taken into account. The views of patients with different medical conditions on deprescribing ‘inappropriate’ medicines may have some similarities, such as the fear of becoming addicted or the harmful effects of the medications, but more research is needed to further explore the perspective of patients with life limiting
illness on deprescribing in relation to different medical conditions as well as various classes of medications.
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