Guidelines for people not for diseases: the challenges of applying UK clinical guidelines to people with multimorbidity

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Abstract

Background: currently one of the major challenges facing clinical guidelines is multimorbidity. Current guidelines are not designed to consider the cumulative impact of treatment recommendations on people with several conditions, nor to allow comparison of relative benefits or risks. This is despite the fact that multimorbidity is a common phenomenon.

Objective: to examine the extent to which National Institute of Health and Clinical Excellence (NICE) guidelines address patient comorbidity, patient centred care and patient compliance to treatment recommendations.

Methods: five NICE clinical guidelines were selected for review (type-2 diabetes mellitus, secondary prevention for people with myocardial infarction, osteoarthritis, chronic obstructive pulmonary disease and depression) as these conditions are common causes of comorbidity and the guidelines had all been produced since 2007. Two authors extracted information from each full guideline and noted the extent to which the guidelines accounted for patient comorbidity, patient centred care and patient compliance. The cumulative recommended treatment, follow-up and self-care regime for two hypothetical patients were then created to illustrate the potential cumulative impact of applying single disease recommendations to people with multimorbidity.

Results: comorbidity and patient adherence were inconsistently accounted for in the guidelines, ranging from extensive discussion to none at all. Patient centred care was discussed in generic terms across the guidelines with limited disease-specific recommendations for clinicians. Explicitly following guideline recommendations for our two hypothetical patients would lead to a considerable treatment burden, even when recommendations were followed for mild to moderate conditions. In addition, the follow-up and self-care regime was complex potentially presenting problems for patient compliance.

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Conclusion: clinical guidelines have played an important role in improving healthcare for people with long-term conditions. However, in people with multimorbidity current guideline recommendations rapidly cumulate to drive polypharmacy, without providing guidance on how best to prioritise recommendations for individuals in whom treatment burden will sometimes be overwhelming.

Keywords: multimorbidity, elderly, family practice, clinical guidelines

Introduction

Clinical guidelines systematically bring together evidence regarding a single condition or group of related conditions, and provide recommendations for patient management based on the evidence where it exists and consensus where it does not. The implementation of clinical guideline recommendations reduces practice variation, and is associated with reduced deaths and hospitalisations [1]. These improvements have been achieved by linking guideline recommendations with financial incentives, such as the quality outcomes framework. Importantly, existing clinical guidelines largely focus on single diseases, and are usually based on evidence from highly selected populations who may not be typical of the actual population with the condition.

Currently one of the major challenges facing clinical guidelines is multimorbidity. Multimorbidity has been defined as ‘the co-occurrence of multiple chronic or acute diseases and medical conditions within one person’ [2]. Current guidelines are not designed to consider the cumulative impact of treatment recommendations on people with several conditions, nor to allow the comparison of relative benefits or risks. This is despite the fact that multimorbidity is a common phenomenon, and in older people is the norm [3–5]. Indeed, Uijen et al. [3] noted that 55% of Dutch people aged 75 and over have four or more chronic conditions.

This paper examines the application of National Institute of Health and Clinical Excellence (NICE) guidelines to people with multimorbidity and the implications for the creation of evidence and future guideline development.

Limitations of existing clinical guidelines

Existing guidelines are usually based on evidence from clinical trials carried out in relatively narrow subsets of the population. Older people have historically been systematically excluded from clinical trials, even though older people usually have the highest prevalence of chronic disease and are therefore the most likely targets of guideline recommendations [6, 7]. Trials also often exclude people with significant comorbidity, further narrowing the population studied [6, 7]. Key clinical trials in heart failure would only have included 13–25% of people with diagnosed heart failure in the community [8], with the corresponding figure for chronic obstructive pulmonary disease (COPD) being 10% [9]. Overall, 81% of randomised controlled trials published in high-impact journals excluded patients with medical comorbidities [6]. Ensuring the internal validity of trials is critical, but the external validity or generalisability of much current evidence is often relatively weak [10].

Driven by the nature of evidence and reflecting current health-care organisation, guidelines usually focus on a single condition, although most people with chronic disease have multiple conditions, and the majority of older people are multimorbid [3–5, 11, 12]. In 2005 Boyd et al. [13] examined the applicability of US clinical guidelines to older individuals with several comorbid diseases. The study reviewed clinical guidelines for nine chronic conditions to determine whether they adequately addressed the care needs of older patients with multiple comorbid diseases. The authors found that clinical guidelines rarely addressed comorbidity, and adherence to guideline recommendations in caring for an older person with multimorbidity would often lead to complex and sometimes contradictory drug and self-care regimes [13]. However, it is unclear whether the same applies in countries where guideline development is more co-ordinated, and the US study only examined guidelines for physical conditions despite physical–mental health comorbidity being common [3].

Methods

Applying NICE guidelines to people with multimorbidity

We examined the extent to which recent UK clinical guideline recommendations for five common conditions addressed care for older people, comorbidity and patient-centred care. The guidelines selected were for type 2 diabetes mellitus, secondary prevention in people with previous myocardial infarction (MI), osteoarthritis, chronic COPD and depression (two guidelines including one for managing depression in people with chronic physical problems) [14–19]. These conditions were chosen because they are common causes of morbidity and a NICE clinical guideline had been published in the past 5 years for each. The majority of people with these conditions will have significant comorbidity (71% of people with diabetes are multimorbid, 92% with coronary heart disease, 82% with osteoarthritis, 83% with COPD and 64% with depression) [2].

L.H. and B.G. extracted information from each full guideline and quick reference guide when available, which summarise the recommendations and are the documents most likely to be used by clinicians. We examined whether and how recommendations gave specific advice about care for older people or those with comorbidities, advice on providing
patient-centred care by accounting for patient choice and preferences, and advice on promoting adherence to treatment recommendations. These criteria were selected as guidelines have been noted in previous studies to be limited in relation to age-specific and multimorbidity-specific clinical recommendations, and in providing information about how patient-centred care can be achieved while following guidelines [13, 20]. In addition, despite patient adherence being recognised as a major problem, particularly in multimorbid patients, there has been limited reference on how this can be promoted in guideline recommendations [5, 13]. The authors wished to assess if UK-based guidelines had similar limitations or provided more comprehensive guidance for clinicians.

The authors noted the extent to which guidelines discussed these criteria and categorised this as none, minimal (criteria specifically noted on ≤2 occasions), moderate (criteria specifically noted on 3–5 occasions) or extensive (criteria specifically noted ≥5 occasions).

For each guideline, recommendations for chronic management were summarised for drug treatment, self-care and health service follow-up. The cumulative recommended treatment, follow-up and self-care regime for two hypothetical patients was then created to illustrate the potential cumulative impact of applying single disease recommendations to people with multimorbidities. These patients were Mrs A, a 78-year-old woman with all five conditions at mild-to-moderate severity, and Mr B, a 75-year-old man with two conditions (type 2 diabetes mellitus and COPD) at mild-to-moderate severity.

Results

Do the guidelines explicitly address age, comorbidity and patient-centred care?

All of the guidelines consider older patients to varying degrees, although usually via general statements suggesting that clinicians should consider individual drug characteristics and prescribe age-adjusted doses of relevant medications. More specific advice ranged from minimal mention of antidepressant choice in older people in the depression guideline to moderate discussion of particular recommendations in other guidelines, such as that age should not influence the offer of cardiac rehabilitation after MI. No guideline explicitly commented on the quality of the evidence in older people, or on the generalisability of trial evidence (Table 1).

Comorbidity was inconsistently accounted for in the guidelines, usually without detailed discussion. Comorbidity was most extensively addressed in the depression guidelines, which provided comprehensive advice on management in the presence of a physical condition with functional limitation and on important interactions of antidepressant drugs. Two of the physical disease guidelines provided extensive discussion for a few topics (holistic assessment in osteoarthritis and the promotion of uptake of cardiac rehabilitation in people with other conditions), but otherwise only relatively minimal comment in relation to particular treatments. Apart from the MI guideline, cross-referencing to other guidelines for important comorbidities was uncommon, and no information was provided on the relative risks and benefits of the different treatments recommended.

All the guidelines examined had a generic introduction emphasising the importance of tailoring treatment to patients’ needs and preferences. However, this generic advice was very similar across guidelines, and provided limited disease-specific recommendations for achieving patient-centred care. In addition to the generic introduction, the depression guideline extensively discussed accounting for individual preference, whereas the physical disease guidelines varied from some discussion of patient preference in relation to particular drugs (oral hypoglycaemics in the diabetes guideline) through general advice on clearly communicating risks and benefits of treatment (osteoarthritis) to no explicit discussion (MI and COPD).

In terms of adherence to treatment recommendations, the depression guideline had a moderate amount of explicit discussion of ensuring adherence to antidepressant drugs by involving patients in the decision to initiate medication, and assessing adherence in non-responders. The physical disease guidelines ranged from moderate discussion in relation to particular topics (cardiac and pulmonary rehabilitation, inhaler technique, exercise) to no explicit discussion (diabetes), although research into the relationship between treatment regime complexity and adherence was recommended by the guidelines for osteoarthritis, secondary prevention of MI and type 2 diabetes mellitus (Table 1).

Overall, there was limited accounting for age, comorbidity, patient centredness and adherence in the recommendations made by guidelines, with the depression guideline providing significantly more comprehensive guidance than the physical disease guidelines which typically only discussed these issues in relation to particular recommendations. It was unclear why these recommendations were prioritised since, for example, adherence to blood pressure lowering medication in type 2 diabetes seems likely to be problematic as adherence to oral hypoglycaemics.

Applying the guidelines to hypothetical patients

We identified guideline recommendations applicable to two patients:

- Mrs A: A 78-year-old woman with previous MI, type 2 diabetes, osteoarthritis and COPD.
- Mr B: A 75-year-old man with type 2 diabetes mellitus and COPD.

These were used to derive a treatment plan that included prescribed drugs, self-care tasks and recommended healthcare follow-up.

Mrs A: 78-year-old multimorbid woman

Our hypothetical patient with 5 mild-to-moderate diseases would be prescribed 11 medications as a minimum, with up to 10 other drugs routinely recommended, depending on the intermediate outcome control, symptoms and progression of disease. She would be advised to routinely engage in nine self-
### Table 1. Comorbidity, patient-centred care and clinical guidelines

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<tbody>
<tr>
<td>Minimal focused on antidepressant drug choice</td>
<td>Minimal focused on oral hypoglycaemic drug choice</td>
<td>Moderate but focused on cardiac rehabilitation</td>
<td>Moderate across multiple areas including smoking cessation, inhaler use, use of theophyllines, referral for surgery</td>
<td>Moderate across several areas including exercise (a core treatment for all ages), avoiding NSAIDs in older people, referral for surgery</td>
<td>Moderate across several areas including exercise (a core treatment for all ages), avoiding NSAIDs in older people, referral for surgery</td>
</tr>
<tr>
<td>Does guideline address comorbidity? (either in terms of comorbid disease or drug treatment recommended for comorbid conditions)</td>
<td>Extensive consideration of detection and management of depression in people with physical conditions with functional limitation</td>
<td>Moderate discussion of oral hypoglycaemic choice in relation to physical comorbidity, and considering the psychological impact of painful neuropathy</td>
<td>Extensive discussion of making cardiac rehabilitation accessible to people with physical and mental health comorbidities.</td>
<td>Moderate discussion of considering statin therapy in the context of comorbidities and life expectancy</td>
<td>Extensive discussion as part of holistic assessment (fitness for surgery, drug choice, falls, comorbidities compounding osteoarthritis) and role of exercise irrespective of comorbidity</td>
</tr>
<tr>
<td>Extensive discussion of antidepressant choice in relation to physical comorbidity and other drug treatment</td>
<td>Cross-referenced to depression guideline</td>
<td>Cross-referenced to depression, anxiety, dyspepsia, hypertension and heart failure guidelines</td>
<td>Cross-referenced to depression guideline</td>
<td>Recommendation to screen for depression</td>
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<tr>
<td>Does guideline explicitly discuss patient choice and preferences?</td>
<td>Generic introduction with later extensive discussion of patient and carer involvement in the decision-making</td>
<td>Generic introduction emphasising self-care, with some later discussion about patient preference with regard to hypoglycaemic agents</td>
<td>Generic introduction only</td>
<td>Generic introduction only</td>
<td>Generic introduction, with some later discussion of clearly communicating risks and benefits of treatment to patients</td>
</tr>
<tr>
<td>Does guideline explicitly discuss potential challenges to patient adherence to recommended treatments?</td>
<td>Moderate discussion of involving patients in decision to use antidepressants, and checking/addressing adherence if no response</td>
<td>None</td>
<td>Moderate discussion focused on actively promoting attendance at cardiac rehabilitation and tailoring components to individual needs</td>
<td>Moderate discussion focused on regular assessment of inhaler technique, and actively promoting attendance at pulmonary rehabilitation and tailoring components to individual needs</td>
<td>Minimal discussion focused on clinicians taking individual circumstances into account to promote exercise</td>
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care/lifestyle alterations, with others recommended under some circumstances. As well as any unplanned appointments, she would be expected to attend 8–10 routine primary care appointments for her physical conditions, 4–6 GP appointments and 8–30 psychosocial intervention appointments for her depression, and multiple appointments for smoking cessation support and pulmonary rehabilitation if she chose to accept a referral. The guideline recommendations are summarised in Table 2.

**Mr B: 75-year-old man with two conditions**

NICE guidelines recommend Mr B be prescribed five medications as a minimum, with up to eight other drugs routinely recommended depending on the intermediate outcome control, symptoms and progression of disease. He would be advised to routinely engage in six self-care/lifestyle alterations, with others recommended under some circumstances (e.g. complications associated with diabetes). As well as any unplanned appointments, he would be expected to attend five to eight routine primary care appointments for his physical conditions, three to five GP appointments and multiple appointments for smoking cessation support and pulmonary rehabilitation if he chose to accept a referral. The guideline recommendations are summarised in Table 3.
Table 3. Recommended management plan for hypothetical patient, Mr B

<table>
<thead>
<tr>
<th>Morbidities and risk factors</th>
<th>Asymptomatic type 2 diabetes with hyperglycaemia uncontrolled on diet alone, but with no microvascular complications</th>
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<tr>
<td>COPD diagnosed 7 years previously currently with moderate airflow obstruction (FEV1/FVC &lt; 0.7, FEV1 ≈ 60%) and grade 3 Medical Research Council dyspnoea scale (walks slower than contemporaries on level ground due to shortness of breath and has to stop for breath)</td>
<td></td>
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<tr>
<td>Smoking cessation medication (nicotine replacement, varenicline or bupropion)</td>
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<tr>
<th>Minimal drug treatment recommendations a</th>
<th>Metformin</th>
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<tr>
<td></td>
<td>Inhaled salbutamol</td>
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<td></td>
<td>Inhaled salmeterol</td>
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<td></td>
<td>Lisinopril</td>
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<td></td>
<td>Simvastatin</td>
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<tr>
<td>Smoking cessation</td>
<td>20–30 min daily of aerobic exercise</td>
</tr>
<tr>
<td>Local muscle strengthening exercise</td>
<td>Alcohol consumption within recommended limits</td>
</tr>
<tr>
<td>Weight loss</td>
<td>Self-monitoring of plasma glucose integrated with educational programme</td>
</tr>
<tr>
<td>Smoking cessation</td>
<td>Appropriate footwear for diabetes</td>
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<th>Self-care recommendations</th>
<th>Smoking cessation medication (nicotine replacement, varenicline or bupropion)</th>
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<tr>
<td></td>
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<td>Appropriate footwear for diabetes</td>
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<th>Follow-up recommendations</th>
<th>Annual clinical review for COPD b</th>
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<tr>
<td></td>
<td>Annual retinal screening by quality-assured digital retinal photography programme</td>
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<tr>
<td></td>
<td>3–6 monthly monitoring of HbA1c and 4–6 monthly monitoring of blood pressure</td>
</tr>
<tr>
<td></td>
<td>One-off pneumococcal and annual influenza immunisation</td>
</tr>
<tr>
<td></td>
<td>Offer referral to smoking intensive support service</td>
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<td></td>
<td>Offer referral for pulmonary rehabilitation</td>
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</tbody>
</table>

aAdditional drugs routinely recommended for more severe disease, notably if poor control of blood pressure (up to three additional drugs), HbA1c control (up to three additional drugs) and/or lipids (up to one additional drug); persistent depression despite initial treatment (initially change of drug rather than addition); progressive symptoms or reduced lung function in COPD (up to two additional inhaled drugs).

bMultiple elements requiring a stand-alone and often extended appointment and/or consultation with more than one professional.

Discussion

Cumulative impact of applying NICE guidelines

Despite examining guidelines produced by a single national organisation (NICE), our findings are consistent with a previous study examining US guidelines for physical disease [13], and are likely to apply in other countries. The cumulative impact of applying all five guidelines for Mrs A and two guidelines for Mr B was considerable, even when only recommendations for mild-to-moderate disease were considered. The treatment, self-care and follow-up regime recommended was highly complex, and would be challenging to adhere to because of the high treatment burden implied [21]. The guidelines studied did not explicitly address the treatment burden or adherence, nor provide any guidance on the relative risks and benefits of the many treatments recommended. Although NICE full evidence summaries do provide information on the risks and benefits of treatment, few clinicians will have the time or expertise to read and interpret these documents, and the information is not consistently presented to facilitate comparison. High treatment burden including polypharmacy is not intrinsically inappropriate, but particularly in people with physical frailty or limited life expectancy, better guidance on the relative risks and benefits of different treatments, and the likely time to benefit would assist clinical decision-making. Similarly, where patients have strong preferences about limiting treatment burden, particularly when treatments are primarily preventive rather than for symptoms, then such guidance would help prioritise decision-making.

Implications for the creation of evidence and future guideline development

Multimorbidity is already common, and will become more so as the population ages and survival from acute disease improves [4, 12]. Multimorbidity is strongly associated with higher mortality, poorer quality of life and functional status, and higher rates of health service use including emergency hospital admission [22, 23]. Better management of people with multimorbidity is therefore a key challenge for health-care systems internationally. Clinical guidelines have an important role to play in meeting this challenge, but are constrained by the evidence on which recommendations are based and by their current design [1, 13, 24]. Ultimately, it will always remain the clinician’s role to assimilate and review the bodies of evidence relevant to the patient in front of them and then exert their clinical judgement. Concerns have been voiced about linking guideline recommendations with targets/financial incentives and whether this might result in prescriptions being made which materially benefit the prescriber but may not be in the best interests of particular patients [25]. Clearly, clinicians do not wish to be in a situation where they have to defend every deviation from guideline recommendations in order to achieve financial targets. Nor do they wish to be the subject of complaints based around their failure to follow guideline recommendation to the letter [26, 27].
Providing summarised and comparable information about the relative
Concerted action is needed to increase the participation of older people in
Guidelines should note some specific advice for practitioners when treating
Clinical guidelines should include a small number of specific patient case
Existing guidelines should explicitly cross-reference each other when recommendations
The depression guideline provides
Secondly, clinical guidelines should include a small number
disease interactions for commonly used antidepressants.
these patient examples may also provide an opportunity for
consider as the patient ages relating, for example, to drug dose
Thirdly, action to increase the participation of
The use of clinical guidelines in health-care services
Current guidelines are largely paper based, and focus on
In caring for people with multimorbidity, what would be more helpful would be a guideline
that summarised and cross-referenced recommendations
relevant to a particular patient from all single-disease guidelines,
identifying when recommendations are synergistic, potentially risky or contradictory. Additionally, providing
summarised and comparable information about the relative
benefits and risks of different recommended treatments
would help inform prioritisation, although in the face of such
complexity, clinical judgement and careful accounting for
patient choice preferences will always be critical. Internet-
based platforms make delivering such guidelines for people
feasible, although there are considerable challenges to their
production. Although there will often be limited evidence to
underpin explicit comparison of different treatments, existing

Table 4. Recommendations for improving clinical guidelines

- Providing summarised and comparable information about the relative
  benefits and risks of different recommended treatments would help inform
  prioritisation in multimorbid patients
- Existing guidelines should explicitly cross-reference each other when
  recommendations are synergistic or contradictory, and identify high-risk
  interactions between recommended treatments and other commonly
  prescribed drugs. *This may be done in an internet-based format*
- Clinical guidelines should include a small number of specific patient case
  examples for common combinations of comorbidity seen in clinical practice
- Guidelines should note some specific advice for practitioners when treating
  older patients (e.g. drug doses or class)
- Concerted action is needed to increase the participation of older people in
  clinical trials

NICE guideline methodology already uses modelling and expert consensus to address evidence gaps, and these could
be applied to this problem. Research is needed to identify the
best way to create such guidelines for people from existing
guidelines for diseases and to evaluate their usability and use-
fulness to clinicians and patients [13, 23].

Conclusion

Clinical guidelines have played an important role in improv-
aging health care for people with long-term conditions. However, in people with multimorbidity current guideline
recommendations rapidly cumulate to drive polypharmacy,
without providing guidance on how best to prioritise recommendations for individuals in whom the treatment
burden will sometimes be overwhelming. Such prioritisation
will always require the exercise of clinical judgement and
meaningful engagement with patient preferences. Developing
guidelines for people rather than guidelines for
diseases will better ensure that treatment is in the indivi-
dual's best interests.

Key points

- The use of clinical guidelines in health-care services has helped to reduce practice variation, deaths and
  hospitalisations
- Clinical guidelines are known to be limited in their focus on single diseases and the evidence which these guidelines
  are based upon apply only to subsets of the population
- This study showed that explicitly following clinical guide-
  lines for two hypothetical patients with physical and
  mental health comorbidities produced complex treatment
  regimes with a significant risk of adverse drug reactions.
- To make clinical guidelines more applicable to patients with
  comorbidity, future clinical guidelines should provide
  practical examples of how patient-centred care can be
  achieved for a disease process. Attempts should be made
  to integrate guidelines for similar disease processes.

Conflict of interest

All the authors have completed the Unified Competing
Interest form at [www.icmje.org/coi_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (avail-
able on request from the corresponding author) and
declare that the study received no external funding and
the authors have no financial conflicts of interest to report.

Ethical approval

This study did not require NHS Research Ethics approval.
Funding

The study was not externally funded.

Provenance

L.H. is a medical student with an interest in care of the elderly and recently completed an intercalated degree in Care of Older People. M.M. is a consultant in medicine for the elderly and B.G. is a general practitioner. Both M.M. and B.G. provide care for people with complex multimorbidity, and physical and mental frailty, in whom treatment burden and balancing multiple aims are an everyday part of care. L.H. and B.G. conceived the study and conducted the guideline reviewing. L.H. led the writing of the paper, in conjunction with B.G. and M.M. B.G. is the guarantor.

References


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