



## **AGREE Standards for the Quality Control of Cancer Datasets and Tissue Pathways published by the Royal College of Pathologists**

**Dr Tim Helliwell on behalf of the Working Group on Cancer Services**

This document was discussed and agreed by the Working Group on Cancer Services on 20 October 2009.

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### **1. Background**

The Working Group on Cancer Services has discussed the AGREE Instrument ([www.agreecollaboration.org](http://www.agreecollaboration.org)) for the audit of clinical guidelines on several occasions. The standards are considered to be generally applicable to the College cancer pathology datasets and to the tissue pathways series of documents, and will facilitate the acceptance of the College guidance by NHS Evidence. Compliance with some standards is not currently required by the College, as noted below, but this policy is subject to review.

There are 23 AGREE standards covered in six domains, each of which should be explicitly mentioned in the published documents:

- Standards 1–3 (scope and purpose)
- Standards 4–7 (stakeholder involvement)
- Standards 8–14 (rigor of development)
- Standards 15–18 (clarity and presentation)
- Standards 19–21 (applicability)
- Standards 22 and 23 (editorial independence)

This document is a commentary for pathologists and authors of cancer datasets and tissue pathways on the specific Standards and includes the AGREE guidance on the interpretation of the Standards. The commentary is largely written in the context of the cancer datasets but most of the comments apply equally to tissue pathways. The Working Group will encourage authors to meet these standards during the production of new and revised datasets and pathways documents.

The College document, 'Guidance on writing cancer datasets' (2008), contains many relevant statements that will assist in compliance. These need to be applied consistently. In some instances, compliance will be achieved through model wording provided by the Working Group for all authors. Each dataset will include, as an appendix, a compliance monitoring sheet (see Appendix B) that indicates which section of the document provides evidence of compliance with each of the specific AGREE Standards.



## 2. AGREE Standards

### **Domain: SCOPE AND PURPOSE**

#### **Standard 1. The overall objective(s) of the guideline is (are) specifically described.**

This deals with the potential health impact of a guideline on society and populations of patients. The overall objective(s) of the guideline should be described in detail and the expected health benefits from the guideline should be specific to the clinical problem.

*Comments with regard to cancer datasets: The introductory section of the dataset covers the relevant areas with consistent text across datasets. All datasets will include a foreword that covers the generic use of guidelines (see Appendix A).*

#### **Standard 2. The clinical question(s) covered by the guidelines is (are) specifically described.**

A detailed description of the clinical Standards covered by the guideline should be provided, particularly for the key recommendations (see also standard 17).

*Comments with regard to cancer datasets: There is usually no problem achieving this standard as the introductory section covers the relevant areas with consistent text across datasets and tissue pathways.*

#### **Standard 3. The patients to whom the guideline is meant to apply are specifically described.**

There should be a clear description of the target population to be covered by a guideline. The age range, sex, clinical description, co-morbidity may be provided.

*Comments with regard to cancer datasets: There is usually no problem achieving this standard as the introductory section covers the relevant areas with consistent text across datasets and tissue pathways.*

### **Domain: STAKEHOLDER INVOLVEMENT**

#### **Standard 4. The guideline development group includes individuals from all the relevant professional groups.**

This item refers to the professionals who were involved at some stage of the development process. This may include members of the steering group, the research team involved in selecting and reviewing/rating the evidence and individuals involved in formulating the final recommendations. This item excludes individuals who have externally reviewed the guideline (see Standard 13). Information about the composition, discipline and relevant expertise of the guideline development group should be provided.

*Comments with regard to cancer datasets: Currently the writing groups tend to comprise experienced, senior pathologists. The details of their appointments and brief details of their expertise should be provided in the document. The College encourages authors to discuss the content of the datasets and pathways with clinical colleagues. All Fellows of the College and other nominated clinical stakeholder groups are invited to participate in the formal consultation of the draft documents.*

#### **Standard 5. The patients' views and preferences have been sought.**

Information about patients' experiences and expectations of health care should inform the development of clinical guidelines. There are various methods for ensuring that patients' perspectives inform guideline development. For example, the development group could involve patients' representatives, information could be obtained from patient interviews, and literature reviews of patients' experiences could be considered by the group. There should be evidence that this process has taken place.

*Comments with regard to cancer datasets: This is currently considered to be 'not applicable' to the cancer datasets and tissue pathways as the pathology component is only one part of the*

*diagnostic pathway that is experienced by patients. The SAC for Histopathology has agreed with this view (May 2008).*

**Standard 6. The target users of the guideline are clearly defined.**

The target users should be clearly defined in the guideline, so they can immediately determine if the guideline is relevant to them. For example, the target users for a guideline on low back pain may include general practitioners, neurologists, orthopaedic surgeons, rheumatologists and physiotherapists.

*Comments with regard to cancer datasets: The primary users of the cancer datasets and tissue pathways are trainee and consultant cellular pathologists and, on their behalf, the suppliers of IT products to laboratories. For cancer datasets, secondary use by surgeons and oncologists and by cancer registries (National Cancer Intelligence Network) is noted in the introduction.*

**Standard 7. The guideline has been piloted among target users.**

A guideline should have been pre-tested for further validation amongst its intended end users prior to publication. For example, a guideline may have been piloted in one or several primary care practices or hospitals. This process should be documented.

*Comments with regard to cancer datasets: This is not usually immediately obvious from the text of the datasets or tissue pathways. For most datasets and pathways, the new editions are revisions and so the first edition could be considered equivalent to a pilot. The first edition is likely to have been piloted in the authors' own practice.*

*In the introduction, authors should briefly describe the methods used to pilot/validate the dataset and proforma. For revisions of datasets and pathways this will largely be through experience with previous versions of the dataset. Authors should consider how to validate any proposed changes to datasets and pathways.*

**Domain: RIGOR OF DEVELOPMENT**

**Standard 8. Systematic methods were used to search for evidence.**

Details of the strategy used to search for evidence should be provided, including search terms used, sources consulted and dates of the literature covered. Sources may include electronic databases, databases of systematic reviews, journals, conference proceedings and other guidelines.

*Comments with regard to cancer datasets: Authors should provide a brief description of methodology.*

**Standard 9. The criteria for selecting the evidence are clearly described.**

Criteria for including/excluding evidence identified by the search should be provided. These criteria should be explicitly described and reasons for including and excluding evidence should be clearly stated. For example, guideline authors may decide to only include evidence from randomised clinical trials and to exclude articles not written in English.

*Comments with regard to cancer datasets: Authors should provide a brief description of methodology.*

**Standard 10. The methods used for formulating the recommendations are clearly described.**

There should be a description of the methods used to formulate the recommendations and how final decisions were arrived at. Methods include, e.g. a voting system, formal consensus techniques (e.g. Delphi, Glaser techniques). Areas of disagreement and methods of resolving them should be specified.

*Comments with regard to cancer datasets: There is generally little information on the methodology in current datasets, and no statements as to how areas of disagreement were resolved. Authors should briefly describe the methods used to evaluate the evidence used and the ways in which disagreements were resolved. Authors should use the modified Scottish*

*Intercollegiate Guidelines Network (SIGN) guidance (Appendix C) to indicate the strength of the evidence used to support their recommendations.*

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

The guideline should consider health benefits, side effects and risks of the recommendations. For example, a guideline on the management of breast cancer may include a discussion on the overall effects of the various outcomes. These may include: survival, quality of life, adverse effects and symptom management, or a discussion comparing one treatment option with another. There should be evidence that these issues have been addressed.

*Comments with regard to cancer datasets: It is difficult to apply this item to pathology guidelines, but some aspects are covered in the standard introductory paragraphs on the anticipated benefits. Clinical risks associated with the College guidance are minimal, other than the perception that they might increase workload.*

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

There should be an explicit link between the recommendations and the evidence on which they are based. Each recommendation should be linked with a list of references on which it is based.

*Comments with regard to cancer datasets: This is usually obvious from the text; referencing should be comprehensive but not exhaustive.*

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

A guideline should be reviewed externally before it is published. Reviewers should not have been involved in the development group and should include some experts in the clinical area and some methodological experts. Patients' representatives may also be included. A description of the methodology used to conduct the external review should be presented, which may include a list of the reviewers and their affiliation.

*Comments with regard to cancer datasets: The review process is documented in the 'Guidance for authors', and is usually carried out by specialist pathology groups and then by histopathological Fellows of the College, although there is often no information in the text about the methodology applied and how variant opinions were reconciled. Comments received during the consultation have to be addressed by the authors to the satisfaction of the Chair of the Working Group and the Director of the Professional Standards Unit. Part of this is covered by the information on the front page of the datasets and tissue pathways. The new foreword to the datasets (see Appendix A) helps to clarify the process.*

**Section 14. A procedure for updating the guideline is provided.**

Guidelines need to reflect current research. There should be a clear statement about the procedure for updating the guideline. For example, a timescale has been given, or a standing panel receives regularly updated literature searches and makes changes as required.

*Comments with regard to cancer datasets: Each year, the authors of the dataset/tissue pathway, in conjunction with the relevant sub-specialty advisor to the College, will consider whether or not the dataset/tissue pathway needs to be revised. This is covered in the new foreword to the datasets (see Appendix A).*

**Domain: CLARITY AND PRESENTATION**

**Section 15. The recommendations are specific and unambiguous.**

A recommendation should provide a concrete and precise description of which management is appropriate in which situation and in what patient group, as permitted by the body of evidence. However, evidence is not always clear cut and there may be uncertainty about the best

management. This should be reflected in the guideline.

*Comments with regard to cancer datasets: This is the guiding principle of the datasets.*

**Section 16. The different options for management of the condition are clearly presented.**

A guideline should consider the different possible options for screening, prevention, diagnosis or treatment of the condition it covers. These possible management options should be clearly presented in the guideline.

*Comments with regard to cancer datasets: This standard is difficult to assess as it relates mainly to options for clinical management. We interpret this as meaning that the datasets should indicate the range of acceptable practice.*

**Section 17. Key recommendations are easily identifiable.**

Users should be able to find the most relevant recommendations easily. These recommendations answer the main clinical Standards that have been covered by the guideline. They can be identified in different ways, e.g. summarized in a box, typed in bold, underlined or presented as flow charts or algorithms.

*Comments with regard to cancer datasets: The Working Group is aiming for greater uniformity in presentation of the datasets and proformas, but, as most cancer types have specific features that need to be emphasized, complete uniformity would not be appropriate. The core and non-core data items need to be summarized as a bulleted list, supplemented by specific guidance where necessary.*

**Section 18. The guideline is supported with tools for application.**

For a guideline to be effective it needs to be disseminated and implemented with additional materials. These may include, for example, a summary document or a quick reference guide, educational tools, patients' leaflets, computer support.

*Comments with regard to cancer datasets: The core data items, supplemented by proformas, are supported by explanatory text. The licensing of datasets to commercial software companies provides a mechanism for facilitating implementation. The College does not have the resource to develop, produce and maintain its own electronic version of the datasets to facilitate structured report generation. This standard is not applicable to tissue pathways.*

**Domain: APPLICABILITY**

**Standard 19. The potential organisational barriers in applying the recommendations have been discussed.**

Applying the recommendations may require changes in the current organisation of care within a service or clinic which may be a barrier to using the guidance in clinical practice. Organisational changes that may be needed in order to apply the recommendations should be discussed.

*Comments with regard to cancer datasets: Datasets and tissue pathways should explicitly comment on whether or not major organizational changes are likely to be required to meet the guidance; this is covered in the new foreword (see Appendix A).*

**Standard 20. The potential cost implications of applying the recommendations have been considered.**

The recommendations may require additional resources in order to be applied, e.g. more specialised staff, new equipment, expensive drug treatment. These may have cost implications for health care budgets. There should be a discussion of the potential impact on resources in the guideline.

*Comments with regard to cancer datasets: The remit of the datasets (and the College) is to provide guidance on the quality of a diagnostic service and detailed consideration of costs is outside the remit of the College. For current datasets that recommend traditional pathological*

*methods to derive data items there should be no cost implications.*

*The developments in molecular and genetic pathology will eventually lead to situations where the provision of core data for patient management will have cost implications, although since the datasets should reflect accepted good practice, the costs may already have been identified through clinical service developments and clinical tariffs.*

*The new foreword (see Appendix A) will include a statement on possible cost implications. If there are cost implications to implementation, the authors should alert the Working Group which will consider drawing the implications to the attention of others, e.g. the National Cancer Action Team.*

**Standard 21. The guideline presents key review criteria for monitoring and/ or audit purposes.**

Measuring the adherence to a guideline can enhance its use. This requires clearly defined review criteria that are derived from key recommendations in the guideline. These should be presented.

*Comments with regard to cancer datasets: Review and audit criteria have not usually been explicitly included. Some criteria are included in the latest colorectal cancer dataset. Authors should explicitly consider audit criteria for their datasets.*

**Domain: EDITORIAL INDEPENDENCE**

**Standard 22. The guideline is editorially independent from the funding body.**

Some guidelines are developed with external funding (e.g. Government funding, charity organizations, pharmaceutical companies). Support may be in the form of a financial contribution for the whole development, or for parts of it, e.g. printing of the guidelines. There should be an explicit statement that the views or interests of the funding body have not influenced the final recommendations.

*Comments with regard to cancer datasets: The new foreword to the datasets (see Appendix A) includes a statement that the dataset was developed without external funding to the writing group. If this is not the case, then the sources of funding should be specified.*

**Standard 23. Conflicts of interest of guideline development members have been recorded.**

There are circumstances when members of the development group may have conflicts of interest. There should be an explicit statement that all group members have declared whether or not they have any conflict of interest.

*Comments with regard to cancer datasets: Potential conflicts of interest are recorded by the College. The new foreword (see Appendix A) states that the College requires the authors of datasets to provide a list of potential conflicts of interest; these are monitored by the Director of the Professional Standards Unit and are available on request.*

## **APPENDIX A. Summary of model wording to be incorporated into College cancer datasets and tissue pathways documents**

Note that this model wording can be modified as necessary to cover specific issues arising in a College document.

The tissue pathways should include a statement that:

The tissue pathways are **guidelines**. Guidelines are systematically developed statements to assist the decisions of practitioners and patients about appropriate health care for specific clinical circumstances and are based on the best available evidence at the time the dataset was prepared. It may be necessary or even desirable to depart from the guidelines in the interests of specific patients and special circumstances. Just as adherence to the guidelines may not constitute defence against a claim of negligence, so deviation from them should not necessarily be deemed negligent.

The cancer datasets will have a foreword that includes the following statements:

The cancer datasets are **guidelines**. Guidelines are systematically developed statements to assist the decisions of practitioners and patients about appropriate health care for specific clinical circumstances and are based on the best available evidence at the time the dataset was prepared. It may be necessary or even desirable to depart from the guidelines in the interests of specific patients and special circumstances. Just as adherence to the guidelines may not constitute defence against a claim of negligence, so deviation from them should not necessarily be deemed negligent.

This dataset was reviewed by the Cancer Services Working Group and was placed on the College website for consultation with the membership between xx and xx. All comments received from the Working Group and membership have been addressed by the authors to the satisfaction of the Chair of the Working Group and the Director of the Professional Standards Unit.

Each year, the authors of the dataset, in conjunction with the relevant sub-specialty advisor to the College, will consider whether or not the dataset needs to be revised.

No major organizational changes or cost implications have been identified that would hinder the implementation of the dataset.

This dataset was developed without external funding to the writing group. (Alternatively, sources of funding should be specified.)

The College requires the authors of datasets to provide a list of potential conflicts of interest; these are monitored by the Director of the Professional Standards Unit and are available on request.

## APPENDIX B. Dataset monitoring sheet (to be added to each new or revised dataset)

The cancer datasets of the Royal College of Pathologists comply with the AGREE standards for good quality clinical guidelines ([www.agreecollaboration.org](http://www.agreecollaboration.org)). The sections of this dataset that indicate compliance with each of the AGREE standards are indicated in the table.

| AGREE Standard   | Section of dataset |
|--|--------------------|
| <b>SCOPE AND PURPOSE</b>   |                    |
| 1. The overall objective(s) of the guideline is (are) specifically described.                            |                    |
| 2. The clinical question(s) covered by the guidelines is (are) specifically described.                   |                    |
| 3. The patients to whom the guideline is meant to apply are specifically described.                      |                    |
| <b>STAKEHOLDER INVOLVEMENT</b>   |                    |
| 4. The guideline development group includes individuals from all the relevant professional groups.       |                    |
| 5. The patients' views and preferences have been sought.   | N/A                |
| 6. The target users of the guideline are clearly defined.  |                    |
| 7. The guideline has been piloted among target users.  |                    |
| <b>RIGOR OF DEVELOPMENT</b>  |                    |
| 8. Systematic methods were used to search for evidence.  |                    |
| 9. The criteria for selecting the evidence are clearly described.  |                    |
| 10. The methods used for formulating the recommendations are clearly described.                          |                    |
| 11. The health benefits, side effects and risks have been considered in formulating the recommendations. |                    |
| 12. There is an explicit link between the recommendations and the supporting evidence.                   |                    |
| 13. The guideline has been externally reviewed by experts prior to its publication.                      |                    |
| 14. A procedure for updating the guideline is provided.  |                    |
| <b>CLARITY OF PRESENTATION</b>   |                    |
| 15. The recommendations are specific and unambiguous.  |                    |
| 16. The different options for management of the condition are clearly presented.                         |                    |
| 17. Key recommendations are easily identifiable.   |                    |
| 18. The guideline is supported with tools for application.   |                    |
| <b>APPLICABILITY</b>   |                    |
| 19. The potential organizational barriers in applying the recommendations have been discussed.           |                    |
| 20. The potential cost implications of applying the recommendations have been considered.                |                    |
| 21. The guideline presents key review criteria for monitoring and/or audit purposes.                     |                    |
| <b>EDITORIAL INDEPENDENCE</b>  |                    |
| 22. The guideline is editorially independent from the funding body.                                      |                    |
| 23. Conflicts of interest of guideline development members have been recorded.                           |                    |

Standard 5 is currently regarded as not directly applicable to this dataset.

## **APPENDIX C. Evaluation of the strength of supporting evidence**

The College cancer datasets and tissue pathways are explicitly produced to provide guidance that is based on published evidence. The strength (quality) of any evidence is a continuum (low–high) so that any categorisation is arbitrary. However, the value of categorisation in terms of transparency and simplicity outweighs any limitations. Essentially, the College is looking for an approach that indicates whether evidence is of high quality and unlikely to change in the near future, or is more uncertain and therefore likely to be subject to future modification.

The Working Group on Cancer Services has discussed the relative merits of different approaches and has agreed to recommend the use of a modification of the Scottish Intercollegiate Guidelines Network (SIGN) guidance for the development of clinical practice guidelines. This is summarised in detail in the SIGN 50 document, published in January 2008 ([www.sign.ac.uk/guidelines/fulltext/50/index.html](http://www.sign.ac.uk/guidelines/fulltext/50/index.html)).

### ***Importance of recommendations***

SIGN emphasises that the assessment of the quality of evidence should be separate from an assessment of the clinical importance of the eventual recommendation. For the cancer datasets, the importance of the recommendations is indicated by whether a data item forms part of the core data list (strongly recommended), or part of the non-core data (less strongly recommended). The Working Group considers that, for simplicity, further categorisation of the importance of the recommendations is not required.

### ***Quality of evidence***

The criteria for assessing the level of evidence and subsequently the grade of recommendation are described in Annex B of the SIGN 50 document. The summary table below is modified from Palmer K, *et al. BMJ* 2008; 337: a1832.

Any evidence evaluated will normally be directly applicable to the relevant cancer type considered in the dataset. For some rare cancers, extrapolation of evidence from more common cancers may be justified in order to provide a uniformity of approach to the pathology (such evidence will never achieve grade A).

For traditional histopathological data items, e.g. prognosis is related to tumour type or size, the strongest evidence is likely to be provided by high quality cohort studies (grade B). For pathological markers of predictive value, in particular molecular and genetic markers, it is likely that there will be evidence of clinical impact from randomised controlled trials (grade A) to justify inclusion as core data. The Working Group considers it unlikely that data items based on grade C evidence would be included in lists of core data.

In the cancer dataset documents, the grade of supporting evidence should be recorded against each item in the core and non-core data lists.

**Table:** Explanation of grades of evidence (modified from Palmer K, *et al. BMJ* 2008; 337: 1832)

| Grade (level) of evidence | Nature of evidence  |
|---------------------------|---|
| Grade A                   | <p>At least one high quality meta-analysis, systematic review of randomised controlled trials or a randomised controlled trial with a very low risk of bias and directly attributable to the target cancer type.</p> <p>or,</p> <p>A body of evidence demonstrating consistency of results and comprising mainly well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias, directly applicable to the target cancer type.</p> |
| Grade B                   | <p>A body of evidence demonstrating consistency of results and comprising mainly high quality systematic reviews of case-control or cohort studies and high quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relation is causal, and which are directly applicable to the target cancer type.</p> <p>or,</p> <p>Extrapolation evidence from studies described in A.</p>   |
| Grade C                   | <p>A body of evidence demonstrating consistency of results and including well-conducted case-control or cohort studies and high quality case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relation is causal, and which are directly applicable to the target cancer type.</p> <p>or,</p> <p>Extrapolation evidence from studies described in B.</p>  |
| Grade D                   | <p>Non-analytic studies such as case reports, case series or expert opinion.</p> <p>or,</p> <p>Extrapolation evidence from studies described in C.</p>  |
| Good practice point (GPP) | <p>Recommended best practice based on the clinical experience of the authors of the writing group.</p>  |