JOURNAL OF COMORBIDITY

Journal of Comorbidity 2015;5:11–14 doi: 10.15256/joc.2015.5.49

Editorial

Coping with complexity: working beyond the guidelines for patients with multimorbidities

Julian Treadwell[1,2]

[1]Hindon Surgery, Wiltshire, UK; [2]Royal College of General Practitioners' Standing Group on Overdiagnosis, UK

Journal of Comorbidity 2015;5:11–14

Keywords: multimorbidity, comorbidity, primary care, general practice, guidelines, over-treatment

Primary care physicians believe they are delivering evidence-based care, understanding that adherence to evidence-based clinical guidelines results in tangible benefits in the populations for which they were developed. Unfortunately, most clinical guidelines are based on trial populations which are very different to primary care populations [1], and do not reflect the reality of multimorbidity in general practice [2–6]. Since patients with multimorbidity account for around eight in every 10 primary care consultations [7], it is unsurprising that many primary care physicians find managing these patients challenging. Additionally, current clinical guidelines do not provide guidance on how best to prioritize recommendations for individuals with multimorbidity, and may therefore result in over-treatment and polypharmacy, and a risk of overlooking patient preferences [2,8].

To illustrate the point, allow me to present Mary, an 82-year-old, socially active woman living alone. Mary has been taking alendronate and calcium/vitamin C following a Colles fracture 5 years ago. She has difficulty walking as a result of osteoarthritis (for which she takes paracetamol and naproxen) and chronic obstructive pulmonary disease (for which she uses salbutamol for short-term symptom relief plus a salmeterol/fluticasone inhaler to prevent exacerbations). Mary is visiting her GP today to discuss her recently diagnosed stage 2 hypertension (ambulatory blood pressure 162/92 mmHg), her fasting total:HDL (high-density lipoprotein cholesterol) of 5.3, and her newly diagnosed chronic kidney disease (CKD) stage 3aA2.

With strict adherence to all the current evidence-based guidelines for her conditions, Mary would be leaving her appointment today with a prescription containing all of the following:

- Paracetamol 1 g four-times per day, as needed
- Naproxen 250 mg twice-daily, as needed
- Calcichew D3 Forte two tablets per day
- Alendronate 70 mg once-weekly
- Salbutamol and/or ipratropium bromide inhalers, as needed
- Salmeterol/Fluticasone 50/500 mg inhaler, one puff twice-daily
- Atorvastatin 20 mg, once daily
- A calcium channel blocker, once daily
- An angiotensin-converting enzyme (ACE) inhibitor, possibly at the maximum dose
- Possibly a thiazide to achieve CKD blood pressure targets.

Patients like Mary are now the norm – not the exception – in primary care [5].

The Quality Outcomes Framework for general practice in the UK has resulted in more consistent use of evidence-based interventions, but has also led to far greater use of pharmacological therapies [9]. This has been compounded by a tendency towards over-diagnosis of premorbid disorders, with many patients receiving aggressive interventions for conditions that would

Correspondence: Julian Treadwell, Hindon Surgery, High Street, Hindon, Wiltshire SP3 6DJ, UK.
Tel.: +44 (0) 1747 820 222; fax: +44 (0) 1747 820736;
E-mail: juliantreadwell@nhs.net

Received: Feb 9, 2015; Accepted: Feb 9, 2015; Published: Mar 4, 2015

never have harmed them [10,11]. Polypharmacy is a risky business associated with causing or exacerbating other conditions, adverse drug reactions and interactions, under-dosing of recommended drugs, medication errors, and poor adherence to treatment [12].

In Mary's circumstances and for many other patients, we need to adopt a more rational, patient-centered approach to care, and consider deviating from the guidelines when it is safe and justifiable to do so. Most guidelines contain a statement encouraging clinicians to exercise "clinical judgement"; to do this we need to consider what the individual patient really wants, prioritize those conditions most likely to do harm, and initiate only those treatments most likely to confer substantial benefits. We must make the best decisions we can in partnership with our patients.

Let us imagine that Mary expresses concern about the number of medications that she is being offered. She will do what her doctor advises, but would rather only take what is really necessary and wants to minimize her risk of side effects. Her treatment priorities are to reduce her risk of having a disabling stroke (a great fear) but she takes a philosophical approach about mortality and is not especially interested in taking drugs to increase longevity at her age; "You've got to die of something". What her doctor needs to know now to help her make a treatment decision is: exactly how much good these treatments are likely to do her, how much harm they might cause, exactly how much risk reduction are they conferring, and a reduction in risk of what, exactly? An exploration of the evidence behind her guideline recommended treatment might lead her and her doctor to make some more prudent choices about her medication regime:

- Treatment of stage 2 hypertension has been shown to reduce the risk of stroke from 5.2% to 3.3% over approximately 4 years [13], and a similar degree of benefit was observed in the Hypertension in the Very Elderly (HYVET) trial [14] with a target blood pressure of <150/90 mmHg. A calcium channel blocker is the first class of drug recommended in current NICE hypertension guidance [15]. It would seem likely that Mary would opt for this treatment.
- An ACE inhibitor is recommended in current NICE guidance for CKD in the presence of moderate albuminuria and hypertension. Examination of the evidence for this recommendation reveals that this intervention is based on trials of patients with diabetes or severe, progressive CKD, and has been shown to reduce biochemical deterioration of CKD and the chance of end-stage CKD [16]. This is not a comparable population, nor a treatment goal that is likely to be relevant for Mary. Treatment with an ACE inhibitor exposes her to risks of hyperkalemia, hypotension, falls, and acute kidney injury.
- Why should she remain on her Salmeterol/Fluticasone inhaler? In chronic obstructive pulmonary disease with an FEV1 (forced expiratory volume in 1 s) <50% of predicted, this is recommended to reduce her risk of exacerbations and hospital admissions [17]. However, the absolute gain for this is very small. A Cochrane review [18] reported a 2.1% absolute risk reduction in the composite endpoint of exacerbations and hospital admissions, but also a 1.4% increase in absolute risk of pneumonia, conferring a 'net benefit' of merely 0.7% absolute risk reduction. Would Mary think this a worthwhile exercise?
- Bisphosphonates have been shown to reduce the risk of osteoporotic fractures in a secondary prevention population [19], although the trial populations were younger than Mary and it is hard to extrapolate her likely gain from these drugs given the multifactorial nature of fracture risk. However, they are likely to be a valuable intervention for her. Nevertheless, given that she has already been taking them for 5 years, it may be reasonable to stop these treatments now as extension trials of bisphosphonates have not shown any longer term reduction in fracture risk [20]. Additionally, these drugs are associated with significant side effects, including gastrointestinal bleeding [21].
- There is little evidence about the benefit for her in continuing oral calcium and vitamin D supplements without bisphosphonates. A trial in a comparable population showed no benefit [22].
- The role of statins in the very elderly in a primary prevention context remains controversial. NICE guidance [23] recommends offering treatment but acknowledges the paucity of evidence in this age group. The PROSPER trial [24] in those aged over 70 years showed no benefit for stroke reduction or total mortality (though some reduction in fatal and non-fatal myocardial infarction was observed) with pravastatin 40 mg versus placebo.
- With regard to her analgesia, paracetamol and naproxen are both recommended in current NICE guidance [25], but Mary and her doctor would wish to know the size of the potential risks of non-steroidal anti-inflammatory drugs, which include GI bleeds, acute kidney injury, and cardiovascular events.

Given all this extra information, it may well be that Mary and her doctor choose to rationalize her long-term medication so that she might remain on just paracetamol, a calcium channel blocker and salbutamol inhaler as needed. In doing so, she may not lose much in terms of risk reduction, but gain a lot in reduced treatment

burden, risk of acute kidney injury, GI bleed, hypotension, falls, and possibly hospital admission.

But how might we achieve this sort of personalized assessment in everyday practice? Gathering this amount of information is prohibitively time consuming and requires high levels of confidence on the part of the doctor interpreting it. Current clinical guidelines tend to be prescriptive and the evidence summaries behind them relatively inaccessible, do not consider the cumulative impact of treatment recommendations on people with multimorbidities, and do not state the potential risks and benefits of different treatments to the individual.

Primary care professionals are becoming increasingly frustrated by the prescriptive and additive nature of current guidelines based on research that excluded most of the types of patients with multimorbidities we see every day [8,26–28]. Ideally, we would like to see clinical guidelines that are generalist-led, readily accessible and relevant to our work [2,4]. We need a clinically meaningful evidence resource that draws on the excellent work presented in current guidelines, but would enable us to make prompt, patient-centred decisions based on an analysis of potential benefits and risk at the individual level. We would like to see data on absolute risk reductions with each intervention, numbers needed to treat in the context of a clear time frame, and numbers needed to harm clearly expressed, wherever possible. Breakdowns of composite endpoints would allow us to target treatment according to what the patient wants to achieve; for example, stroke versus non fatal myocardial infarction. We would like to have information about the applicability of study results to 'real-world' patients, with consideration given to the needs of different age groups, ethnicities, and patients with comorbidities/multimorbidities [29].

Primary care physicians need rapid access to evidence that matters – expressed in a way that is useful for patients – that can be found quickly during a consultation. A framework for a web-based resource is being explored by the Royal College of General Practitioners Standing Group on Overdiagnosis [30], and we hope to engage with others in the world of shared decision making to take this further. In the meantime, we should continue to be alert to the perils of polypharmacy in our patients with multimorbidity, aim to balance the risk of under-treatment against that of over-treatment, and to maximize use of the most important interventions that offer the greatest benefit with the smallest harm [9].

We have a long way to go before we are adequately equipped to provide evidence-based, patient-centered care for our patients with multimorbidity, but at least the issues of over-diagnosis and over-treatment are now on the agenda, and there is a palpable hunger for change in primary care in the UK.

Conflicts of interest

None declared.

Funding

None declared.

References

1 Steel N, Abdelhamid A, Stokes T, Edwards H, Fleetcroft R, Howe A, et al. A review of clinical practice guidelines found that they were often based on evidence of uncertain relevance to primary care patients. J Clin Epidemiol 2014;67:1251–7. View Item.

2 Hughes LD, McMurdo ME, Guthrie B. Guidelines for people not for diseases: the challenges of applying UK clinical guidelines to people with multimorbidity. Age Ageing 2013;42:62–9. View Item.

3 Greenhalgh T, Howick J, Maskrey N; Evidence Based Medicine Renaissance Group. Evidence based medicine: a movement in crisis? Br Med J 2014;348:g3725. View Item.

4 Guthrie B, Payne K, Alderson P, McMurdo ME, Mercer SW. Adapting clinical guidelines to take account of multimorbidity. Br Med J 2012;345:e6341. View Item.

5 Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. Lancet 2012;380:37–43. View Item.

6 Smith SM, Soubhi H, Fortin M, Hudon C, O'Dowd T. Interventions for improving outcomes in patients with multimorbidity in primary care and community settings. Cochrane Database Syst Rev 2012;4:CD006560. View Item.

7 Salisbury C, Johnson L, Purdy S, Valderas JM, Montgomery AA. Epidemiology and impact of multimorbidity in primary care: a retrospective cohort study. Br J Gen Pract 2011;61:e12–21. View Item.

8 Heath I, Treadwell J. Bad guidelines and overtreatment in primary care. Report from the First Preventing Overdiagnosis Conference, Dartmouth, NH, USA, 2013 Sep 10–12. Available from: http://www.preventingoverdiagnosis.net/documents/PODC2013.pdf [Last accessed Dec 10, 2014].

9 Duerden M, Avery T, Payne R. Polypharmacy and medicines optimisation: making it safe and sound. London: The King's Fund, 2013. Available from: http://www.kingsfund.org.uk/sites/files/kf/field/field_publication_file/polypharmacy-and-medicines-optimisation-kingsfund-nov13.pdf [Last accessed Dec 11, 2014].

10 Moynihan R, Doust J, Henry D. Preventing overdiagnosis: how to stop harming the healthy. Br Med J 2012;344:e3502. View Item.

11 McCartney M. The patient paradox: why sexed-up medicine is bad for your health. London: Printer & Martin Ltd.; 2012. View Item.

12 Mannucci PM, Nobili A; REPOSI Investigators. Multimorbidity and polypharmacy in the elderly: lessons from REPOSI. Intern Emerg Med 2014;9:723–34.View Item.
13 Diao D, Wright JM, Cundiff DK, Gueyffier F. Pharmacotherapy for mild hypertension. Cochrane Database Syst Rev 2012;8:CD006742. View Item.
14 Beckett NS, Peters R, Fletcher AE, Staessen JA, Liu L, Dumitrascu D, et al. Treatment of hypertension in patients 80 years of age or older. N Engl J Med 2008;358:1887–98.View Item.
15 National Institute for Health and Care Excellence. NICE clinical guideline 127. Hypertension: clinical management of primary hypertension in adults. Manchester: NICE; 2011. Available from: http://www.nice.org.uk/guidance/cg127 [Last accessed Jan 12, 2015].
16 National Institute for Health and Care Excellence. NICE clinical guideline 182. Chronic kidney disease: early identification and management of chronic kidney disease in adults in primary and secondary care. Manchester: NICE; 2014. Available from: http://www.nice.org.uk/guidance/cg182 [Last accessed Jan 12, 2015].
17 National Institute for Health and Care Excellence. NICE clinical guideline 101. Chronic obstructive pulmonary disease: management of chronic obstructive pulmonary disease in adults with primary and secondary care (partial update). Manchester: NICE; 2010. Available from: http://www.nice.org.uk/guidance/cg101 [Last accessed Jan 12, 2015].
18 Nannini LJ, Poole P, Milan SJ, Holmes R, Normansell R. Combined corticosteroid and long-acting-beta$_2$-agonist in one inhaler versus placebo for chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2013;11:CD003794.View Item.
19 Wells GA, Cranney A, Peterson J, Boucher M, Shea B, Welch V, et al. Alendronate for the primary and secondary prevention of osteoporotic fractures in postmenopausal women. Cochrane Database Syst Rev 2008;1:CD001155.View Item.
20 Black DM, Bauer DC, Schwartz AV, Cummings SR, Rosen CJ. Continuing bisphosphonate treatment for osteoporosis--for whom and for how long? N Engl J Med 2012;366:2051–3.View Item.
21 Peng YL, Hu HY, Luo LC, Hou MC, Lin HC, Lee FY. Aldendronate, a bisphosphonate, increased upper and lower gastrointestinal bleeding risk: risk factor analysis from a nationwide population-based study. Osteoporos Int 2014;25:1617–23.View Item.
22 Grant AM, Avenell A, Campbell MK, McDonald AM, MacLennan GS, McPherson GC, et al. Oral vitamin D3 and calcium for secondary prevention of low-trauma fractures in elderly people (Randomized Evaluation of Calcium Or vitamin D, RECORD): a randomized placebo-controlled trial. Lancet 2005;365:1621–8.View Item.
23 National Institute for Health and Care Excellence. NICE clinical guideline 181. Lipid modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease. Manchester: NICE; 2014. Available from: http://www.nice.org.uk/guidance/cg181 [Last accessed Jan 12, 2015].
24 Shepherd J, Blauw GJ, Murphy MB, Bollen EL, Buckley BM, Cobbe SM, et al. Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial. Lancet 2002;360:1623–30.View Item.
25 National Institute for Health and Care Excellence. NICE clinical guideline 177. Osteoarthritis: care and management in adults. Manchester: NICE; 2014. Available from: http://www.nice.org.uk/guidance/cg177 [Last accessed Jan 12, 2015].
26 Mercer SW, Guthrie B, Furler J, Watt GCM, Hart JT. Multimorbidity and the inverse care law in primary care. Br Med J 2012;344:e4152. View Item.
27 Smith SM, Bayliss EA, Mercer SW, Gunn J, Vestergaard M, Wyke S, et al. How to design and evaluate interventions to improve outcomes for patients with multimorbidity. J Comorbidity 2013;3:10–7.View Item.
28 Mercer SW, Gunn J, Bower P, Wyke S, Guthrie B. Managing patients with mental and physical multimorbidity. Br Med J 2012;345:e5559. View Item.
29 Salisbury CJ, Mercer SW, Fortin M. The ABC of Multimorbidity. Oxford: Wiley-Blackwell; 2014.
30 McCartney M, Treadwell J. The RCGP's new standing group on overdiagnosis. Br Med J 2014;349:g4454.View Item.