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In the Context of Palliative Care

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Most, if not all, consultations often end with a sentence which sounds similar to the following, "I will be prescribing to you this list of medications....". Evidently, medical practitioners, and medical students alike, are often most keen about the medications they prescribe to their patients. Drugs are akin to a doctor's toolbox in their attempt to fix their patients' illnesses. Furthermore, several hospitals and healthcare systems globally mandate medication reconciliation as part of the hospital visit, highlighting the increased development and purchase of new drugs (Porcelli et al., 2010). Unfortunately, this can open a Pandora's box of problems, which ultimately may not confer solely benefit for the patients.

"Deprescribing," a process aimed at optimizing a patient's treatment regime by stopping medications deemed to be unnecessary or inappropriate, is a relatively newer concept to most practitioners, and particularly important for the geriatric population. However, pharmaceutical companies have not supported the practice for commercial reasons, and it is rarely taught to medical students (Mishori, 2018).

Polypharmacy is common, particularly with palliative care patients. These patients often have multiple comorbidities that have numerous complications and symptoms, including but not limited to pain, nausea, and breathlessness. It is no wonder that these patients often have a significant increase in the number of medications used (Akinbolade, Husband, Forrest & Todd, 2016).

Pharmacologically, changes to drug pharmacokinetics happen with aging and certain terminal illnesses, thereby affecting drug distribution, metabolism and excretion. Elderly patients have an increase in total fat mass, and a decrease in lean muscle mass and blood volume. This is similar in chronic disease patients with cachexia (fat and skeletal muscle loss). As a result of the patient's body composition, there is an increase in the volume of distribution of lipophilic drugs and a decrease in the volume of distribution of hydrophilic drugs thereby altering the loading dose and half-life. This is compounded by impaired liver function that affects drug metabolism, particularly phase II metabolism. Coupled with reduced renal clearance, drugs may have significantly longer half-lives, leading to potentially toxic effects (Hardy & Hilmer, 2011). For these reasons, polypharmacy can be particularly dangerous in elderly and chronically ill patients.

In addition, the concept of "time to benefit" (TTB) is a crucial consideration that doctors must note. TTB is defined as the time for the drug to have its intended effect on the patient (Holmes et al., 2006). Two commonly prescribed drugs, such as statins and zoledronic acid, have an estimated TTB of more than two years (Akinbolade et al., 2016), and 16 months (Hardy & Hilmer, 2011) respectively. Hence, there may be no reasonable justification to initiate these drugs which may not have an appreciable effect on patients in their twilight years.

Some drug classes have greater potential for adverse drug reactions (ADRs) in terminal care patients. ADRs are between the fourth and sixth leading cause of death in the United States, and have cost approximately 5% of the national health budget (Bain et al., 2008). The Beers criteria provides consensus-derived classification of *high* and *low* risk drugs (American Geriatric Society, 2015). Unfortunately, high-risk drugs such as cardiovascular, psychotic, and non-steroidal anti-inflammatory drugs, are often prescribed for elderly and terminally ill patients to help control symptoms, such as night-time awakenings and sundowning, which patients with altered mental status or dementia often experience. However, the risk of ADRs is greater than 80% when eight or more drugs are taken regularly (Currow et al., 2007), as a result of drug-drug interaction (Bernard & Bruera, 2000).

Polypharmacy can also be expensive. Financial costs are a huge burden of polypharmacy for both patients and the government. A Canadian study involving 248 palliative care patients revealed that inpatient hospital stay was the largest cost component33.2%). In addition, the cost of prescription medication alone was 6.5% of the mean total cost of

healthcare expenditure per patient (Dumont et al., 2009). More importantly, there is a shift, in many developed countries, towards palliative care delivery from hospitals into community settings since most patients wish to die in their own homes (Emanuel, 2018). The implication, then, is a shift in the burden of medical costs towards patients and their families.

Despite the reasons in favour, the deprescribing process is not without risks and barriers, often increasing the risk of withdrawal reactions, disease progression, or relapse, as in the case of donepezil, for instance, discontinuation of which was found to lead to a decline in cognitive scores. (Reeve et al., 2014). A retrospective study showed that 26% of medication stoppage led to adverse withdrawal reaction (Reeve, Shakib, Hendrix, Roberts & Wiese, 2014). Furthermore, a doctor's decision to deprescribe can be resisted by patient preference, especially when there is a noticed improvement after medication. Benefits are often psychological in nature, giving patients mental comfort and hope in curing the disease (Reeve et al., 2013). Lastly, both doctors and patients suffer from a lack of support. The former lack support in terms of proper guidelines with regards to deprescribing, the latter in terms of poor support from their doctors to discuss deprescription.

What is the way forward? Although several guidelines and tools such as the *NO TEARS tool* (Lewis et al., 2004), *Beers Criteria*, the *Screening Tool of Older Person's Prescriptions* (STOPP) / *Screening Tool to Alert Doctors to Right Treatment* (START) criteria have been created to address the issue of polypharmacy, there is still a need for further guidance and dissemination of work so that more primary care providers and hospice physicians participate in deprescribing. Nevertheless, these efforts must continue to be supported by scientific research. Unfortunately, much of the emphasis and financial investments on drug research today is to investigate methods and reasons to start drug treatment; there is little done conversely to study the discontinuing.

Doctors must continue to reassess their patients' medication regime, and if need be, seriously consider deprescribing certain medications that are unnecessary and inappropriate for patients receiving palliative care. Furthermore, deprescription should be heavily emphasized in medical schools. Student need to critically understand not just the 'when's and 'why's of starting a medication, but also stopping it.

"*Primum non nocere*". We are taught to practice by this principle of "doing no harm." When it comes to prescribing medications, we must bear in mind that sometimes the treatment itself can be a source of harm.

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