Ontario Health
Cancer Care Ontario

Guideline Endorsement 3-22 REQUIRES UPDATING

A Quality Initiative of the Program in Evidence-Based Care (PEBC), Ontario Health (Cancer Care Ontario)

An Endorsement of the 2018 Guideline on Hypofractionated Radiation Therapy for Localized Prostate Cancer: An ASTRO, ASCO, and AUA Evidence-Based Guideline

H. Lukka, J. Brown, C. Catton, B. Shayegan and the Hypofractionated Radiation Therapy for Prostate Cancer Guideline Development Group

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This publication is an OH (CCO) Hypofractionated Radiation Therapy for Prostate Guideline Development Group Endorsement of the 2018 Guideline on Hypofractionated Radiation Therapy for Localized Prostate Cancer: An ASTRO, ASCO and AUA Evidence-based Guideline. The original publication is available at: https://www.astro.org/Patient-Care-and-Research/Clinical-Practice-Statements/ASTRO-39;s-guideline-on-hypofractionation-for-loca

An assessment conducted in January 2022 indicated that Guideline Endorsement 3-22 REQUIRES UPDATING. It is still appropriate for this document to be available while this updating process unfolds. The PEBC has a formal and standardized process to ensure the currency of each document (PEBC Assessment & Review Protocol).

GL-END 3-22 is comprised of 2 sections. You can access the summary and full report here: https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/65431

Section 1: Guideline Endorsement
Section 2: Endorsement Methods Overview

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For information about this document, please contact H. Lukka through the PEBC via: Phone: 905-527-4322 ext. 42822 Fax: 905 526-6775 E-mail: ccopgi@mcmaster.ca

For information about the PEBC and the most current version of all reports, please visit the OH (CCO) website at https://www.cancercareontario.ca/en/guidelines-advice or contact the PEBC office at: Phone: 905-527-4322 ext. 42822 Fax: 905 526-6775 E-mail: ccopgi@mcmaster.ca

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An Endorsement of the 2018 Guideline on Hypofractionated Radiation Therapy for Localized Prostate Cancer: An ASTRO, ASCO, and AUA Evidence-Based Guideline

Section 1: Guideline Endorsement

GUIDELINE OBJECTIVES

The objectives of this guideline are to assess the advantages of hypofractionated radiation therapy compared to conventional fractionation in terms of prostate control, toxicity, and quality of life. Our recommendations are based on the 2018 Guideline on Hypofractionated Radiation Therapy for Localized Prostate Cancer: An ASTRO, ASCO, and AUA[1] Evidence-Based Guideline [1].

TARGET POPULATION

Men with localized prostate cancer.

INTENDED USERS

The guideline document will support providers in recommending the most optimal radiation therapy schedules to their patients.

ENDORSEMENT

The Hypofractionated Radiation Therapy for Prostate Cancer Guideline Development Group (GDG) of Ontario Health (Cancer Care Ontario) endorses the recommendations of Hypofractionated Radiation Therapy for Localized Prostate Cancer: an ASTRO, ASCO and AUA Evidence-Based Guideline modified by the endorsement process described in this document. Sixteen of the 18 questions were endorsed without modifications or comments. Two recommendations (KQ3B and KQ4A) were endorsed with comments as listed in Table 1-1.

Table 1-1. ASTRO/ASCO/AUA evidence-based guideline recommendations: Hypofractionated radiation therapy for localized prostate cancer [1]

Recommendations	Assessment
KQ1A: In men with low-risk prostate cancer who decline active surveillance and receive external beam radiotherapy (EBRT) to the prostate with or without radiation to the seminal vesicles, moderate hypofractionation should be offered.	**ENDORSED**
KQ1B: In men with intermediate-risk prostate cancer receiving EBRT to the prostate with or without radiation to the seminal vesicles, moderate hypofractionation should be offered.	**ENDORSED**
KQ1C: In men with high-risk prostate cancer receiving EBRT to the prostate, but not including pelvic lymph nodes, moderate hypofractionation should be offered.	**ENDORSED**
KQ1D: In patients who are candidates for EBRT, moderate hypofractionation should be offered regardless of patient age, comorbidity, anatomy, or urinary function. However, physicians should discuss the	**ENDORSED**

[1] ASTRO = American Society for Radiation Oncology; ASCO = American Society of Clinical Oncology; AUA = American Urological Association

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limited follow-up beyond five years for most existing randomized controlled trials (RCTs) evaluating moderate hypofractionation.	
KQ1E: Men should be counselled about the small increased risk of acute gastrointestinal (GI) toxicity with moderate hypofractionation. Moderately hypofractionated EBRT has a similar risk of acute and late genitourinary (GU) and late GI toxicity compared with conventionally fractionated EBRT. However, physicians should discuss the limited follow-up beyond five years for most existing RCTs evaluating moderate hypofractionation.	**ENDORSED**
KQ2A: Regimens of 6000 cGy delivered in 20 fractions of 300 cGy and 7000 cGy delivered in 28 fractions of 250 cGy are suggested since they are supported by the largest evidentiary base. One optimal regimen cannot be determined because most of the multiple fractionation schemes evaluated in clinical trials have not been compared head to head.	**ENDORSED**
KQ2B: One moderately hypofractionated regimen is not suggested over another for cancer control for specific risk groups, and the efficacy of moderately hypofractionated EBRT regimens does not appear to be affected by patient age, comorbidity, anatomy, or urinary function.	**ENDORSED**
KQ3A: In men with low-risk prostate cancer who decline active surveillance and choose active treatment with EBRT, ultrahypofractionation may be offered as an alternative to conventional fractionation.	**ENDORSED**
KQ3B: In men with intermediate-risk prostate cancer receiving EBRT, ultrahypofractionation may be offered as an alternative to conventional fractionation. The task force strongly encourages that these patients be treated as part of a clinical trial or multi-institutional registry. **Comment:** There is additional RCT evidence to support the recommendation of KQ3B that may increase the quality of evidence for the use of ultrahypofractionation in intermediate-risk disease from low to at least moderate [2].	**ENDORSED with comment**
KQ3C: In men with high-risk prostate cancer receiving EBRT, the task force does not suggest offering ultrahypofractionation outside of a clinical trial or multi-institutional registry due to insufficient comparative evidence.	**ENDORSED**
KQ4A: Ultrahypofractionated prostate EBRT of 3500 to 3625 cGy in five fractions of 700 to 725 cGy to the planning target volume may be offered to low- and intermediate-risk patients with prostate sizes less than 100 cm^3. The key dose constraints in KQ5B should be followed. **Comment:** A regimen of 4270 cGy delivered in seven fractions of 610 cGy is suggested since it is supported by the highest-level evidence [2]. One optimal regimen cannot be determined because most of the multiple fractionation schemes evaluated in clinical trials have not been compared head to head. It is strongly encouraged that these patients be treated as part of a clinical trial or multi-institutional registry.	**ENDORSED With comment**
KQ4B: Five-fraction prostate ultrahypofractionation at doses above 3625 cGy to the planning target volume is not suggested outside the setting of a clinical trial or multi-institutional registry due to risk of late toxicity.	**ENDORSED**
KQ4C: Five-fraction prostate ultrahypofractionation using consecutive daily treatments is not suggested due to potential increased risk of late urinary and rectal toxicity.	**ENDORSED**
KQ5A: At least two dose-volume constraint points for rectum and bladder should be used for moderately or ultrahypofractionated EBRT: one at the	**ENDORSED**

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high-dose end (near the total dose prescribed) and one in the mid-dose range (near the midpoint of the total dose).	
KQ5B: Use of normal tissue constraints for moderately or ultrahypofractionated EBRT that differ from those of a published reference study is not recommended due to the risk of both acute and late toxicity.	**ENDORSED**
KQ6A: Use of target volume and associated margin definitions for hypofractionated EBRT that deviate from those of a published reference study is not recommended, especially for ultrahypofractionated regimens.	**ENDORSED**
KQ7A: Image-guided radiation therapy is universally recommended when delivering moderately or ultrahypofractionated EBRT.	**ENDORSED**
KQ8A: Nonmodulated three-dimensional conformal radiation therapy techniques are not recommended when delivering moderately fractionated or ultrahypofractionated prostate EBRT.	**ENDORSED**
ASCO = American Society of Clinical Oncology; ASTRO = American Society for Radiation Oncology; AUA = American Urological Association	

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An Endorsement of the 2018 Guideline on Hypofractionated Radiation Therapy for Localized Prostate Cancer: An ASTRO, ASCO, and AUA Evidence-Based Guideline

Section 2: Endorsement Methods Overview

THE PROGRAM IN EVIDENCE-BASED CARE

The Program in Evidence-Based Care (PEBC) is an initiative of the Ontario provincial cancer system, Ontario Health (Cancer Care Ontario) (OH [CCO]). The PEBC mandate is to improve the lives of Ontarians affected by cancer through the development, dissemination, and evaluation of evidence-based products designed to facilitate clinical, planning, and policy decisions about cancer control.

The PEBC is a provincial initiative of OH (CCO) supported by the Ontario Ministry of Health (OMH). All work produced by the PEBC is editorially independent from the OMH.

BACKGROUND FOR GUIDELINE

There is currently no established guideline, specific to Ontario, in this area; other jurisdictions are reviewing the evidence for hypofractionation. It is of interest to our clinicians such that we can alter our care if the evidence supports it.

GUIDELINE ENDORSEMENT DEVELOPERS

This endorsement project was developed by the Hypofractionated Radiation Therapy for Prostate Cancer GDG, which was convened at the request of the Radiation Treatment Program. The project was led by a small Working Group of the GDG, which was responsible for reviewing the evidence base and recommendations in "Hypofractionated Radiation Therapy for Localized Prostate Cancer: An ASTRO, ASCO, and AUA Evidence-Based Guideline [1]" in detail and making an initial determination as to any necessary changes, drafting the first version of the endorsement document, and responding to comments received during the document review process. The Working Group members had expertise in radiation oncology and urology. Other members of the Hypofractionated Radiation Therapy for Prostate Cancer GDG served as the Expert Panel and were responsible for the review and approval of the draft document produced by the Working Group. Conflict of interest declarations for all GDG members are summarized in Appendix 1, and were managed in accordance with the *PEBC Conflict of Interest Policy*.

ENDORSEMENT METHODS

The PEBC endorses guidelines using the process outlined in OH (CCO)'s Guideline Endorsement Protocol [3]. This process includes selection of a guideline, assessment of the recommendations (if applicable), drafting the endorsement document by the Working Group, and internal review by content and methodology experts.

The PEBC assesses the quality of guidelines using the AGREE II tool [4]. AGREE II is a 23-item validated tool that is designed to assess the methodological rigour and transparency of guideline development and to improve the completeness and transparency of reporting in practice guidelines.

Implementation considerations such as costs, human resources, and unique requirements for special or disadvantaged populations may be provided along with the recommendations for information purposes.

Selection of Guidelines

UNDER PEER REVIEW

The Radiation Treatment Program, Disease Pathway Management, Ontario GU Cancers Advisory Committee, GU disease site group (DSG) chairs reviewed the ASTRO, ASCO, and AUA evidence-based guideline on hypofractionated radiation therapy for localized prostate cancer and accepted it as potentially useful and relevant to guide practice in Ontario.

Assessment of Guideline(s)

The Working Group selected the ASTRO guideline because the rigour of development domain, which assesses the methodological quality of the guideline, had the highest score.

Details of the AGREE II assessment can be found in Appendix 2. The overall quality of the guideline was rated as "6" by both appraisers (on a scale from 1 to 7). Both appraisers stated that they would recommend this guideline for use. The AGREE II quality ratings for the individual domains were varied; they were assessed at 97% for scope and purpose, 89% for stakeholder involvement, 89% for rigour of development, 94% for clarity of presentation, 46% for applicability, and 71% for editorial independence.

DESCRIPTION OF ENDORSED GUIDELINE(S)

The ASTRO guideline presented recommendations addressing eight key questions regarding moderately hypofractionated and ultrahypofractionated radiation therapy for localized prostate cancer. The recommendations were based on a systematic literature review and created using a predefined consensus-building methodology and approved tools for grading evidence quality and recommendation strengths. The guidelines recommended moderate hypofractionation across risk groups to patients choosing EBRT (based on high-quality evidence and high consensus). The guideline conditionally recommended that ultrahypofractionated radiation therapy may be offered for low- and intermediate-risk prostate cancer but strongly encourages treatment of intermediate-risk patents on a clinical trial or multi-institutional registry. The guideline conditionally recommended against routine use of ultrahypofractionated EBRT for high-risk patients. The guideline recommended image-guided radiation therapy and avoidance of non-modulated three-dimensional conformal technique with any hypofractionated approach [1].

ENDORSEMENT PROCESS

The Working Group assessed the 2018 ASTRO Guideline in detail and reviewed each recommendation of the guideline to determine whether it could be endorsed, endorsed with modifications, or rejected. There are 18 recommendations based on eight research questions. The Working Group considered the following issues for each of the recommendations:

1) Does the Working Group agree with the interpretation of the evidence and the justification of the original recommendation?
2) Are modifications required to align with the Ontario context?
3) Is it likely there is new, unidentified evidence that would call into question the recommendation?
4) Are statements of qualification/clarification to the recommendation required?

ENDORSEMENT and MODIFICATIONS

Sixteen of the 18 key recommendations were endorsed without modifications or comments. Two recommendations (KQ3B and KQ4A) were endorsed with comments as listed in Table 2-1 (see Section 1, Table 1-1 for a list of all 18 recommendations).

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Table 2-1. ASTRO/ASCO/AUA Evidence-based guideline recommendations: Hypofractionated Radiation Therapy for localized prostate cancer [1]	
Recommendations	**Assessment**
KQ3B: In men with intermediate-risk prostate cancer receiving EBRT, ultrahypofractionation may be offered as an alternative to conventional fractionation. The task force strongly encourages that these patients be treated as part of a clinical trial or multi-institutional registry. **Comment:** There is additional RCT evidence to support the recommendation of KQ3B that may increase the quality of evidence for the use of ultrahypofractionation in intermediate-risk disease from low to at least moderate [2].	**ENDORSED with comment**
KQ4A: Ultrahypofractionated prostate EBRT of 3500 to 3625 cGy in five fractions of 700 to 725 cGy to the planning target volume may be offered to low- and intermediate-risk patients with prostate sizes less than 100 cm^3. The key dose constraints in KQ5B should be followed. **Comment:** A regimen of 4270 cGy delivered in seven fractions of 610 cGy is suggested since it is supported by the highest-level evidence [2]. One optimal regimen cannot be determined because most of the multiple fractionation schemes evaluated in clinical trials have not been compared head to head. It is strongly encouraged that these patients be treated as part of a clinical trial or multi-institutional registry.	**ENDORSED With comment**
ASTRO = American Society for Radiation Oncology; ASCO = American Society of Clinical Oncology; AUA = American Urological Association	

EXPERT PANEL REVIEW AND APPROVAL

Following the formulation of the first draft, the recommendation endorsement was reviewed by the Director and Assistant Director of the PEBC and the Working Group was responsible for ensuring the necessary changes were made. An Expert Panel of clinical content experts (members of the radiation treatment and GU community) reviewed the draft endorsement document, provided feedback, and approved the final version (See Appendix 1 for a list of Expert Panel members and conflict of interest declarations).

Of the 10 members of the GDG Expert Panel, nine members voted and one abstained, for a total of 90% response in March 2020. Of those nine who voted, all approved the document (100%). The main comments from the Expert Panel and the Working Group's responses are summarized in Table 2-2.

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Table 2-2. Summary of the Working Group's responses to comments from the Expert Panel.

Comments	Responses
1. KQ4A: Should we add a comment regarding additional evidence to support the use of 42.7 Gy/7 fractions (ref 2 - Widmark Lancet 2019)	The change we made to KQ4A only referenced the paper (Widmark Lancet 2019). The comments below suggest for #1, including some actual data, and for #2, making a recommendation about adopting the specifics of the trial. Comment 1 provides additional granularity to what we recommended, and is quite reasonable. Comment 2 raises the recommendation to another level by supporting a specific dose/fractionation scheme for ultrahypofractionation. Since KQ2A did the same thing for moderate fractionation it is also reasonable to include this for KQ4A. If we do, we should use the same general wording as in KQ2A ie: **"A regimen of 4270 cGy delivered in seven fractions of 610 cGy is suggested since it is supported by the highest-level evidence. One optimal regimen cannot be determined because most of the multiple fractionation schemes evaluated in clinical trials have not been compared head to head."**
2. KQ4A should have a comment 'Doses above are based on non-RCT data and since RCT data are now available ultrahypofractionated EBRT of 4270 cGy in seven fractions may be the preferred alternative' or words to that effect.	

DISSEMINATION

The endorsement document will be published on the OH (CCO) website. OH (CCO)-PEBC guidelines are routinely included in several international guideline databases including the CPAC Cancer Guidelines Database, the CMA/Joule CPG Infobase database, NICE Evidence Search (UK), and the Guidelines International Network (GIN) Library.

UPDATING THE ENDORSEMENT

OH (CCO)/PEBC will review the endorsement on an annual basis to ensure that it remains relevant and appropriate for use in Ontario.

ACKNOWLEDGEMENTS

The Hypofractionated Radiation Therapy for Prostate Cancer GDG would like to thank the following individuals for their assistance in developing this report:

- Jonathan Sussman and Sheila McNair for providing feedback on draft versions.
- Sara Miller for copy editing.

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CONCLUSION

The final endorsed recommendation contained in Section 1 reflect the integration of feedback obtained through the internal review processes with the document as drafted by the GDG Working Group and approved by the GDG Expert Panel.

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References

1. Morgan SC, Hoffman K, Loblaw DA, Buyyounouski MK, Patton C, Barocas D, et al. Hypofractionated radiation therapy for localized prostate cancer: An ASTRO, ASCO, and AUA evidence-based guideline. J Clin Oncol. 2018;36(34):JCO1801097-JCO.
2. Widmark A, Gunnlaugsson A, Beckman L, Thellenberg-Karlsson C, Hoyer M, Lagerlund M, et al. Ultra-hypofractionated versus conventionally fractionated radiotherapy for prostate cancer: 5-year outcomes of the HYPO-RT-PC randomised, non-inferiority, phase 3 trial. Lancet. 2019;394(10196):385-95.
3. Program in Evidence-based Care. Cancer Care Ontario quideline endorsement protocol. http://pebctoolkitmcmasterca/dokuphp?id=projectdev:cco_endorsement_protocol.Toronto Ontario, Accessed January 20, 2020.
4. 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. 2010;182(18):E839-E42.

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Appendix 1: Affiliations and Conflict of Interest Declarations

Members of the Hypofractionated Radiation Therapy for Prostate Cancer Guideline Development Group

Name	Affiliation	Conflict of Interest
Working Group		
Judy Brown	Health Research Methodologist McMaster University, Department of Oncology, Program in Evidence-Based Care, Hamilton, ON	None declared
Charles Catton	Princess Margaret Cancer Centre Toronto, ON	[a] See below
Himu Lukka	Faculty of Health Sciences and Department of Oncology McMaster University Hamilton, ON	[b] See below
Bobby Shayegan	St. Joseph's Healthcare Institute of Urology Hamilton, ON	None declared
Expert Panel and Members of the Guideline Development Group		
Patrick Cheung	Sunnybrook Health Sciences Centre, Toronto, ON	[c] See below
Peter Chung	Princess Margaret Cancer Centre, Toronto, ON	[d] See below
Louis Fenkell	Stronach Regional Cancer Centre, Newmarket, ON	None declared
Wayne Koll	Lakeridge Health Corp Oshawa Site Durham Regional Cancer Centre, Oshawa ON	[e] See below
Joelle Helou	Radiation Oncology, University of Toronto, Toronto, ON	[f] See below
Gerard Morton	Odette Cancer Centre Sunnybrook Health Sciences Centre, Toronto, ON	[g] See below
Srinivas Raman	Princess Margaret Cancer Centre, Toronto, ON	[h] See below
George Rodrigues	London Regional Cancer Program, London, ON	None declared
Kara Schnarr	Department of Oncology McMaster University, Hamilton ON	None declared
Danny Vesprini	Sunnybrook Health Sciences Centre, Toronto, ON	[i] see below

[a] Employment at Himanshu Lukka Medicine Professional Corporation. Served as consultant for AbbVie, ASTRA, Zeneca, Astellas, Sanofi, Tersera, Bayer, Jansen, Ferring. Own business entity Himanshu Lukka Medicine Professional Corporation. Have stocks, etc. in Vertex Pharma. In the past have published several papers on hypofractionation.
[b] Served on Advisory Boards of AbbVie Corp, Bayer Corp, Astellas Ltd. Previous research grants AbbVie Corp. Principal Investigator on OGOG PROFIT trial. Published "The evolution of fractionated prostate cancer radiotherapy" Catton C et al, Lancet 2019. Managerial responsibility GU site leader, Princess Margaret Cancer Centre.
AbbVie Corp
[c] Invited speaker honoraria from TerSera, and Bayer

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Investigator initiated grant support from: Sanofi Aventis, AbbVie, Pfizer, TerSera
Sunnybrook Odette Cancer Centre hypofractionated prostate trial, specifically pHART2, which evaluates the use of moderately hypofractionation in localized high risk prostate cancer along with elective nodal irradiation in one simultaneous integrated boost type of radiotherapy plan.
Published: Elective Pelvic Nodal Irradiation With a Simultaneous Hypofractionated Integrated Prostate Boost for Localised Prostate Cancer: Ready for Prime Time?
Cheung P, Niazi T, Faria S, Loblaw A. Clin Oncol (R Coll Radiol). 2020 Mar;32(3):181-188. doi: 10.1016/j.clon.2019.12.002. Epub 2020 Jan 8.
[d] Principle investigator for MRI-Guided HDR Brachytherapy for Prostate Cancer Tumor-Targeted Radiotherapy for Patients with Localized Prostate Cancer
[e] Recruited patients for Profit RCT
[f] Medical Professional Corporation but no relevant conflicts
[g] Employment: Sunnybrook Health Sciences Centre
CCTG PR19: randomized trial of HDR and LDR mono therapies for low and intermediate risk prostate cancer
HDR Monotherapy Randomized Trial: comparison of two and one fraction of HDR. Single centre study
[h] Consulting and speaking fees for Astra Zeneca. Consulting fees for Sanofi
Co-investigator on grants received from Varian Medical Systems, unrelated to hypofractionation in prostate cancer
[i] Am the PI on an ongoing clinical trial looking at the feasibility of using an MRI integrated into a linear accelerator (MRI-Linac) to treat prostate cancer with stereotactic body radiotherapy (SBRT). The trial is named "The PRISM Odette Cancer Centre Study- Prostate Radiotherapy Integrated with Simultaneous MRI"

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Appendix 2: Agree II Score Sheet

Domain	Item	AGREE II Appraiser Ratings[1]	
		1	2
1) Scope and purpose	1. The overall objective(s) of the guideline is (are) specifically described.	7	7
	2. The health question(s) covered by the guideline is (are) specifically described.	7	7
	3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.	7	6
Domain score[2] - (41-6/42-6)*100 = 35/36*100 = .9722*100 = **97.2%**		Score 41	
2) Stakeholder involvement	4. The guideline development group includes individuals from all the relevant professional groups.	7	7
	5. The views and preferences of the target population (patients, public, etc.) have been sought.	7	7
	6. The target users of the guideline are clearly defined.	6	4
Domain score[2] - (38-6/42-6)*100 = 32/36*100 = .8888*100 = **88.8%**		Score 38	
3) Rigor of development	7. Systematic methods were used to search for evidence.	7	7
	8. The criteria for selecting the evidence are clearly described.	6	7
	9. The strengths and limitations of the body of evidence are clearly described.	6	5
	10. The methods for formulating the recommendations are clearly described.	6	7
	11. The health benefits, side effects and risks have been considered in formulating the recommendations.	7	7
	12. There is an explicit link between the recommendations and the supporting evidence.	6	7
	13. The guideline has been externally reviewed by experts prior to its publication.	7	7
	14. A procedure for updating the guideline is provided.	5	4
Domain score[2] - (101-16/112-16)*100 = 85/96*100 = .8888*100 = **88.8%**		Score 101	
4) Clarity of presentation	15. The recommendations are specific and unambiguous.	7	7
	16. The different options for management of the condition or health issue are clearly presented.	6	6
	17. Key recommendations are easily identifiable.	7	7
Domain score[2] - (40-6/42-6)*100 = 34/36*100 = .9444*100 = **94.4%**		Score 40	
5) Applicability	18. The guideline describes facilitators and barriers to its application.	5	3
	19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	5	3
	20. The potential resource implications of applying the recommendations have been considered.	5	5
	21. The guideline presents monitoring and/or auditing criteria.	3	1
Domain Score[2] - (30-8/56-8)*100 =22/48*100 = .4583*100 = **45.8%**		Score 30	
6) **Editorial independence**	22. The views of the funding body have not influenced the content of the guideline.	5	8

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Domain	Item	AGREE II Appraiser Ratings[1]	
		1	2
	23. Competing interests of guideline development group members have been recorded and addressed.	6	7
Domain Score[2] - (21-4/28-4)*100 = 17/24*100 = .7083*100 = **70.8%**		Score 21	
Overall Guideline Assessment	1. Rate the overall quality of this guideline.	**6**	**6**
Overall Guideline Assessment	2. I would recommend this guideline for use.	**Yes**	**Yes**

[1] Rated on a scale from 1 to 7, [2] Domain score = (Obtained score – Minimum possible score)/(Maximum possible score – Minimum possible score)

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