



Canadian Association of Radiologists Diagnostic Imaging Referral Guidelines: Guideline development methodology

Journal:	<i>CMAJ Open</i>
Manuscript ID	CMAJOpen-2022-0098
Manuscript Type:	Other
Date Submitted by the Author:	27-Apr-2022
Complete List of Authors:	Hamel, Candyce; The Canadian Association of Radiologists, Margau, Ryan; North York General Hospital Pageau, Paul; Ottawa Hospital Venturi, Marc; The Canadian Association of Radiologists Esmaeilisaraji, Leila; The Canadian Association of Radiologists Avard, Barb Campbell, Samuel; Dalhousie University, Emergency Medicine; Queen Elisabeth II Health Sciences Centre, Emergency Medicine Corser, Noel Dea, Nicolas; Vancouver General Hospital, Combined Neurosurgical and Orthopedic Spine Program Kwok, Edmund; University of Ottawa, Emergency Medicine MacLean, Cathy Sarrazin, Erin Yong-Hing, Charlotte Zaki-Metias, Kaitlin
Keywords:	Diagnostics, Radiology and imaging, Statistics and research methods
More Detailed Keywords:	Diagnostic imaging referral guideline, Methodology
Abstract:	<p>Background: Comprehensive diagnostic imaging referral guidelines are an important tool for facilitating referring clinicians and radiologists to determine the safest and best clinical value diagnostic imaging study for their patients. The Canadian Association of Radiologists (CAR) last produced their diagnostic imaging referral guidelines in 2012. In partnership with several national organizations, referring clinicians, radiologists, and patient and family advisors from across Canada, the CAR are redoing their referral guidelines using a new methodology for guideline development. These guideline recommendations will be suited for integration into clinical decision-support (CDS) systems.</p> <p>Methods: Expert Panels of radiologists, referring clinicians, and a patient advisor, will work with epidemiologists at the CAR to create guidelines across 13 sections. The Expert Panel for each section will first create a comprehensive list of clinical/diagnostic scenarios to include in the guideline. CAR epidemiologists will then conduct a systematic rapid evidence review to identify systematically produced guidelines from</p>

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	<p>other guideline groups. The corresponding Expert Panel will develop diagnostic imaging recommendations for each clinical/diagnostic scenario using the recommendations identified from the evidence review and contextualize them to the Canadian healthcare system. They will accomplish this using an adapted Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework, which reflects the benefits and harms of imaging, values and preferences, equity, accessibility, resources, and cost.</p> <p>Interpretation: Freely available, up-to-date, comprehensive Canadian specific diagnostic imaging referral guidelines are needed. A transparent and structured guideline development approach will aid the CAR and its partners in producing guidelines across its 13 sections.</p>



PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Page
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	n/a
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	n/a
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	n/a
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	1
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	n/a
Support:			
Sources	5a	Indicate sources of financial or other support for the review	1
Sponsor	5b	Provide name for the review funder and/or sponsor	1
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	1
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	n/a
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	9
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	10
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	n/a

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Section and topic	Item No	Checklist item	Page
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	10
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	10-11
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	11-12
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	11-12
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	11-12
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	12
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	n/a
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2 , Kendall's τ)	n/a
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	n/a
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	n/a
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	n/a
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	12-13

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

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Canadian Association of Radiologists Diagnostic Imaging Referral

Guidelines: Guideline development methodology

Candyce Hamel, PhD, Canadian Association of Radiologists, 294 Albert Street, Ottawa, ON

Ryan Margau, MD, North York General, 4001 Leslie Street, Toronto, ON

Paul Pageau, MD FRCPC, The Ottawa Hospital, 501 Smyth Road, Ottawa, ON

Marc Venturi, MHA, Canadian Association of Radiologists, 294 Albert Street, Ottawa, ON

Leila Esmailisaraji, MD, Canadian Association of Radiologists, 294 Albert Street, Ottawa, ON

and members of the CAR Diagnostic Imaging Referrals Working Group

CAR Diagnostic Imaging Referrals Working Group members (alphabetically)

Barb Avard, Sam Campbell, Noel Corser, Nicolas Dea, Edmund Kwok, Cathy MacLean, Ryan Margau (co-chair), Paul Pageau (co-chair), Erin Sarrazin, Charlotte J. Yong-Hing, Kaitlin Zaki-Metias

Corresponding author: chamel@car.ca

Contributor's statement: All authors contributed to the concept and design of the guideline development process described. CH drafted the manuscript, and all other authors critically revised the draft version, gave final approval for the version to be published, and agree to act as guarantors of the work described.

Support: This work has been funded by the Canadian Medical Association (CMA). The funder did not have any role in the content, in the writing of this manuscript, or in the decision to submit for publication.

Abstract

Background: Comprehensive diagnostic imaging referral guidelines are an important tool for facilitating referring clinicians and radiologists to determine the safest and best clinical value diagnostic imaging study for their patients. The Canadian Association of Radiologists (CAR) last produced their diagnostic imaging referral guidelines in 2012. In partnership with several national organizations, referring clinicians, radiologists, and patient and family advisors from across Canada, the CAR are redoing their referral guidelines using a new methodology for guideline development. These guideline recommendations will be suited for integration into clinical decision-support (CDS) systems.

Methods: Expert Panels of radiologists, referring clinicians, and a patient advisor, will work with epidemiologists at the CAR to create guidelines across 13 sections. The Expert Panel for each section will first create a comprehensive list of clinical/diagnostic scenarios to include in the guideline. CAR epidemiologists will then conduct a systematic rapid evidence review to identify systematically produced guidelines from other guideline groups. The corresponding Expert Panel will develop diagnostic imaging recommendations for each clinical/diagnostic scenario using the recommendations identified from the evidence review and contextualize them to the Canadian healthcare system. They will accomplish this using an adapted Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework, which reflects the benefits and harms of imaging, values and preferences, equity, accessibility, resources, and cost.

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3 **Interpretation:** Freely available, up-to-date, comprehensive Canadian specific diagnostic imaging
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5 referral guidelines are needed. A transparent and structured guideline development approach
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8 will aid the CAR and its partners in producing guidelines across its 13 sections.
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Confidential

Introduction

A 2022 systematic review, which included 34 studies evaluating practices undertaken by healthcare professionals in a Canadian healthcare setting, reported that diagnostic imaging was “inappropriately used” (defined as underused and/or overused) a median of 13.8% of the time (interquartile range 4.5 to 29.0%) (1). This over- and underuse of diagnostic imaging may result in iatrogenic harms to the patient, longer wait times, poorer health outcomes due to delays in diagnosis, and inefficient use of scarce health care resources (1,2). Imaging referral guidelines can be an important tool in ensuring that patients get the safest and best clinical value diagnostic imaging study at the right time (3,4). Trustworthy guidelines, and the recommendations within, should be evidence-based and developed using rigorous methodology (5). Guidelines developed for other countries can serve as an important reference. However, Canadian guidelines are required to ensure that geographic distribution, population characteristics, and the structure of the healthcare system are considered in the guideline development process. This highlights the need to develop country-specific, systematically produced diagnostic imaging referral guidelines.

In 2012, the Canadian Association of Radiologists (CAR) produced a comprehensive set of diagnostic imaging referral guideline recommendations (6). These recommendations were categorized into 13 sections and included recommendations for 338 clinical/diagnostic scenarios (**Table 1**). In some instances, sections cover specific anatomy or organ systems (e.g., head and neck, musculoskeletal system); in other instances, the sections refer to clinical or referral pathways or scenarios (e.g., trauma, pediatrics). These guidelines are now over a decade old and must be revised to reflect updated evidence and be produced using a different guideline

development approach. In 2020, the CAR, in collaboration with the Canadian Medical Association (CMA) through an unrestricted sponsorship grant, developed a plan to update the CAR diagnostic imaging referral guideline recommendations, tailored to the Canadian healthcare context. An oversight Working Group (WG) was created, made up of radiologists, referring medical professionals (e.g., referring physicians, nurse practitioners), and a patient and family advisor. The WG formed partnerships with national associations, including the Canadian Association of Emergency Physicians, the College of Family Physicians of Canada, Choosing Wisely, the Nurse Practitioners Association of Canada, and the Society of Rural Physicians of Canada.

Table 1. 2012 CAR Sections

CAR Section	Clinical/diagnostic problems
A. Central nervous system	15
B. Head and neck	15
C. Spine	6
D. Musculoskeletal systems	19
E. Cardiovascular	13
F. Thoracic	26
G. Gastrointestinal system	33
H. Urological, adrenal and genitourinary systems	12
I. Obstetrics and gynaecology	16
J. Trauma	29
K. Cancer	68
L. Pediatrics	78
M. Breast disease	8

A systematic rapid evidence review will inform each section and each sectional Expert Panel (EP) will formulate recommendations using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework (7,8) as guidance, adapted where necessary. The CAR WG has opted to use the concepts found in GRADE for guidelines, as it is a robust framework which not only considers the data when formulating the recommendations, but also

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3 the contextual criteria (9). These include the desirable and undesirable effects and the balance
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5 of these effects, values and preferences, equity, accessibility, resources required, and costs.
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8 ***Project Mandate and Objectives***

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11 The project mandate is to develop a comprehensive set of evidence-based diagnostic imaging
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13 referral guidelines, suited for integration into clinical decision-support (CDS) systems. A CDS
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15 system is defined as “a computer-based program that analyses data within electronic health
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17 records to provide prompts and reminders to assist health care providers in implementing
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19 evidence-based clinical guidelines at the point of care” (10). The CAR will also make these
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21 guideline recommendations publicly available on their website.
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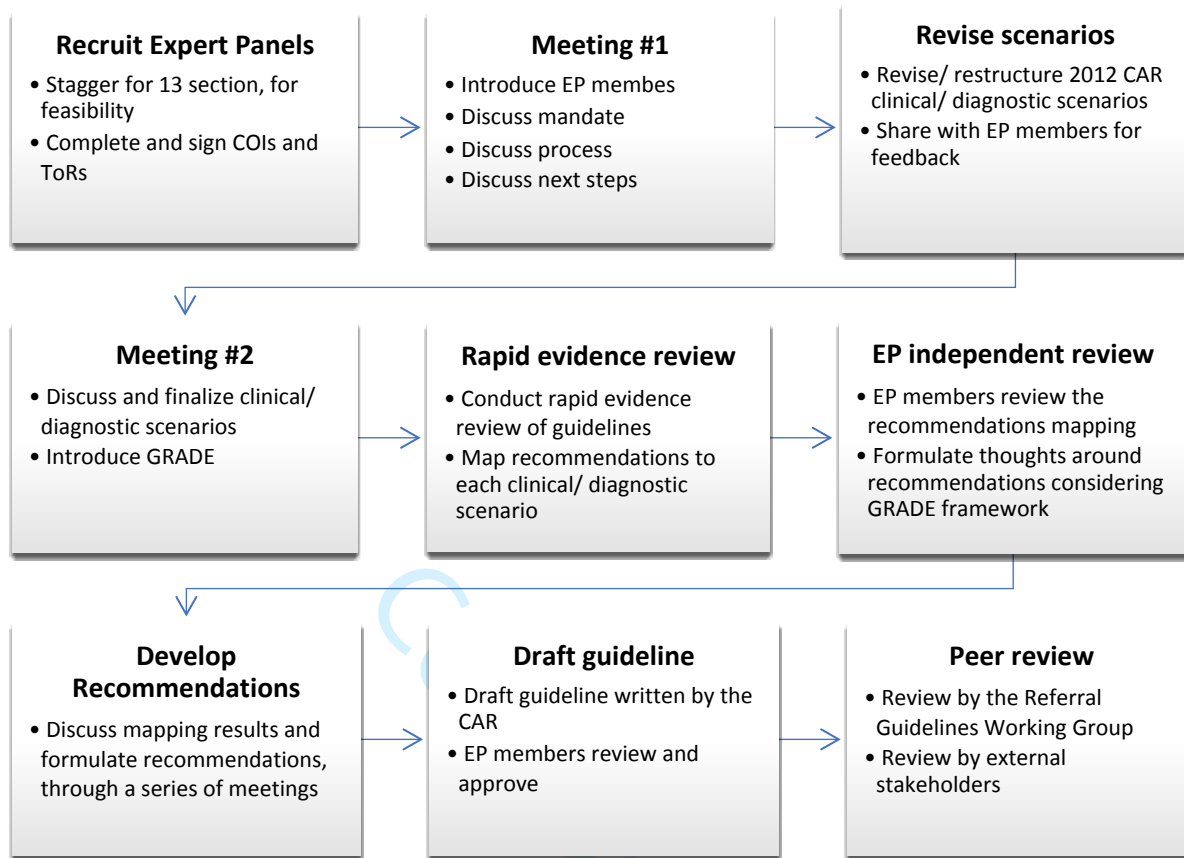
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27 It is important to note that guidelines cannot always account for variability between
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29 patients (e.g., patient values). The recommendations developed as part of this initiative are not
30
31 intended to replace clinical expertise and judgment of the referring clinician but provide
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33 guidance. Depending on the clinical scenario, expert opinion may supplement and/or override
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35 the recommendation.
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40 This document describes the process and methodology for developing the 2021-2022 CAR
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42 Diagnostic Imaging Referral recommendations. This robust methodology also presents a guide
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44 for other organizations/associations to collaboratively develop rapid guidelines.
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48 **Methods**

49 ***Guideline Development***

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55 **Figure 1** displays the overall schematic of the guideline development process.
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Abbreviations: CAR = Canadian Association of Radiologists; COI = Conflict of Interest; EP = Expert Panel; GRADE = Grading of Recommendations Assessment, Development and Evaluation; ToR = Terms of Reference

Figure 1 - Project flow diagram

1. Recruitment of Expert Panel

Each EP will comprise six to nine members, lead by a chair (or co-chairs) with representation from radiologists, referring physicians, and at least one patient advisor, with geographic representation from across Canada (11). Members of the WG will provide candidates for the EP chair and other EP members. Recruited EP members may also provide names of other candidate EP members.

Following the GIN-McMaster Guideline Development Checklist (11), members of each EP will complete and sign a conflict of interest (COI) form, which includes any financial, intellectual,

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3 and/or academic COIs. We will use the CARs COI policy to manage any potential COIs.
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6 Additionally, EP members will receive a terms of reference document, which describes the
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8 purpose of the project, mandate of the project and of EP members, along with other support
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10 information (e.g., quorum, target audience, staff liaison).
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13 **2. Meetings**

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16 EPs will meet a minimum of four times over the guideline development process. EP member
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18 availability will determine the meeting schedule, and each meeting should include at least one
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20 radiologist, one referring clinician, and one patient advisor.
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23 **3. Revise and restructure list of clinical/diagnostic scenarios**

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26 After the initial meeting to introduce the project and discuss the mandate of the EP, members
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28 will revise and restructure the clinical/diagnostic scenarios that were included in the 2012 CAR
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30 recommendations. They may do this virtually or offline, depending on EP member preference.
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33 EP members can review and provide feedback on the draft set of clinical/diagnostic scenarios via
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35 email or on Microsoft Teams.
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39 **4. Conduct rapid evidence review**

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42 Producing guidelines can be time and resource intensive, particularly when recommendations
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44 are developed using evidence from systematic reviews and the GRADE framework. As the 2012
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46 CAR Diagnostic Imaging guideline included recommendations for 338 clinical/diagnostic
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48 scenarios, we will use a systematic rapid evidence review approach, with evidence-based
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50 guidelines as the unit of analysis. “A rapid review is a form of knowledge synthesis that
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52 accelerates the process of conducting a traditional systematic review through streamlining or
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omitting a variety of methods to produce evidence for stakeholders in a resource-efficient manner.” (12) The Cochrane Handbook (13), with additional guidance on conducting rapid reviews (14), will guide the conduct of the systematic rapid evidence review for each of the 13 sections.

The relevant items in the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) statement (15) were used as a guide to ensure reporting standards are met for the description of the systematic rapid evidence review methods.

Eligibility Criteria

The inclusion criteria are presented in **Table 2**.

Table 2. Inclusion criteria

	Details
Study design	<p>Evidence-based guidelines that meet AGREE-II checklist items 7, 8 and 9 (16,17)</p> <ul style="list-style-type: none"> ▪ Question 7. Systematic methods were used to search for evidence: <ul style="list-style-type: none"> ○ Searched and named at least 1 electronic database using an electronic search strategy (e.g., Medline, Embase, PubMed, CENTRAL) ▪ Question 8. The criteria for selecting the evidence are clearly described: <ul style="list-style-type: none"> ○ Described a formal process for study selection; AND ○ Reported the inclusion and exclusion criteria; OR ○ If it is based on a systematic review but does not provide explicit methods. ▪ Question 9. The strengths and limitations of the body of evidence are clearly described: <ul style="list-style-type: none"> ○ Performed critical appraisal on the included studies (e.g., risk of bias, describe study limitations); OR ○ If it is based on a systematic review and GRADE is performed.
Population	Adults (≥ 18 years) and/or children (< 18 years)
Intervention/ Comparison	Recommendations on diagnostic imaging modalities (e.g., radiography, magnetic resonance imaging, computed tomography)
Outcomes	Diagnostic imaging recommendations for a clinical/diagnostic scenario identified by the Expert Panel

	Details
Timing	Published in the last five years (as of the date of the search)
Language	Published in English [†]

[†] Although the search strategy will not have a language filter, we will only include guidelines published in English. An appendix within the guideline will provide a list of potentially relevant guidelines published in other languages.

Information sources

An experienced information specialist will develop a search strategy using the updated list of clinical/diagnostic scenarios produced by the EP. A senior epidemiologist will review this search strategy for completeness. The library scientist will execute the search in Medline and Embase using controlled vocabulary (e.g., MeSH) and title and abstract keywords. For feasibility and to capture the newest evidence-base, we will limit the search to guidelines published in the last five years.

We will perform supplemental searching to identify guidelines not captured in the electronic databases. For feasibility, we will search the American College of Radiology (ACR) Appropriateness Criteria[®], the National Institute for Health and Care Excellence (NICE) guidelines, and relevant section-specific specialty societies [e.g., Society of Obstetricians and Gynaecologists of Canada (SOGC)]. We will also include the recommendations found in the Royal College of Radiologists (RCR) iRefer 8th Edition (2017) (4).

Study selection

Title and abstract screening

Following published guidance (18), we will use artificial intelligence (AI) active-machine learning during title and abstract screening. Using a standardized form in DistillerSR, an online systematic review software (19), one reviewer will screen the records in prioritized order, using the AI re-

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3 ranking tool. Once 95% of the predicted included studies have been identified, we will implement
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5 a stop-screening approach (20,21). The re-rank tool screen has four ways to display the screening
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7 progress and the number of predicted references included. An example of the re-ranking tool
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9 displays is provided in **Appendix 2**.

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13 To identify any excluded records that have a high score for inclusion (i.e., a prediction
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15 score of 0.85 and above), we will run the AI audit tool once 95% of the predicted included records
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17 are identified. One reviewer will rescreen these records to ensure their exclusion was accurate.
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19 Then, the AI reviewer tool in DistillerSR will exclude the remaining records. A second reviewer
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21 will verify a random sample of 10% of the included records and 20% of the excluded records,
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23 without knowledge of the inclusion or exclusion decision by the first reviewer. The two reviewers
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25 will resolve any disagreements by consensus, and when required, will contact the EP chair for
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27 further guidance.
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33 Full-text screening

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35 Using a standardized form in DistillerSR, two reviewers will conduct a pilot exercise on
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37 approximately 25-50 records against the eligibility criteria, as described in **Table 2**. The two
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39 reviewers will resolve any disagreements by consensus. After the pilot exercise, one reviewer will
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41 evaluate the remaining full texts.
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46 *Data extraction/Recommendations mapping*

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48 One reviewer will map the recommendations from each included guideline to the relevant
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50 clinical/diagnostic scenario in the updated CAR guideline section. Other data extraction items
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52 include: the Guideline group name(s); Year of publication (or last update); Method of evaluating
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3 the quality/certainty of the recommendation (e.g., Oxford Centre for Evidence-based Medicine,
4 GRADE); Recommendation grade; and the GRADE Evidence Profile or Summary of Findings tables,
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6 when available.
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10 *Critical appraisal*

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13 One reviewer will critically appraise the included guidelines using the AGREE-II checklist (updated
14 in December 2017) (16,17), using a modified scale (**Appendix 3**). Briefly, the AGREE-II tool uses a
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16 scale from 1 to 7 for each question, which we have modified to three options: Agree (~6-7),
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18 Partially agree (~4-6), and Disagree (~1-3). The EP will consider the quality of the guideline during
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20 the discussions and formulation of the recommendations.
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26 **5. Expert Panel member review**

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29 Once completed, the CAR epidemiologists will share the results of the evidence review with the
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31 EP members for independent review over a three-to-four-week period. In addition to the
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33 complete evidence mapping tables, which are lengthy, we will also provide a synopsis of the
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35 information across guidelines for each clinical/diagnostic scenario. These synopses are useful
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37 during recommendation formulation, as concordance and discordance among the
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39 recommendations are highlighted. When additional information is required, the EP may refer to
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41 the full evidence mapping tables or the full-text guideline.
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46 **6. Development of recommendations**

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49 The EP members will meet over a series of 1-hour meetings to formulate the recommendations
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51 for each clinical/diagnostic scenario in the section. Using a modified GRADE for guidelines
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53 approach, in addition to the recommendations from the included guidelines, the EP discussions
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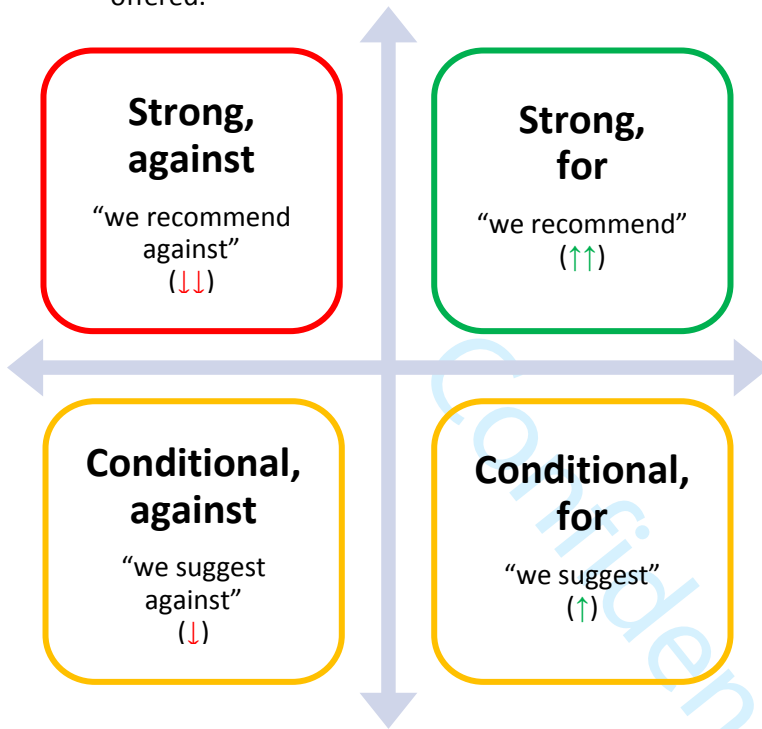
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3 will consider the following contextualization factors when formulating the recommendations: the
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5 certainty of the evidence (where available); the balance of benefits and harms; patient values
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7 and preferences; equity, acceptability and feasibility; and resource use and cost (7,8). Although
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9 there are limitations to this approach, for feasibility, we will extract the judgements around the
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11 certainty of the evidence (i.e., very low, low, moderate, high) as presented in the guidelines.
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16 Using GRADE as guidance (8), EP members will assign the strength (i.e., strong,
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18 conditional) and direction (i.e., for, against) of the recommendation using consistent phrasing
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20 and graphical representation for the recommendations (**Error! Reference source not found.**). For
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22 clinical/diagnostic scenarios that do not have any included guidelines, the EP members will
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24 formulate the recommendations through discussion and consensus considering their clinical
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26 expertise, patient values and preferences, equity, accessibility, resources, and costs.
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STRONG RECOMMENDATION

- All or almost all informed people would want the recommended course of action and only a small proportion would not.
- Request discussion if the intervention is not offered.



CONDITIONAL RECOMMENDATION

- Most informed people would choose the recommended course of action, but a substantial number would not.
- Different choices will be appropriate for different patients (e.g., their values and preferences).

Figure 2 - Determining the strength of the recommendation

7. Draft guideline

A senior epidemiologist, who is also the guideline methodologist, at the CAR will draft the guideline. A draft table ^{Strong} _{For} contents is available in **Appendix 4**, and includes a brief methods section, which will contain a link to this publication to provide additional details.

8. Peer review

Once the EPs finalize the guideline, WG members will provide a peer-review around the contextualization and clarity of the recommendations. Once WG feedback is incorporated into the guideline, EP members will nominate additional external stakeholders to approach for external peer-review. The goal of the external feedback is not for endorsement, but to ensure that the guidelines and recommendations are clearly written.

Statistical analysis

EP members will use recommendations from existing guidelines to inform discussions during recommendation formulation. Therefore, there is no statistical analysis.

Ethics approval

No ethics approval was required for this work.

Interpretation

Using a transparent and structured approach will help in developing reproducible guidelines across the 13 CAR sections. Other organizations producing diagnostic imaging guidelines have also published their processes (3,22,23).

The CAR website will host the publicly available guidelines, per section, as they are produced. This will allow free access to referring clinicians, radiologists, patients and families, and other diagnostic imaging guideline producers. The CAR will also configure the recommendations to optimize integration into CDS systems of both community medical facilities and hospitals. For dissemination to offline users, the CAR will produce a digital and paper book,

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3 once all sections are complete. We will seek additional funding to work with patient groups to
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5 develop patient-friendly summaries, a valuable tool implemented by several organizations,
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7 including Cochrane (24) and the American College of Radiology (25). Using the 2012 CAR
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9 recommendations as an estimation, we expect recommendations for over 350 clinical/diagnostic
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11 scenarios. For feasibility, we will prioritize with patient groups which scenarios require patient-
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13 friendly summaries.
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19 **Limitations**

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21 There are some limitations to our approach. First, having guidelines as the unit of
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23 inclusion in our evidence review does not allow for the evaluation of the five GRADE domains
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25 when conducting a systematic review of primary studies (i.e., risk of bias, imprecision,
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27 indirectness, inconsistency, publication bias) (26). Therefore, we must rely on the level of
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29 evidence as reported by the guideline group. To ensure we have some level of certainty/quality
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31 of the recommendations in the guidelines, we are only including guidelines that have used a
32
33 systematic approach to identify the primary studies, and that have performed critical appraisal
34
35 on these studies. Second, the outcomes judged as critical for decision making for the guideline
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37 group may not be the same as the outcomes that would have been voted as critical for the CAR
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39 EPs (27). However, this limitation is specific to guidelines that rate patient-important outcomes
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41 prior to the conduct of the systematic review, which is not always performed depending on the
42
43 guideline methodology used. Third, as we are using this process over 13 EPs, we may be required
44
45 to modify the process. This may be influenced by the EP members' availability, by the number of
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47 clinical/diagnostic scenarios covered, and by timelines. We aim to adhere to these methods
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49 across sections and will report any large deviations to the process in the guideline.
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3 **Conclusion**
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5 A set of up-to-date, Canadian specific, diagnostic imaging referral guidelines are needed for safe,
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7 high-value diagnostic imaging referrals and improved patient care in the Canadian healthcare
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9 system. We have described the guideline development process that the CAR is applying across
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11 the 13 sections.
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References

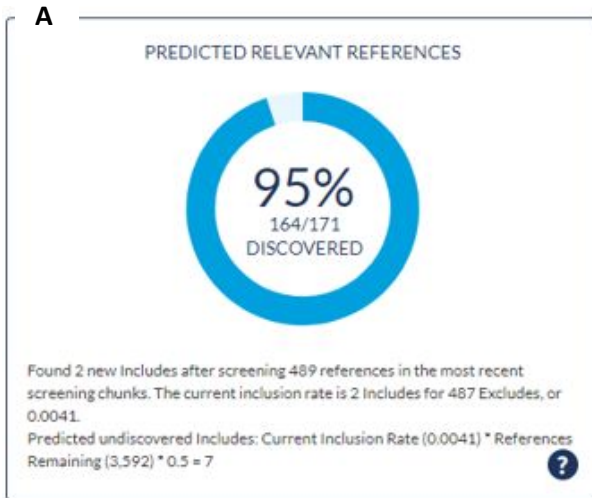
1. Squires JE, Cho-Young D, Aloisio LD, Bell R, Bornstein S, Brien SE, et al. Inappropriate use of clinical practices in Canada: a systematic review. *CMAJ*. 2022 Feb 28;194(8):E279–96.
2. O’Sullivan JW, Albasri A, Nicholson BD, Perera R, Aronson JK, Roberts N, et al. Overtesting and undertesting in primary care: a systematic review and meta-analysis. *BMJ Open*. 2018 Feb 1;8(2):e018557.
3. European Society of Radiology (ESR). Methodology for ESR iGuide content. *Insights Imaging*. 2019 Mar 13;10(1):32.
4. The Royal College of Radiologists. RCR iRefer Guidelines: Making the best use of clinical radiology. London: The Royal College of Radiologists; 2017.
5. Zhang Y, Akl EA, Schünemann HJ. Using systematic reviews in guideline development: the GRADE approach. *Res Synth Methods*. 2018 Jul 14;
6. Canadian Association of Radiologists. 2012 CAR Diagnostic Imaging Referral Guidelines [Internet]. Canadian Association of Radiologists; 2012 [cited 2022 Mar 31]. Available from: <https://car.ca/patient-care/referral-guidelines/>
7. Andrews J, Guyatt G, Oxman AD, Alderson P, Dahm P, Falck-Ytter Y, et al. GRADE guidelines: 14. Going from evidence to recommendations: the significance and presentation of recommendations. *J Clin Epidemiol*. 2013 Jul;66(7):719–25.
8. Andrews JC, Schünemann HJ, Oxman AD, Pottie K, Meerpohl JJ, Coello PA, et al. GRADE guidelines: 15. Going from evidence to recommendation—determinants of a recommendation’s direction and strength. *J Clin Epidemiol*. 2013 Jul;66(7):726–35.
9. Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, et al. GRADE guidelines: 1. Introduction—GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol*. 2011 Apr;64(4):383–94.
10. Implementing Clinical Decision Support Systems [Internet]. Centers for Disease Control and Prevention. 2021 [cited 2022 Mar 31]. Available from: <https://www.cdc.gov/dhbsp/pubs/guides/best-practices/clinical-decision-support.htm>
11. Schünemann HJ, Wiercioch W, Etzeandia I, Falavigna M, Santesso N, Mustafa R, et al. Guidelines 2.0: systematic development of a comprehensive checklist for a successful guideline enterprise. *CMAJ*. 2014 Feb 18;186(3):E123–42.
12. Hamel C, Michaud A, Thuku M, Skidmore B, Stevens A, Nussbaumer-Streit B, et al. Defining Rapid Reviews: a systematic scoping review and thematic analysis of definitions and defining characteristics of rapid reviews. *Journal of Clinical Epidemiology*. 2021 Jan 1;129:74–85.

13. Higgins J, Thomas J, Chandler J, Cumpston M, Li T, Page M, et al. Cochrane Handbook for Systematic Reviews of Interventions version 6.2 (updated February 2021) [Internet]. 2021. Available from: www.training.cochrane.org/handbook
14. Garritty C, Gartlehner G, Nussbaumer-Streit B, King VJ, Hamel C, Kamel C, et al. Cochrane Rapid Reviews Methods Group offers evidence-informed guidance to conduct rapid reviews. *J Clin Epidemiol*. 2021 Feb;130:13–22.
15. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews*. 2015 Jan 1;4(1):1.
16. 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 Dec 14;182(18):E839-842.
17. AGREE Next Steps Consortium (2017). The AGREE II Instrument [Electronic Version]. 2017 [cited 2022 Mar 3]; Available from: <https://www.agreetrust.org/wp-content/uploads/2017/12/AGREE-II-Users-Manual-and-23-item-Instrument-2009-Update-2017.pdf>
18. Hamel C, Hersi M, Kelly SE, Tricco AC, Straus S, Wells G, et al. Guidance for using artificial intelligence for title and abstract screening while conducting knowledge syntheses. *BMC Medical Research Methodology*. 2021 Dec 20;21(1):285.
19. Evidence Partners. DistillerSR [Internet]. Ottawa, ON, Canada: Evidence Partners; 2011. Available from: <https://v2dis-prod.evidencepartners.com/>
20. Hamel C, Kelly SE, Thavorn K, Rice DB, Wells GA, Hutton B. An evaluation of DistillerSR's machine learning-based prioritization tool for title/abstract screening - impact on reviewer-relevant outcomes. *BMC Med Res Methodol*. 2020 Oct 15;20(1):256.
21. Howard BE, Phillips J, Tandon A, Maharana A, Elmore R, Mav D, et al. SWIFT-Active Screener: Accelerated document screening through active learning and integrated recall estimation. *Environ Int*. 2020 May;138:105623.
22. Cascade PN. The American College of Radiology. ACR Appropriateness Criteria project. *Radiology*. 2000 Jan;214 Suppl:3–46.
23. Developing NICE guidelines: the manual [PMG20] [Internet]. National Institute for Health and Care Excellence (NICE); 2014 Oct [cited 2022 Mar 7]. Available from: <https://www.nice.org.uk/process/pmg20/chapter/introduction>
24. New Standards for Plain Language Summaries [Internet]. Cochrane Consumer Network. [cited 2021 Oct 14]. Available from: <https://consumers.cochrane.org/PLEACS>
25. ACR Expands First-of-Its-Kind Patient-Friendly Appropriateness Criteria Summary Resource [Internet]. American College of Radiology. 2018 [cited 2021 Oct 14]. Available from: <https://www.acr.org/Media-Center/ACR-News-Releases/2018/ACR-Expands-First-of-Its-Kind-Patient-Friendly-Appropriateness-Criteria-Summary-Resource>

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26. Balshem H, Helfand M, Schünemann HJ, Oxman AD, Kunz R, Brozek J, et al. GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol*. 2011 Apr;64(4):401–6.
27. Guyatt GH, Oxman AD, Kunz R, Atkins D, Brozek J, Vist G, et al. GRADE guidelines: 2. Framing the question and deciding on important outcomes. *Journal of Clinical Epidemiology*. 2011 Apr 1;64(4):395–400.

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Graph A displays the number of predicted relevant references identified. This is based on a calculation, which is provided below the chart.

Graph B displays the reviewing progress. Each dot on the line chart is an iteration (i.e., a set of screened records informing the active machine-learning tool). As the AI is presenting the most relevant records in prioritized order, there will be a step incline to the curve for the first few iterations. As additional records are screened, and most of the included records should have already been identified, you can see how that the curve begins to level off.

Graph C displays the value of the likelihood of inclusion of the remaining unscreened records. In this example, you will see that there are 3592 records that have not been screened and the likelihood of inclusion falls in the 0% to 9% range.

Table D displays a tabular format of the reviewing progress. It displays the date and time the re-rank was run, the highest remaining score (likelihood of inclusion) of the remaining unscreened records, the training size (the number of records screened), the number of records included, the number of records excluded, and the values of the bars in the histogram/bar chart (as displayed in Graph C).

Appendix 1. DistillerSR AI Re-ranking output

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Appendix 2. Modified AGREE-II tool

Domain 1. Scope and purpose

1. **The overall objective(s) of the guideline is (are) specifically described.**
 Strongly agree Partially agree Strongly disagree
2. **The health question(s) covered by the guideline is (are) specifically described.**
 Strongly agree Partially agree Strongly disagree
3. **The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.**
 Strongly agree Partially agree Strongly disagree

Domain 2. Stakeholder involvement

4. **The guideline development group includes individuals from all relevant professional groups.**
 Strongly agree Partially agree Strongly disagree
5. **The views and preferences of the target population (patients, public, etc.) have been sought.**
 Strongly agree Partially agree Strongly disagree
6. **The target users of the guideline are clearly defined.**
 Strongly agree Partially agree Strongly disagree

Domain 3. Rigour of Development

7. **Systematic methods were used to search for evidence.**
 Agree Partially agree Disagree
8. **The criteria for selecting the evidence are clearly described.**
 Agree Partially agree Disagree
9. **The strengths and limitations of the body of evidence are clearly described.**
 Agree Partially agree Disagree
10. **The methods for formulating the recommendations are clearly described.**

Agree Partially agree Disagree

11. The health benefits, side effects, and risks have been considered in formulating the recommendations.

Agree Partially agree Disagree

12. There is an explicit link between the recommendations and the supporting evidence.

Agree Partially agree Disagree

13. The guideline has been externally reviewed by experts prior to its publication.

Agree Partially agree Disagree

14. A procedure for updating the guideline is provided.

Agree Partially agree Disagree

Domain 4. Clarity of Presentation

15. The recommendations are specific and unambiguous.

Agree Partially agree Disagree

16. The different options for management of the condition or health issue are clearly presented.

Agree Partially agree Disagree

17. Key recommendations are easily identifiable.

Agree Partially agree Disagree

Domain 5. Applicability

18. The guideline describes facilitators and barriers to its application.

Agree Partially agree Disagree

19. The guideline provides advice and/or tools on how the recommendations can be put into practice.

Agree Partially agree Disagree

20. The potential resource implications of applying the recommendations have been considered.

Agree Partially agree Disagree

21. The guideline presents monitoring and/or auditing criteria.

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Agree Partially agree Disagree

Domain 6. Editorial Independence

22. The views of the funding body have not influenced the content of the guideline.

Agree Partially agree Disagree

23. Competing interests of guideline development group members have been recorded and addressed.

Agree Partially agree Disagree

Scoring

Agree = 2 points

Partially agree = 1 point

Disagree = 0 points

Overall quality of the guideline

High Moderate Low

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Appendix 3. Draft guideline table of contents

The report will include the following sections:

1. Introduction
2. Who are these recommendations for?
3. Methods of the Evidence Review
4. Formulating the recommendations: a description on the process of how the recommendations were formulated
5. Included guidelines
6. Limitations of the evidence review
7. Recommendations
8. References
9. Appendix 1: Search strategy(ies)
10. Appendix 2: Evidence tables (modified as appropriate to adhere to copyright)
11. Appendix 3: Summary of recommendations: including the strength of the recommendation and the dose of ionized radiation associated with that imaging modality
12. Appendix 4: List of potentially relevant guidelines published in non-English
13. Appendix 5: Modified AGREE-II assessments