Mod Pathol 37 (2024) 100515

MODERN PATHOLOGY

USCAP UNITED STATES AND CANADIAN ACADEMY OF PATHOLOGY
Creating a Better Pathologist

Journal homepage: https://modernpathology.org/

Review Article

Moving Forward on Tumor Pathology Research Reporting: A Guide for Pathologists From the World Health Organization Classification of Tumors Living Evidence Gap Map by Tumour Type Group

Richard Colling[a,b,*], Iciar Indave[c], Javier Del Aguilla[c], Ramon Cierco Jimenez[c], Fiona Campbell[d], Magdalena Chechlinska[e], Magdalena Kowalewska[f], Stefan Holdenrieder[g], Inga Trulson[g], Karolina Worf[g], Marina Pollán[h,i], Elena Plans-Beriso[h], Beatriz Pérez-Gómez[h,i], Oana Craciun[h], Ester García-Ovejero[h], Irmina Maria Michalek[j], Kateryna Maslova[e], Grzegorz Rymkiewicz[j], Joanna Didkowska[k], Puay Hoon Tan[l], Nur Diyana Bte MD Nasir[l], Nickolas Myles[c], Christine Giesen[c], Gabrielle Goldman-Lévy[c], Dilani Lokuhetty[c], Ian A. Cree[c]

[a] *Nuffield Department of Surgical Sciences, University of Oxford, Level 4, John Radcliffe Hospital, Oxford, United Kingdom;* [b] *Department of Cellular Pathology, Oxford University Hospitals NHS FT, Oxford, United Kingdom;* [c] *International Agency for Research on Cancer (IARC), World Health Organization, Lyon, France;* [d] *Population Health Sciences, Newcastle University, Newcastle Upon Tyne, United Kingdom;* [e] *Department of Cancer Biology, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland;* [f] *Department of Molecular and Translational Oncology, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland;* [g] *Institute of Laboratory Medicine, German Heart Centre Munich, Munich, Germany;* [h] *National Center for Epidemiology. Instituto de Salud Carlos III, Madrid, Spain;* [i] *Consortium for Biomedical Research in Epidemiology and Public Health (CIBERESP), Madrid, Spain;* [j] *Department of Cancer Pathomorphology, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland;* [k] *Polish National Cancer Registry, Department of Epidemiology and Cancer Prevention, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland;* [l] *Luma Medical Centre, Singapore, Singapore*

ARTICLE INFO

Article history:
Received 27 February 2024
Revised 30 April 2024
Accepted 4 May 2024
Available online 17 May 2024

Keywords:
checklist
evidence-based medicine
guidance
guidelines

ABSTRACT

Evidence-based medicine (EBM) can be an unfamiliar territory for those working in tumor pathology research, and there is a great deal of uncertainty about how to undertake an EBM approach to planning and reporting histopathology-based studies. In this article, reviewed and endorsed by the Word Health Organization International Agency for Research on Cancer's International Collaboration for Cancer Classification and Research, we aim to help pathologists and researchers understand the basics of planning an evidence-based tumor pathology research study, as well as our recommendations on how to report the findings from these. We introduce some basic EBM concepts, a framework for research questions, and thoughts on study design and emphasize the concept of reporting standards. There are many study-specific reporting guidelines available, and we provide an overview of these. However, existing reporting guidelines perhaps do not always fit tumor pathology research papers, and hence, here, we collate the key reporting data set together into one

The content of this article represents the personal views of the authors and does not represent the views of the authors' employers and associated institutions. Where authors are identified as personnel of the International Agency for Research on Cancer/World Health Organization, the authors alone are responsible for the views expressed in this article and they do not necessarily represent the decisions, policy or views of the International Agency for Research on Cancer/World Health Organization.

* Corresponding author.
E-mail address: richard.colling@nds.ox.ac.uk (R. Colling).

ELSEVIER

0893-3952/© 2024 THE AUTHORS. Published by Elsevier Inc. on behalf of the United States & Canadian Academy of Pathology. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).
https://doi.org/10.1016/j.modpat.2024.100515

pathology
reporting

generic checklist that we think will simplify the task for pathologists. The article aims to complement our recent hierarchy of evidence for tumor pathology and glossary of evidence (study) types in tumor pathology. Together, these articles should help any researcher get to grips with the basics of EBM for planning and publishing research in tumor pathology, as well as encourage an improved standard of the reports available to us all in the literature.

© 2024 THE AUTHORS. Published by Elsevier Inc. on behalf of the United States & Canadian Academy of Pathology. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

Introduction

The aim of evidence-based medicine (EBM) is to guide clinical decision-making by integrating the best available evidence with clinical expertise and patient values.[1] Evidence-based practice is now well established in modern health care. For diagnostic histopathology, which underpins the fundamental basis of management of patients with tumors, the need for an EBM approach is self-evident. To boost this EBM approach in tumor pathology, the Word Health Organization's International Agency for Research on Cancer[2] set out to systematically find and rank all published research related to the World Health Organization Classification of Tumours (WCT).[3-5] The WCT serves as the internationally acknowledged basis for cancer classification, forming the foundation for all research and clinical management in oncology globally.[6] The "Mapping the Evidence for the World Health Organization Classification of Tumours: a Living Evidence Gap Map by Tumour Type" (WCT EVI MAP) project[7] aims to produce evidence gap maps, visually highlighting and ranking existing evidence to identify pockets of low-level or absent data in the evidence base.[3,4,7-9] Similar to systematic reviews of the literature, WCT EVI MAP will rely heavily on well-reported manuscripts to facilitate screening and appraisal of the studies identified. In this guide, which is focused on tumor pathology and based on the WCT EVI MAP Group's experience with reviewing the citations of the WCT literature, we make recommendations for pathologists and researchers who are designing and reporting the results of their work. We hope that this guide will help researchers improve the quality of published work to guide evidence-based pathology practice.

Tumor Pathology Research

In this guide, we use the term "tumor pathology" to refer to the biological and clinical pathological study of benign and malignant neoplasia. We encompass within this studies of etiology, epidemiology, pathogenesis, clinical and diagnostic features (from patient characteristics to macroscopic, microscopic, and molecular diagnostics), prognosis, and (where relevant) treatment response prediction. This is essentially any topic that lies within the scope of the WCT.

Design Phase: The Most Important Phase

Planning the Work: What Is the Research Question?

All research commences with a question. The importance of this stage cannot be overstated—the research question needs to be clear, focused, succinct, unambiguous, clinically important, and answerable. We recommend using a system such as PICOT (Fig. 1)—to help structure this process.[10]

Gathering the Background Information

The questions identified may, or may not, have already been answered, and hence, all research *should* now proceed to "what do we already know?" It can be a waste of time, resources, and patient tissue if we repeat work that has already been answered; hence, the first part of research is gathering and synthesizing the existing evidence pertaining to the research question, and asking what work is left to do. This is often an iterative process and can take much longer than expected, but this should not discourage pathologists/researchers from spending this time at the planning stage, as it will always result in a more meaningful and publishable piece of work. We hope that this the WCT EVI MAP project, once completed (scheduled for 2026), will facilitate this stage. The project is dedicated to developing an online living tool that provides a synthesis of available evidence, categorized by tumor classification-related topics and evidence levels.

Study Design

In an ideal world, the stage outlined above would always be done via a systematic review, which may, in itself, be a study that needs to be published. However, for most practicing pathologists, this is unrealistic or not possible due to a lack of published work. We recommend that when a genuine question needing answering is identified, careful consideration is given to the best study needed to answer the question, and how this will fit with (or improve upon) the evidence currently available. Hierarchies of evidence for tumor pathology (Fig. 2),[7] are a useful guide for this, where the aim should be to use the highest level of study design possible—it is important to remember, however, that not every question can be answered with a randomized controlled trial

P – patients/participants/problem
I – intervention or index test/marker
C – comparison or reference test
O – outcome measure
T – timing of test or intervention

Figure 1.
The PICOT framework for structuring research questions. Here, we propose to modify the model to include test and biomarker evaluation to make allow coverage for various pathology studies—similar systems are sometimes abbreviated to PICO (eg, in clinical trials) or re-ordered as PIRTO (where the "C" is replaced by "R," for example in diagnostic test accuracy studies). Outcomes may include trial end points such as recurrence or death, or test accuracy measure such as sensitivity or specificity. Not all letters may be applicable in all studies, and purely descriptive studies (such as case series) may not fit this model at all.

WCT topics:	Etiology		Clinical features Radiology Localisation Macroscopy, Histopathology Immunohistochemistry Cytology	Diagnostic molecular pathology Diagnostic immunohistochemistry	Prognosis Staging	Prediction
	Epidemiology Prevalence Incidence Risk factors	Mechanisms & Pathogenesis				
Research focus:	Population	Cellular, molecular & genetic biology	Pathological characterisation and diagnosis of the tumor	Diagnostic tests (accuracy) and reproducibility (precision)	Prognostics	Predictive biomarkers
Clinical questions:	How common is this tumor? What factors influence the probability of developing this tumor? Who is at risk?	What are the molecular alterations in this tumor? What mechanisms cause this tumor?	What are the key features of this tumor? How to we define the tumor?	How well does this test confirm the diagnosis?	What features influence five-year survival?	Can this marker predict treatment?
Level P1	*Systematic reviews**	*Systematic reviews**	*Systematic reviews**	*Systematic reviews**	*Systematic reviews**	*Systematic reviews**
Level P2	*Cancer registry data* *Prospective cohort studies* *Randomised-controlled trials*	*Prospective cohort studies* *Studies derived from randomised-controlled trials*	*Case-control studies* *Diagnostic agreement/ reproducibility studies* *Diagnostic test accuracy studies* *Prospective cohort studies* *Studies derived from randomised-controlled trials*	*Case-control studies* *Diagnostic agreement/ reproducibility studies* *Diagnostic test accuracy studies* *Prospective cohort studies* *Randomised-controlled trials of diagnostic tests* *Studies derived from randomised-controlled trials*	*Prospective Cohort studies* *Studies derived from randomised-controlled trials*	*Prospective Cohort studies* *Randomised-controlled trials* *Studies derived from randomised-controlled trials*
Level P3	*Case-control studies* *Retrospective cohort studies* *Other cross-sectional studies*	*Case-control studies* *Mechanistic clinical studies* *Other cross-sectional studies* *Retrospective cohort studies*	*Consensus studies* *Other cross-sectional studies* *Retrospective cohort studies*	*Case series* *Consensus studies* *Other cross-sectional studies* *Retrospective cohort studies*	*Case-control studies* *Observational trials* *Other cross-sectional studies* *Retrospective Cohort studies*	*Case-control studies* *Retrospective Cohort studies*
Level P4	*Case series*	*Animal studies* *Case series* *Mechanistic laboratory studies* *Molecular database entries* *Observational trials*	*Case series*	*Clinical laboratory test validation studies*	*Cancer registry data* *Diagnostic accuracy studies*	*Diagnostic accuracy studies*
Level P5	*Case reports*	*Case reports*	*Case reports*	*Not used*	*Case reports* *Case series*	*Case reports* *Case series* *Mechanistic clinical studies*

Figure 2.
The World Health Organization Classification of Tumours: a Living Evidence Gap Map by Tumour Type (WCT EVI MAP) hierarchy of evidence for tumor pathology. Here, the higher levels (eg, P1/P2) represent preferable study designs with a lower risk of bias, and lower levels (eg, P5) represent study designs in which the reader may have less confidence due to a higher risk of bias.[11]

(although some can, even in diagnostic research). There are also practical and funding considerations, and it is common in research to compromise and deviate from the ideal design. What is important is that this is carefully considered, clearly outlined in the resulting manuscript, and the limitations discussed. Here, we will try to provide an overview of the main categories of study, and we have attempted as far as possible to align the terminology around study design used with that suggested in our previously published glossary.[11] Not every type of study imaginable is specifically covered in this guide, but we hope our data set (outlined below) can be applied to almost any manuscript.

Ethics and Conflicts

It goes without saying that research should be conducted within the framework of the Declaration of Helsinki[12] and other international agreements, and that all research should be conducted with a research ethics committee or equivalent oversight, as well as peer review. It is also worth reminding readers that not all work is primary biomedical research, some evidence is derived from audits, quality or service improvement (sometimes called service research), and methodology development. Researchers should also make sure that they follow the best legal, institutional, medical, and integrity practices and ensure that they are appropriately trained for the work they are doing. Research misconduct is obviously not acceptable, but “questionable research practices” (eg, poor record keeping—material compliance and poor reporting practices) should also be minimized as far as possible. Conflicts of interest, especially financial, should be given careful consideration before work begins and clearly disclosed in any manuscript. Work needs to be carried out in accordance with national and international data protection, governance, and confidentiality requirements. It is also a good idea to ensure that there are no conflicts arising from contractual obligations, intellectual property, collaborative agreements, or funding restrictions. The participation of industry in research is increasingly encouraged and necessary to fund work and produce meaningful technology; however, there is an important line not to cross where industry or financially interested parties can bias study protocol or manuscripts. Increasingly, commercial stakeholders wish to review manuscripts and comment upon these—the best practice is to outline to what extent the text was edited to incorporate this (if changed). All journals publish detailed guidance about how to disclose such relationships and interactions, and it is beyond the scope of this guide to go into detail here, but journals often adhere to the International Committee of Medical Journal Editors recommendations.[13]

Thinking Ahead to Publishing

As will be outlined in the rest of this article, there are many guidelines and check lists available for reporting research. Thinking ahead of this at the planning stage is highly recommended, as trying to fit a report to a checklist can be impossible after the data collection and analysis. We would also here advocate the involvement of a statistician as early as possible in the planning stage.

Conducting the Study

Before commencing work, it is important that all researchers involved know what the plans are and how to conduct the work. In most cases, this is best handled with a study protocol, although sometimes this is perhaps not necessary (eg, 1 or 2 authors narratively examining a small case series they have identified). Where a protocol is used, best practice is to publish or deposit this online where possible (for a list of suitable online depositories, eg, see the National Health Service (NHS) Heath Research Authority guide).[14] In all cases, good documentation of what should be done is key. Careful consideration should be taken over data collection and storage, and a piloting phase is always recommended as details overlooked at the planning stage very often come to light. Some funders will support feasibility studies for larger projects.

Reporting the Study

Reporting Best Practices

Arguably the most important part of the research cycle is the publication of results. Data can sometimes speak for themselves, but only when adequately reported. Researchers know (hopefully) what they have done and can have confidence in their results because they know it was done right, but the reader also needs to have this level of confidence, particularly if the research is ultimately going to impact patient care or further scientific developments. Good reporting practices and guidelines have been published for most study designs (https://www.equator-network.org). Using these "check lists" to produce a well-written and detailed manuscript (ie, substantiated by data, explicit methods, and analyses) allows the reader to understand and interpret the data for themselves and may help reduce bias.[15] In addition, a well-documented piece of research may allow systematic reviewers to use the data in future synthesis and meta-analyses, making the authors work even more impactful. It is difficult however for some pathologists/pathology researchers as authors to know exactly what details to include in a manuscript, and this has been clear to us in the WCT EVI MAP project. Here, we aim to provide guidance to pathologists/pathology researchers to overcome this obstacle. Table is a generalized overview of the data set we would recommend for reporting any tumor pathology manuscript. This data set checklist is based upon, and adapted from, other existing checklists mentioned throughout this article. However, many of these existing checklists are not well suited for tumor pathology studies, and hence, here, we have attempted to tailor these for the pathologist/pathology researcher. We hope that our list will complement those we mentioned below and that authors will use these at the planning stage of their research.

Studies Describing Tumor Characteristics

Much of tumor pathology literature is descriptive, defining features or characteristics of a particular tumor type. These may describe clinical presentation, findings from imaging, biochemistry, and cytology test results, and macroscopic and microscopic features including immunohistochemical features and typical molecular alterations. A distinction should be made here between descriptive studies that define a tumor for classification purposes (what a pathologist usually means when they talk about making a diagnosis) and those that evaluate diagnostic tests (refer to the following sections). Many studies in this descriptive category are essentially reporting a case series—similar cases collected and described by pathologists/researchers. See our glossary for a more detailed explanation.[11] When reporting these studies, we would recommend the minimum data set as outlined in our checklist (Table). Although aimed at surgical case series, we would also recommend authors review the very useful Preferred Reporting of CasE Series in Surgery guidelines.[16] Some studies outlining tumor characteristics may follow a classical epidemiologic cohort (refer to the following sections) or case-control design, and for these, we would also recommend authors take into account the relevant Strengthening the Reporting of Observational Studies in Epidemiology (cohort studies or case-control) checklists.[17]

Diagnostic and Reproducibility Studies

Studies that evaluate a specific method or test to aid reaching a diagnosis may follow the design of a diagnostic test accuracy (DTA) study. These could be studies looking at the accuracy (eg, sensitivity and specificity) of a specific histologic feature, an immunohistochemical (IHC) stain, or a molecular test. For these, we would strongly recommend following our data set (Table) or the Standards for Reporting of Diagnostic Accuracy Studies (STARD) checklist.[18,19] We distinguish diagnostic test studies from more descriptive type studies that characterize a tumor (which pathologists will probably more commonly think of as "diagnostic" papers), the latter are described above ("studies describing tumor characteristics"). We also distinguished studies using tests to provide prognostic or predictive information (again for these, refer to the following sections). See our glossary for a more detailed explanation.[11] There is no good checklist available for reproducibility studies (where pathologists' test results are compared against each other for concordance), but there is sufficient overlap with DTA studies that we recommend following our checklist or STARD for these as well (as far as possible).

For DTA and reproducibility studies, we recommend in our checklist, in addition to STARD, adding an outline of how the cases were selected from a diagnostic archive—the search strategy and details about which cases were eligible or excluded—how a sample size was chosen, how many cases were missing results or were unusable and why (eg, referral cases, blocks were lost or tissue exhausted), and consider any biases in selecting only from their institution (eg, tertiary center with expertise in tumor type versus more generalist setting). Brief details of the reagents and equipment used should also be outlined. We recommend giving full details of the pathology review—number of pathologists involved, level of training and experience in the subspeciality/tumor type, if blinding was used (from each other and the gold standard test results), detail of any wash out periods that were used between case re-reviews (if applicable), handling of interpretation disagreements and consensus reaching, and specific

Table
The "Mapping the Evidence for the World Health Organization Classification of Tumours: a Living Evidence Gap Map by Tumour Type" group data set checklist for reporting tumor pathology research

TITLE		Identify study design (cohort, case series, case-control, etc.) and tumor type (if appropriate) in addition to the main result/discovery
Abstract		Provide the premises and aim of the study. State study design, prospective or retrospective (where relevant)
		State sample size and source? And main statistical results. Provide conclusions
Introduction	Background	Rationale and context for the study. State clinical relevance of issue—why is the study important?
	Objectives	Clinical/biological question to be investigated/tested—state a PICO or similar
Methods	Study design	State study design type, prospective or retrospective (where relevant), why this study was chosen
		State sample size (no. of cases) and how the sample size was determined
		State if the question was formed before cases were selected, or on an existing cohort
		State if a study protocol was prepared and published/deposited and where prospective recruitment registry data are available
		Ethics review and approval details, any anonymization carried out (or state if it was not needed)
	Setting	State geographic (country) settings, multi or single center
		State health care setting (community, secondary, tertiary, etc.)
	Participants[a]	Case selection (where applicable): inclusion and exclusion criteria, where/how cases were identified, description of material used and how it was handled, database search criteria, what cases had in common, how controls were selected (if needed), how many were missing from an archive, how many cases lack enough tissue for inclusion, random inclusion or consecutive inclusion, how cases were enrolled/identified if done prospectively.
	Pathologists	Details of pathology review: to what extent were cases reviewed, how many pathologists, level training (qualifications, experience, and current practice), method of review (digital or glass), what stains were reviewed, method of reporting results, AI involvement, pathologist blinding (to each other or other pertinent results/data, wash out periods for individuals), handling borderline interpretations and discordance, consensus meetings, audit of any cases by other parties, learning curves that were overcome during study
	Diagnostics	Diagnostic criteria (where relevant) for included cases, outline if these were changed over the study/since cases reported (criteria updated, stage or grade drift)
		Details of index/comparator test (where relevant)
		Define outcomes to be analyzed and how these were derived/confirmed (where relevant)
		Describe any other efforts to limit bias
	IHC/molecular/ other	Briefly outline methods (performed manually or by automated machine), timings
		State assay/antibody and clone/target/probe/reagents and companies/suppliers
		State equipment used and companies/suppliers
	Analysis	Outline statistical methods (including subgrouping or sensitivity analyses) and software used
		Details of how missing data and/or loss to follow up was addressed
		State that all analyses were planned a priori
Results	Participants[a]	Outline cases at each stage of study (number in archive, number selected, number available, number analyzed, and number missing or lost to follow up). Use a flow diagram (eg, CONSORT, PRISMA) where appropriate
		Baseline characteristics of patients (clinical data, age at time of sampling) and cases (tumor type, grade, stage, ancillary tests, and any other). Summarize in data tables where appropriate
		Time between samples acquired and study (age of cases, variation of this within the cohort).
		Adverse effects of any intervention/test where applicable.
	Descriptives	Results of pathology review (where applicable). Use tables or flow diagrams where appropriate
		Results of outcome data (where applicable) and follow up time. Use tables or flow diagrams where appropriate
		As far as possible or practical, include all raw data (or include in supplementary files, or provide a link to deposited data) that would allow repeat independent analysis
	Statistics	Relevant statistics with 95% CIs and/or *P* values where applicable, adjusted and unadjusted (where relevant)
		Detail how boundaries or dichotomies were derived
		Include all analyses that were carried out (selective inclusion of results is to be avoided)
Discussion	Findings	Summarize key findings
	Limitations	Study limitations, potential sources of bias, statistical uncertainty
		Areas where further work is needed
	Relevance	Relevance to clinical practice and generalizability, and taking into consideration the context of existing published data
		Ability to adopt findings into clinical practice
Conflicts		Funding sources and involvement by funders, Authors conflicts of interest—all funding to be stated even if not directly influencing the work
		Other publications using the same data/cases
Key points (if used)		State the problem and what has been done before State what the study has found and adding up to the evidence base
		State what is still unknown

[a] Participants may be included in either methods or results, or both.

methods of interpreting a test result (eg, how an IHC stain was interpreted). These additional data are included in our checklist (Table 1).

Not all studies follow the DTA design encompassing comparison of a new test with an established reference (a.k.a. gold) standard (or existing practice) in a representative cohort of samples. For example, a technical validation or verification type of design with selected positive and negative cases. Nonetheless, we would encourage authors to follow our checklist or STARD as far as possible in these cases and adapt the data set where appropriate. Identifying the type of study design in the abstract or title would be best practice.

Prognostic Studies

These tend to be cohort studies where the outcomes for patients with a particular tumor are evaluated (see our glossary for a more detailed explanation[11]). This could be a morphologic feature, the grade or stage, or an IHC or molecular characteristics. In cohort studies, outcomes are either already known (retrospective) or patients are later followed up (prospective). We recommend following the Strengthening the Reporting of Observational Studies in Epidemiology (cohort studies) checklist, or our checklist, for these in general or the REporting recommendations for tumor MARKerprognostic studies checklist for specific tumor markers[17,20,21] and would emphasize the need to be clear in the abstract which study design has been used, the sample size, and if the study is prospective or retrospective (the latter having more risk of bias). Many authors like to present these cohort baseline and outcome data in tables, but others may prefer to summarize using a flow diagram, similar to the Consolidated Standards of Reporting Trials (CONSORT) or Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) diagram. Both of these approaches can be helpful to the reader and/or a systematic reviewer, and we would encourage the use of such visualization methods where possible. As for DTA studies, we would recommend outlining how the cases were selected, the details of the pathology review, and stating clearly how the feature was defined/morphologic criteria used (or test interpreted). Case series are usually smaller collections of isolated but similar cases that are grouped together, occasionally to look at outcomes. Usually, there is no exposed/unexposed for comparisons to be made. The distinction from cohort studies can be sometimes difficult, but guidance exists.[22-24] Also, see our glossary for a more detailed explanation.[11] For more complex modeling, the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis checklist may be more appropriate.[25,26]

Case Reports

Case reports (usually just one case, or sometimes, a very small collection of similar cases) usually have limited utility in EBM. However, in pathology, case reports often bring useful practice points, highlight rare (or hitherto undocumented) exceptions to the generally accepted rule (it could be the first report of a false positive IHC result for example), provide data on rare tumors, or can be useful educational material (discussions around differential diagnoses). See our glossary for a more detailed explanation.[11] We recommend using our checklist or following the CARE (CAse REport)[27] or Surgical CAse REport[28] checklists when reporting cases. We would emphasize and add to this that for pathology case reports, certain information should be included, such as background, clinical and family history, any available imaging results, the specimen and dissection procedures and reporting data sets used, where relevant (national or international guidelines), details of tissue stains used, IHC antibody clones and manufacturers, and details of clinical outcomes, where known should be included.

Clinical Trials

Clinical trials (including randomized controlled trials) do not often feature in the WCT, particularly for rare tumor types. However, these are included here for completeness, as they play an increasingly important role in personalized medicine (companion diagnostics development). Pathologists are often involved in clinical trial research and are perhaps asked to help draft relevant sections of manuscripts. The CONSORT guidelines[29] are well known for general clinical trial reporting, but we recommend following the SPIRIT-Path (Standard Protocol Items: Recommendations for Interventional Trials—pathology extension)[30] checklist for pathology aspects of clinical trials. A CONSORT diagram (or similar) should be used.[31] Finally, it is worth noting that the information and/or samples collected in a clinical trial can be used to test a different research question (eg, the prognostic value of a biomarker) related to histopathology.

Prediction Studies

We use the term “predictive” here to refer to markers predictive of treatment response and companion testing. For most situations, this will be based on clinical trial data as above as well as on diagnostic test accuracy/validation studies.

Mechanisms and Pathogenesis

Reporting guidelines are less well developed for mechanistic and basic science or wet laboratory (experimental pathology) type studies. Nature Cell Biology has produced detailed guidance on these however, and we would recommend following these in most cases. For studies using animal models, the Animal Research: Reporting of In Vivo Experiments (ARRIVE) guidelines are recommended.[32]

Systematic Reviews

Systematic reviews attempt to find, appraise, and summarize all the existing evidence on a topic. They are carried out with a specific clinical question and search criteria and may or may not include a meta-analysis. Systematic reviews are not common in the pathology research literature, but when conducted, we recommend following the PRISMA guidelines[33] and the use of a PRIMSA flow diagram.[34] Systematic review studies include a big picture review type of studies, such as evidence gap maps.[7]

We do wish to distinguish between systematic reviews that are published primarily as a piece of research and guidelines from institutions (such as College of American Pathologists, American Society of Oncology, Royal College of Pathologists, and others), many of whom commonly use systematic methods in the development of such documents. The development and reporting of guidelines are very much the domain of those institutions publishing them and as such we consider them to fall outside of the scope this guide, other than to say that we hope this guide helps improve the reporting of evidence upon which these commonly cited guidelines rely.

Conclusions

In this brief guide we have outlined the basis for planning, conducting, and reporting good quality research in tumor pathology. This guide is not intended to be all-encompassing or to replace any existing EQUATOR checklists. However, we hope this will complement existing guidelines, and can be easily adopted into the planning and writing up of pathology studies of tumor

pathology. Following this guidance should help to improve the level of detail in tumor pathology research publications, which in turn should make systematic reviewing of the literature much easier and encourage secondary researchers to focus more attention on this underrepresented area of medicine for evidence synthesis.

Acknowledgments

The authors would like to thank Laura Brispot and Benjamin Duclos for their contribution in coordinating this work at IARC. The authors would also like to thank IARC for supporting the work.

Endorsement

This work has been reviewed and endorsed by the WHO IARC International Collaboration for Cancer Classification and Research (IC^3R) Core Members.

Author Contributions

The paper was conceived by R.C., I.I., and I.C. The manuscript was drafted by R.C., and all authors reviewed, significantly contributed to, and approved the final version.

Data Availability

All data generated or analyzed during this study are included in this published article.

Funding

The overall project, IARC, and beneficiaries (DHM, MSCI, ISC III) are funded by the European Commission (HORIZON Grant No 101057127). R.C. and F.C. are funded by United Kingdom Research and Innovation (UKRI). R.C. is partly funded by mdxhealth inc. S.H. has received research funding or honoraria from Roche, BMS, Merck, Sysmex, Thermo, Volition, Trillium, Medica, and Instand and is founder of SFZ BioCoDE and CEBIO. P.H.T. has received honoraria from AstraZeneca.

Declaration of Competing Interest

Not reported.

References

1. Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn't. *BMJ*. 1996;312:71–72.
2. IARC. About IARC. Accessed June 3, 2024. https://www.iarc.who.int/cards_page/about-iarc/
3. Del Aguila Mejía J, Armon S, Campbell F, et al. Understanding the use of evidence in the WHO Classification of Tumours: a protocol for an evidence gap map of the classification of tumours of the lung. *BMJ Open*. 2022;12(10), e061240.
4. Md Nasir ND, Koh VCY, Cree IA, et al. Phyllodes tumour evidence gaps mapped from the 5th edition of the WHO classification of tumours of the breast. *Histopathology*. 2023;82:704–712.
5. Cree IA, Indave Ruiz BI, Zavadil J, et al. The international collaboration for cancer classification and research. *Int J Cancer*. 2021;148:560–571.
6. IARC. *WHO Classification of Tumours*. Accessed June 3, 2024. https://tumourclassification.iarc.who.int/welcome/
7. IARC. *WCT EVI MAP Project Overview*. 2023. Accessed June 3, 2024. https://wct-evi-map.iarc.who.int/project-overview/
8. White H, Albers B, Gaarder M, et al. Guidance for producing a Campbell evidence and gap map. *Campbell Syst Rev*. 2020;16, e1125.
9. Campbell F, Tricco AC, Munn Z, et al. Mapping reviews, scoping reviews, and evidence and gap maps (EGMs): the same but different—the "Big Picture" review family. *Syst Rev*. 2023;12:45.
10. Riva JJ, Malik KM, Burnie SJ, Endicott AR, Busse JW. What is your research question? An introduction to the PICOT format for clinicians. *J Can Chiropr Assoc*. 2012;56:167–171.
11. Colling R, Indave I, Del Aguila J, et al. A new hierarchy of research evidence for tumor pathology: a Delphi study to define levels of evidence in tumor pathology. *Mod Pathol*. 2024;37:100357.
12. World Medical Association General Assembly. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA*. 2013;310:2191–2194.
13. ICMJR. *Recommendations*. Accessed June 3, 2024. https://www.icmje.org/recommendations/
14. HRA. *Research Registration and Research Project Identifiers*. Accessed June 3, 2024. https://www.hra.nhs.uk/planning-and-improving-research/research-planning/research-registration-research-project-identifiers/
15. Bradley SH, DeVito NJ, Lloyd KE, et al. Reducing bias and improving transparency in medical research: a critical overview of the problems, progress and suggested next steps. *J R Soc Med*. 2020;113:433–443.
16. Agha RA, Sohrabi C, Mathew G, et al. The PROCESS 2020 guideline: updating consensus preferred reporting of CasE series in surgery (PROCESS) guidelines. *Int J Surg*. 2020;84:231–235.
17. von Elm E, Altman DG, Egger M, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *BMJ*. 2007;335:806–808.
18. network e. STARD2015: *An Updated List of Essential Items for Reporting Diagnostic Accuracy Studies*. Accessed June 3, 2024. https://www.equator-network.org/reporting-guidelines/stard/
19. Bossuyt PM, Reitsma JB, Bruns DE, et al. STARD 2015: an updated list of essential items for reporting diagnostic accuracy studies. *BMJ*. 2015;351, h5527.
20. Equator Network. *REportingrecommendations for Tumour MARKerprognostic Studies (REMARK)*. Accessed June 3, 2024. https://www.equator-network.org/reporting-guidelines/reporting-recommendations-for-tumour-marker-prognostic-studies-remark/
21. McShane LM, Altman DG, Sauerbrei W, et al. REporting recommendations for tumour MARKer prognostic studies (REMARK). *Br J Cancer*. 2005;93:387–391.
22. Dekkers OM, Egger M, Altman DG, Vandenbroucke JP. Distinguishing case series from cohort studies. *Ann Intern Med*. 2012;156:37–40.
23. Mathes T, Pieper D. Clarifying the distinction between case series and cohort studies in systematic reviews of comparative studies: potential impact on body of evidence and workload. *BMC Med Res Methodol*. 2017;17:107.
24. Song JW, Chung KC. Observational studies: cohort and case-control studies. *Plast Reconstr Surg*. 2010;126:2234–2242.
25. Equator Network. *Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD): The TRIPODstatement*. Accessed June 3, 2024. https://www.equator-network.org/reporting-guidelines/tripod-statement/
26. Collins GS, Reitsma JB, Altman DG, Moons KG. Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD): the TRIPOD Statement. *Eur J Clin Invest*. 2015;45:204–214.
27. Gagnier JJ, Kienle G, Altman DG, et al. The CARE guidelines: consensus-based clinical case reporting guideline development. *BMJ Case Rep*. 2013;2013:bcr2013201554.
28. Agha RA, Franchi T, Sohrabi C, et al. The SCARE 2020 Guideline: updating consensus surgical CAse REport (SCARE) guidelines. *Int J Surg*. 2020;84:226–230.
29. Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMJ*. 2010;340:c332.
30. Kendall TJ, Robinson M, Brierley DJ, et al. Guidelines for cellular and molecular pathology content in clinical trial protocols: the SPIRIT-Path extension. *Lancet Oncol*. 2021;22:e435–e445.
31. Falci SG, Marques LS. CONSORT: when and how to use it. *Dental Press J Orthod*. 2015;20:13–15.
32. Percie du Sert N, Hurst V, Ahluwalia A, et al. The ARRIVE guidelines 2.0: Updated guidelines for reporting animal research. *PLoS Biol*. 2020;18:e3000410.
33. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71.
34. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Syst Rev*. 2021;10:89.