Deprescribing in Advanced Illness

Olusola Akinbolade[1], Andy Husband[1], Simon Forrest[1], Adam Todd[1*]

1. Division of Pharmacy, School of Medicine, Pharmacy and Health, Durham University, UK

*Corresponding author:

E-mail: adam.todd@durham.ac.uk

Telephone: +44 (0) 191 33 40542

Room number: C138, Holliday Building, Queen's Campus, Stockton on Tees, TS17 6BH

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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 often accompanied with acute symptoms, such as pain, breathlessness and fatigue. As a consequence, many 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, as well as increased risk of developing drug-related toxicities through drug-drug interactions. Furthermore, as patients approach end of 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);[7] this can, in theory, further increase the probability of developing a drug-related toxicity.

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 [10] have been developed to assist healthcare professionals in their decision-making with regards to prescribing medication. 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 to assess medication appropriateness specific for patients late in life.[12] 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.

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 [12] and defined as the time for a population to realise the intended effect of the medication.[13] The 'time to benefit' of some medications commonly prescribed to manage co-morbid illness ranges from several months to years. For example, statins 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. Indeed, and in view of this, several studies have shown that statins are inappropriately prescribed to patients who have life limiting illness.[14] Other inappropriately prescribed medications reported in the literature include: mineral and vitamin supplements; anti-platelets; anti-hypertensive; and, anti-diabetic agents.[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 may result in symptom recurrence or adverse drug withdrawal events.

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] 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, as well as patients with life-limiting illness. To support the deprescribing approach, Woodward et al developed a 5-step patient-centred deprescribing process, which engages patients throughout the process with the aim of improving health outcomes:[16] this approach includes obtaining an accurate medication history; identifying medications that could be stopped; planning a regimen for deprescribing; working with patients and carers; and review and support the patient. A more recent article by Scott and colleagues, describe the development of a 5-step protocol to deprescribing.[17] This protocol also involves prioritization 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.

Despite these advances, there is at present, a dearth of published empirical research exploring how deprescribing approaches affect the outcome for patients with advanced illness. One such study by Garfinkel & Mangin tested the feasibility of applying the Good Palliative – Geriatric Practice (GP-GP) 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.[18] 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, 256 medications were discontinued with consent from the patients, guardians and physicians. The study reported that, in 88 per cent of patients, the application of the algorithm was associated with subjective, functional, mood or cognitive improvement. The discontinued medicines included anti-hypertensives, aspirin, statins, benzodiazepines, and metformin; importantly, only 2% of the discontinued medicines were re-started due to symptom recurrence.[18] A similar study by the same group, 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] These finding show that when thinking about deprescribing, it is essential to consider the class of medication, as some classes of medication should not be discontinued abruptly, but tapered to prevent drug withdrawal events or recurrence of disease (e.g. antihypertensive medication). Focusing on the discontinuation of statins with patients in a palliative care setting, Kutner and colleagues have shown that continuing statin treatment in patients near end-of-life does not provide clinically significant positive (or negative) outcomes, compared to patients who have their statin treatment stopped.[20] 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. Though the findings of this study suggests 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.

For the deprescribing process to be successful, both healthcare professionals and patients should be actively engaged in it. Studies have shown that some general practitioners (GPs) find it challenging to deprescribe medications in elderly patients with multimorbidity, as they believe patients could perceive it as a sign of being given up on.[21] A systematic review by Anderson *et al* highlighted perceived barriers faced by primary care physicians toward minimising potentially inappropriate medication; themes included: 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.[22] Prescribers usually have to consider a number of factors before embarking on deprescribing, as well as being mindful of risks of harm, blame and litigation. 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: a recent qualitative study using a phenomenological approach, showed medication formed a significant part of a patient's day-to-day routine; the same study also showed that there is a point in a patient's disease journey where less importance is placed on taking certain medications (such as statins); this was also recognized by healthcare professionals who referred to it as a 'transition'.[23] Further studies have shown that patients have reservations about taking medications and usually balance these with the perceived benefits they obtain from them.[24] Some of the challenges identified by patients and related to deprescribing were resistance to change and poor acceptability or trust in alternative options.[22] While 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 are patient barriers toward deprescribing.[25] 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, the timing of a discussion in relation to initiating a deprescribing event – especially in patients with advanced illness – appears to be is crucial. If the timing of such a discussion is not correct, the patient may not be willing to change their medication regimen; this will make it challenging for healthcare professionals to fully engage in the 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 professional. 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.[25] Mindful of these factors, Reeve and colleagues used the 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.[26] It was found that the readiness of patients to cease medications does not correlate with age, number of concomitant medications or number of medical conditions. The authors also found that more than 60 per cent of participants felt that they were taking a large number of medications, while 92 per cent would be willing to stop one of more medications if this was possible.[26]

It is clear from the literature that an individual patient approach to deprescribing should be at the centre of any deprescribing decision. Indeed, 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 by 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.

In summary, this review has identified: 1) advances in understanding the prevalence and detection of inappropriate medication used by patients with advanced illness; and 2) the processes and issues involved in discontinuation or deprescribing of such medication. The consideration for discontinuation of inappropriate medication 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 both patients and healthcare professionals has revealed the challenges around the acceptance of deprescribing: some healthcare professionals also find it difficult to deprescribe due to time constraints and the sensitivities around discussing medication discontinuation. 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. In certain circumstances, the benefits of deprescribing medications may outweigh the risks; nonetheless patients should work in partnership with healthcare professionals to identify which, of any, medication can be stopped; this is crucial as patients are at the centre of every prescribing (or 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 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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