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The delicate choice of optimal basic therapy for multimorbid older adults: A cross-sectional survey

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ABSTRACT

Background: Clinical practice guidelines are useful to suggest pharmacological therapies for the treatment of single chronic diseases. However, there is little guidance for multimorbidity, and specific quality measures for people with multimorbidity that can be used at a population level are lacking.
Objective: To describe what pharmacists and geriatricians consider to be an optimal basic pharmacological therapy for an older individual with type 2 diabetes (DM), chronic obstructive pulmonary disease (COPD) and heart failure (HF).
Methods: An online cross-sectional survey among 162 pharmacists and geriatricians, in Quebec, Canada, was performed. Participants were invited to choose, from a list of 32 medications or classes, the optimal basic therapy for an individual aged 65–75 years with the 3 chronic diseases. Descriptive statistics were used to calculate the median number of medications chosen and the proportions of participants who chose each medication, according to the participant's specialty. A Kruskall-Wallis test was performed to detect whether there were differences in the median number of medications recommended according to speciality.
Results: There was little consensus on the optimal basic pharmacological therapy for this hypothetical multimorbid individual, with 157 different combinations provided by the 162 participants. Nevertheless, 5 classes were chosen by at least 75% of the participants: metformin, long-acting anticholinergic agents, angiotensin-converting enzyme (ACE) inhibitors/angiotensin receptor blockers (ARBs), beta-blockers, and short-acting beta-agonists. The median number of recommended medications was 10 (interquartile range [IQR]: 6–13). There was a statistically significant difference between specialties ($p = 0.0396$). Geriatricians recommended the lower median number of medications, 7 (IQR: 5–10).
Conclusions: At least half of the participants considered polypharmacy (≥10 medications) inevitable for an optimal basic treatment of DM, COPD and HF. The heterogeneity of responses raises issues when considering quality indicators in population-based studies.

Introduction

Aging is almost unavoidably associated with the presence of multimorbidity,[1] defined as the co-occurrence of two or more diseases in a single person.[2] It has been reported that 62% of U.S. Medicare individuals aged 65–74 years live with two or more chronic diseases, while multimorbidity rises to 81.5% for individuals 85 years old and older.[3] Similarly, 65% of people aged 65–79 years in Canada report two or more chronic diseases and the proportion rises to 78% for those aged 80 years and above.[4] Considering the constant aging of the population,[5] a considerable number of individuals will live with multiple diseases for several decades.

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While clinical practice guidelines are extremely useful tools for the treatment of single chronic diseases, there is little guidance for evidence-based pharmacological therapies in multimorbidity.[6] Thus, for the treatment of individuals with complex comorbid diseases, clinicians tend to follow clinical practice guidelines for each disease. This behaviour can lead to competing or conflicting situations and increase the risk for the individuals to be exposed to an unnecessary number of medications.[6]

In terms of public health, ensuring most individuals receive the medications believed to provide the greatest benefits without causing harm can translate into substantial gains for the healthcare system. However, once again, quality indicators for pharmacological treatments or prescription use, which are markers of quality of care, often rely on individual diseases. They may prove inadequate for the ever-increasing number of individuals suffering from multimorbidity, especially in the older population.

To the best of our knowledge, no studies have explored the complex topic of managing multimorbidity in terms of pharmacological treatments in older adults at a population level. Therefore, it is worthwhile to examine how different healthcare professionals address multimorbidity in a hypothetical older individual. The objective of this study was to investigate what pharmacists and geriatricians consider to be an optimal basic pharmacological therapy of a multimorbid person—that is, the basic therapy most individuals would need in a population-based point of view. Specifically, the study aimed to describe the professional opinion of pharmacists and geriatricians on the optimal basic therapy for an older individual (65–75 years old) affected by 3 diseases: type 2 diabetes (DM), chronic obstructive pulmonary disease (COPD) and heart failure (HF).

Methods

Ethics

This study was approved by the Ethical Committee of the *CHU de Québec—Université Laval* (project 2017–3274).

Study design

A cross-sectional Internet-based survey was performed between October 2016 and April 2017 to determine which medications should be included in the basic treatment of an older individual with the 3 chronic diseases.

Survey participants

Pharmacists and geriatricians in the Canadian province of Quebec were invited to respond to the online survey. Pharmacists were targeted because of their expertise with medications. Geriatricians were regarded as an interesting comparative group, as their area of expertise is the global health of older people, without focusing exclusively on medications.

First, a link to the survey was sent to all pharmacists of the Quebec College of Pharmacists through the College's newsletter (*L'Express*) in December 2016. The College of Pharmacists also provided us with the list of pharmacists who have agreed to be contacted for research purposes. A random selection of 1000 pharmacists among the 5421 pharmacist members was performed. An invitation to participate in the survey was mailed in February 2017, providing the selected pharmacists with the Internet link written in the letter. The pharmacists were also offered the opportunity to write an e-mail to the researchers so the link would be provided by e-mail. Geriatricians were recruited with the help of the Geriatrician association of Quebec through the organisation's e-mailing list. An e-mail invitation to the 90 geriatricians was sent in February 2017. A pharmacist and a geriatrician, separately and on their own initiative, also forwarded the survey link in a Facebook group of pharmacists and geriatricians of Quebec, respectively, in March 2017. Finally, personal contacts were invited to take part in the survey, either by e-mail or by phone.

Survey

The survey was created using the Survey Monkey platform (https://www.surveymonkey.com). The survey presented the hypothetical case: an individual aged 65–75 years with 3 chronic diseases, DM, COPD and HF. These comorbidities were chosen because they can pose significant clinical challenges: their management may include an important number of medications, potential medication-medication interactions and medication-disease interactions. No clinical information was provided as the purpose of the survey was to obtain a professional opinion on an optimal basic pharmacological therapy that would be acceptable at a population level, with the use of administrative data that lack such clinical details. The participants were asked to choose from a list of 32 medications or medication classes approved for use in the treatment of the 3 chronic diseases. All medications either approved or used in Canada for the treatment of the 3 diseases were included (appendix 1). The participants were invited to comment on their answers as needed. Finally, the participants were asked to provide information on their professional background, by selecting the appropriate category (community pharmacist; hospital pharmacist [specialized in geriatrics]; hospital pharmacist [not specialized in geriatrics]; geriatricians; other).

No nominal or sensitive data were collected; the participants provided only their professional opinion. Participants had also been advised that the data would be stored in the United States. The participants were offered the possibility to receive the survey results once the consultation process terminated. Those participants who provided their e-mail at the end of the survey received a summary of the results in May 2017.

Analysis

Descriptive statistics were used to evaluate the number and proportions of responders who chose each of the individual medications and classes of medications, according to their specialty. The number of medications chosen by each participant (and according to their specialty) was also calculated. Then the median number of medications chosen, with the interquartile range [IQR] was established. A Kruskall-Wallis test was performed to detect whether there were differences in the median number of medications recommended according to speciality. Finally, the number of different overall treatments the participants recommended was determined.

In order to evaluate the quality of suggested optimal basic pharmacological treatments, information about medication-medication interactions involving the 32 medications or classes of medications listed in the survey was collected. The analysis was based on Micromedex® Solutions data. The evaluations were restricted to contraindicated interactions as defined by Micromedex, as they represent the most serious interactions that must be avoided because of their significant likelihood of important clinical consequences. The number of responders who chose at least 2 medications or classes of medications being part of a contraindicated interaction was analysed.

All quantitative analyses were performed with SAS, version 9.4.1 (SAS Institute, Inc., Cary, NC).

Qualitative content analysis was used to interpret comments the participants entered at the end of the survey. The aim of the qualitative analysis was to identify what consideration had driven or influenced the choice of medications. Simple content analysis was performed by one researcher (CS), with major themes identified to explicit what elements played a role in the decisions. An inductive approach was privileged, and the themes were identified at a semantic (explicit) level. The following phases were done: 1) familiarization with the data; 2) generation of initial codes; 3) search for themes; 4) review of themes; 5)

naming of themes; 6) selection of quotes particularly illustrative of the identified themes.[7]

Results

A total of 162 responses to the online survey was received. Among the participants, 92 (56.8%) were community pharmacists, 43 (26.5%) were hospital pharmacists (including 12 specialized in geriatrics), and 17 (10.5%) were geriatricians. The participation rate was similar for pharmacists and geriatricians, 13.5% and 18.9%, respectively (135 out of 1000 pharmacists selected and 17 out of 90 geriatricians of the province of Quebec).

There was very little consensus on the optimal basic therapy for an older individual suffering from DM, COPD and HF. Indeed, 157 different combinations of medications were chosen by the 162 responders among the list of 32 medications or classes. The 92 community pharmacists chose 90 different combinations. For the hospital pharmacists without specialization in geriatrics, 31 combinations out of 43 responders were calculated, while 12 combinations were obtained out of 12 responders for the hospital pharmacists specialized in geriatrics. Finally, the 17 geriatricians reported 17 different combinations.

Nevertheless, as summarized in Fig. 1, 5 medications or classes were chosen by at least 75% of respondents. Three medications or classes (metformin, long-acting anticholinergic agents and angiotensin-converting enzyme [ACE] inhibitors/angiotensin receptor blockers [ARBs]) were chosen by at least 90% of participants. The 2 others chosen by at least 75% of the participants were beta-blockers and short-acting beta-agonists.

The median number of medications considered to be part of an optimal therapy was 10 (interquartile range [IQR]: 6–13). Geriatricians recommended a median of 7 (IQR: 5–10) medications; community pharmacists suggested a median of 10 (IQR: 7–13) medications, hospital pharmacists without a specialization in geriatrics also recommended a median of 10 (IQR: 8–10) medications while hospital pharmacists specialized in geriatrics suggested a median of 10.5 (IQR 8–16) medications. There were statistically significant differences in the median number of medications chosen according to the specialty of the participant ($p = 0.0396$).

A proportion of 21.6% participants chose at least two medications or classes of medications that should not be prescribed together because of a contraindicated interaction. In a subgroup analysis performed according to the specialty of the responder, similar proportions of participants including a contraindicated combination were found among pharmacists (26.1% of community pharmacists, 19.3% of hospital pharmacists not specialized in geriatrics, 25.0% of hospital pharmacists specialized in geriatrics). None of the 17 geriatricians choose two contraindicated medications together (Table 1).

The content analysis performed with the comments provided by 65 participants yielded two major themes in relation to the choice of medications. The first theme involved the clinical aspects of the decisions and included three subthemes: the difficulty of identifying relevant medications without clinical data; the importance of evidence-based information to orientate the decisions; and the consideration of medication-disease interactions. The second theme referred to financial and organisation aspects, notably the role of reimbursement in the choice of the optimal therapy.

Theme 1: Clinical aspects of the decisions

Subtheme 1: Participants commented on the difficulty of determining which medication is appropriate without clinical data:

"*It is difficult to establish the optimal treatment because we don't*

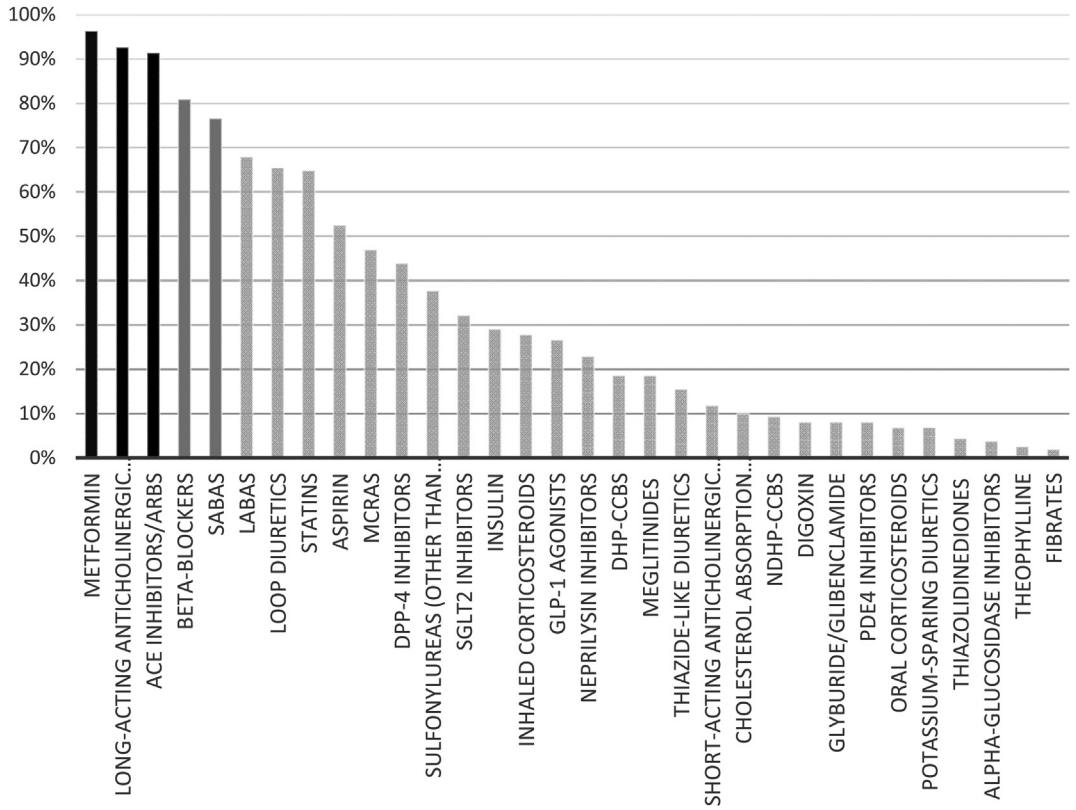

Fig. 1. Proportion of responders who included the medication or medication classes in their optimal basic therapy.
ACE: Angiotensin-Converting-Enzyme; ARBs: Angiotensin II Receptor Blockers; DHP-CCBs: DiHydroPyridine Calcium Channel Blockers; DPP4: DiPeptidyl Peptidase-4; GLP-1: Glucagon-Like Peptide-1; LABAs: Long-Acting Beta-Agonists; MCRAs: MineraloCorticoid Receptors Antagonists (Antimineralocorticoids); NDHP-CCBs: Non-DiHydroPyridine Calcium Channel Blockers; PDE4: PhosphoDiEsterase-4; SABAs: Short-Acting Beta-Agonists; SGLT2: Sodium/Glucose coTransporter 2.

Table 1
Contraindicated interactions mentioned by responders according to their specialty.

Type of Contraindicated interaction	Specialty of the responder					
	All specialties (N = 162)	Community pharmacist (N = 92)	Hospital pharmacist non-specialized (N = 31)	Hospital pharmacist specialized in geriatrics (N = 12)	Geriatrician (N = 17)	Other or non-disclosed (N = 10)
ACE inhibitors— [ARBs/Neprilysin inhibitors]	31 (19.4%)	21 (22.8%)	6 (19.4%)	2 (16.7%)	0 (0.0%)	2 (20.0%)
Antimineralocorticoid— Potassium-sparing diuretics	9 (5.6%)	7 (7.6%)	0 (0.0%)	2 (16.7%)	0 (0.0%)	0 (0.0%)
Fibrates—Meglitinides	2 (1.2%)	1 (1.1%)	0 (0.0%)	1 (8.3%)	0 (0.0%)	0 (0.0%)
Fibrates—Statins	2 (1.2%)	1 (1.1%)	0 (0.0%)	1 (8.3%)	0 (0.0%)	0 (0.0%)
At least one of the above combinations	35 (21.6%)	24 (26.1%)	6 (19.4%)	3 (25.0%)	0 (0.0%)	2 (20.0%)

necessary know how severe the disease is (COPD, heart failure), how the patient responds to treatment (Type 2 diabetes controlled with metformin only?), how is the renal function and other factors (left ventricular ejection fraction?)" (#78)

Accordingly, some participants mentioned what medications they would add, provided the individual presented distinct clinical characteristics, considering one disease at a time:

"Heart failure: in addition to ACEI / ARB, ASA, b-blocker and statin we can consider loop diuretic if symptomatic. Potassium sparing diuretic if functional class II / IV or post-infarction. Aldosterone antagonist if functional class III-IV / IV (if kaliemia allows it). Digoxin may be added if [patient] remains symptomatic despite treatment above. Diabetes: metformin or dpp4 inhibitor in first line. Others as needed ad insulin. (…) COPD: at least short-acting beta-agonist prn. According to symptoms consider long-acting beta-agonist and long-acting anticholinergic. Inhaled cortico if moderate to severe symptoms with frequent exacerbations." (# 140)

Other clinical conditions particular to older individuals were also mentioned, such as physical or mental characteristics:

"Cognitive state provides required information to optimize the pharmacotherapy" (#61).

Nonetheless, the possibility to identify the essential medications to add to the pharmacological profile remained present:

"The medications listed are the bare minimum, that is, those that I deem necessary in first intention to treat the comorbidities mentioned, those that seem absolutely necessary. Many of the other medications may be appropriate in the case of a poorly controlled or progressive disease, or according to various symptoms that may or may not occur in the course of the disease or even according to the cause of heart failure, for example." (#138)

Subtheme 2: Clinical practices guidelines for each individual disease appeared to be of utmost importance in the choice of treatments for participants, explicitly or implicitly. Many participants explained their choices by providing the list of medications they picked for each of the 3 diseases:

"I used the clinical guidelines that I knew. For COPD, I chose (…)" (#29)

"Diabetes: metformin is the first-line medication with very low risk of hypoglycemia which is often problematic with old people. (…) COPD: LAAC is firs-line medication for moderate to severe COPD plus SABA prn. Heart failure: for those with low ejection fraction, beta-blockers and ACE-I are first-line treatments. Adding an aldosterone antagonist is also recommended according to the recent clinical guidelines." (#63)

Furthermore, specific consensus guidelines for older adults, such as lists of potentially inappropriate medications such as Beer's criteria, also influenced the choice of medications:

"*Avoid digoxin for older people (Beers).*" (#84)

Subtheme 3: The case provided the opportunity to balance the benefits and the risks of various treatments according to the diseases treated. Drug-disease interactions played a role in the participants' choice of pharmacological combinations.

"If it is a decompensated HF, considering their nephroprotective effects in type 2 DM, I would put this patient under ACEI/ARB only; I would not add beta-blockers because they are contra-indicated in COPD. However, if I have a decompensated HF and a mild COPD, the benefits of beta-blockers in HF would overcome the risks in COPD." (#38)

"The principal criterion was efficacy on health outcomes for the disease without negative impacts on the other diseases" (#88)

"I know that in theory metformin should be avoided in heart failure, but in practice, we use it anyway" (#8).

Theme 2: Financial and organisational aspects

Participants mentioned that costs and reimbursement issues had to be taken into account when choosing a combination of medications. Older people in the province of Quebec are insured through the universal public health plan (RAMQ). However, some medications are not reimbursed under the plan and therefore, the choice of certain treatments may be limited because costs become an issue:

"Coverage by the public health care insurance plan is always a concern for older people, unless they have private insurance plans that are very comprehensive." (#61)

"For SLGT-2 inhibitors, the patient must fulfill the reimbursement criteria. Idem for Entresto." (#2)

"Entresto is an excellent choice, but expensive and not covered by the RAMQ." (#79)

Discussion

From a population-based perspective, the results show that there is no clear consensus on what an optimal basic pharmacological therapy should include for an older individual suffering from DM, COPD and HF. The number of medications comprised in suggested therapies proved elevated for many participants, making polypharmacy inevitable most of the time. Pharmacists, both in community and hospital settings, tended to recommend more medications than geriatricians.

Many chronic diseases necessitate a combination of pharmacological therapies in order to achieve guideline-recommended treatment goals. The treatments of the 3 targeted diseases are particularly prone to the use of many medications. To our knowledge, there is no specific data on the mean number of medications those individuals with the 3 chronic diseases might use, but it is likely to be elevated.

Most first-line medications recommended in individual guidelines were chosen by the participants. According to the Canadian clinical guidelines in DM, metformin, which 96.3% of respondents identified, should be the first antidiabetic medication to be initiated.[8] Similarly, ACE inhibitors/ARBs are recommended both for DM and HF[9–11] and were included in the optimal basic therapy by 91.4% of participants. Optimal therapy for HF should also include a beta-blocker according to guidelines.[10,11] Those were chosen by 80.9% of participants. On the other hand, nondihydropyridine calcium channel blockers are not recommended in the treatment of HF with low left ventricular ejection fraction and can be harmful.[12] Nonetheless, they were included in the optimal basic therapy by 9.3% of participants. Regarding COPD, medications chosen by a larger proportion of participants are inhaled long-acting anticholinergic agents (92.6%), inhaled short-acting beta-agonist (76.5%) and inhaled long-acting beta-agonist (67.9%). In fact, according to COPD Canadian guidelines and the Global Initiative for Chronic Obstructive Lung Disease, optimal therapy of stable COPD should include long-acting anticholinergic agents or long-acting beta-agonists in monotherapy or a combination of these agents.[13,14] Short-acting beta-agonists are recommended in the acute treatment of COPD exacerbation.[13,14]

Treating older individuals according to guidelines is hard enough for single diseases; it proves a complex task when it comes to treating them at once in one individual. As Hugues et al. noticed, clinical guidelines often drive to polypharmacy and provide little guidance on how to prioritize recommendations for multimorbid individuals.[15] According to U.S. clinical practice guidelines, an individual aged 45–54 years with 3 chronic diseases among hypertension, DM, coronary heart diseases, COPD, osteoarthritis and depression, would take from 6 to 13 medications per day.[16] Furthermore, reviewing recommendations from 12 national clinical guidelines, Dumbreck et al. concluded that following guidelines would result in potentially serious medication-medication interactions.[17] Moreover, the concomitant use of first-line medications with opposite actions (e.g. beta-blockers for HF and beta-agonists for COPD) may result in a loss of efficacy for both treated diseases. Some of the participants did acknowledge such facts. Establishing the balance between efficacy and side effects is often challenging, and may need to be individualized in many circumstances, depending on the severity of the diseases, the life expectancy and the overarching goals of treatment.

In fact, as stated earlier, the participants commented on the difficulty of determining which medication is appropriate without clinical data. There was indeed no clinical information provided because the aim was to determine what a basic pharmacological treatment should be for a majority of individuals, the so-called “must have” treatments for most individuals, regardless of the severity or the course of the disease. The overarching intent was to be able to build indicators of optimal polypharmacy that can be used at a population-based level, using administrative data that do not contain such clinical information. However since the participants were clinicians, it is understandable that there is a gap between the study request and their professional practice, which makes the process of choosing much less tangible. Hence, the survey indicates how difficult the creation of quality of care measures for this population is, when information about the severity of diseases or patients' goals is not available. The contribution of the patient in the process of medication selection was seldom mentioned by the participants. It may be troubling that this element did not emerge as a distinct theme, as the process would ensure treatment is aligned with the patient's expectations and goals. However, some participants may not have mentioned it because the overarching goal was to identify medications that would benefit most individuals in the population, therefore individualization of therapy was not possible under this perspective.

Striking differences were observed between the number of medications that pharmacists and geriatricians recommended. The visions of pharmacists with different trainings and geriatricians could be further explored, for example in focus group, to identify the underlying reasons that led to these differences. The discrepancy may stem from the fact that pharmacists are trained to treat diseases, while geriatricians may have a more holistic point of view of the individuals. It was previously shown that physicians were inclined to deprescribe more medications than pharmacists,[18] which tend to support the fact that pharmacists and physicians may have diverging views regarding optimal medication regimens. In fact, pharmacists tended to justify their choices in citing guidelines and recommendations, which may result in using more treatments.

The number of contraindicated interactions reported in the optimal therapies suggested by the participants is not negligible. A proportion of 20% of participants included both ACE inhibitors and the combination neprisilyn inhibitor-ARB in their proposed optimal basic therapy. This should be avoided because the dual blockade provided by the concurrent use of an ACE inhibitor and ARBs is not recommended and the use of ACE inhibitors with the combination neprisilyn inhibitor-ARB may result in an increased risk of angioedema.[19,20] On the one hand, the real proportion of people who would recommend using the two together may have been overestimated. Indeed, it seems that some people checked all medications that would be possible to use, without considering their concomitant use. Nevertheless, no geriatricians checked this combination of contraindicated medications or classes. On the other hand, it may also be the result of considering each disease individually when determining the optimal treatment: while the neprisilyn inhibitor would be included for HF (although only for severe cases), the ACE inhibitors could have been judged appropriate for DM for example, without realizing their concomitant use would be contraindicated. As such, this result may demonstrate the complexity of treating an individual with various diseases for whom the treatments may not have the same benefits as for the population without these comorbidities.

The study did not yield a result that could be translated into specific indicator(s) to perform polypharmacy surveillance at a population level. The challenge in creating such indicators is important because the indicators have to be applied to undifferentiated data as the one provided in the case, and therefore do not account for the individualized treatment of patients. Nonetheless, such indicators would be helpful to evaluate quality of care and ensure that older individuals with multimorbidity benefit from a standard basic pharmacological treatment. Although no consensus emerged from our consultation, there were still a number of medications that elicited a high proportion of agreement, which may indicate that further steps, including discussions and consultations among experts, may end up in consensus decisions. However, considering the importance evidence-based data had in the participants' decisions, it appears essential that more data on the impact of medications in the context of multimorbidity be acquired. Well-conducted population-based studies, in real-life care settings, could notably provide interesting bases for supporting decisions and guiding the opinions of experts.

The study has several strengths. It included both pharmacists from hospital and community settings and geriatricians with a comparable participation rate between specialties, making a comparison of professional background and clinics possible. Although the study did not include a formal discussion, 65 participants (40%) provided comments and rationale for choosing specific medications or combinations. This clearly enriched the analysis by providing deeper comprehension of the participants’ decisions.

The study presents some limitations. First, only 15% of the total number of participants contacted were reached, although different solicitation methods were used to achieve a high response level. Nonetheless, we believe that the study still provides valuable information, because it did not seek personal opinion, but professional perspective, which is mostly influenced by training received rather than personal experience. Furthermore, considering the wide variety of responses obtained, it is unlikely that a larger number of respondents would have generated less heterogeneity. Although responses were

compared according to professional roles, other potential modifiers (e.g. number of years of experience, rural/urban settings of practice, training university) were not assessed. Finally, no post-hoc analysis was performed following Kruskall-Walis tests to identify where lied the specific differences between disciplines.

Other limitations of the study include the fact that the lack of clinical details may have led to misunderstandings. For example, the non-specific use of HF may have cause misinterpretations, because the pharmacological treatment may differ according to the type of HF. Indeed, non-dihydropyridine calcium channel blockers are not contra-indicated in HF with preserved ejection fraction, which could explain why some of the participants chose this class of medications. Also, some participants did not fully understand the questionnaire. Some of them claimed that the directives were vague. However, they answered as expected by choosing medications that would be first-line therapy for the three diseases, which suggests that the vagueness was rather linked to the lack of specific clinical details. Others appear to have checked all cases that could apply. Such behaviour obviously overestimates the number of medications included in an optimal therapy. Interestingly, participants often explained in the comments part why they would add medications, but rarely explicitly mentioned that they would take medications off. The overarching trend was therefore towards poly-pharmacy.

Conclusion

All in all, most of the participants considered polypharmacy ($\geq$10 medications) inevitable for an optimal basic treatment of DM, COPD and HF. The difficulty reaching a clear indication of an optimal basic therapy for multimorbidity raises issues when considering quality indicators in population-based studies. Indeed, the concept of appropriate polypharmacy is still to be defined. This concept needs to incorporate a holistic view of older adults rather than individual diseases.

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Conflicts of interest

The authors have no other conflict of interest to declare.

Meetings

Results were presented at the European Drug Utilisation Research Group (EuroDURG) Conference 2017 at Glasgow, United Kingdom.

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Appendix A. Supplementary data

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References

1. Marengoni A, Angleman S, Melis R, et al. Aging with multimorbidity: a systematic review of the literature. *Ageing Res Rev.* 2011;10(4):430–439. https://doi.org/10.1016/j.arr.2011.03.003.
2. Formiga A, Ferrer A, Sanz H, et al. Patterns of comorbidity and multimorbidity in the oldest old: the Octabaix study. *Eur J Intern Med.* 2013;24(1):40–44. https://doi.org/10.1016/j.ejim.2012.11.003.
3. Salive ME. Multimorbidity in older adults. *Epidemiol Rev.* 2013;35:75–83. https://doi.org/10.1093/epirev/mxs009.
4. Public Health Agency of Canada. *The Chief Public Health Officer's Report on the State of Public Health in Canada 2010: Growing Older - Adding Life to Years.* 2010; 2010.
5. Institut de la statistique du Québec. *Le bilan démographique du Québec. Édition 2016.* Gouvernement du Québec; 2016.
6. Boyd CM, Darer J, Boult C, Fried LP, Boult L, Wu AW. Clinical practice guidelines and quality of care for older patients with multiple comorbid diseases: implications for pay for performance. *J Am Med Assoc.* 2005;294(6):716–724.
7. Braun V, Clarke V. Using thematic analysis in psychology. *Qual Res Psychol.* 2006;3(2):77–101. https://doi.org/10.1191/1478088706qp063oa.
8. Harper W, Clement M, Goldenberg R, et al. Canadian diabetes association 2013 clinical practice guidelines for the prevention and management of diabetes in Canada: pharmacologic management of type 2 diabetes. *Can J Diabetes.* 2013;37(Suppl 1):S61–S68. https://doi.org/10.1016/j.jcjd.2013.01.021.
9. Howlett JG, MacFadyen JC. Canadian diabetes association 2013 clinical practice guidelines for the prevention and management of diabetes in Canada: treatment of diabetes in people with heart failure. *Can J Diabetes.* 2013;37:S126–S128. https://doi.org/10.1016/j.jcjd.2013.01.036.
10. Ezekowitz JA, O'Meara E, McDonald MA, et al. Comprehensive update of the canadian cardiovascular society guidelines for the management of heart failure. *Can J Cardiol.* 2017;33(11):1342–1433. https://doi.org/10.1016/j.cjca.2017.08.022.
11. Yancy CW, Jessup M, Bozkurt B, et al. ACC/AHA/HFSA focused update of the 2013 ACCF/AHA guideline for the management of heart failure: a report of the american College of cardiology/american heart association task force on clinical practice guidelines and the heart failure society of America. *J Card Fail.* 2017;23(8):628–651. https://doi.org/10.1016/j.cardfail.2017.04.014.
12. Yancy CW, Jessup M, Bozkurt B, et al. ACCF/AHA guideline for the management of heart failure: a report of the american College of cardiology foundation/american heart association task force on practice guidelines. *J Am Coll Cardiol.* 2013;62(16):e147–239. https://doi.org/10.1016/j.jacc.2013.05.019.
13. Bourbeau J, Bhutani M, Hernandez P al. CTS position statement: pharmacotherapy in patients with COPD – an update. *Can J Resp Crit Care Sleep Med.* 2017;1(4):222–241. https://doi.org/10.1080/24745332.2017.1395588.
14. Vogelmeier CF, Criner GJ, Martinez FJ, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive Lung disease 2017 report: GOLD executive summary. *Arch Bronconeumol.* 2017;53(3):128–149. https://doi.org/10.1016/j.arbres.2017.02.001.
15. Hughes LD, McMurdo ME, Guthrie B. Guidelines for people not for diabetes: the challenges of applying UK clinical guidelines to people with multimorbidity. *Age Ageing.* 2013;42(1):62–69. https://doi.org/10.1093/ageing/afs100.
16. Buffel du Vaure C, Ravaud P, Baron G, Barnes C, Gilberg S, Boutron I. Potential workload in applying clinical practice guidelines for patients with chronic conditions and multimorbidity: a systematic analysis. *BMJ Open.* 2016;6(3):e010119. https://doi.org/10.1136/bmjopen-2015-010119.
17. Dumbreck S, Flynn A, Nairn M, et al. Drug-disease and drug-drug interactions: systematic examination of recommendations in 12 UK national clinical guidelines. *BMJ.* 2015;350:h949. https://doi.org/10.1136/bmj.h949.
18. Page AT, Etherton-Beer CD, Clifford RM, Burrows S, Eames M, Potter K. Deprescribing in frail oder people – do doctors and pharmacists agree? *Res Soc Adm Pharm.* 2016;12(3):438–449. https://doi.org/10.1016/j.sapharm.2015.08.011.
19. Messerli FH. The sudden demise of dual renin-angiotensin system blockade or the soft science of the surrogate end point. *J Am Coll Cardiol.* 2009;53(6):468–470. https://doi.org/10.1016/j.jacc.2008.10.036.
20. Fala L. Entresto (Sacubitril/Valsartan): first-in-class angiotensin receptor neprilysin inhibitor FDA approved for patients with heart failure. *Am Health Drug Benefits.* 2015;8(6):330–334.