Evidence-based Clinical Practice Guideline for Deprescribing Cholinesterase Inhibitors and Memantine

Administrative Report

The full guideline and supporting documents are available at:
http://sydney.edu.au/medicine/cdpc/resources/deprescribing-guidelines.php

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Developing organisations:

The University of Sydney, NHMRC Partnership Centre: Dealing with Cognitive and Related Functional Decline in Older People (Cognitive Decline Partnership Centre) and Bruyère Research Institute, Deprescribing Guidelines in the Elderly Project

Table of Contents

List of Tables

Guideline Development

The development, publication and dissemination of the Guideline were funded through an NHMRC-ARC Dementia Research Development Fellowship awarded to Dr Emily Reeve (APP1105777).

The project proposal and fellowship application was led by Dr Emily Reeve with Prof Sarah Hilmer (University of Sydney, Australian supervisor), Dr Kenneth Rockwood (Dalhousie University, overseas supervisor) and Dr Barbara Farrell (Bruyère Research Institute, collaborator and mentor) and submitted for consideration in March 2015. The fellowship/project was awarded in October 2015, commenced February 2016 and is administered through the Northern Clinical School, University of Sydney. This overseas fellowship entails the fellow (Dr Emily Reeve) spending years 1 and 2 at an overseas institution (Dalhousie University, Nova Scotia, Canada) and years 3 and 4 at their Australian institution (University of Sydney, NSW, Australia).

This guideline was developed in line with the procedures and requirements for meeting the 2011 NHMRC standard for clinical practice guidelines (May 2011 version 1.1) [1]. It was registered on the Australian Clinical Practice Guideline Register on the 20th of April 2016 (https://www.clinicalguidelines.gov.au/register/evidence-based-clinical-practice-guideline-deprescribing-cholinesterase-inhibitors-and).

The recommendations made in the guideline were approved by the National Health and Medical Research Council (NHMRC) on 27 October 2017.

Organisation

Organisations responsible for developing and publishing the guideline:

- The University of Sydney
- NHMRC Partnership Centre: Dealing with Cognitive and Related Functional Decline in Older People (Cognitive Decline Partnership Centre)
- Bruyère Research Institute/Deprescribing Guidelines in the Elderly Project

Funding breakdown

The NHMRC-ARC Dementia Research Development Fellowship provides salary support, living overseas allowance/maintenance, Research Implementation and Outreach Loading and project funding. The total GST exclusive funding amount is AUD$623,362.50. The funding allocated to project costs (development and implementation) is AUD$241,830.50. Additional salary support

for Dr Emily Reeve is provided by the Northern Clinical School and Faculty of Medicine, University of Sydney.

The funding body had no involvement in guideline development and as such the views and/or interests of the funding body have not influenced the final recommendations.

Contributors

Process and criteria for selecting members

We recruited Guideline Development Team (GDT) members who were one or more of the following: content experts, end-users, methodology experts or consumers. We sought to include healthcare professionals who are involved in the prescription and/or monitoring/management of prescriptions of cholinesterase inhibitors and/or memantine (end-users). At a minimum, we intended our GDT to have at least one member of the following groups: general practitioner (family physician, primary care physician), geriatrician, pharmacist and nurse. This guideline was developed as a partnership between Australian and Canadian institutions and therefore we intended to have a balance of members from both countries.

To recruit potential content experts, end-users and methodology experts we utilised the networks of the people involved in the submission of the fellowship/project.

Where possible, potential conflicts of interest (COIs) were reviewed prior to inviting members (for example, recent publications reviewed for COIs). All potential members were invited via email which briefly explained the aim of the guideline and the process involved in development. If a potential member declined, they were asked to suggest another person in their place. If they expressed an interest in participating, they were provided with more information (via email or in person) and they were asked to complete the COI form.

GDT members received no reimbursement for their involvement. Travel costs were covered to attend the first GDT meeting (setting the scope).

All GDT members and other individuals involved in the development of the guideline are listed in Table 1 and Table 2. Additionally, we express gratitude to Robin Parker, academic librarian (Dalhousie University) for assistance in creating the search strategy for the systematic review. The guideline (main document) underwent professional editing by Elite Editing.

Consumer involvement in the GDT

We sought to recruit two consumer representatives to be on the GDT: a current/past carer of a person with dementia and a person with dementia. The carer was recruited through the NHMRC Cognitive Decline Partnership Centre (Australia) and the person with dementia was recruited through the Alzheimer Society of Nova Scotia (Canada). As GDT members they were involved throughout the development process. The carer representative was present at the first GDT team meeting where the scope of the guideline was determined and provided ongoing input to the guideline and recommendations via email/telephone communication. The person with dementia was not able to be recruited until after the first meeting (setting the scope) had occurred, as such they did not participate in this meeting. During the development phase the person with dementia provided input via one-on-one meetings with the guideline lead in a place that was suitable to them. Other communication occurred via email and telephone contact.

GDT members

Table 1: GDT members, role and affiliations

Name	Discipline/role/expertise	Organisational affiliation(s)
Emily Reeve *Guideline coordinator and lead*	NHMRC-ARC Dementia Research Development Fellow Pharmacist	NHMRC Cognitive Decline Partnership Centre, Kolling Institute of Medical Research, Northern Clinical School, Sydney Medical School, University of Sydney, New South Wales (NSW), Australia Geriatric Medicine Research, Faculty of Medicine, Dalhousie University and Nova Scotia Health Authority, Nova Scotia (NS), Canada Adjunct Appointee, College of Pharmacy, Faculty of Health Professions, Dalhousie University, NS, Canada
Sarah Hilmer	Geriatrician and Clinical Pharmacologist Professor of Geriatric Pharmacology and Head of Department, Clinical Pharmacology and Senior Staff Specialist, Royal North Shore Hospital	NHMRC Cognitive Decline Partnership Centre, Kolling Institute of Medical Research, Northern Clinical School, Sydney Medical School, University of Sydney, NSW, Australia Departments of Clinical Pharmacology and Aged Care, Royal North Shore Hospital, NSW, Australia
Lynn Chenoweth	Professor of Nursing Professor of Aged and Extended Care Nursing Adjunct Professor	Centre for Healthy Brain Ageing, University of NSW, NSW, Australia Faculty of Health Sciences, University of Macau, Macau, China School of Nursing, The Notre Dame University, NSW, Australia
Lyntara Quirke	Consumer representative: carer	Consumer Network, Alzheimer's Australia, Australian Capital Territory (ACT), Australia Bribie-Moreton Hospice Health Service, Queensland (QLD), Australia Rotary Club Bribie Island, QLD, Australia Dementia Training Australia, Australia

Parker Magin	General practitioner Director Conjoint Professor	NSW and ACT Research and Evaluation Unit, GP Synergy, NSW, Australia Discipline of General Practice, School of Medicine and Public Health, University of Newcastle, NSW, Australia
Barbara Farrell	Pharmacist Methodology expert in deprescribing guideline development	Bruyère Research Institute, Ontario (ON), Canada Department of Family Medicine, University of Ottawa, ON, Canada School of Pharmacy, University of Waterloo, ON, Canada
Mary Gorman	General practitioner, aged care specialty	Faculty of Medicine, Dalhousie University, NS, Canada
Nathan Herrmann	Geriatric psychiatrist Head, Division of Geriatric Psychiatry	Division of Geriatric Psychiatry, Sunnybrook Health Sciences Centre, ON, Canada Faculty of Medicine, University of Toronto, ON, Canada
Graeme Bethune	General practitioner, aged care specialty Medical Director of Veterans' Services	Veterans' Services, Nova Scotia Health Authority, NS, Canada Hydrostone Medical Centre, NS, Canada
Wade Thompson	Pharmacist in residential aged care services Methodology expert in deprescribing guideline development process	Medisystem Pharmacy, ON, Canada Bruyère Research Institute, ON, Canada School of Epidemiology, Public Health and Preventive Medicine, University of Ottawa, ON, Canada
Ingrid Sketris	Pharmacist Methodology expert in systematic reviews and pharmacoepidemiology	College of Pharmacy, Faculty of Health Professions, Dalhousie University, NS, Canada
Faye Forbes	Consumer: person with dementia	Alzheimer's Society of Canada (board member)

Table 2: Non-GDT members involved in guideline development

Name	Profession/discipline *Role in the guideline development process*	Organisational affiliation(s)
Lisa Kouladjian O'Donnell	Pharmacist Postdoctoral research associate *Reviewer for systematic review (title/abstract screening, full text screening and eligibility assessment, and data extraction)*	NHMRC Cognitive Decline Partnership Centre, Kolling Institute of Medical Research, Northern Clinical School, Sydney Medical School, University of Sydney, NSW, Australia
Judith Godin	Researcher *Conducting meta-analysis of the systematic review*	Nova Scotia Health Authority, NS, Canada Geriatric Medicine Research, Faculty of Medicine, Dalhousie University, NS, Canada
Caitlin Lees	Medical doctor, research student *Second reviewer for systematic review (title/abstract screening)*	Maritime Resident Doctors, PGY3 Internal Medicine & Clinician Investigator Program, Dalhousie University, NS, Canada
Emma Squires	Research assistant *Data extraction of systematic review (full text screening and eligibility assessment, and data extraction)*	Geriatric Medicine Research, Nova Scotia Health Authority, NS, Canada
Ivanka Hendrix	Senior clinical pharmacist, postgraduate research fellow *Reviewed Dutch-language article for potential inclusion in the systematic review*	Department of Pharmacy, Queen Elizabeth Hospital, Woodville, South Australia (SA), Australia School of Nursing and Adelaide Geriatrics Training and Research with Aged Care (GTRAC), School of Medicine, University of Adelaide, SA, Australia NHMRC Centre of Research Excellence: Frailty Trans-Disciplinary Research to Achieve Health Ageing, SA, Australia

Table 3: Specific roles and responsibilities of GDT members

Note: All GDT members were provided the opportunity to review/comment on all sections of the guideline. Roles and responsibilities were discussed and agreed upon by GDT members prior to writing the guideline.

Activity	Most responsible person[†]	Support people[±]
Scoping review	ER	-
Setting the scope of the guideline	ER	All GDT
Systematic review	ER	PM, MG, WT, IS, NH, SH Also non-GDT members and academic librarian
Guideline sections		
Introduction	ER	SH
Scope	ER	SH
Methods	ER	LC, BF
Summary of findings and quality of evidence	ER	NH, IS, SH
GRADE review (including assessing the quality of the evidence)	ER	WT, IS
Recommendations (and introductory pages)	ER	SH, BF (All GDT members voted on recommendations to achieve consensus)
Summary of benefits	ER	MG, NH
Review of harms	ER	SH, PM, IS
Consumer values and preferences	BF	LQ, ER, FF
Resource implications and cost effectiveness	ER	IS, LC
Clinical considerations	ER	SH, MG, GB, NH, FF (consumer section)
Implementation and follow-up	ER	LC
Other guidelines	ER	LQ
Gaps in knowledge	ER	GB, PM
Conclusion	ER	SH

[†]Person responsible for leading task and/or drafting section

[±]People responsible for reviewing and revising the first draft of the section/assisted with completion of the task prior to sending to whole GDT

Organisations endorsing the guideline

- Australian and New Zealand Society of Geriatric Medicine (ANZSGM)
- The Royal Australian and New Zealand College of Psychiatrists (RANZCP)
- Tasmanian Health Service: Royal Hobart Hospital
- Canadian Geriatrics Society (CGS)
- Canadian Society of Hospital Pharmacists (CSHP)

Declaration of conflicts of interest policy

The procedure for declaring and managing Conflicts of Interest (COI) was conducted as per the University of Sydney External Interests Policy and is in accordance with the National Health and Medical Research Council (NHMRC) Guideline Development and Conflicts of Interest Policy. The purpose of disclosure of interests was to provide information on financial, business/professional, and intellectual competing interests related to the topic addressed.

COI policy

- **Completion of the Disclosure of Interests Form is a prerequisite for being a Guideline Development Team (GDT) member.** (The NHMRC Disclosure of Interest Form was used: https://www.nhmrc.gov.au/guidelines-publications/information-guideline-developers/guideline-development-and-conflicts-interes). GDT members will be asked at all meetings and prior to public consultation period and submission to the NHMRC for approval if they have any new interests which have arisen and their disclosure form must be updated accordingly. Members must also inform the GDT lead at any point between meetings if a new conflict has arisen.
- Disclosure is required in relation to disbursement/activities over the **three years preceding**, and any anticipated disbursements in the **twelve months following** appointment to the GDT.
- If at any point in time a person is found to have purposely withheld/not disclosed information, that person will be removed from the GDT.
- When the GDT lead has received completed disclosures from all prospective GDT members they will review them and, if a COI has been declared, they will decide upon a potential management plan. This will then be discussed with the person who has the COI and the management plan will be confirmed and documented. If necessary (for example, disagreement about management plans) the COI and management plan will be reviewed by a University of Sydney staff member external to the GDT. The GDT lead (Dr Emily Reeve) had their COIs reviewed by Australian supervisor, Prof Sarah Hilmer.
- Management will include declaration and disclosure of all COIs and may additionally include:
    - restriction of involvement: non-voting member and not involved in drafting recommendations (on all or only relevant recommendations)
    - restriction of involvement: exclusion from relevant discussion(s)
    - relinquish external interests
    - appointment as a member of the GDT is precluded

- All COIs and management plans will be disclosed and discussed at the first GDT meeting. This will provide all members an opportunity to voice any concerns about interests relating to other prospective committee members.
- Completed Disclosure Forms and management plans will be kept electronically by the GDT lead (Dr Emily Reeve).
- All COIs and management plans will be published with the final guideline.

Disclosures of Interest

Table 4: Disclosure of potential conflicts of interest of GDT members

Name	Financial COIs	Professional and organizational experience	Other relationships or activities	Management plan
Emily Reeve	NHMRC-ARC Dementia Research Development Fellowship. Total value $623,362.50 paid through the University of Sydney. Includes salary and grant money to complete the project 'Development and implementation of evidence-based deprescribing guidelines to guide person-centred care for people with dementia.' Bupa Health Foundation Emerging Health Researcher Finalist: prize money awarded (2016) Support to attend conferences/travel received from: Canadian Frailty Network, TUTOR-PHC Program (Western University), University of Sydney Medical School, Ramsay Research and Teaching Fund (Kolling Institute Travel Award, Royal North Shore Hospital Scientific Staff Council), Brocher Foundation (Geneva, Switzerland)	Author of a number of publications and presentations on deprescribing in older adults and people with dementia.	Nil	Declaration
Sarah Hilmer	NHMRC-Cognitive Decline Partnership Centre provides funds for research into quality use of medicines in dementia.	No specific publications/lectures on this subject but many on prescribing and deprescribing for people with dementia. Convened the National Stakeholders Meeting on Quality Use of Medicines to Optimise Ageing in Older Australians, Aug 2 2015	Nil	Declaration
Lynn Chenoweth	Nil	Nil	Nil	N/A

Lyntara Quirke	Reimbursement of flight costs to attend Deprescribing GDT meeting (Funding from the NHMRC-ARC Dementia Research Development Fellowship, administered through University of Sydney)	Consumer representative on the development of resource material for Alzheimer's Australia 'Medicines in Dementia' campaign	Member of Alzheimer's Australia Consumer Network	Declaration
Parker Magin	Royal Australian College of General Practitioners Expert Committee: Research. Honorarium for attending Committee Meetings Potentially relevant grant received from Judith Jane Mason & Harold Stannett Williams Memorial Foundation Medical Program Grants.	Several publications on the diagnosis and screening for dementia as well as anticholinergic medication load.	Nil	Declaration
Barbara Farrell	Consultancy fees and grants (including reimbursement for travel for research meetings or education sessions) received from: Institute for Healthcare Improvement, Canadian Society of Hospital Pharmacists, Ontario Pharmacists Association, Canadian Institute of Health Research, Ontario Ministry of Health and Long-Term Care, European Association of Hospital Pharmacists and Bruyère Research Institute	Author of a variety of publications and presentations on deprescribing and deprescribing guidelines. Co-lead of the Deprescribing in the Elderly project which involves development of Deprescribing Guidelines	Member of the Canadian Deprescribing Network and chair of a subcommittee on provider awareness.	Declaration
Mary Gorman	Nil	Several talks to healthcare professionals on dementia and stroke diagnosis and treatment	Nil	Declaration
Nathan Herrmann	Consultancy fees for dementia drug development received from Lilly, Astellas and Merck. Grants received from Lundbeck and Roche for dementia investigational drug trials. Support from the Canadian Consortium on Neurodegeneration in Aging (CCNA) funded by the Canadian Institute of Health Research and several partners.	A number of publications and speeches/lectures on medication use in dementia. Development of related guidelines, standards, educational material or fact sheets.	Nil	Declaration
Graeme Bethune	Nil	Nil	Nil	N/A

Wade Thompson	Received Master of Science stipend from government of Ontario for work on deprescribing project 2014-2016. Speaking fees to present at conferences on deprescribing: Advanced Learning in Palliative Medicine Conference May 2016 and Geriatrics in Primary Care (University of Ottawa) 2016	Relevant experience includes publications, speeches and lectures on deprescribing and involvement in the development of guidelines on the deprescribing of proton pump inhibitors, benzodiazepines, antihyperglycemics and antipsychotics.	Nil	Declaration
Ingrid Sketris	Receives a salary stipend from Canadian Institute of Health Research (CIHR) as part of the Canadian Network for Observational Effect Studies. Grants from CIHR and the Nova Scotia Department of Health and Wellness (including funds utilized to present research results). Meals/beverages at workshops sponsored by Nova Scotia Health Research Foundation and CIHR	Several publications and speeches/lectures related to the STOPP criteria. Gave a presentation on STOPP and optimal drug use to the Patented Medicines Prices Review Board (travel costs covered)	Management committee member of the Nova Scotia government funded Drug Evaluation Alliance of Nova Scotia and CIHR funded CNODES researcher	Declaration
Faye Forbes	Nil	Nil	Nil	N/A

Table 5: Disclosure of potential conflicts of interest of non-GDT members involved in guideline development

Name	Financial COIs	Professional and organizational experience	Other relationships or activities	Management plan (NB: individuals below did not have voting privileges)
Lisa Kouladjian O'Donnell	Salary through the University of Sydney, funded by the NHMRC Partnership Centre: Dealing with Cognitive and Related Functional Decline in Older People (Cognitive	Various publications and presentations on deprescribing and medication use in older adults.	Board member of the Pharmaceutical Society of Australia Branch	Declaration

	Decline Partnership Centre) (receives support from the NHMRC and Funding Partners including HammondCare, Alzheimer's Australia, Brightwater Care Group and Helping Hand Aged Care) Received honorarium from Journal of Pharmacy Practice and Research. Received PhD Scholarship from the NHMRC		Committee 2011-2016	
Judith Godin	Nil	Nil	Nil	N/A
Caitlin Lees	Honoraria received to attend the Canadian Medical Association General Council as a delegate of Doctors' of Nova Scotia Grants received from Dalhousie University, Canadian Institutes of Health Research and Nova Scotia Health Research Foundation	Nil	Nil	Declaration
Emma Squires	Nil	Nil	Nil	N/A
Ivanka Hendrix	Nil	Nil	Nil	N/A

Method to achieve group consensus in the development of the recommendations

The recommendations were drafted by the guideline lead and then disseminated electronically to the whole GDT (along with the full guideline including summary of the systematic review). Where possible, a group teleconference or individual meetings with the guideline lead was conducted to discuss recommendations. After the meeting/initial feedback, a revised version was sent out electronically which GDT members provided further feedback on. This was repeated until the guideline lead determined that it was appropriate to put the recommendations to a vote. Voting on recommendations occurred via email. An 80% or greater agreement was chosen to indicate consensus. This level of consensus was agreed upon by all GDT members at the beginning of the development process. Any members who did not agree with the recommendations were provided the opportunity to report their concerns in the section following the recommendations: 'Areas of major debate' (main guideline document).

Independent review

In accordance with the process of developing class specific deprescribing guidelines developed by the 'Deprescribing guidelines in the elderly' project [2], the draft guideline underwent external clinical review by two end-users/content experts. The external clinical reviewers were Dr Kenneth Rockwood (geriatrician, Kathryn Allen Weldon Professor of Alzheimer's Research, Professor of Geriatric Medicine at Dalhousie University and Staff Physician, Department of Medicine, QEII Health Sciences Centre, Halifax, NS, Canada) and Amy Page (consultant pharmacist, experienced in geriatric clinical pharmacy, credentialed advanced practice pharmacist, Vic, Australia). These experts were chosen based on their expertise and relevant experience in the field of prescribing and deprescribing in people with dementia. They also represent the two countries involved in guideline development (Australia and Canada) and are from two relevant professions (geriatrician and pharmacist).

The guideline has also undergone independent assessment using the AGREE II instrument [3] by two individuals external to the GDT. This methodological review (using the AGREE-II criteria) was to assess that the guideline had been developed robustly and according to internationally recognised methods. One of the external clinical reviewers (Amy Page) also conducted methodological review due to experience in this field. The external clinical reviews and the first methodological review were conducted after GDT consensus on the recommendations and prior to the public consultation period. A second methodological reviewer was recruited to conduct a review after the public consultation period; Dr Saravana Kumar is a senior lecturer at the Sansom Institute for Health Research, University of South Australia. This individual was chosen due to their experience in developing and reviewing guidelines and familiarity with the AGREE-II criteria.

We express immense gratitude to the external reviewers for their valuable feedback on the drafts of the guideline. Appropriate changes were made to the guideline based on their feedback, ensuring alignment with the evidence base.

Public consultation

The public consultation period was conducted in accordance with the 'Public Consultation Information for Guideline Developers Seeking NHMRC Approval of their Guideline' Version 3, effective date: 16/12/2016 [4].

The dates of the public consultation period were: 5th June to the 6th of July 2017 (inclusive).

A consultation notice was published on a publically available website: http://sydney.edu.au/medicine/cdpc/news-events-participation/deprescribing-guideline.php

The full guideline, summary of recommendations, technical report and administrative report were all publically available via this website. Instructions on how to make a submission (with alternatives) and guideline lead contact details were provided.

The following Australian organisations were specifically targeted to provide comment on the draft guideline:

- Director-General, Chief Executive or Secretary of each state, territory and Commonwealth health department
- Therapeutic Goods Administration
- Pharmaceutical Benefits Advisory Committee
- Consumers Health Forum of Australia
- Australian Deprescribing Network (ADeN)
- NHMRC National Institute of Dementia Research (NNIDR)
- NPS MedicineWise*
- Alzheimer's Australia*
- Carers Australia*
- Australian Medical Association*
- Royal Australasian College of General Practitioners*
- Royal Australasian College of Physicians*
- Royal Australian and New Zealand College of Psychiatrists*
- Australian New Zealand Society of Geriatric Medicine*
- Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists*
- Australasian Pharmaceutical Science Association*
- Pharmaceutical Society of Australia *
- Society of Hospital Pharmacists of Australia *
- The Pharmacy Guild of Australia*
- Australian Primary Health Care Nurses Association*
- Australian Nursing and Midwifery Federation*

- Australian College of Nurse Practitioners*
- COTA Australia (Council on the Ageing)

* These organizations were invited to endorse the guideline

The following Canadian organisations were specifically targeted to provide comment on the draft guideline:

- Health Canada
- Canadian Deprescribing Network
- Canada Health Infoway
- Canadian Consortium on Neurodegeneration in Aging (CCNA)
- Choosing Wisely Canada*
- Alzheimer Society of Canada*
- Caregivers Canada*
- Canadian Medical Association*
- The College of Family Physicians Canada*
- Canadian Primary Care Sentinel Surveillance Network*
- Royal College of Physicians and Surgeons of Canada*
- Canadian Psychiatric Association*
- Canadian Geriatrics Society*
- Canadian Society of Pharmacology and Therapeutics*
- Canadian Pharmacists Association*
- Canadian Society of Hospital Pharmacists *
- Canadian Nurses Association*
- Canadian Family Practice Nurses Association*
- Canadian Association of Advanced Practice Nurses*
- Canadian Academy of Geriatric Psychiatry*
- Canadian Coalition for Seniors' Mental Health*

* These organizations were invited to endorse the guideline

De-identified submissions and GDT responses are provided in the Appendix.

Administrative Report References

1. National Health and Medical Research Council. Procedures and requirements for meeting the 2011 NHMRC standard for clinical practice guidelines. Melbourne: National Health and Medical Research Council; 2011.

2. Farrell B, Pottie K, Rojas-Fernandez CH, Bjerre LM, Thompson W, Welch V. Methodology for developing deprescribing guidelines: Using evidence and GRADE to guide recommendations for deprescribing. *PLoS One*. 2016;11:e0161248.

3. Brouwers MC, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, et al. AGREE II: advancing guideline development, reporting and evaluation in health care. *CMAJ. Canadian Medical Association*; 2010;182:E839–42.

4. Public Consultation Information for Guideline Developers Seeking NHMRC Approval of their Guideline. Australia: Australian Government, National Health and Medical Research Council; 2016. Report No.: Version 3.

Appendix: Public Consultation Responses Summary

Note: Some organizations provided their responses in text of an email only, others used the online response form or word template which contained specific sections for comment (comments on the actual recommendations, comments on other aspects of the guideline and supporting materials, invitation for endorsement and comments regarding endorsement). Responders were also asked to provide information on whether their comments reflected an organization or individual. We have provided their comments in the format as close as possible to how it was submitted.

This table has been de-identified for publication (including comments about endorsement).

Response #	Comments	Responses to comments	Corresponding changes made to guideline
#1 (Organisation)	Although we appreciate being made aware of your proposed Guideline, it does not come under our purview. We suggest that you contact the Canadian Institutes of Health Research at this link: http://www.cihr-irsc.gc.ca/e/9833.html.	We thank the organisation for their response. As per their advice, we invited the CIHR to comment on the guideline.	N/A
#2 (Organisation)	Thank you for your correspondence of June 5, 2017 in which you invite [organisation] to make a submission on the draft Guideline for Deprescribing Cholinesterase Inhibitors and Memantine in People with Dementia. Please note that prescribing practices, including the choice to taper patients off of these types of drugs, do not normally fall under [organisation]'s mandate; this is part of the practice of medicine which is regulated by the provincial and territorial governments. If you have not already done so, you may wish to share the draft Guideline with the provincial/territorial ministers of health and the colleges of physicians and surgeons. Please	We thank this organisation for their response and suggestion of other organizations to contact.	N/A

	find attached a contact list for your reference.		
#3 (Organisation)	Thank you for the invitation to [organisation] to review the CPG on deprescribing. This exceeds our clinical expertise but we will redirect it to the Canadian Geriatrics Society for their consideration.	We thank this organization for their response and suggestion to contact the Canadian Geriatrics Society. We had previously contacted the Canadian Geriatrics Society for comment.	N/A
#4 (Organisation)	Thank you very much for your email. I am a coordinator in the [organisation]. We believe this is request is highly relevant to them, and I will pass along the request for comments on the Evidence-Based Clinical Practice Guideline for Deprescribing Cholinesterase Inhibitors and Memantine in People with Dementia.	We thank the organisation for their response – however, no further comments were received.	N/A
#5 (Organisation)	**Comments on recommendations:** Recommendations are well balanced, practical and process is well laid out in the various documents. Our organization is primarily made up of [profession] so comments are from the context of ...[clinical] practice	We thank the organisation for their feedback.	
	Comments on other aspects of the guideline and supporting materials: A couple of comments from reviewers include: 1) Suggest listing the benefits and harms of continuing and discontinuing medications	The benefits and harms of continuing and discontinuing the medications are discussed throughout the guideline. However, we appreciate the suggestion to have the potential benefits and harms clearly outlined.	A new table has been created which clearly outlines the potential benefits and harms of both continuing and discontinuing ChEIs and memantine. This new table has been placed following the recommendations. *Page 9*
	2) It is not possible to halve the dose every 4 weeks for some cholinesterase inhibitors (like galantamine ER)	Thank you for highlighting the issue of the inability to halve the dose of certain formulations. The recommended dose tapering schedule outlined in Table 5 takes into account the available dose forms in Australia and Canada. Not all dose reductions correspond to a halving of the dose (and extended release	Based on this, we have made a minor alteration to the wording of this Practice Point: **"PP:** The dose of the cholinesterase inhibitors and/or memantine should be tapered prior to discontinuation by halving the dose *(or by stepping down through available dose formulations)* every four

		formulations/capsules are unable to be cut in half).	weeks to the lowest available dose, followed by discontinuation." *Page 7* We have also added a box after the recommendations with some further general details about tapering and what to do after discontinuation which provides more information about tailoring the tapering regimen to available dosage regimens.
	Well balanced. Appreciated the focus on the context of the individual.		
#6 (Organisation)	Thank you for inviting the [organisation] to provide feedback on the draft Evidence-Based Clinical Practice Guideline for Deprescribing Cholinesterase Inhibitors and Memantine in People with Dementia. After receiving the invitation, [organisation] invited selected members to provide feedback on the guideline. I received very little feedback, but it is overall positive: please see the attached file *(comments have been extracted from attached file and included below)*. I wish you and the developing organisations all the best as this important work continues. **Comments on the actual recommendations:** Pg 2 (Plain English Summary) Appreciated this section to help summarise and define terms before embarking on reading the rest of/ body of the document.	We are glad that the plain English summary was well received and appreciate the positive comments from this organisation.	N/A
	Pg 3 Cost implications of deprescribing – uncertain benefit or cost if there is a change in function – further research required – would like to see some research around impact on	We thank the individual for sharing their experience of deprescribing these medications and the potential for harm and therefore need for close monitoring after discontinuation.	We have added a box following the recommendations to highlight the need for a process of deprescribing with close monitoring after discontinuation. *Page 8*

	mobility and worsening of muscle contractures following deprescribing - personal experience where an entire AD floor in NH with mainly severe AD were deprescribed at same time following change in MD coverage and showed rapid progression (i.e. within 2 months or so) from independently mobile to wheel chair bound and severe contractures from a sig number of patients.	Unfortunately very few of the included articles measured mobility/functional outcomes and agree that this should be a focus of future research. We have previously mentioned in the main guideline that there is a lack of research in this area.	
	Pg 5 Appreciated the important warning (NB)" This is not a treatment guideline" as this helps to set the context of the guideline purpose and not limitations of these recommendations.	Thank you for this comment – the GDT felt that it was extremely important to ensure that the deprescribing guideline was not misused outside its intended purpose.	No changes made.
	Pg 7 Content: "(as outlined in Error! Reference source not found.Error! Reference source not found. and Error! Reference source not found.)." Please clarify the source. "Error! Reference source not found" – I find that this is an odd placement/ statement– I wonder if the search continuing to find the reference source and this will be added later??)	Thank you for highlighting this issue with our cross referencing – this has now been fixed. It was referring to sections later in the guideline which discussed the issue in further detail and provided references	Cross referencing to other parts of the guideline has been fixed to remove the error message.
	Interesting that you include the debate issues that the team wrestled with in trying to reach consensus or practice point. These points helped/ helps to underline the issues at hand, especially when the evidence is weak or low in defining how recommendations are being applied or viewed. General comment: The guidelines are well	We thank the organisation for their positive comments.	N/A

thought out and reasonable. It makes sense to taper the aforementioned drugs when effectiveness has been lost in order to decrease side effects.

Comments on other aspect of the guideline and supporting materials:

Pg 26 to 30 More in depth review concerning Memantine, combinations of therapies. Helpful to understand the reasoning behind the recommendations

Pg 34 - Potential Harms Review ChEIs - understandable and appears thorough

Pg 37 Potential Harms Review Memantine - understandable and appears thorough

Pg 39 – 41 Helpful chart to summarize published findings for drug-drug interactions

Pg 42 Consumer values and preferences – useful discussion to appreciate the care and conversation that is necessary as background to incorporate into practice

Pg 45 Cost of prescribed ChEIs and memantine – helps with understand the overall prescribing and cost implications for these therapies.

Pg 49 Clinical context – weighing benefits and harms for use of meds. – useful background

Pg 51 How to go about de-prescribing process – is helpful for details

Pg 53 Chart summary – easy reference to follow for tapering schedules for RXs

Pg 55 Chart summary – helpful for monitoring and management

	Pg 58 – 60 When to consult specialist or other healthcare professional – appreciated inclusion for resources and how to consult for specific purposes. Pg 68 Gaps in knowledge – appreciate that this is work in progress for patterns of use		
#7 (Organisation)	On behalf of [organisation], please find attached ... input to the Evidence-Based Clinical Practice Guideline for Deprescribing Cholinesterase Inhibitors and Memantine in People with Dementia. The [organisation] is supportive of the public consultation and development of the Evidence-Based Clinical Practice Guideline for Deprescribing Cholinesterase Inhibitors and Memantine in People with Dementia. The [organisation] would appreciate being kept informed about the development of the Guideline, through its secretariat (refer to contact details above), particular if changes to clinical practice are recommended ... [removed to de-identify submission]	We thank the [organisation] for their support of the development of this guideline. We will keep them informed if there are any changes to recommendations in the future that are relevant to their organisation.	N/A
#8 (Organisation)	Thank you for the opportunity to comment on Public Consultation: Draft - Evidence-Based Clinical Practice Guideline for Deprescribing Cholinesterase Inhibitors and Memantine in People with Dementia. [Organisation] does not have the clinical expertise to comment on the guidelines so we can't offer any specific comment at this time.	We thank this organisation for their response.	N/A
#9	The [organisation] commends the development of this clinical practice guideline	Thank you	N/A

(Organisation)	to date and welcomes the opportunity to consult on this draft. On a general note it was felt that the draft guideline is a useful and comprehensive guideline which consolidates the evidence well regarding a controversial approach.		
	Comments on the actual recommendations: It is suggested that the executive summary and recommendations would benefit from the inclusion of a summary of 'what to do' after discontinuation. It is noted that this appears in Table 6: Guidance on management of change in condition following discontinuation on page 55 of the guideline.	We thank this organization for this suggestion. We agree that it would be helpful to add a 'what to do' after discontinuation section in the preliminary pages.	We have added a box after the recommendations with some additional guidance on monitoring and follow-up (with reference to the relevant sections later in the guideline). *Page 8*
	On page 6, it is suggested that the review after deprescribing of cholinesterase inhibitors and/or memantine should be at 4 weeks. The [organisation] feels that the initial review period may benefit from occurring earlier as it is felt that most change will occur in the first few weeks if the agent is 'active'.	There was very little available evidence to guide our recommendation of a follow-up during tapering and after discontinuation. But we thought that it was important to include a specific recommendation on this, to ensure that follow-up was conducted. Our time period of 4 weeks was based on allowing time for the reappearance of dementia-related symptoms (re-emergence of the condition and need for ongoing medication use), while also considering the rate of clearance of the medication. Studies indicate that, after short-term use, the cognitive symptomatic effect of ChEIs reduced to the level of placebo-treated participants after approximately four to six weeks. Also considered was a time period that would allow for appropriate monitoring of fluctuating symptoms and the quantity of tablets that	Based on a previous recommendation of this organisation we have added a Box after the recommendation with further details about monitoring and follow-up. Here we have noted that a shorter time period may be appropriate in individuals where there is a high concern about return of symptoms. *Page 8*

		usually come in a package (one month's supply). We have noted in the clinical considerations section that duration between dose reduction/monitoring can be altered to suit the person with dementia/family/carer. We do agree that a shorter period (such as 1-2 weeks) may be appropriate in some circumstances, for example where there is a high risk or concern about worsening of cognitive impairment.	
	On page 7, it is felt the second and fourth CBR (as in bullet points below) would benefit from increased clarity regarding the circumstances in which a trial of AChEI/memantine discontinuation should be undertaken for the patient groups in question, especially regarding emphasising an individualised approach be undertaken for each patient and considering that patients with Lewy body dementia and dementia of Parkinson's disease tend to do very well on ACHEI's. • 'For individuals taking a cholinesterase inhibitor (donepezil, rivastigmine or galantamine) for an indication other than Alzheimer's disease, dementia of Parkinson's disease, Lewy body dementia or vascular dementia, we recommend trial discontinuation' • 'For individuals taking memantine for indications other than Alzheimer's disease, dementia of Parkinson's disease or Lewy body dementia, we	We have considered this comment – however, it is unclear how we can make this recommendation clearer. We have included dementia of Parkinson's disease and Lewy body dementia as conditions similar to AD and these indications fall under the first and 3rd CBRs – where there are more details of when to consider deprescribing In the CBRs highlighted by this organisation – these refer to any indication that is not AD, PDD or LBD.	No changes.

	recommend trial discontinuation'		
	In Table 6: on page 55, in the longer term tab, it was felt further clarity could be beneficial here to explain the timeframes as it was felt that it may be difficult to ascertain whether ongoing decline is due to the agent being withdrawn or the natural progression of the dementia.	The GDT agrees that it may be very difficult to ascertain if ongoing decline is due to the agent being withdrawn (i.e. return of condition) or natural progression of dementia. We have provided some guidance related to the timing of when symptoms/changes occur to help clinicians with this determination – and therefore whether the medication should be restarted. Unfortunately, there was scarce evidence to support this, especially in the period of 6 weeks to 3 months where we have noted that decline may be due either to progression of the disease or return of condition. The GDT did not feel that there was sufficient evidence to provide only one probable cause during this time frame – however, based on a few studies that report return of symptoms to placebo treatment levels after about 6 weeks we have slightly altered the wording to accommodate the greater likelihood of progression of disease after this time point.	Previously for the 6 week to 3 month time period, possible cause was: "Progression of condition or possible re-emergence of symptoms that were being treated by ChEI/memantine" This has been changed to: "*Likely* progression of condition or possible re-emergence of symptoms that were being treated by ChEI/memantine" *Page 56*
	It is suggested that the wording of the grading of the strength of the recommendations be reviewed as it may appear confusing as the strength grading appears contradictory to the level of evidence for each stance.	The wording of the strength of the recommendations and quality of the evidence is in accordance with the recommendations of NHMRC and GRADE. It is understandable that these are not intuitive assessment. We have the following explanation in the executive summary: "The rating of strong is primarily based on the evidence presented (despite its low quality) and a reasonable judgement of the limited	No changes

		potential for harm in a carefully monitored **trial of discontinuation**." And the following in the section of areas of major debate: "It is also important to remember that the strength of the recommendation is based not only on the systematic review evidence, but also on the review of benefits and harms, consumer values and preferences, and economic considerations."	
	Comments on other aspects of the guideline and supporting materials: It is suggested that the recommendations section would benefit from the inclusion of a statement as to what constitutes "severe/end stage" dementia.	Thank you for this recommendation, we have added a brief definition for what constitutes severe/end stage dementia.	Definition: "(some characteristics of this stage include dependence in most activities of daily living, inability to respond to their environment and/or limited life expectancy)." *Page 7*
#10 (Organisation)	Thank you for the opportunity to provide feedback to the above Guidelines. [Organisation] commends the authors on a well constructed paper. It deals with a difficult clinical area that has not previously been extensively addressed and in which a relatively sparse evidence based exists with more research required. We are supportive of the indications for trial of discontinuation that are presented and agree that the terms 'trial of discontinuation' or 'trial deprescribing' are appropriate. We are also pleased that there is a clear focus on the key role of discussing decision making around deprescription with persons with dementia and their carers.	We thank this organisation for their positive feedback.	N/A

	[Organisation] ... make the following comments for consideration: 1. Given that most of the recommendations are based on consensus rather than a strong evidence base, the guideline may be more appropriately titled a 'Consensus Clinical Practice Guideline.'	While the recommendations are termed Consensus Based Recommendations (CBRs) they are still based on evidence. As per the definition we provided: "CBRs are recommendations based on a systematic review where there is limited or low-quality evidence." (Executive Summary). We have followed a robust method for evidence sourcing and synthesis and development of recommendations. While there are significant limitations to the evidence available, this is discussed extensively throughout the guideline. The GDT is confident that the title of 'evidence-based' accurately reflects our processes and the recommendations. Recommendations which are not based on a systematic review of the evidence (Practice Points, PP) are clearly labelled as such.	No changes
	2. Our view is that decisions on deprescribing and tapered withdrawals should be individualised. We note that there was considerable debate around this issue between the authors of the guideline.	We thank the organisation for this comment and agree that decisions on deprescribing and tapered withdrawals should be individualized. The debate between GDT members focused not on this point (it was generally agreed that individual review/consideration was required) but how to express this need for individualisation in the recommendations – which we also wanted to be clear and concise. We resolved this debate by adding a preamble and having an introductory line to the recommendations: **"We present these recommendations for clinicians to consider within the context of**	No changes required.

		each individual:"	
	3. There could be a greater emphasis placed in the recommendations on the importance of close monitoring of persons with dementia for cognitive decline following commencement of deprescribing.	Thank you for this suggestion. We have added the word 'close' to the PP. We have also added a box after the recommendations on what to do after deprescribing where we emphasise the importance of monitoring.	Revised PP: **"PP:** Deprescribing of cholinesterase inhibitors and/or memantine should be a **trial discontinuation**, with *close* periodic monitoring (such as every four weeks) and re-initiation of the medication if the individual evidences clear worsening of condition after withdrawal." *Page 7* Box 1: "Close monitoring during and after withdrawal of ChEIs and memantine is very important." *Page 8*
	4. The recommended tapering appears very reasonable but is incongruous with the immediate cessation that is generally appropriate in circumstances where side-effects have prompted discontinuation. It may be worthwhile making this distinction clearer.	We thank the organisation for this suggestion. This is an important point that was not clear previously.	We have added a Box after the recommendations with guidance on how to taper and monitor after discontinuation. We have included the point here that abrupt cessation may be appropriate in some circumstance: "Abrupt cessation may be appropriate in some individuals such as if they are experiencing a severe adverse drug reaction. Instructions should be provided to the individual and/or carer/family on what to look out for and what to do if symptoms occur (particularly the possible risk of adverse drug withdrawal event)." *Page 8* We have also added comment about this to the section on Tapering in the main part of the guideline: "In the situation of severe or concerning adverse drug reactions, abrupt discontinuation may be the most

			appropriate cessation method (as exposure even to a lower dose for an extra four weeks may be inappropriate). As above, the potential risk of abrupt cessation should be discussed." *Page 55*
	5. Nursing home admission in and of itself should not necessarily equate to ongoing prescription futility unless associated with other features of end-stage disease (eg. language, mobility, swallowing and oral intake deterioration).	Our GDT agrees with – we originally considered it as a 'trigger' to review and consider deprescribing but decided not to because of the reasons outlined by this organisation. We have added a brief definition to 'severe/end stage dementia' to ensure that this is not mistaken to mean admission to a residential aged care facility.	We have added a brief definition of 'severe/end stage dementia': "(some characteristics of this stage include dependence in most activities of daily living, inability to respond to their environment and/or limited life expectancy)." *Page 7*
#11 (Organisation)	Thank you for the opportunity to provide feedback on the Guidelines released for public consultation: evidence-based clinical practice guideline deprescribing cholinesterase inhibitors and memantine in people with dementia.	We thank the organisation for their comments.	N/A
	• Recommendations document Page 2: Paragraph 1: Last Sentence: "These medications can have important benefits to people with dementia and their carers" This statement is not referenced and is broad and nonspecific. The [organisation] suggests: • adding a summary of benefits such as 'improvement on cognitive testing' to the statement adding an overarching statement indicating that these medications are not a disease-modifying agent, may increase	We thank the [organisation] for this suggestion and agree that greater details were required for this sentence. The inclusion of this sentence was to ensure that there was a positive and balanced tone to the guideline to recognise that some individuals may experience important benefits from these medications.	This sentence now reads: "These medications are not disease modifying, but they can have important benefits to people with dementia and their carers (such as through improvement of cognitive function)." *Page 3*

	practitioner comfort when considering deprescribing.		
	• Consumer feedback suggests that the language used in the documents is complex and limits their understanding and likely receptiveness to changes advocated in treatment plans. Developing and ensuring information is presented in plain English may assist carers in adopting any recommendations. I trust you will consider these comments in your review of the guideline.	Thank you for highlighting this concern. We have made it a priority to develop a version of this guideline which contains language more appropriate for the consumer audience. This is, however, not yet available. We considered ensuring that the introduction section and recommendations were appropriate for the lay audience – however, we did not feel that we were able to completely achieve this at this time given the primary audience of prescribers and the overall complex nature of this guideline.	No changes to guideline – however developing a consumer companion version of the guideline is a priority for the GDT.
#12 (Individual)	**Comments on actual recommendations:** I am fully supportive of the recommendations being applied to patients on an individual basis, after consultation with the patient and family / carers. There is a lot of anxiety regarding deprescribing these drugs, particularly here as they are rarely commenced outside our [organisation]. It seems that often they are ceased by the GP once the patient goes into residential care, and that this can be associated with significant cognitive decline. I hope that these guidelines will reduce the frequency of this happening. **Comments on other aspects of the guideline and supporting materials:** No Comment	Thank you for your positive feedback. The GDT consciously chose not to include admission to residential aged care facility as a reason for deprescribing – as highlighted, we agreed that this is not always appropriate.	No changes required.
#13	We have no dissent with the recommendations.	We thank this organisation for their positive feedback.	

(Organisation)	We have no dissent with the guideline and supporting materials		
#14 (Organisation)	**Comments on the actual recommendations:** The initial advice when this drug was released was not to cease or miss doses because once cognitive decline occurs it is permanent. There is no concern for patients who have a dose reduction or medication ceased where cognitive decline does not occur because the benefits outweigh the risk. However, there is concern that other patients will experience what was an avoidable decline in cognition had the medication not been ceased or reduced. The [organisation] has raised this concern since there is not necessarily a robust way for determining which patients may fall into the second category. Clinicians will need to carefully consider the risks and benefits plus family and patient wishes when deciding to dose reduce or discontinue this medication.	Thank you for this comment. Regarding the concern about 'permanent' cognitive decline, we have discussed this concern in the clinical considerations section: 'Will temporary dose reduction/cessation cause irreversible harm?' While there some evidence to support this concern, the overall picture is unclear as there also exists conflicting evidence and significant limitations of the studies. Our recommendations aim to identify those who are at the least risk of reduced cognitive decline upon withdrawal of the medication. The time recommendation of >12 months use in several of the recommendations is to specifically minimise this concern which seems to be an issue early in the treatment course (if indeed it does occur). We agree that there is potential for harm through deprescribing and with the comment that there is no robust way to identify which specific individuals will experience harm. We have aimed to emphasise throughout the guideline that the potential benefits and risks of deprescribing need to be weighed up against the potential harms – and also that there is considerable uncertainty in these benefits and harms. Additionally, our plain English summary emphasises the need to discuss the potential for harm with the consumer: "Good	We have added a table which clearly outlines the potential for benefit and harm with both continuing and discontinuing medication use to further highlight that there are potential harms and benefits to both continuation and discontinuation. *Page 9* We have also added a box after the recommendations with a summary of follow-up and monitoring guidance to emphasise the need for this to minimise the potential for harm though deprescribing. *Page 8*

		communication between clinicians and people with dementia and/or carers/family on the benefits and harms of continuing versus discontinuing, in the context of their values and preferences, is necessary when discussing a potential trial of deprescribing."	
	The [organisation] wishes to note that even high level care patients may benefit from the behaviour control properties of this medication. This should be a factor used when considering if tapering or discontinuation is appropriate for a patient.	We thank the organisation for highlighting this. We chose not to include residential care facility admission or requiring 'high level of care' as specific criteria for deprescribing. We have provided a definition of severe/end stage dementia to ensure that this is not misinterpreted to be a specific level of care required. As a GDT we debated the need to add caveats/explanations to all the recommendations versus the need to provide clear guidance for the primary audience (prescribers) – this means that there will be exceptions (for example those in high level of care whose behavioural symptoms responded well to medication use). From our systematic review, there is a potential for behavioural symptoms to worsen upon withdrawal – however, the evidence was unclear and we concluded that the overall risk was likely to be small (although noting there may be significant individual variability in this). Measurement of behavioural symptoms over time in people with dementia is complicated by the fluctuating nature of these symptoms.	We have added a brief definition of 'severe/end stage dementia': "(some characteristics of this stage include dependence in most activities of daily living, inability to respond to their environment and/or limited life expectancy)." *Page 7* This is also listed as a potential harm from discontinuation in our new table which outlines the potential benefits and harms of continuation and discontinuation. *Page 9*
	Comments on other aspects of the guideline and supporting material:	We thank the organisation for raising this concern as it has provided us with the ability to	In order to clarify the definition of a 'strong' recommendation we have added "[based on

	The [organisation] is concerned that the material is titled as evidence based however throughout the documents it is noted that the evidence is very limited and that the decision was based on what the majority of clinical staff would do rather than on scientific evidence. This appears misleading.	clarify. The reference to the recommendation being graded as strong based on what a majority of clinicians would do does not specifically relate to a lack of evidence. The definition states that it is what a majority of informed people would choose – i.e. based on the evidence. This reflects the consideration that all recommendations will involve a trade-off. This is summarised by the GRADE working group: "Recommendations involve a trade-off between benefits and harms. Making that trade-off inevitably involves placing, implicitly or explicitly, a relative value on each outcome. It is often difficult to judge how much weight to give to different outcomes, and different people will often have different values. People making judgments on behalf of others are on stronger ground if they have evidence of the values of those affected. For instance, people making recommendations about chemotherapy for women with early breast cancer will be in a stronger position if they have evidence about the relative importance those women place on reducing the risk of a recurrence of breast cancer relative to avoiding the side effects of chemotherapy." Additionally, while the recommendations are termed Consensus Based Recommendations (CBRs) they are still based on evidence. As per the definition we provided: "CBRs are recommendations based on a systematic review where there is limited or	the evidence available]" to the describing text. *Page 10*

		low-quality evidence." (Executive Summary). We have followed a robust method for evidence sourcing and synthesis and development of recommendations. While there are significant limitations to the evidence available, this is discussed extensively throughout the guideline. The GDT is confident that the title of 'evidence-based' accurately reflects our processes and the recommendations. Recommendations which are not based on a systematic review of the evidence (Practice Points, PP) are clearly labelled as such.	
#15 (Individual)	Recommend adding in a preamble on not starting these drugs!	We thank the individual for their response. Unfortunately, it was outside the scope of the guideline to recommend when (or not) these medications should be initiated. We have referred readers to relevant guidelines and also provided a review of the potential benefits and harms of these medications.	No changes required.