

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Barriers and facilitators to deprescribing of cardiovascular medications: a systematic review
<b>AUTHORS</b>	Brunner, Laureline; Rodondi, Nicolas; Aubert, Carole

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Vander Stichele, Robert Universiteit Gent, Unit of clinical Pharmacology
<b>REVIEW RETURNED</b>	30-Mar-2022

<b>GENERAL COMMENTS</b>	<p>This is a systematic review of qualitative and quantitative studies on barriers and facilitators of deprescribing, focussing on cardiovascular medications.</p> <p>The review is well conducted according to PRISMA guidelines, and well reported. The data extraction and analysis is well performed and represented in the result tables. The discussion is a profound comparison of the results with existing literature and a useful overview for researchers designing future interventions in the field. The conclusions are within the limitations of the study.</p> <p>The authors rightly advocate the need for approaching deprescribing in a framework of shared-decision making with patients and proxies, providing the topics to explore and discuss during such interactions.</p>
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<b>REVIEWER</b>	Zimmerman, Kirstin Virginia Commonwealth University School of Pharmacy, Pharmacotherapy and Outcomes Sciences
<b>REVIEW RETURNED</b>	04-Apr-2022

<b>GENERAL COMMENTS</b>	<p>There are a plethora of systematic reviews published within the past year or two and that may make the reader weary to read yet another. I'd love for yours to stand out. While the comparison/contrast of themes is nice, I would really like this team to consider reframing the work to add a quantitative component of frequency (e.g. what are the most common barriers/facilitators referenced) as this otherwise feels like confirmation of what is already known and the addition to the body of literature (impact) feels low. I'd rather hear about "what is the resounding theme" that may indicate the greatest impetus to address. Alternatively, I feel that this work would be well suited for a "call to action" paper, rather than a strict reporting of outcomes. I recognize that these are additional workload burdens, but we are often so focused on bringing our work to publication that we forget how to maximize the impact of our work. If you elect not to reframe the paper or add a quantitative component, please do consider the following:</p> <p>--Your results section often cites "some patients", "many patients</p>
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	<p>and one GP even stated” which often sounds quantitative. If you do not want to take the route of addressing frequency, please be clear that “in one study of x, many patients...”</p> <p>--Table 4: Legend is quite confusing with the normal/italic/bold. I know it makes the table huge, but might be worth considering breaking out the components for readability.</p> <p>--Table 4: What does this mean, “ADEs foster deprescribing discussion with HCP” in context as a patient barrier?</p> <p>--Table 4: Under “Influences” category, consider reordering “(QOL improvement, no stroke, restart medication, stroke)” to be consistent with the prior formatting (normal &gt; italic); same with “Dose-lowering scheme; close monitoring; Time constraints” under “Processes” category if you DO keep the normal/italic/bold formatting.</p> <p>--Table 4: In your "Appropriateness" text, you state, “Patient and HCP agreement or disagreement with appropriateness of CVM deprescribing were based on three main themes: CVM necessity, CVM benefit, and ADE occurrence” but Table 4 lumps these all together. Consider if it’s more impactful to delineate these for the reader.</p> <p>These types of reviews are a lot of work, and I commend you on a paper well executed and written. I encourage you to consider the reflections above and to make the best decision for your research team. Thanks for the opportunity to review.</p>
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**VERSION 1 – AUTHOR RESPONSE**

	Reviewer’s comment	Authors’ answer
Reviewer 1	1	<p>The review is well conducted according to PRISMA guidelines, and well reported. The data extraction and analysis is well performed and represented in the result tables. The discussion is a profound comparison of the results with existing literature and a useful overview for researchers designing future interventions in the field. The conclusions are within the limitations for the study.</p> <p>The authors rightly advocate the need for approaching deprescribing in a framework of shared-decision making with patients and proxies,</p>
		We are glad that the reviewer appreciated our work.

		providing the topics to explore and discuss during such interactions.	
Reviewer 2	1	<p>There are a plethora of systematic reviews published within the past year or two and that may make the reader weary to read yet another. I'd love for yours to stand out. While the comparison/contrast of themes is nice, I would really like this team to consider reframing the work to add a quantitative component of frequency (e.g. what are the most common barriers/facilitators referenced) as this otherwise feels like confirmation of what is already know and the addition to the body of literature (impact) feels low. I'd rather hear about "what is the resounding theme" that may indicate the greatest impetus to address.</p> <p>Your results section often cites "some patients", "many patients and one GP even stated" which often sounds quantitative. If you do not want to take the route of addressing frequency, please be clear that "in one study of x, many patients..."</p> <p>Alternatively, I feel that this work would be well suited for a "call to action" paper, rather than a strict reporting of outcomes.</p>	<p>Thank you for this constructive comment. We reconsidered our presentation of the results, and added a quantitative component to our thematic analysis to quantify how frequently the barriers and facilitators were mentioned by patients, informal caregivers and/or healthcare providers throughout the articles included in the review. We mention this additional component in the methods (<b>page 6, lines 138-140</b>), and reframed our result section accordingly (<b>pages 13-14, lines 192-205; page 18, lines 217-219; page 19, lines 233-235; page 21, lines 269-272 &amp; line 279; page 22, lines 294-296; page 23, lines 323-324 &amp; lines 335-336</b>). We added a table describing the frequency of reporting of each category/theme (<b>Table 3</b>). To keep with the journal guidelines, we merged previous Tables 1, 2 and 3 into one table (<b>Table 1</b>).</p> <p>This additional quantitative component enabled us to identify subtle differences between healthcare provider and patient/informal caregiver barriers and facilitators, which we addressed in the discussion (<b>page 25, lines 366-378; page 26, lines 394-406; page 27, lines 419-426</b>). We think that the discussion now better reflects the differences between patient/informal caregiver and healthcare provider barriers and facilitators, as well as the differences in the needs for future actions. Finally, while keeping the original structure of our article, we added a paragraph on implications, to call for actions needed to address 1) the lack of evidence on the risks and benefits of deprescribing that exists for some cardiovascular medications, and 2) the need for deprescribing tools and strategies for healthcare providers to adequately convey the risks and benefits of deprescribing to patients (<b>page 29, lines 469-485</b>). We shortened the conclusion accordingly (<b>page 29, lines 487-492</b>).</p>
	2	Table 4: Legend is quite confusing with the normal/italic/bold. I know it makes the table huge, but it might be	We reformatted <b>Table 2</b> (previous Table 4) accordingly. The components are now displayed by barriers or facilitators, and at patient and/or informal caregiver and/or healthcare provider level,

		worth considering breaking out the components for readability.	respectively. We deleted Supplementary Table S3 as it was similar to Table 2.
	3	Table 4: Under “Influences” category, consider reordering “(QOL improvement, no stroke, restart medication, stroke)” to be consistent with the prior formatting (normal > italic); same with “Dose-lowering scheme; close monitoring; Time constraints” under “Processes” category if you DO keep the normal/italic/bold formatting.	Given the reformatting of <b>Table 3</b> (previous Table 4, see answer to comment number 2 of Reviewer 2), we did not need to address this point.
	4	Table 4: In your "Appropriateness" text, you state, “Patient and HCP agreement or disagreement with appropriateness of CVM deprescribing were based on three main themes: CVM necessity, CVM benefit, and ADE occurrence” but Table 4 lumps these all together. Consider if it's more impactful to delineate these for the reader.	We added the three themes that are mentioned in the text to the “Appropriateness” category of <b>Table 3</b> (previous Table 4).
	5	Table 4: What does this mean, “ADEs foster deprescribing discussion with HCP” in context as a patient barrier?	This item was meant as a facilitator and not a barrier, which might have been confusing with the previous format of <b>Table 3</b> (previous Table 4). We hope that this is clearer in the new format of the table. We clarify that in the text as well ( <b>page 21, paragraph 3.3.1.3, lines 260-261</b> ).

**VERSION 2 – REVIEW**

<b>REVIEWER</b>	Zimmerman, Kirstin Virginia Commonwealth University School of Pharmacy, Pharmacotherapy and Outcomes Sciences
<b>REVIEW RETURNED</b>	24-Jun-2022
<b>GENERAL COMMENTS</b>	Thank you for the hard work revising this paper. There are still some

	<p>recommendations listed here to optimize this paper.</p> <ul style="list-style-type: none"> <li>• There is limited reporting of characteristics of papers in your text— would be worth mentioning the number of studies (number of studies total, number in HCPs, etc.). Maybe include some of the highlights from the characteristics table.</li> <li>• Quantification of necessity, benefit, ADE, fear, dislike, previous experience, social influences, etc. For example, change (line 260-261) “CVM dislike was one of the most common facilitators to deprescribing for patients and informal caregivers, but not for HCPs” to “CVM dislike was a facilitator to deprescribing for patients and informal caregivers (n=7 papers), but not for HCPs (n=0).” There is no context to your current descriptive results section.</li> <li>• Compare barriers and facilitators between groups (as you do with dislike, influences) within your results section. For example, benefit as a facilitator was much more common for HCP than for pts/caregivers, dislike as not a facilitator in any HCP evaluation but was for pts/caregivers; uncertainty and process were barriers for HCPs but not for pts/caregivers, etc.</li> <li>• I would like to hear more about how this compares with the remainder of the deprescribing literature. What is unique about this focused review on cardiovascular medications?</li> <li>• Limitations: It’s worth mentioning that your pool of HCP papers utilizes primarily GP’s and we know (Goyal, et al) that the perspectives of GPs and specialists vary significantly re: deprescribing CVM.</li> </ul>
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### VERSION 2 – AUTHOR RESPONSE

1	<p>There is limited reporting of characteristics of papers in your text – would be worth mentioning the number of studies (number of studies total, number in HCPs, etc.). Maybe include some of the highlights from the characteristics table.</p>	<p>The total number of studies identified, included for full-text assessment and finally those kept for data extraction and analysis are mentioned on <b>page 7, lines 155-157</b>. We added characteristics of the studies included in the review on <b>page 7, lines 157-162</b>.</p>
2	<p>Quantification of necessity, benefit, ADE, fear, dislike, previous experience, social influences, etc. For example, change (line 260-261) “CVM dislike was one of the most common facilitators to deprescribing for patients and informal caregivers, but not for HCPs” to “CVM dislike was a facilitator to deprescribing for patients and informal caregivers (n=7 papers), but not for HCPs (n=0).” There is no context to your current descriptive results section.</p> <p>Compare barriers and facilitators between groups (as you do with dislike, influences) within your results section. For example, benefit as a facilitator was much more common for HCP than for pts/caregivers, dislike as not a facilitator in any HCP evaluation but was for pts/caregivers; uncertainty and process were barriers for HCPs but not for pts/caregivers, etc.</p>	<p>Thank you for this constructive comment which enabled us to further develop the quantitative component of our thematic analysis and give a clearer context to the readers as to where healthcare providers and/or patients and informal caregivers stand on the different categories/themes reported in this review. For readability purposes, we often grouped the comparison between the two groups’ barriers and facilitators (e.g., dislike was a frequently reported facilitator for patients/informal caregivers but not for healthcare providers) and the quantification of each theme/category per group (i.e., the theme of necessity is reported in n=5 as a barrier and in n=3 as a facilitator for patients).</p> <p>We reframed the abstract and text result section accordingly: <b>page 2, lines 41-42 and 44-45; pages 10-11, lines 195-203; page 15, line 217, lines 220-223, lines 235-238; page 16, lines 252-254, lines 257-259; page 17 lines 266-267, line 276, lines 279-281; page 18, lines 294-299; page 19, lines 326-328, lines 339-342; page 20,</b></p>

		<b>line 361, line 364.</b>
3	I would like to hear more about how this compares with the remainder of the deprescribing literature. What is unique about this focused review on cardiovascular medications?	While there is increasing literature on deprescribing, there is little literature focusing on barriers and facilitators to deprescribing cardiovascular medications from the perspectives of different stakeholders (i.e., patients, informal caregivers and HCPs). Our review aims at addressing this gap, especially since deprescribing of some cardiovascular medications remains controversial (e.g., statins). Our review shows that deprescribing such medications can generate fear and uncertainty, although the current evidence for some of them cannot state with certainty which of deprescribing or continuing is safer. Our review shows this component and reinforces the need for more evidence. To better articulate this message, we modified the second paragraph of the discussion section ( <b>pages 21-22, lines 386-409</b> ).
4	Limitations: It's worth mentioning that your pool of HCP papers utilizes primarily GP's and we know (Goyal, et al) that the perspectives of GPs and specialists vary significantly re: deprescribing CVM.	Thank you for this comment. We added this limitation on <b>page 24, lines 455-457</b> and on <b>page 3, lines 64-65</b> .