Deprescribing Guidelines

Proposal: guideline production plan for England

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The first stop for professional medicines advice

Background

Deprescribing is the technical process of reducing or stopping a medication. This process is a useful tool for clinicians who have identified, following a thorough review of a person's medicines, that a specific medicine may no longer be indicated or may be causing undesirable side effects.

In November 2018, the London Regional Medicines Optimisation Committee (RMOC) identified the need to produce high quality guidelines that support clinicians in the technical process of deprescribing. The RMOC requested that a plan be produced for the development of these guidelines. This document proposes a method for development of deprescribing guidelines in England.

In Canada, a project led by the Bruyere Research Institute in Ottawa has so far produced four deprescribing guidelines according to a published methodology. [1] [2] Additionally, they have worked with the University of Sydney to produce a fifth deprescribing guideline. As deprescribing guidelines as a concept are in their infancy, and there are many potential clinical areas to be covered, the project plan in this document is based on the assumption that England will collaborate with international partners (e.g. Canada) to allow pooling of resources and production of larger volumes of guidelines. This would require registering development of each individual guideline with the Bruyere Research Institute and inviting a member of their team to join England guideline development team(s) as either an author or reviewer. The process that the Bruyere Research Institute has already published will have to be followed. [2]

At the same time, NICE is in the process of endorsing one of the four deprescribing guidelines produced in Canada (benzodiazepines). An update will be required on plans for endorsing the remaining deprescribing guidelines.

Acknowledgements

The process described below is based on that originally described by the Bruyere Research Institute for Canada. This is referred to below as *The Manual*. [2]

Purpose of project

1. To establish the system for creating evidence-based deprescribing guidelines that can be approved for use in England by the Regional Medicines Optimisation Committee.
2. To highlight, where necessary, key aspects of the guideline development process which need to be agreed initially

Purpose of this document

This document describes the overall system of deprescribing guideline development that the RMOC is being asked to approve. It provides details of the resource input required to develop robust deprescribing guidelines.

The document maps out aspects of a process that deprescribing guideline development teams would be expected to follow.

Project plan

Task	Who	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12	M13
Agree Deprescribing Guideline writing process	London RMOC													
Agree project plan and budget	London RMOC													
Approve guideline topic	London RMOC													
Approve guideline development scope	London RMOC													
Receive project update	London RMOC													
Approve final guideline	London RMOC													

Develop project plan

The project plan has been developed by a project team comprised of:

- London RMOC Secretary, SPS
- Assistant Head of Medicines Optimisation, SPS
- Regional Medicines Information Manager, London Medicines Information Service
- Chief Pharmaceutical Officer Clinical Fellow, NHS England

The project plan has already been shared with the following key stakeholders to gain comments before presentation to the London RMOC:

- RMOC Operational Group, SPS
- UK Medicines Information Executive
- Medicines Use and Safety Team, SPS
- Clinical Pharmacologist RMOC members

An additional element of the project that needs agreeing is the choice of clinical topic. This will be dependent on the following factors:

- Topics identified as a priority in Canada
- Results of scoping reviews
- Consensus that a topic is a priority in England

Agree project plan and budget

The London RMOC is being asked to agree the project principles laid down in this document. If the project is agreed, the RMOC secretary will write to NHS England (Medicines and Diagnostics Policy Unit) outlining the proposal and funding required.

Determine Guideline Development Team

The composition of the Guideline Development Team (GDT) will be important to the success of the project. *The Manual* (page 12) describes who should be invited to join the team. This includes team members from the professional groups that will be expected to use the guidance, and patient membership. In England, it is possible to include Clinical Pharmacologists in the GDT. Recruitment should start once the topic for review has been agreed.

Literature scoping review

This starts before the GDT is recruited. A method to follow is provided in *The Manual* (page 15). It may be necessary to repeat the scoping review if it is found that the first topic chosen has insufficient evidence available to proceed.

Guideline Development Team meeting

Two face-to-face meetings are scheduled, with a budget requested for these. The first meeting of the GDT should be face-to-face. Additional meetings can use video and teleconferencing facilities that are already available. Meetings should be held whenever there is something key that the GDT needs to agree.

Define and agree project scope

A Co-ordinator will define the scope for the project based on the findings of the scoping review and input from the GDT. The RMOC should be asked to agree the project scope.

The Manual (page 19) includes examples of questions on clinical consideration that they have included in previous deprescribing guidelines. It would be sensible to consider at least the following when scoping guidelines in England: [2]

- How should tapering be approached?
- What should be monitored and how often?
- How to manage recurring symptoms?
- What factors warrant continued use?

Plan and conduct systematic review

The Manual provides clear information on how to plan and conduct the systematic review. [2] There should be sufficient members of the project team trained and experienced in conducting systematic reviews. Where a training need exists, there are courses that could be used to fill the gap.

The **Required reading** section below includes documents that project team members need to read before embarking on this project. These documents may also be useful for GDT members who want a better understanding of the methods followed.

The process should be developed according to PRISMA-P and registered on the PROSPERO site. The search strategy should be critiqued by a second reviewer. A suitable tool (such as the PRESS Peer Review tool listed below) should be used to do this. GRADE should be used to assess the evidence found.

Develop recommendations

The Manual provides details on how to produce the draft guidance with recommendations (page 34) [2]. This will be compiled by the Co-ordinator with input from anyone engaged in the review process. Once a full draft is compiled it will be shared with the GDT to gain consensus (as described below).

There is a format for the draft suggested in *The Manual*, but this may have to change if the journal identified for publication differs.

Clinical review of guidelines

Clinical reviewers should be identified from within clinical groups that are likely to use this guidance. As all clinical comments will need to be responded to, caution should be given to ensure that this stage is manageable.

Stakeholder review

This step is to seek out external support for the guideline. *The Manual* (page 41) gives an example of seeking out support from gastroenterologists for PPI deprescribing guidance, for example. This stage can take a long time and therefore should be started as early as possible.

Finalise and disseminate guidelines

The guideline should be finally approved by the Guideline Development Team. In England, the finished guideline, together with relevant project documents should be presented to the RMOC for approval. Dissemination of the guidelines should then begin.

The Canadian project found that the flow charts that they created are an incredibly valuable part of the guideline, therefore should be repeated here. A software licence to produce the chart has been included in the budget request. Budget has also been requested to seek Open Access publication for the finished guideline. This will increase the credibility of the document, and should be used alongside anything published on other websites.

The RMOC network will be engaged to help disseminate these guidelines nationally once completed. If the methodology is followed as per the description in *The Manual*, there will be opportunity for them to impact internationally.

Required reading

- Cochrane Handbook for Systematic Reviews of Interventions (http://handbook-5-1.cochrane.org/) [3]
- PRISMA statement for systematic reviews and meta-analyses (https://doi.org/10.1136/bmj.b2535) [4]
- GRADE evidence profiles and summary of findings tables (https://www.jclinepi.com/article/S0895-4356(10)00330-6/fulltext) [5]
- PRESS Peer Review of Electronic Search Strategies (https://www.sciencedirect.com/science/article/pii/S0895435616000585) [6]

Choice of topic for guideline development

The choice of what to develop deprescribing guidelines for is important as there are many competing suggestions. For example, in May 2018, RMOC South had preliminary discussions about the need for antidepressant deprescribing guidelines. To address the issue of competing interests in Canada, the Bruyere Research Institute sought stakeholder consensus on which clinical areas should be prioritised for development of deprescribing guidelines in the elderly. [7] To reach the list of priority areas described below, the research institute conducted a literature search to identify potentially inappropriate medicines in the elderly, subsequently conducting three rounds of Delphi review to determine the priority list. There were sixty five stakeholders enrolled in round one (composed of geriatricians, family physicians, pharmacists and nurse practitioners), and forty seven stakeholders who continued to contribute by round three of the Delphi process. Column three of the table below represents the number of times a stakeholder listed the drug class in their "top 5" priority areas.

Table 5. Round Three Ranking: by number of participants who indicated drug class was a high priority for deprescribing guideline development.

Rank	Drug	Number of participants who indicated drug class was a high priority (%)	Mean	Standard deviation
#1	Benzodiazepines	43/47 (91%)	1.49	0.87
#2	Atypical antipsychotics	38/47 (81%)	2.32	1.05
#3	Statins	22/47 (47%)	3.14	1.22
#4	Tricyclic antidepressants	21/47 (45%)	3.29	1.16
#5	Proton-pump inhibitors	20/47 (43%)	3.5	0.92
#6	Urinary anticholinergics	17/47 (36%)	3.82	1.15
#7	Typical antipsychotics	16/47 (34%)	3.38	0.93
#8	Cholinesterase inhibitors	16/47 (34%)	3.88	1.32
#9	Opioids	12/47 (26%)	3.42	1.5
#10	Selective serotonin reuptake inhibitors	9/47 (19%)	4.11	1.1
#11	Bisphosphonates	8/47 (17%)	3.75	1.3
#12	Anticonvulsants	7/47 (15%)	4.14	0.83
#13	Beta-blockers	3/47 (6%)	4	1.41
#14	Antiplatelets	3/47 (6%)	5	0

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Guidelines topics already developed

Topic	Developer	NICE status
Benzodiazepines	Bruyere Research Institute	In Endorsement process
Proton Pump Inhibitors	Bruyere Research Institute	
Antihyperglycemics	Bruyere Research Institute	
Antipsychotics for BPSD & insomnia	Bruyere Research Institute	
Cholinesterase Inhibitors	University of Sydney	

Options for identifying topic for development

1. Select from Canadian reference above
2. Seek consensus from Area Prescribing Committees

Questions for consideration by RMOC

1. Does the RMOC support the project plan described?
2. Does the RMOC support the proposed cost estimate for the project?
3. From where should capacity for this project be sought?
4. From where will expertise for this project be sought?
5. What topic should be explored for the first guideline?

Appendix 1 Anticipated resources to develop one guideline

Item	Cost
Co-ordinator 12 months at 50% WTE	£50k
Support to co-ordinator 6 months at 50% WTE	£12k
Supplies & expenses	£2k
Graphic design	
Face to face meetings	£1k
Systematic Review Training	£1.2k
Literature searching by library services	£2k
Statistical input	£600
Methodological input	£600
Meeting attendance expenses	£2.8k
IT equipment	£2k
Open Access Journal fees	£7k
Total	***£81.2k***

The template in *The Manual* (page 9) suggests a budget of $130,090 (approx. £77,000). [2]

This doesn't include fees to pay members of the guideline development team (GDT).

Appendix 2 GANTT Chart for development of one guideline

Task	Who	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12	M13
Agree guideline topic	London RMOC													
Determine Guideline Development Team	RMOC Secretariat													
Recruit Guideline Development Team	RMOC Secretariat													
Literature scoping review	Co-ordinator													
Guideline Development Team meeting	GDT													
Define project scope	Co-ordinator													
Agree project scope	London RMOC													
Plan systematic review	Co-ordinator													
Conduct systematic review	Co-ordinator													
Develop recommendations	Co-ordinator													
Update report received	London RMOC													
Guidelines clinical review	GDT													
Finalise guideline following review	Co-ordinator													
Stakeholder review and endorsement	Co-ordinator													
Finalise guideline	Co-ordinator													
Approve guideline	London RMOC													
Knowledge mobilisation	Co-ordinator													

References

[1] B. Farrell, K. Pottie, C. Rojas-Fernandez, L. Bjerre, W. Thompson and V. Welch, “Methodology for Developing Deprescribing Guidelines: Using Evidence and GRADE to Guide Recommendations for Deprescribing,” *PLOS One,* 2016.

[2] W. Thompson, L. Pizzola, M. Hogel, C. Black and B. Farrell, Developing an evidence-based deprescribing guideline: instruction manual for guideline coordinators (working document), 2018.

[3] J. Higgins and S. Green, “Cochrane Handbook for Systematic Reviews of Interventions (Version 5.1.0),” March 2011. [Online]. Available: http://handbook-5-1.cochrane.org/. [Accessed 08 Jan 2019].

[4] D. Moher, A. Liberati, J. Tetzlaff and D. Altman, “Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement,” *BMJ,* vol. 339, no. doi: https://doi.org/10.1136/bmj.b2535, 2009.

[5] G. Guyatt, A. Oxman, E. Akl, R. Kunz, G. Vist, J. Brozek, S. Norris, Y. Falck-Ytter, P. Glasziou, H. deBeer, R. Jaeschke, D. Rind, J. Meerpohl, P. Dahm and H. Schunemann, “GRADE guidelines: 1. Introduction - GRADE evidence profiles and summary of findings tables,” *Journal of Clinical Epidemiology,* vol. 64, no. 4, pp. 383 - 394, 2011.

[6] J. McGowan, M. Sampson, D. Salzwedel, E. Cogo, V. Foerster and C. Lefebvre, “PRESS Peer Review of Electronic Search Strategies: 2015 Guideline Statement,” *Journal of Clinical Epidemiology,* vol. 75, pp. 40 - 46, 2016.

[7] B. Farrell, C. Tsang, L. Raman-Wilms, H. Irving, J. Conklin and K. Pottie, “What Are Priorities for Deprescribing for Elderly Patients? Capturing the Voice of Practitioners: A Modified Delphi Process.,” *PLoS ONE,* vol. 10, no. 4, p. e0122246, 2015.