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EDITORIAL

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# Avoiding harm from overprescribing: What are the challenges and how do we overcome them?

Increasingly complex and innovative medicines are a significant contributor to the extended life expectancy that we currently enjoy in the United Kingdom (83 years for women and 79.4 years for men).[1] The proportion of people living with multimorbidity, the co-existence of two or more long-term health conditions, increases substantially with age which in turn promotes the increased use of medications. Today, the average 70-year-old takes an additional two tablets each day compared to 10 years ago.[2–4] Combinations of medications prescribed for multiple long-term conditions often have unintended consequences, including harms through drug–drug and drug–disease interactions. An example of where this can be particularly harmful is in those with both physical and mental health conditions. Extensive evidence links cardiovascular mortality with psychiatric illness and metabolic disturbance caused by antipsychotic medications.[5]

Improvements in health surveillance have led to the earlier detection of asymptomatic conditions such as hypertension and hyperlipidaemia, which are, in themselves, risk factors for diseases such as cardiovascular and cerebrovascular disease. This has led to an era of preventative prescribing: tackling concordant diseases that have similar aetiology and therefore complementary therapeutic strategies. Less well understood are the discordant disease clusters, those that develop independently through distinct mechanisms and are treated with therapies that have differing and sometimes, contradictory mechanisms. An example of this includes the co-existence of osteoarthritis (OA) and chronic kidney disease, both more common in older people in whom renal function and hence drug clearance declines. Non-steroidal anti-inflammatory drugs (NSAIDS) prescribed for OA are useful agents for management of chronic pain; however, they exert a deleterious effect on renal function and can lead to direct harm and also exacerbate any co-existing hypertension. This can lead to iatrogenic harm owing to drug–drug interactions (DDIs) and adverse drug reactions (ADRs), responsible for 6.5% of hospitalisations.[6]

The major challenge for the prescriber is weighing up the balance between benefit and harm for each individual medication in the context of the complete prescription. Added to this, the increasing subspecialisation of medicine means that there are fewer prescribers with generalist skills available to consider the prescription, and the patient, as a whole. Indeed, treatment guidelines are developed for single diseases, using data from trials involving patients with single diseases that do not account for multimorbidity or extreme spectrums of age. As a result, conflicting medications with high risk for DDIs and ADRs can go unrecognised for considerable periods.

In the United Kingdom, the NHS Long Term Plan (www.longtermplan.nhs.uk) includes measures to optimise prescribing, including deprescribing. Deprescribing has been defined as "the withdrawal of an inappropriate medication, supervised by a health care professional with the goal of managing polypharmacy and improving outcomes."[7] The 2020–2021 Primary Care Network Direct Enhanced Service specification[8] requires offering Structured Medication Reviews (SMRs) to patients who would benefit most, but there is little guidance on how to target these patients or how to optimise prescribing for particular groups. Clinicians care for increasingly complex older multimorbid patients with different degrees of frailty. Effective medicines optimisation is impeded by scattered care records leading to poorly integrated care across different providers. There is little expert support for holistic medication reviews. The prescriber is faced with trying to apply multiple guidelines, across different disease and therapeutic areas, to a complex and heterogenous population that is characterised by a high inter-individual variability in organ function, homeostatic capacity, and physical and cognitive function.

In this themed issue, we summarise the existing challenges and attempt to present solutions to the expanding problem associated with a vast therapeutic arsenal and increasing medical complexity. The context of this thematic issue follows a meeting held at the Royal College of Physicians in London in November 2019 entitled "Avoiding harm from overprescribing: how to reduce waste and dependence on prescription drugs." Mattishent and Loke argue for a paradigm shift in the management of older people with diabetes: away from the relentless pursuit of an ideal glycated haemoglobin target and towards a more pragmatic, blood glucose monitoring with adaptive therapeutic response.[9] Older people are well recognised to be at increased risk of hypoglycaemia, a particularly dangerous problem for those with cognitive impairment who are less able to detect and self-treat.[10] They raise an extremely pertinent question, one that we should, as care providers, ask ourselves about all treatments that we prescribe: is it really appropriate to chase a benefit in risk-reduction derived over 10–20 years in those who are over 90 years of age, or indeed even younger? Which begs the inevitable question, at what stage of life does the benefit of risk reduction therapeutics become less than the

potential harm from ADRs? Is there a "tipping point" and if so, how do we define it? More evidence, from well-designed, inclusive studies that are more representative of the complex population that we live in, that tells us about true benefits and harm in the context of multimorbidity and polypharmacy, is needed before we are able to answer this question with greater certainty. In this context, a repeated cross-sectional observational study by Oktora et al. reports an increased prevalence of polypharmacy in middle-age and older patients with diabetes over a 5-year period in the Netherlands.[11] An increased prevalence over time of diabetic patients with at least one potentially inappropriate medication in the middle-age group was also observed. In a separate commentary, Yoke and Mattishent caution against the widespread use of computerised tools and algorithms for the identification of ADRs and the consequent implementation of deprescribing strategies.[12] Such tools might have been developed and validated in patient populations that are significantly different from those in whom they are routinely used (i.e., hospitalised vs. community patients). Furthermore, significant uncertainties remain regarding the actual clinical impact of most ADRs in individual patients. More research is advocated to develop and validate current and novel tools in representative populations and to investigate their effects on tangible clinical outcomes.

The long-term effects of systemic glucocorticoids for the treatment of inflammatory disorders, and the possible strategies for their withdrawal, are discussed by Baker (RC-00792-20). A slow withdrawal strategy, primarily determined by the treatment requirements of the underlying condition, is advocated. Once physiological doses are reached, further dose reduction is determined by the rate of recovery of the hypothalamic–pituitary–adrenal axis and the need for exogenous glucocorticoid during this phase. A better understanding of these principles by healthcare practitioners will ensure a safe and effective withdrawal of these agents in individual patients. Kendrick discusses the inappropriate long-term use of antidepressants and the risks associated with their withdrawal, including the lack of access to psychological treatments as a substitute.[13] While studies are currently investigating the role of internet and telephone support in patients willing to reduce their antidepressant more research is warranted to investigate the efficacy and safety of different tapering interventions.

Decision making in older adults with multimorbidity is very complex. Numerous tools exist to support identification of problematic polypharmacy including the Beer's Criteria, STOPP/START and the Drug Burden Index. However, the clinical utility of these tools is limited in clinical practice as they do not provide explicit decision support. We are developing a comprehensive list of the problems; however, solutions are much harder to come by in complex patients. The barriers and facilitators to effective deprescribing are discussed further by Bennett et al.[14]

A collaborative approach between patient and prescriber is required to facilitate shared decision making, particularly when there are complex risk to benefit ratios to consider. Limited health literacy (LHL) has been reported as a significant barrier to clear communication and appropriate decision making. LHL and low numeracy have been associated with a range of adverse health effects, including worse self-management skills and poor adherence to medication. In this issue, Scott et al. describe the behavioural processes pertinent to shared decision making in the context of deprescribing and argue for a greater focus on behavioural change of the prescriber.[15] Conservatism and inertia, from both patients and physicians, have also been recognised as key barriers to effective deprescribing. The "if it ain't broke don't fix it" approach can lead to patients remaining on multiple medications long past the point at which they are beneficial. This undoubtedly contributes to the 51.1% of palliative patients still in receipt of preventative drugs on their day of death.[16] Changing the behaviour of prescribers towards regular and rigorous scrutiny of medications requires a systematic approach. Understanding what barriers and facilitators exist is something Hughes and colleagues explore in this issue in their Theoretical Domain Framework.[17] They describe the development of a behavioural change technique, grounded in theory and evidence-based, that has been and co-developed with patients and healthcare practitioners, to improve appropriate prescribing.

In 2018, the Short Life Working Group on Overprescribing was commissioned by the U.K. Secretary of State for Health to conduct a review on the burden of problematic polypharmacy in the United Kingdom, the interventions to reduce it, including the efficient handover between primary and secondary case, and the implementation of activities to increase the uptake of such interventions. A rapid review of systematic reviews, conducted by Martyn-St James et al., identified three systematic reviews on the burden of polypharmacy and six systematic reviews on interventions.[18] The reviews on burden reported a high prevalence of polypharmacy in long-term care. Although this was associated with mortality, there was no information regarding associated costs or consequences on health. The reviews on interventions showed a tangible effect on polypharmacy but no clear effects on health outcomes. One review on handover between primary and secondary care showed that medicine reconciliation can reduce problematic polypharmacy. By contrast, there were no systematic reviews on implementation activities. As also suggested by the authors, more research is required to investigate the burden of problematic polypharmacy and the effects of intervention and implementation strategies. Another review on problematic polypharmacy by Reeve focuses on the state of play in three important areas, how we make shared decisions with patients, how we design specific systems that support this decision-making process, and how we generate the much-needed knowledge that informs practice.[19] The need for a sustained shift in healthcare goals, including the awareness of the importance of whole-person outcomes, the continuing support of healthcare professionals, and the design of systems supporting learning from practice, is advocated to better tackle problematic polypharmacy.

Miller et al. discuss the potential of extensive viral vaccination programmes to curb the increasing trend of antibiotic use and its negative consequences, particularly antimicrobial resistance, by reducing infectious disease health care presentation and, consequently, antibiotic prescribing (COMT-00758-20.R1). The reduced use of antibiotics

might further impact on the selection of antimicrobial resistance, preventing the need for additional antibiotic treatment. In this context, the cost-effect analysis of vaccines should also take into account the potential impact on antibiotic use and resistance.

In summary, the contributions in this thematic issue describe some key contemporary challenges faced by prescribers and policy makers in regard to the general aspects of problematic polypharmacy as well as the practical management of specific therapeutic agents in complex patient groups. The investigation of the proposed solutions is likely to drive the research agenda in this area of clinical pharmacology over the next 5–10 years and hopefully lead to more appropriate therapeutic regimens and better patient outcomes.

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