Review

Multi-Morbidity and Polypharmacy in Older People: Challenges and Opportunities for Clinical Practice

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Abstract: Multi-morbidity and polypharmacy are common in older people and pose a challenge for health and social care systems especially in context of global population ageing. They are complex and interrelated concepts in the care of older people that require early detection and patient centred decision making that are underpinned by the principles of multidisciplinary led comprehensive geriatric assessment (CGA). Personalised care plans need to remain responsive and adaptable to the needs of a patient, enabling an individual to maintain their independence.

Keywords: multi-morbidity; CGA; frailty; polypharmacy; deprescribing

Introduction

The number of people aged 60 or over globally are set to rise from 841 million to more than 2 billion between 2013 and 2050; this equates to 21.1% of the world’s population (1). The proportion of people aged 80 years or over is growing even faster. Estimated to be 125 million in 2015 contrasted to 71 million worldwide at the turn of the millennium. This number is projected to increase by 61 per cent over the next 15 years, reaching nearly 202 million in 2030 (2). In the UK, a male aged 85 could expect to live to age 90.8 years and a female to 91.8 years (Office of National Statistics 2016, ONS.gov.uk). These demographic changes are largely due to the advances in public health and modern medicine that have allowed people to live with one or more long term conditions. Whilst a cause for celebration, these changes pose significant challenges in the provision of health and social care to older people (3, 4).

Multi-morbidity refers to the presence of two or more simultaneous long-term health conditions that may not share a causal link for the individual concerned (4). These can span both physical and psychosocial domains and include conditions such as cardiovascular disease, metabolic diseases diabetes and osteoporosis, mental health illness, chronic pain, learning disabilities, sensory deprivation, as well as substance misuse (5, 6). Multi-morbidity increases with age but is not only
limited to older people. For example, in a cross sectional study of over 1 million patients in Scotland, the prevalence of multi-morbidity was 30.4% in those aged 45-64 years increasing to 81.5% in those >85 years (7). Higher prevalence of multi-morbidity is present in women, those who have a lower socio-economic status and educational attainment. In addition, there are racial and ethnic differences that affect prevalence rates (4, 8).

Long-term health conditions account for approximately 50% of general practitioner (GP) appointments, 64% of hospital outpatient appointments and 70% of inpatient hospital admissions (8) and is therefore responsible for approximately 70% of the United Kingdom, National Health Service (UK NHS) current healthcare expenditure. People living with multi-morbidity are at greater risk work absenteeism, mental health problems, unplanned hospital admission, experience higher rates of polypharmacy and adverse drug events and have a reduced quality of life (9-13). Living with multi-morbidity is associated with increased rates of mortality. For example, adults aged >60 years with ≥2 or ≥3 health conditions have a 73% and 172% increased risk of dying respectively, compared to those who are not multi-morbid (14). The proportion of patients living with multi-morbidity is likely to climb as life expectancy continues to rise (5) and is fast becoming a global health problem (15-17).

The association with poor outcome is likely to be multifactorial. Health conditions have a tendency to cluster and interact with other related diseases and can worsen the severity of each disease or result in the development of a further potentially more serious condition (18). For example, the metabolic syndrome is characterised by central obesity alongside the presence of insulin resistance, hypertension and raised cholesterol and triglycerides (19). The interaction of these disease mechanisms leads to a worsening of each individual condition, as well as an increased risk of cardiovascular events such as stroke or myocardial infarction (20, 21). Another example relevant for older people is dementia – where individuals have several co-existent long term conditions often have impairments in function and are at risk of polypharmacy (22). Patients who are multi-morbid and have functional limitations experience the poorest health outcomes (23).

Healthcare infrastructure has not been optimised to manage multiple diseases simultaneously, which can lead to disorganised care for those who are multi-morbid. The norm amongst most medical professionals out with geriatric medicine is to specialise and manage single organ systems, or even a single disease within a given specialty. Whilst this is sometimes necessary, treating diseases in isolation leads to the duplication of efforts within the healthcare system as well as fragmented, poorly co-ordinated healthcare assessments and follow up (24-26). The emphasis on managing single diseases in isolation ignores the unique dynamics of disease clusters. Clinical trials of new medications often exclude participants who have an additional health problem to the one being investigated (27-30). This causes uncertainty regarding the potential risks and benefits of starting evidenced based medications for a patient in the context of their multi-morbidity and invariably leads to additional treatment burden, lower adherence and increased risk of adverse drug interactions (ADR) (31).

**Management of multi-morbidity**

Key points to managing individuals living with multi-morbidity include early identification of those living with multiple health conditions, identification of frailty and patient centred shared decision making (32-34). These key points embody the core principles of comprehensive geriatric assessment
where a holistic and balanced approach to individualise and prioritise management opinions take centre stage. Exploring a person’s personal goals, which health problems have the most impact on their day-to-day life and choice on their medication regime allows a tailored approach, which can facilitate an improvement in individual quality of life. Practical guidance for the management of multi-morbidity underpinned by core principles of CGA are summarised in Figure 1.

**Relationship between multi-morbidity and frailty**

Multi-morbidity and frailty are associated conditions, and there may be inevitable overlap between these concepts in older adults especially since the presence of multiple co-existent conditions increases the risk of a chronic pro-inflammatory state, hormonal dysregulation and susceptibility to disease states and hospitalisation (35). Frailty characterised by a vulnerability to stressor events that can be both internal (e.g. infections and changes to medication) as well as external (e.g. changes in a person’s immediate environment or a breakdown in social care) (36, 37) as a consequence of poor reserve across multiple physiological systems (38). A recent meta-analysis of 78,122 participants across 48 studies found that, on average, seven out of ten frail adults were also multi-morbid (39). However, people living with multi-morbidity will not necessarily also be frail, as many people with multiple health conditions have the sufficient physiological reserve to recover from insults and return to their previous baseline of health.

**Polypharmacy**

Polypharmacy, defined as the concurrent use of at least 4-5 medications rises considerably as the number of health problems and healthcare service use increases (40, 41). In the health survey for England 2016, 56% of individuals aged 85 and over were taking five or more medicines compared to 9% of those aged 45-54. A study of 180,815 primary care records found that amongst patients with two comorbidities, 20.8% received four to nine medications and 1.1% received ten or more medications (42). In contrast, amongst patients with six or more comorbidities, these values increased to 47.7% and 41.7% respectively. Several studies have also found that number of medications increased after hospital admission with prescription on average of two additional drugs (43, 44).

In the past decade the average number of items prescribed for each person per year in England has increased. For example, the proportion of patients receiving ≥10 medications was 1.9% in 1995, increasing to 5.8% in 2010 (40). One explanation for this rise is that asymptomatic people are increasingly treated with preventative interventions to reduce their future risk of mortality; this is seen particularly with cardiovascular disease. If each morbidity illness is treated in accordance to national guidelines patients would be on many more medications (45).

Polypharmacy is appropriate in instances where medicines have been optimised and prescribed for complex conditions according to best evidence. Advanced age in itself should not be a reason for withholding effective therapies (46). Problematic polypharmacy occurs when there is the prescription of multiple medicines and the risk of harm outweighs benefits and the consequent pill burden leads to lower adherence or risks of potentially harmful interactions (ADR) (46). ADR can lead to further morbidity. For example, within two hospitals in the UK, a study suggested that the prevalence of ADR related admissions was 6.5%, with ADR directly leading to acute admission in 80% of cases (47). In a follow up study of hospital wards, it was estimated that one in seven patients experienced a ADR that contributed to health deterioration and increased length of hospital stay (48).
Managing polypharmacy

Balancing the recommendations of multiple guidelines for those who are multi-morbid inevitably leads to polypharmacy and danger of the prescribing cascade where medications are prescribed to counter side-effects of another medication. Medicines optimisation is defined as a person-centred, evidence based, approach to safe and effective medicines use to ensure people obtain the best possible outcomes from their medicines and that they continue to provide benefit for the individual. Medicines optimisation ensures that there is a specific and justifiable reason for every medication the patient is taking and that this is as optimum it can be based on evidence. This includes stopping medications that are having no benefit or causing side effects, interacting and or are contra-indicated (49). Several guides are available to help with medicines optimisation such as the Beers Criteria, Medications Appropriateness Index, STOPP-START, NO TEARS and the PINCER tool (50-53). These guides rely on actions taken by all health and social care practitioners and requires patient engagement and professional collaboration across health and social care settings (54, 55).

Deprescribing requires an intimate knowledge of drug pharmacodynamics and potential for side effects and ADR and patient factors affecting pharmacokinetics. When planned, is patient centred and backed up by education and training, deprescribing is not associated with significant side effects or adverse outcomes (56-58).

Medication use in older people

Physiological changes with age include a reduction in total body water, increase in blood brain barrier permeability, lower hepatic mass, decreased renal cortical mass, lower nephron numbers and a lower capacity for glomerular filtration. Older people have mild renal impairment and this is not always reflected by a rise in serum creatinine due to sarcopenia. These changes increase the risk of ADR and potentially harmful drug-drug interactions. This especially important for drugs with a narrow therapeutic index (NTI) such as digoxin, warfarin, aminophylline, lithium and some antidepressants.

In addition, older people are more susceptible to anticholinergic side effects from commonly prescribed drugs such as amitriptyline, oxybutynin, cetirizine, mirtazapine, which include delirium, reduced cognition, gait and balance problems, constipation, urinary retention and dry mouth (59). These conditions may be misinterpreted as new conditions and can initiate a prescribing cascade. Individuals who have a shorter life expectancy may not benefit from prescribed medications that take time before therapeutic benefit is established. Examples include anti-hypertensives, drugs used to treat hyperlipidaemia and osteoporosis treatments (60). Given the heterogeneity of disease trajectories in older people, symptoms and individual patient preferences, goals of care will vary between individuals. This should be driven by patient centred decision making, underpinned by CGA (61).

Comprehensive geriatric medicine (CGA): a useful paradigm in the management of older people across primary and secondary care.

Individuals generally do not like taking prescribed medications for several reasons such as complex dosing regimens, fear, scepticism especially when asymptomatic, and media portrayal. These factors affect adherence and studies suggest that up to 50% of prescribed medications may not be taken by older people (62). GPs are in a position to make shared decisions with patients and families to
prescribe, deprescribe, rationalise and optimise medications (54, 63). It is also clear that the impact of multi-morbidity, frailty and polypharmacy spans both primary and secondary care. Geriatricians and pharmacists are therefore also ideally placed within the MDT and alongside GPs to implement principles of personalised care planning consequent to CGA across this arbitrary divide. This provides an exciting opportunity for future models of care (64) (Figure 1).

Conclusions

Older age is characterised by and increased risk of accumulating multiple long term conditions. Multi-morbidity and polypharmacy are interrelated and are associated with progressive loss of resilience, impaired homeostasis and contribute to a significant health and social care burden. Routine assessment of long term conditions, presence of frailty and medicines optimisation should form part of a patient centred, multidisciplinary, personalised and comprehensive assessment across all health and social care settings.

Competing interests

The authors declare no conflict of interest

Author contributions

All authors were involved in the preparation of this manuscript. HPP edited and critically revised the final version. All authors read and approved the final version of this manuscript.

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Figure 1 Principles of comprehensive geriatric assessment (CGA)

CGA is an evidence-based multidimensional and interdisciplinary assessment of medical, psychological, and functional capabilities aimed at developing an integrated plan for treatment and care and is associated with favourable clinical and health care outcomes. The core principles of CGA include comprehensive history taking, multidisciplinary-led assessment culminating in goals for current and future management. These principles can be applied across any health and social care setting and have been shown to be highly effective in the management of older people living with frailty and multimorbidity. The process is iterative and the key to its success is timely review and coordination so that the care plan generated from a CGA remains responsive to the patient’s needs.