

## Commissioning Brief - Supporting Information

### 17/69 – Safely and effectively stopping medications in older people with multimorbidity and polypharmacy

**Closing date: 28 September 2017**

This supporting document provides further information to support applicants for this call. It is intended to summarize what prompted the call and the existing evidence base, including relevant work from the HTA and wider NIHR research portfolio. It was researched and written on the basis of information from a search of relevant sources and databases, and in consultation with a number of experts in the field. Searches and information provided were up to date as of May 2017.

#### Source of topic

This topic was suggested by the Royal College of General Practitioners.

In addition, NICE guideline NG56 contains a research recommendation suggesting research to assess the clinical and cost-effectiveness of stopping preventive medicines in people with multimorbidity who may not benefit from continuing them.

#### Patient group

In the UK, most people aged 65 years or older have two or more long term conditions and the majority of people aged 75 years or older have three or more.

One study found that the proportion of adults in their studied population dispensed  $\geq 5$  drugs was 20.8%, and the proportion dispensed  $\geq 10$  was 5.8%. Receipt of  $\geq 10$  drugs was strongly associated with increasing age (those  $\geq 80$  years, 24.0%).<sup>1</sup>

#### NICE and other guidance

*NICE NG56 Multimorbidity: clinical assessment and management. September 2016.*

One of the aims of this guideline is to reduce treatment burden (polypharmacy and multiple appointments).

Recommendations relevant to this research brief:

1.6.2 Discuss with the person the purpose of the approach to care, that is, to improve quality of life.

1.6.4 Establish treatment burden by talking to people about how treatments for their health problems affect their day-to-day life. Include in the discussion.

Reviewing medicines and other treatments

1.6.9 When reviewing medicines and other treatments, use the database of treatment effects to find information on: the effectiveness of treatments; the duration of treatment trials; the populations included in treatment trials.

1.6.10 Consider using a screening tool (for example, the STOPP/START tool in older people) to identify medicine-related safety concerns and medicines the person might benefit from but is not currently taking. [This recommendation is adapted from the NICE guideline on medicines optimisation.]

1.6.11 When optimising treatment, think about any medicines or non-pharmacological treatments that might be started as well as those that might be stopped.

1.6.12 Ask the person if treatments intended to relieve symptoms are providing benefits or causing harms. If the person is unsure of benefit or is experiencing harms from a treatment: discuss reducing or stopping the treatment; plan a review to monitor effects of any changes made and decide whether any further changes to treatments are needed (including restarting a treatment).

1.6.13 Take into account the possibility of lower overall benefit of continuing treatments that aim to offer prognostic benefit, particularly in people with limited life expectancy or frailty.

1.6.14 Discuss with people who have multimorbidity and limited life expectancy or frailty whether they wish to continue treatments recommended in guidance on single health conditions which may offer them limited overall benefit.

1.6.15 Discuss any changes to treatments that aim to offer prognostic benefit with the person, taking into account:

Agreeing the individualised management plan

1.6.17 After a discussion of disease and treatment burden and the person's, personal goals, values and priorities, develop and agree an individualised management plan with the person. Agree what will be recorded and what actions will be taken. These could include: starting, stopping or changing medicines and non-pharmacological treatments; prioritising healthcare appointments; anticipating possible changes to health and wellbeing; assigning responsibility for coordination of care and ensuring this is communicated to other healthcare professionals and services; other areas the person considers important to them; arranging a follow-up and review of decisions made. [...]

1.6.16 Tell a person who has been taking bisphosphonate for osteoporosis for at least 3 years that there is no consistent evidence of: further benefit from continuing bisphosphonate for another 3 years; harms from stopping bisphosphonate after 3 years of treatment. Discuss stopping bisphosphonate after 3 years and include patient choice, fracture risk and life expectancy in the discussion.

- *NICE NG5 Medicines optimisation: the safe and effective use of medicines to enable the best possible outcomes. March 2015*

Recommendations on management of polypharmacy are similar to those described in NICE NG56 above.

### **Current practice and proposed intervention**

Multimorbidity is associated with polypharmacy, which is generally described as prescription of five or more different drugs. A 50% increase in the number of prescription items was reported between 2005 and 2015. It is believed that this is due to an increase in the average number of medications from 14 to 20 per head of population in England.

It is not unusual for people with multimorbidity to be prescribed medications that are intended to prevent future morbidity and mortality from certain health conditions. However, there are concerns over the actual benefits of preventive medicines and their potential harms. The evidence of benefit of many drugs comes from trials that did not include people with multimorbidity. Hence there is no evidence to support their use in multimorbid patients, and it is possible that the benefits of multiple medications are reduced, and there may be higher risk of adverse events.

The King's Fund distinguishes between appropriate and inappropriate polypharmacy.

Appropriate polypharmacy is described as 'Prescribing for a person for complex conditions or for multiple conditions in circumstances where medicines use has been optimised and where the medicines are prescribed according to best evidence.'

Problematic polypharmacy is described as 'The prescribing of multiple medicines inappropriately, or where the intended benefit of the medicines are not realised.' This may be the case where there is lack of evidence, risk of drug interactions, high burden to the patient, difficulty with adherence to treatment, or where a drug is prescribed as a treatment of side effects coming from another medication (especially if there are alternative solutions).

[Sources: Multimorbidity and polypharmacy. NICE Key therapeutic topic [KTT18] Published date: January 2017 <https://www.nice.org.uk/advice/ktt18/chapter/Options-for-local-implementation>; [The King's Fund report 2013](#) ].

## Completed research

### *Evidence Synthesis*

Some of the following reviews are believed to be out of date.

- *Effectiveness of Interventions to Deprescribe Inappropriate Proton Pump Inhibitors in Older Adults*. Wilsdon 2017.<sup>2</sup> Australia.

Searches up to January 2017. 21 studies included. Effective interventions included a population-wide education and promotion strategy, academic detailing for general practitioners, and inpatient geriatrician-led deprescribing. Clinical outcome data were not available. Meta-analysis was not possible due to heterogeneity.

- *Deprescribing versus continuation of chronic proton pump inhibitor use in adults*. Boghossian 2017.<sup>3</sup>

Searches up to November 2016. Six trials (n = 1758) included. Authors' conclusions: In people with mild GERD, on-demand deprescribing may lead to an increase in GI symptoms (e.g. dyspepsia, regurgitation) and probably a reduction in pill burden. There was a decline in participant satisfaction, although heterogeneity was high. There were insufficient data to make a conclusion regarding long-term benefits and harms of PPI discontinuation, although two trials (one on-demand trial and one abrupt discontinuation trial) reported endoscopic findings in their intervention groups at study end.

- *The feasibility and effect of deprescribing in older adults on mortality and health: a systematic review and meta-analysis*. Page 2016.<sup>4</sup>

Searches up to February 2015. 132 papers included (n = 34,143). Primary outcome: mortality. Eligibility for inclusion: studies where older adults had at least one medication deprescribed. In nonrandomized studies, deprescribing polypharmacy was shown to significantly decrease mortality. However, this was not statistically significant in the randomized studies.

- *Statin withdrawal in people with dementia*. McGuinness 2016.<sup>5</sup>

Searches up to February 2016. 28 references identified but all excluded.

- *Medication review in hospitalised patients to reduce morbidity and mortality*. Christensen & Lundh 2016.<sup>6</sup>

Searches up to November 2014. 10 trials (3575 participants) included. Authors' conclusions: No evidence that medication review reduces mortality or hospital readmissions; some evidence that medication review may reduce emergency department contacts. However, because of short follow-up ranging from 30 days to one year, important treatment effects may have been overlooked.

- *Interventions to improve the appropriate use of polypharmacy for older people*. Patterson 2014.<sup>7</sup>

Searches up to November 2013. 12 studies included. Authors' conclusions: It is unclear whether interventions to improve appropriate polypharmacy, such as pharmaceutical care, resulted in clinically significant improvement; however, they appear beneficial in terms of reducing inappropriate prescribing.

- *Can medications be safely withdrawn in patients with stable chronic heart failure? Systematic review and meta-analysis*. Hopper 2014.<sup>8</sup>

Searches up to January 2014. Twenty-six studies included (total number of participants not reported). Authors' conclusions: Current evidence discourages any attempt to discontinue renin-angiotensin-aldosterone system inhibitors or beta-blockers in patients with stable heart failure, regardless of clinical and/or echocardiographic status. Formal withdrawal trials of other classes are needed.

- *Patient barriers to and enablers of deprescribing: a systematic review*. Reeve 2013.<sup>9</sup>

Searches up to August 2011. Twenty-one studies were included (total number of participants not reported). Authors' conclusions: Patients' understanding of the appropriateness of (and having a process for) cessation facilitates willingness to trial medication cessation. Disagreement with cessation and fear of consequences may prevent patients agreeing to cessation. The decision to stop a medication by an individual is influenced by multiple competing barriers and enablers. Knowledge of these will aid in the development of a deprescribing process, particularly in approaching the topic of cessation with the patient and what process should be utilised. However, further research is required to determine if the proposed patient-centred deprescribing process will result in improved patient outcomes.

### Primary Research

A MedLine search produced >50 papers of interest published during the past five years.

A proportion of these are qualitative studies investigating attitudes and beliefs of clinicians and patients towards deprescribing, including barriers and facilitators.

Other papers report on research to develop and/or assess guidance, tools, and decision aids for the management of polypharmacy, including deprescribing.

A third group of studies investigates patient outcomes when defined treatments are withdrawn.

Some of the most relevant studies found include the following:

- *Deprescribing in a family health team: a study of chronic proton pump inhibitor use.* Walsh 2016.<sup>10</sup> Canada.

A PPI Deprescribing Tool was uploaded into the electronic medication record as a second reminder and to guide reassessment and deprescribing where indicated. Ten weeks after implementation, a survey found that 43 of 46 (93%) patients had their PPI reassessed, resulting in 11 patients (26%) having their PPI deprescribed.

- *Deprescribing in Frail Older People: A Randomised Controlled Trial.* Potter 2016.<sup>11</sup> Australia.

N=95 people aged over 65 years living in four RACF in rural mid-west Western Australia. Of the 348 medicines targeted for deprescribing (7.4 +/- 3.8 per person, 78% of regular medicines), 207 medicines (4.4 +/- 3.4 per person, 59% of targeted medicines) were successfully discontinued. The mean change in number of regular medicines at 12 months was -1.9 +/- 4.1 in intervention group participants and +0.1 +/- 3.5 in control group participants. Twelve intervention participants and 19 control participants died within 12 months of randomisation. There were no significant differences between groups in other secondary outcomes.

- *A medication review and deprescribing method for hospitalised older patients receiving multiple medications.* McKean 2016.<sup>12</sup> UK

Prospective pilot study. N=50 patients aged >=65years admitted acutely to general medicine units in a tertiary hospital (convenience sample). Intervention: education programme and paper-based or computerised proforma listing clinical and medication data linked with a five-step decision support tool for selecting drugs eligible for discontinuation. Selected drugs were ceased or were being weaned by the time of discharge. 186 of 542 (34.3%) regular medications were discontinued. Reduction by at least 2 medications occurred in 84% of participants, and by four or more in 50%. Statins, gastric acid suppressive agents, angiotensin-converting enzyme inhibitors/angiotensin receptor antagonists and inhaled bronchodilators were the most frequently ceased medications. During the 78 days' follow-up, ceased medications were recommenced among three patients because of symptom relapse.

- *What factors are important for deprescribing in Australian long-term care facilities? Perspectives of residents and health professionals.* Turner 2016.<sup>13</sup> Australia.

Qualitative research using nominal group technique. Participants were 11 residents/representatives, 19 GPs, 12 nurses and 14 pharmacists. GPs ranked 'evidence for deprescribing' and 'communication with family/resident' as most important factors. Nurses ranked 'GP receptivity to deprescribing' and 'nurses ability to advocate for residents' as most important. Pharmacists ranked 'clinical appropriateness of therapy' and 'identifying residents' goals of care' as most important. Residents ranked 'wellbeing of the resident' and 'continuity of nursing staff' as most important. The multidisciplinary groups ranked 'adequacy of medical and medication history' and 'identifying residents' goals of care' as most important.

- *Reduction of inappropriate benzodiazepine prescriptions among older adults through direct patient education: the EMPOWER cluster randomized trial.* Tannenbaum 2014.<sup>14</sup> Canada.

Participants: 303 long-term users of benzodiazepine aged 65-95 years, recruited from 30 community pharmacies. Intervention: Deprescribing patient empowerment intervention describing the risks of benzodiazepine use and a stepwise tapering protocol. Control: usual care. At 6 months, 27% of the intervention group had discontinued benzodiazepine use compared with 5% of the control group. Dose reduction occurred in an additional 11%.

- *Safety of discontinuing statins among patients with life limiting illness.* Kutner 2014.<sup>15</sup> USA.

Pragmatic RCT. Participants: 381 adults with life-limiting illness on statin for primary or secondary prevention for > 3months, life expectancy >1 month, declining functional status. Rate of death within 60 days was 0.238 in the intervention group (where statins were deprescribed) and 0.203 in the control group (difference statistically not significant). The intervention group had longer median time-to-death

(229 vs. 190 days), and higher quality of life (using validated tools). Incidence of cardiovascular events was 13 in the intervention group, and 11 in the control group.

## Research in progress

### *Evidence Synthesis*

A number of ongoing evidence syntheses were identified, but none of these are expected to answer the research question and outcomes specified in this research brief.

- *Systematic review of the effectiveness of deprescribing interventions in older hospitalised patients on prescribing and clinical outcomes.*

Primary outcomes: Reduction in potentially inappropriate medications, including number of medications, drug burden index score, medication appropriateness index, and prescribing quality index. Secondary outcomes: Clinical outcomes including mortality, falls, cognitive function, adverse drug withdrawal events, quality of life, and hospitalisations. Anticipated completion date: 11 January 2018. PROSPERO 2017:CRD42017060236. Available from

[http://www.crd.york.ac.uk/PROSPERO/display\\_record.asp?ID=CRD42017060236](http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42017060236)

- *Computer decision support to reduce potentially inappropriate medication in older adults: a systematic review.*

Anticipated completion date: 31 December 2017. PROSPERO 2017:CRD42017067021. Available from

[http://www.crd.york.ac.uk/PROSPERO/display\\_record.asp?ID=CRD42017067021](http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42017067021)

- *Health outcomes of deprescribing interventions by healthcare professionals in the nursing home setting: a systematic review.*

Primary outcomes: Fall rates, pill burden, quality of life, hospitalisation and mortality rates. Anticipated completion date: 30 June 2017. PROSPERO 2016:CRD42016050028. Available from

[http://www.crd.york.ac.uk/PROSPERO/display\\_record.asp?ID=CRD42016050028](http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016050028)

- *Systematic review of polypharmacy tools and association with clinical outcomes.*

Review question(s): 1) Systematic review of polypharmacy tools and criteria; 2) Systematic reviews of shortlisted tools and their association with clinical outcomes (external validation). Anticipated completion date: 23 June 2017. PROSPERO 2017:CRD42017067233. Available from

[http://www.crd.york.ac.uk/PROSPERO/display\\_record.asp?ID=CRD42017067233](http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42017067233)

- *Effectiveness of deprescribing interventions in adults: a systematic review.*

Review question(s): To determine the effectiveness of deprescribing interventions in reducing prescribed medications in adults. To identify behaviour change components present in interventions and whether they are deemed to be effective or non-effective. Primary outcomes: Number of prescriptions per patient and/or change in dosages of prescriptions per patient. Secondary outcomes: Medication Appropriateness Index (MAI) and/or Quality of Life (QOL). Anticipated completion date: 01 May 2017. Status reported as ongoing. PROSPERO 2016:CRD42016037730. Available from

[http://www.crd.york.ac.uk/PROSPERO/display\\_record.asp?ID=CRD42016037730](http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016037730)

- *Inappropriate pharmacological treatment in older adults affected by cardiovascular disease and other chronic comorbidities: a systematic literature review to identify potentially inappropriate prescription indicators.*

Anticipated completion date: 31 March 2017. Status reported as ongoing. PROSPERO 2017:CRD42017057795. Available from

[http://www.crd.york.ac.uk/PROSPERO/display\\_record.asp?ID=CRD42017057795](http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42017057795)

- *Developing and evaluating a measure of inappropriate polypharmacy in primary care.*

Review question(s): This review is being undertaken as part of a wider study aiming to develop a measure of polypharmacy for use in primary care. The findings of this review will be used to inform the development of this measure. Anticipated completion date: 31 January 2017. Status reported as ongoing. PROSPERO 2016:CRD42016049176. Available from

[http://www.crd.york.ac.uk/PROSPERO/display\\_record.asp?ID=CRD42016049176](http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016049176)

- *Health impacts and characteristics of deprescribing interventions in older adults: a systematic review.*

Review question(s): What are the health outcomes of interventions to deprescribe, i.e. reduce the number or dosage of chronic medications, in seniors? What are the characteristics of deprescribing

interventions, or elements thereof, that achieve positive or at least neutral outcomes on health or quality of life in these seniors? Anticipated completion date: 23 December 2016. Status reported as ongoing. PROSPERO 2015:CRD42015020866. Available from [http://www.crd.york.ac.uk/PROSPERO/display\\_record.asp?ID=CRD42015020866](http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015020866)

#### *Primary Research*

- ISRCTN16560559 The Prevention of Polypharmacy in Primary Care Patients Trial (4P-RCT). Scientific title: Systematic Deprescribing of medicaments in polymorbid primary care patients: a randomized-controlled study in Swiss General Practices. N=430 (from 16-17 practices). Expected completion: 01/07/2017. Switzerland.
- NCT02379455 Cooperation for Improved Pharmacotherapy in Home-dwelling Elderly People Receiving Polypharmacy - The COOP Study (COOP). N=200. Expected completion: August 2017. Norway.
- ISRCTN42003273 Polypharmacy reduction in patients treated for chronic diseases. N= 1,626. Expected completion: 31/08/2017. Germany.
- ISRCTN10137559 PRIMA-eDS: Polypharmacy in chronic diseases: Reduction of Inappropriate Medication and Adverse drug events in elderly populations by electronic Decision Support. N= 335 practices. Expected completion: 30/09/2017. International study (Germany, UK, Austria, Italy).
- NCT03091153 Deprescribing in a Long Term Care Facility. N=66. Expected completion: October 2017. Canada.
- NCT02866799 Multi-PAP RCT: Improving Prescription in Primary Care Patients With Multimorbidity and Polypharmacy (Multi-PAP). N=400. Expected completion: November 2017. Spain.
- NCT02928939 Therapeutic Conflicts and Multimorbidity. N=1600. Expected completion: December 2017. Switzerland.
- NCT02863341 Nursing Home Team-Care Deprescribing Study. N=295. Expected completion: June 2018. Singapore.
- NCT02830425 Potentially Inappropriate Prescription Associated to Multimorbidity (PIMyC). N=800. Expected completion: December 2018. Spain.
- NCT02958800 Deprescribing Antipsychotics in Long-Term Care. N=20. Expected completion: December 2018.
- ISRCTN12752680 Supporting medicines management in older adults with multiple medical conditions. N= 450 patients from 30 GP practices. Expected completion: 28/08/2019. Ireland. Funder: The Health Research Board - Centre for Primary Care Research (Ireland).
- NCT02942927 Team Approach to Polypharmacy Evaluation and Reduction (TAPER-RCT). N=360. Expected completion: October 2020. Canada.
- NCT02979353 A Randomized Controlled Trial to Deprescribe for Older Patients With Polypharmacy (Shed-Meds). N=1300. Expected completion: April 2021.
- ACTRN12616000721404 Deprescribing anticholinergic and sedative medicines: A Feasibility Trial (DEFEAT-polypharmacy) in residential aged care facilities. N=150. Expected completion: Not reported. Status: Not yet recruiting. New Zealand.

#### **NETS research**

- HS&DR 11/2003/27 Better guidelines for better care: accounting for multimorbidity in clinical guidelines – structured examination of exemplar guidelines and health economic modelling. Guthrie et al. Health Services and Delivery Research Volume 5 Issue 16, 2017.
- HS&DR 12/130/15 Improving the management of patients with multimorbidity in general practice. Christopher Salisbury, Bristol. Expected completion 30/09/2017.
- HS&DR 15/12/22 Accounting for multimorbidity, competing risk and direct treatment disutility in risk prediction tools and model-based cost-effectiveness analysis for the primary prevention of cardiovascular disease and osteoporotic fracture. Bruce Guthrie, Dundee. Expected completion: 31/08/2019.
- HS&DR 15/137/01 Developing a framework for a novel multi-disciplinary, multi-agency intervention(s), to improve medication management in older people on complex medication regimens resident in the community. Ian Maidment, Aston University. Expected completion: 31/12/2018.

## References

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