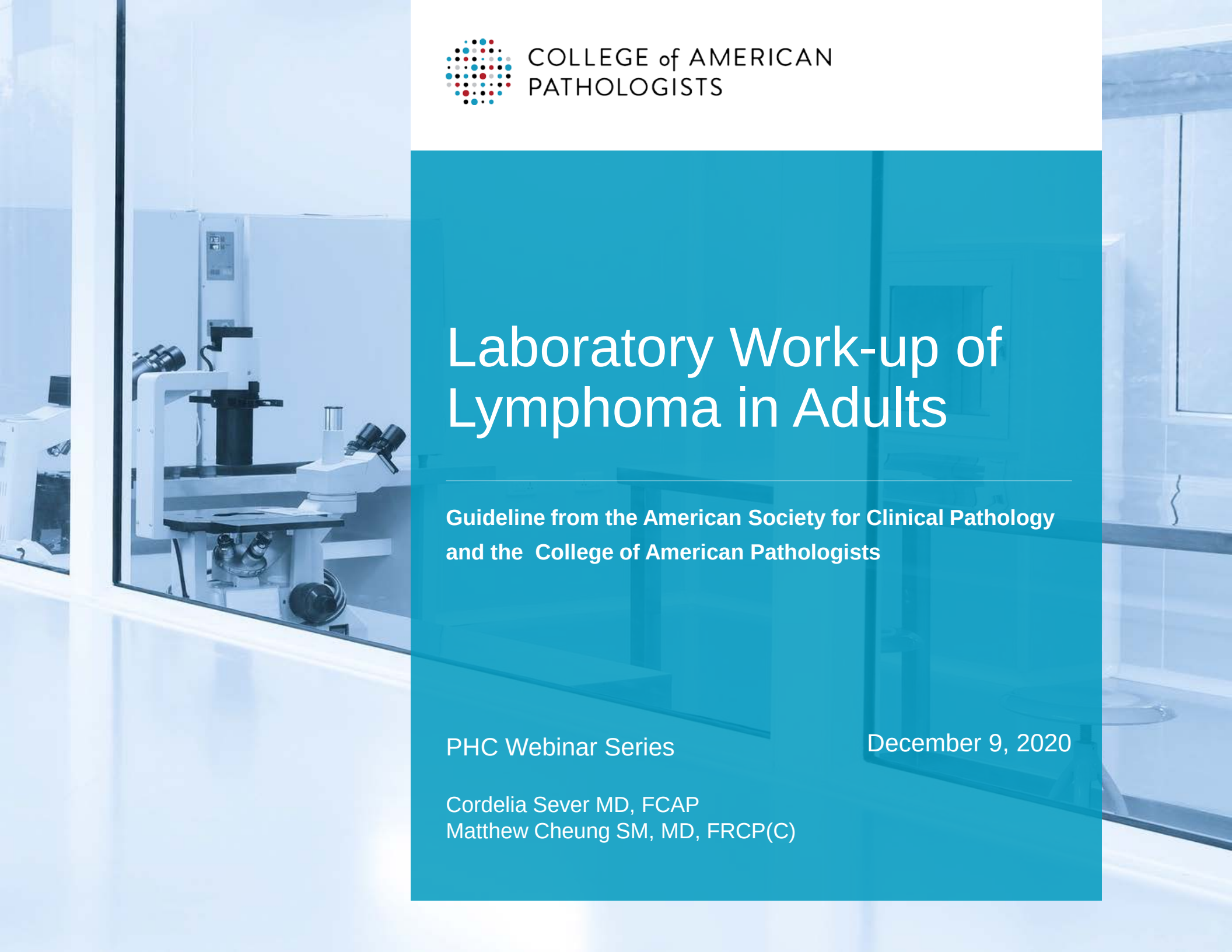

COLLEGE of AMERICAN PATHOLOGISTS

Laboratory Work-up of Lymphoma in Adults

Guideline from the American Society for Clinical Pathology and the College of American Pathologists

PHC Webinar Series

December 9, 2020

Cordelia Sever MD, FCAP
Matthew Cheung SM, MD, FRCP(C)

Webinar Host

- **This series is sponsored by the Personalized Healthcare Committee (PHC)**
- **Today's webinar host is Joseph Willis MD**

Housekeeping

- **This presentation will be recorded. The recording and PDF will go out to all registrants in one week**
- **All lines are muted during the presentation**
- **Please send in your questions as you think of them via the "Question Box" in your control panel**

Cordelia Sever MD, FCAP

- **Vice-President and Director of Clinical Pathology of Pathology Associates of Albuquerque, PA**
- **Medical Director of Presbyterian Hospital laboratory, clinical laboratory hematology, and Presbyterian urgent care branch labs in Albuquerque for TriCore Reference Laboratories**
- **Served as co-chair of the ASCP-CAP-ASH Requirements for the Workup of Lymphoma Expert Panel**

Matthew Cheung SM, MD, FRCP(C)

- **Clinician-Investigator and Clinical Hematologist at the Odette Cancer Centre/Sunnybrook Health Sciences Centre**

- **Medical Assistant Professor in the Department of Medicine at the University of Toronto**

- **Served as co-chair of the ASCP-CAP-ASH Requirements for the Workup of Lymphoma Expert Panel**

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Disclaimer, continued

- **Opinions expressed by the speaker are the speaker's own and do not necessarily reflect an endorsement by the CAP of any organizations, equipment, reagents, materials, or services used by participating laboratories.**

Disclosures

- Both presenters have no relevant disclosures.

Outline

- Introduction
- Key questions and results
- Guideline statements (recommendations)
- Good Practice Statements
- Conclusion
- Guideline development process (appendix)

Introduction

- **Diagnosis and classification of lymphoma has become a highly complex, multi-modality process that requires rigorous attention to and quality assurance of pre-analytical, analytical, and post-analytical details**
- **However, little guidance exists regarding the appropriate handling, testing, and reporting of lymphoma specimens**

Introduction, continued

- **Practitioners do not generally have the bandwidth to assimilate the universe of evidence into coherent conclusions and apply them**
  - **Highly variable quality of scientific evidence**
  - **Highly variable practice environments with different diagnostic capabilities need tailored approach**
  - **Often conflicting or confusing evidence across studies**
  - **Highly biased publications dominated by retrospective single institution studies**
  - **Insufficient focus on patient perspective and preference**

Collaboration

- **The ASCP, CAP, and ASH convened a multi-disciplinary expert panel to systematically review published documents and develop a formal, evidence-based guideline for the pre-analytic phase of testing with a focus on specimen requirements for the diagnosis of lymphoma**

Multi-disciplinary Guideline Panel

CO-CHAIRS
Steven H. Kroft, MD – ASCP
Cordelia Sever, MD – CAP
Matthew Cheung, MD – ASH

EXPERT PANEL
Adam Bagg, MD
David Dorfman, MD
Catherine Diefenbach, MD
William Finn, MD
Dita Gratzinger, MD, PhD
Patricia Gregg, MD
John Leonard, MD
Sonali Smith, MD
Ronald Weiss, MD, MBA

ADVISORY PANEL
Catalina Amador, MD
Peter Banks, MD
Diane D. Davey, MD
Christopher Flowers, MD
Christopher E. Fundakowski, MD
Sara E. Gibson, MD
Kent Hootman, MD
M. Elizabeth Hammond, MD
Annette S. Kim, MD, PhD
Catherine Leith, MD
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Gwen Nichols, MD
Lauren B. Smith, MD
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Robert Kunkle, MS – ASH
Lesley Souter, PhD
Christina Ventura, MPH, MLS(ASCP) – CAP

Key Questions and Results

Overarching Key Question

- **What are the specimen requirements for accurate diagnosis in all adult patients with clinical features raising consideration of lymphoma?**

OUR KEY QUESTIONS

KQ1a:	To what degree do specimen types allow for accurate primary diagnosis of indolent, aggressive and Hodgkin lymphoma?
KQ1b:	For each specimen type, what are the optimum and minimum requirements for accurate primary diagnosis or exclusion of lymphoma?
KQ1c:	What are the appropriate analytical triage processes by which fresh tissue can be distributed for indolent, aggressive and Hodgkin lymphoma?
KQ2:	What are the diagnostic test characteristics of the available additional assays and how does additional testing of the primary specimen influence the diagnostic accuracy to enable actionable therapy for indolent, aggressive and Hodgkin lymphoma?

Results

- **13 guideline statements were developed to optimize specimen selection, ancillary diagnostic testing, and appropriate follow up for safe and accurate diagnosis of indolent and aggressive lymphoma**

Guideline Statements

Statement 1

1. *Strong Recommendation*. – Clinical care providers should use surgical biopsy when feasible in a clinical setting where Hodgkin lymphoma is highly suspected.

Rationale

- **Studies compared core needle biopsy (CNB) to surgical biopsy (where available) and indicated lower diagnostic sensitivity of CNB for HL than for NHL**
  - **Positive predictive value of CNB is high**
  - **Negative predictive value is low (as many as 50% of patients may require follow up with open biopsy)**

Rationale, continued

Other factors:

- **Bias in site selection (most accessible versus likelihood of involvement)**
- **Paucity of neoplastic cells and mimickers**

Statement 2

2. *Recommendation.* – Clinical care providers should obtain excisional or core needle biopsy (CNB) specimens in patients with high suspicion of lymphoma.

Rationale

- **Core needle biopsy equivalent or superior to open biopsy in 2 well-controlled prospective trials:**
  - **CNB not statistically different from surgical biopsy:**

    sensitivity 92%, PPV 97%, NPV 85%
  - **Surgical biopsy also has false negative results (selection bias):**

    sensitivity 88.7%, NPV as low as 54.3%

Statement 3

3. Strong Recommendation. Clinical care providers should *not* use fine needle aspiration (FNA) cytomorphology alone without ancillary testing to achieve a definitive diagnosis of lymphoma.

- ***Note:*** **Cytomorphology alone without ancillary studies has low sensitivity and low predictive value.**
- ***Note:*** **A defined subset of lymphoma requires architectural assessment and cannot be reliably diagnosed and subclassified by FNA.**

Statement 3

Rationale

- **FNA most frequently used to diagnose non-hematopoietic tumors, lymphoma incidence is 6-7%**
- **Sensitivity for lymphoid lesion versus “not lymphoma” as high as 95%**
- **High rate of incorrect classification, particularly high for T-cell lymphomas (30%), Hodgkin lymphoma (nearly 50%)**
- **Addition of immunophenotyping and cell blocks markedly improves diagnosis of B-cell lymphomas with sensitivity as high as 89-93%**

Statement 3

Rationale

- **In difficult to reach areas (such as lung), FNA can also have significant complication rates**
- **Study of transthoracic FNA showed 25% complication rate:**
  - **Pneumothorax 20%**
  - **Bleeding 8%, including 1 death in patient with coagulopathy**

Statement 4

4. *Strong Recommendation.* Clinical care providers should follow-up patients with "negative" results for persistent signs and symptoms of lymphoma and pursue larger volume biopsy when clinical suspicion for lymphoma persists.

Statement 5

5. *Conditional Recommendation*. – Clinical care providers may use positron emission tomography with 2-deoxy-2-[fluorine-18]fluoro-D-glucose (FDG-PET) to identify sites for biopsy in patients with suspected transformed/aggressive-histology lymphoma. As feasible, biopsies should be directed to the site of greatest FDG avidity.

Rationale

- **Application of PET or PET-CT: to guide the initial biopsy site for patients with suspected lymphoma, or to investigate the potential for histologic transformation in patients with suspected or known indolent lymphoma**
  - **Consensus guidelines recommend the use of PET in combination with computed tomography (PET-CT) for staging and end of treatment response assessment**
  - **Studies also suggested that FDG uptake, generally quantified by measuring the standardized uptake value (SUV), trended higher in patients with aggressive histology lymphomas**

Rationale, continued

- **Application of PET or PET-CT: to guide the initial biopsy site for patients with suspected lymphoma, or to investigate the potential for histologic transformation in patients with suspected or known indolent lymphoma**
  - **Data supports the ability of PET to distinguish between indolent vs aggressive histologies**
    - **patients with indolent lymphomas had PET scans that were reliably associated with SUV ≤13**
    - **sensitivity and PPV of PET-based biopsy: 94%**
    - **specificity and NPV of PET-based biopsy: 95%**

Statement 6

6. *Conditional Recommendation*. – Clinical care providers may obtain bone marrow biopsies for the primary diagnosis in select patients with suspected lymphomas.

***Note*: For certain lymphoma types (eg, splenic low-grade lymphomas, lymphoplasmacytic lymphomas [LPL]) bone marrow biopsy may be preferred over more invasive surgical methods.**

Rationale

- **A majority of splenic lymphomas have bone marrow involvement and can be safely diagnosed with bone marrow examination with sufficient information for therapy planning**
- **Some lymphomas only involve bone marrow and require bone marrow examination, e.g. lymphoplasmacytic lymphoma**
- **Most literature on bone marrow lymphoma is on staging efficacy; some high grade lymphomas (eg Burkitt lymphoma) have high incidence of BM involvement and can potentially be diagnosed with a low risk staging BM examination**

Statement 7

7. *Conditional Recommendation*. – Clinical care providers may use cerebrospinal fluid (CSF) for the evaluation of primary or secondary central nervous system (CNS) lymphoma in select patients.

Statement 8

8. *Strong Recommendation*. – Clinical care providers should use a combined morphologic and flow cytometric evaluation of cerebrospinal fluid (CSF) in the investigation of possible primary or secondary central nervous system (CNS) lymphoma in select patients.

Rationale

- **Flow cytometric evaluation of CSF improves diagnostic accuracy in the diagnosis of primary or secondary CNS lymphoma when compared with morphologic examination alone**
  - **combined morphologic and flow cytometric evaluation of CSF increased the PPV from 50% (morphology only) to 92% (combined morphology and flow cytometry) for CNS lymphoma.**
  - **NPV for combined morphologic and flow cytometric evaluation was 52% in unselected patients; however, in higher risk patients (history of lymphoma and/or suspicious findings on brain imaging) the NPV of combined analysis was 89%**

Statement 9

9. *Strong Recommendation*. – Based on low negative predictive values, clinical care providers should follow-up patients with “negative” results for persistent signs and symptoms of CNS lymphoma and pursue repeat CSF examination or biopsy when clinical suspicion for lymphoma persists.

Rationale

- **There is historical documentation of high false negative rates for CSF evaluation of lymphoma likely due to:**
  - **Low cellularity of CSF samples**
  - **Inadequate sample volumes**
  - **Challenges in differentiating lymphoma cells from reactive cells**
  - **Sites of CNS involvement distant from the leptomeninges**
  - **Exposure to corticosteroids prior to sampling**

Rationale, continued

- **An initial negative or non-diagnostic test result may not definitively rule out the presence of lymphoma**
  - **Continued monitoring is required to determine if open brain biopsy (in patients with parenchymal brain lesions) or further CSF sampling is necessary**
  - **Repeated sampling, sending larger volumes, and addition of ancillary testing may reduce false negative CSF evaluations**
- **Clinical judgment is required to determine whether further sampling or pursuit of tissue (brain) biopsy is preferred when clinical or radiographic suspicion for lymphoma remains**

Statement 10

10. *Strong Recommendation*. – Clinical care providers should use immunophenotyping by flow cytometry and/or immunohistochemistry (IHC) in addition to morphology for the evaluation of specimens for the diagnosis and subclassification of lymphomas.

Rationale

- **Immunophenotyping by IHC staining and/or flow cytometry, in addition to morphology, is well established as critical for lymphoma diagnosis and subtyping**
  - **Numerous studies support that flow cytometry of fresh, unfixed tissue can be used to identify clonal B-cell populations in a variety of specimens and lymphoma subtypes**
    - **Identification of clonal B-cell populations in biopsies from 382 of 471 patients (81%) with B-cell NHLs, including low and high-grade B-cell lymphomas; also identified clonal B-cell populations in 147 of 169 lymph node biopsy or FNA specimens (87%) involved by B-cell lymphoma**
    - **Flow cytometric analysis identified clonal B-cells, based on restricted immunoglobulin light chain expression, with a sensitivity of 82-88%, specificity of 72-100%, PPV of 93% and NPV of 48%**

Statement 11

11. *Conditional Recommendation* – Clinical care providers may use fluorescence in situ hybridization (FISH) analysis when evaluating specimens in patients with suspected or confirmed lymphoma, or in the subclassification of lymphoma. FISH analysis is feasible on specimens obtained by fine needle aspiration (FNA) and may increase diagnostic yield.

Note: **Demonstration of the appropriate rearrangements is required for a diagnosis of high-grade B-cell lymphoma with *MYC* and *BCL2* and/or *BCL6* rearrangements.**

Rationale

- **Two studies reported directed use of particular FISH probes to aid in diagnosis of lymphoma in FNA specimens**
- **FISH probes were chosen based on clinical history, morphologic features, and/or immunophenotype**
  - **Study did not use up-front panels of FISH probes, which would be expected to significantly increase costs and risk of false positive results**
  - **FISH evaluation was requested for subclassification of DLBCL, Burkitt lymphoma, high-grade B-cell lymphoma, FL, and mantle cell lymphoma**
  - **Results: FISH was positive in 61% of cases, negative in 26% of cases, and indeterminate in 12% (including 2% that failed to hybridize) in one study; successful results in 95% of the 298 cases in which FISH was deployed**

Rationale, continued

- **The revised *WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues* state that rearrangements such as high-grade B-cell lymphoma with *MYC* and *BCL2* and/or *BCL6* (double- or triple-hit lymphomas require detection by cytogenetic or molecular methods)**
- **It is reasonable to perform FISH for *MYC* translocations on all samples with large B-cell morphology and if positive, proceed with *BCL2* and/or *BCL6* FISH**

Statement 12

12. *Conditional Recommendation* – Clinical care providers should not routinely use up-front polymerase chain reaction (PCR)-based clonality studies of antigen receptor genes (ie, T-cell receptor and immunoglobulin) in the initial investigation of lymphoma. There may be a confirmatory role in certain settings for these studies.

Rationale

- **The evidence base shows high but imperfect sensitivity and specificity of molecular testing for immunoglobulin (IG) gene rearrangements.**
  - **Data is scarce on the performance characteristics of up-front molecular testing for T-cell receptor (TCR) gene rearrangements in formulating the recommendation.**
- **Concerns about the potential harms associated with up-front molecular testing that could lead to possible false positive or false negative diagnoses, unnecessary medical costs, and use of limited biopsy material for unnecessary testing.**

Rationale, continued

- **Study with 98 patients were tested for B- and T-cell clonality testing in patients with B-cell lymphoma and reactive lymphadenopathy.**
  - **The reported sensitivity and specificity of B-cell clonality testing for B-cell lymphoma were 77% (95% CI, 58-90%) and 88% (95% CI, 78-95%) respectively.**
  - **false positive T-cell clonality results were reported in 10% of B-cell lymphomas and 13% of reactive lymphadenopathies**

Rationale, continued

- **Flow cytometry alone combined with morphology is highly effective in establishing diagnosis without molecular studies**
- **The added value of up-front IG molecular clonality studies in the initial diagnosis setting combined with routine flow cytometry immunophenotyping appears to be quite limited.**
- **Study with 149 B-cell lymphomas, 131 (88%) showed light chain restriction by flow immunophenotyping; Of the 18 cases without light chain restriction, 14 (78%) were DLBCLs, which generally can be diagnosed based on histologic features without the need for clonality studies of any sort.**

Rationale, continued

- **Data on T-cell clonality testing were scant in the evidence base; neither sensitivity nor the "added value" of T-cell clonality testing for detection of T-cell lymphoma could be assessed based on the 5 identified studies in the evidence base.**
  - **Study reported T-cell clonality testing on 30 B-cell lymphomas and 68 reactive lymphadenopathies; false positive T-cell clonality results were reported in 10% of B-cell lymphomas and 13% of reactive lymphadenopathies.**
  - **Given the low incidence of T-cell lymphoma, even relatively high specificity could still lead to significant numbers of false positive TCR clonality results in unselected patients.**

Statement 13

13. *Conditional Recommendation* – Clinical care providers may use molecular tests to aid in classification of lymphomas. For example, pathologists may use *MYD88* L265P to aid in the classification of indolent B-cell lymphoma.

***Note:* This recommendation statement refers to non-FISH molecular tests.**

Rationale

- **The *MYD88* L265P mutation is the only example of a mutation that can be used to facilitate the diagnosis of a specific lymphoma, namely lymphoplasmacytic lymphoma**
  - **Sanger sequencing and allele-specific PCR can detect the L265P mutation in formalin-fixed and decalcified bone marrow samples**
  - **PCR was able to detect the mutation in bone marrow infiltrations below 1% of lymphoma cells and clearly distinguish patients with confirmed Waldenström macroglobulinemia (WM)/LPL and other indolent lymphomas, including CLL/SLL and splenic marginal zone lymphoma.**
- **Panel members agreed that mutational analysis may be valuable when classifying lymphoma subtypes**

Good Practice Statements

Good Practice Statements

- **Good practice statements (GPS) are recommendations panels may consider important but are not appropriate to be formally rated for quality of evidence**
- **GPSs reflect expert consensus opinions supported by a limited number of studies and data that were not formally included in the evidence-base or systematically rated.**

Good Practice Statements

Secondary reviews

For the diagnosis of difficult-to-classify lymphomas, laboratories should have a robust peer review process. Peer review may include a second review by a more experienced pathologist or a consensus review by a group of pathologists.

Clinical information

Pathologists should use clinical information in the work-up and classification of lymphoma and lymphoma subtypes.

Good Practice Statements

Reporting elements

Laboratorians should include specimen handling elements in the final pathology report.

Tissue Utilization

Laboratories should establish policies to ensure efficient allocation and utilization of tissue for lymphoma testing.

Good Practice Statements

Turnaround times

- **Laboratories should provide appropriate turnaround times for lymphoma test results to inform clinical decision-making**
  - Conventional cytogenetics 8-10 days
  - FISH for unique translocations 5-7 days
  - Flow cytometric analysis 1-2 days
  - Immunohistochemistry 1-2 days
  - Morphological assessment 1-2 days
  - PCR for Ag receptor gene rearrangements 5 days

- **Laboratories that send out tests for lymphoma diagnosis should have a process in place to ensure that specimens are sent and reviewed by outside reference laboratories in a timely manner.**

What's Missing?

- **No Recommendations related to key question 1b**

  For each specimen type, what are the optimum and minimum requirements for accurate primary diagnosis or exclusion of lymphoma?

  - Specifically, nothing related to:
    - Optimal biopsy techniques (needle gauge, number of passes, operator experience/training)
    - Handling (ischemic time, type and length of fixation, etc.
  - Common themes:
    - "more than one needle core", (2-5)
    - Radiographic guidance (ultrasound, CT) for needle biopsies
    - Formalin fixation better antigen preservation for immunohistochemistry

What's Missing?

- **No Recommendations related to key question 1c**

  What are the appropriate analytical triage processes by which fresh tissue can be distributed for indolent, aggressive and Hodgkin lymphoma?

- **Practical considerations influencing triage process:**
  - Institutional capabilities and objectives:
    - Frequency of lymphoma specimens, communication between departments, work flow
    - On-site versus off-site immunophenotyping capabilities potentially introducing delays and specimen deterioration
    - Tissue needed for research?

Conclusions

Conclusions

- **The primary diagnosis and classification of lymphoma can be achieved through analysis of a variety of specimen types.**
- **The evidence-based recommendations may guide decision-making regarding appropriate specimens, diagnostic capabilities, and correct utilization of ancillary testing.**
- **Disease prevalence in patient populations, availability of ancillary testing, and diagnostic goals should be incorporated into algorithms tailored to each practice environment.**

Conclusions, continued

- **To fully inform decision-making, it is important not only to examine the advantages of the available approaches, but also assess their limitations.**
- **Understanding the limitations and advantages as demonstrated by the available evidence will help health care providers and patients manage expectations and choose a diagnostic testing strategy that is best suited to their goals and resources.**

References

Refer to Early Online Release Nov. 11, 2020

Guideline From the American Society for Clinical Pathology and the College of American Pathologists

(Arch Pathol Lab Med. doi: 10.5858/arpa.2020-0261-SA)

Guideline Development Process

Guideline Funding and Management of Conflict of Interest

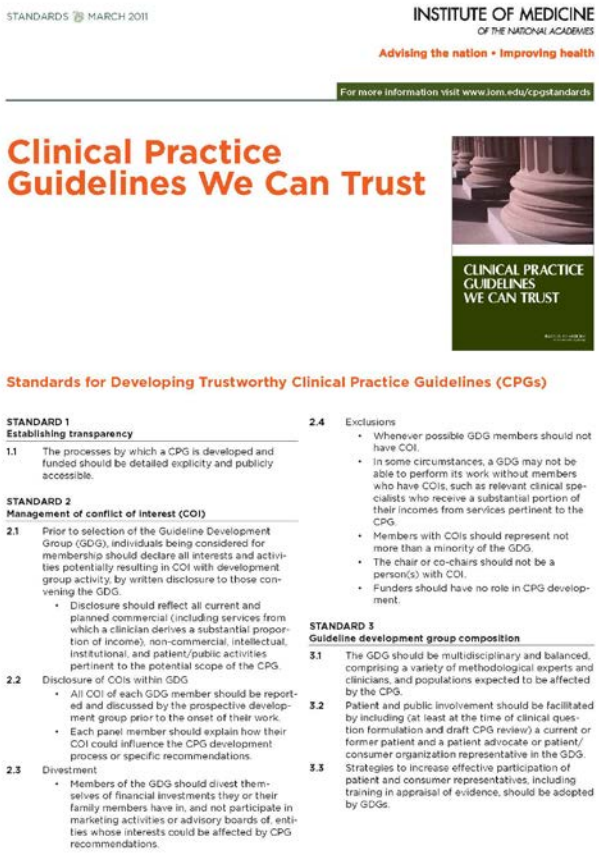
- **The ASCP, CAP, and ASH provided funding for the administration of the project**
  - **Direct funding from for-profit companies was not accepted.**
  - **All EP members volunteered their time and received travel support from their organizations to attend project meetings.**
- **Members disclosed all financial relationships with and interests from 24 months prior to appointment as well as during the guideline development process.**
  - **Also disclosed nonfinancial interests relevant to the guideline topic.**
- **Disclosures were reviewed by a DOI Review Committee composed of members and staff of the three organizations.**

Panel proceedings

- **The expert panel met multiple times via conference call/webinar throughout the guideline development and met twice in-person to review data and draft the recommendations.**
- **The draft recommendations were released to the public for comments September 27 through October 29, 2018.**
- **Comments were reviewed and the panel agreed to revisions. 13 recommendations were made.**
- **All changes were incorporated prior to manuscript approval.**

Institute of Medicine CPG Standards

- Establishing transparency
- Management of COI
- Group composition
- Systematic review
- Rating strength of recommendations
- Articulating recommendations
- External review
- Updating



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CLINICAL PRACTICE GUIDELINES WE CAN TRUST

Standards for Developing Trustworthy Clinical Practice Guidelines (CPGs)

STANDARD 1
Establishing transparency

1.1 The processes by which a CPG is developed and funded should be detailed explicitly and publicly accessible.

STANDARD 2
Management of conflict of interest (COI)

2.1 Prior to selection of the Guideline Development Group (GDG), individuals being considered for membership should declare all interests and activities potentially resulting in COI with development group activity, by written disclosure to those convening the GDG.
- Disclosure should reflect all current and planned commercial (including services from which a clinician derives a substantial proportion of income), non-commercial, intellectual, institutional, and patient/public activities pertinent to the potential scope of the CPG.

2.2 Disclosure of COIs within GDG
- All COI of each GDG member should be reported and discussed by the prospective development group prior to the onset of their work.
- Each panel member should explain how their COI could influence the CPG development process or specific recommendations.

2.3 Divestment
- Members of the GDG should divest themselves of financial investments they or their family members have in, and not participate in marketing activities or advisory boards of, entities whose interests could be affected by CPG recommendations.

2.4 Exclusions
- Whenever possible GDG members should not have COI.
- In some circumstances, a GDG may not be able to perform its work without members who have COIs, such as relevant clinical specialists who receive a substantial portion of their incomes from services pertinent to the CPG.
- Members with COIs should represent not more than a minority of the GDG.
- The chair or co-chairs should not be a person(s) with COI.
- Funders should have no role in CPG development.

STANDARD 3
Guideline development group composition

3.1 The GDG should be multidisciplinary and balanced, comprising a variety of methodological experts and clinicians, and populations expected to be affected by the CPG.

3.2 Patient and public involvement should be facilitated by including (at least at the time of clinical question formulation and draft CPG review) a current or former patient and a patient advocate or patient/consumer organization representative in the GDG.

3.3 Strategies to increase effective participation of patient and consumer representatives, including training in appraisal of evidence, should be adopted by GDGs.

http://www.iom.edu/Reports/2011/Clinical-Practice-Guidelines-We-Can-Trust.aspx

Systematic Reviews and Clinical Practice Guidelines Improve Healthcare Decision Making

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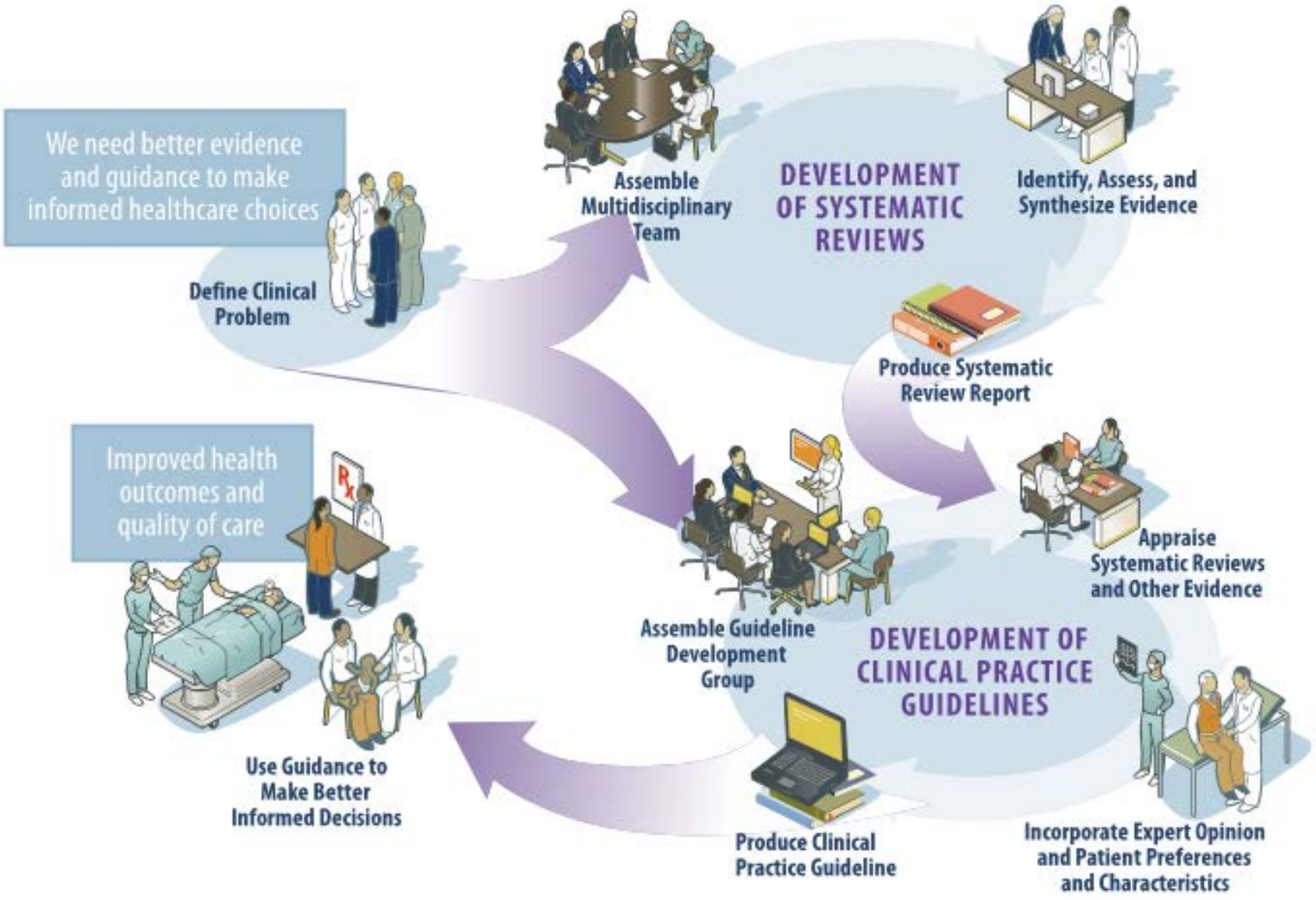
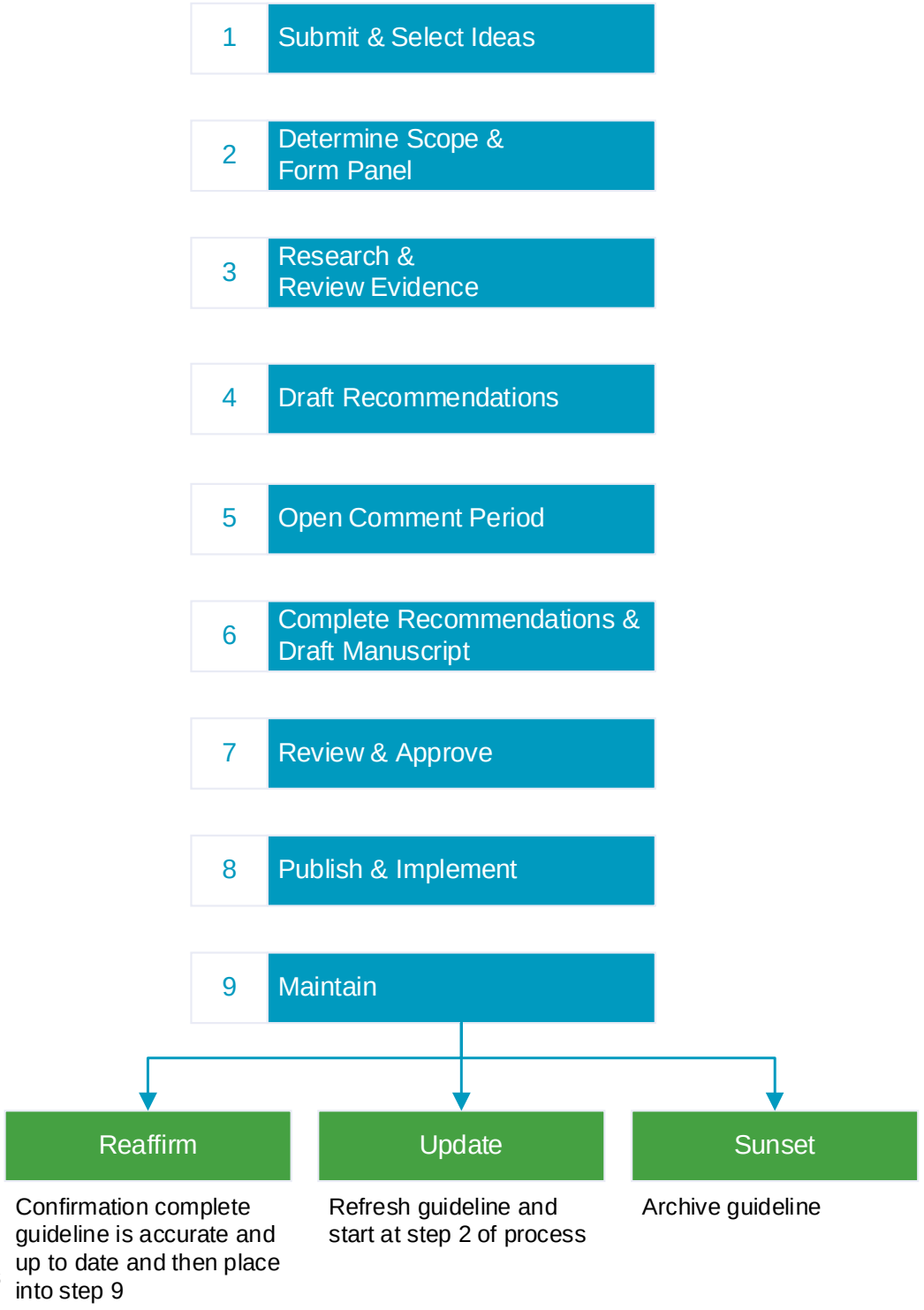


http://resources.iom.edu/widgets/systematic-review/infographic.html



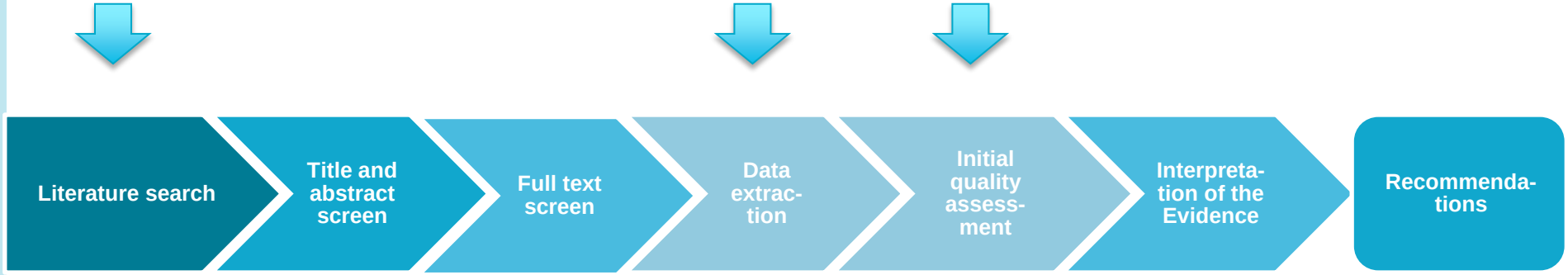
Using the GRADE Approach

- **Grading of Recommendations Assessment, Development and Evaluation (GRADE)**
- **GRADE uses a standardized method which promotes transparency in the rating of evidence and strength of recommendations, including standardized language.**
- **GRADE is internationally recognized and allows a common platform to collaborate with other clinical societies that use the methodology.**

Literature Search

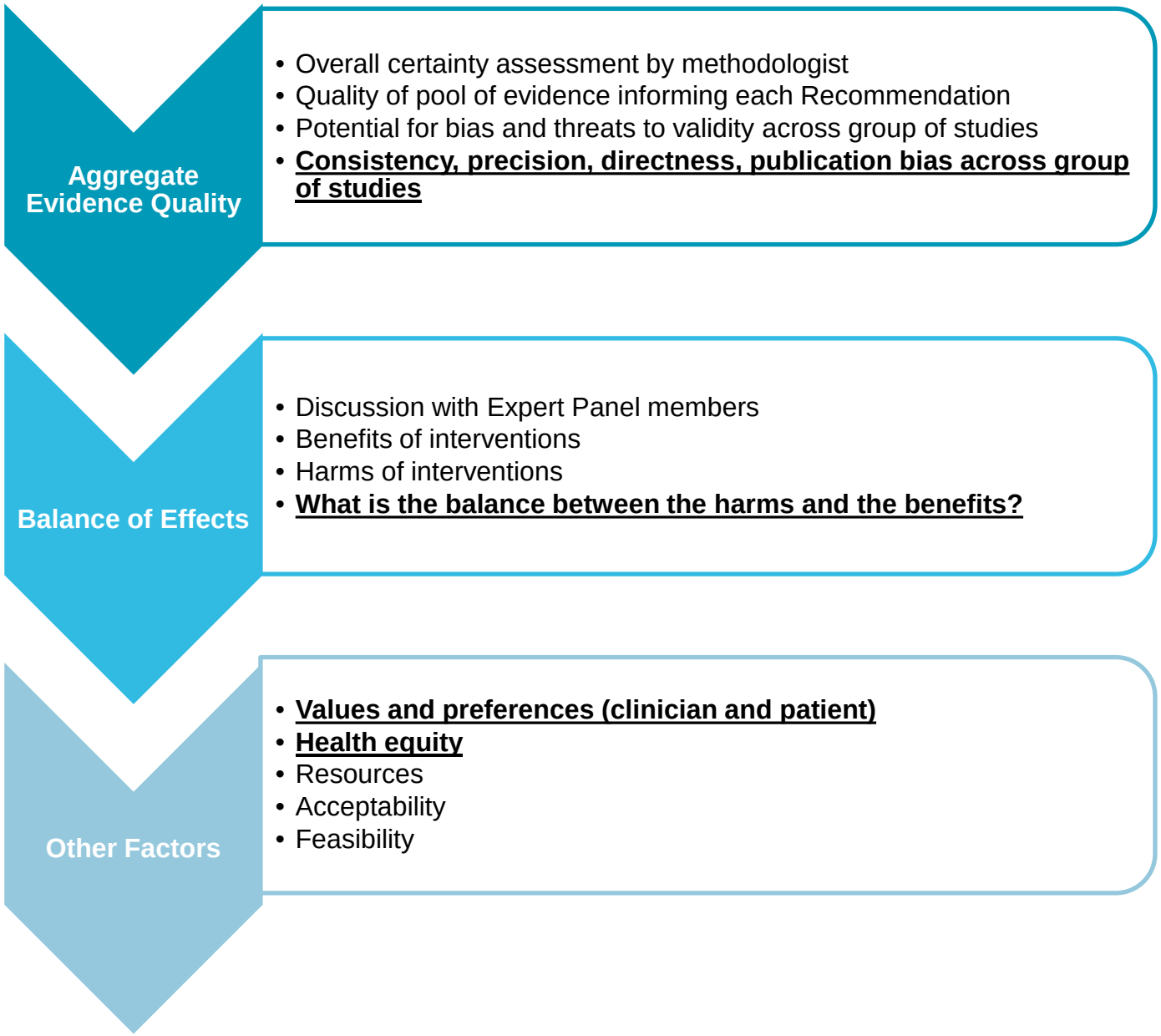
- **Search dates were January 1, 2007 – July 28, 2017 and refreshed in PubMed and Embase September 15, 2018 and October 11, 2019**
- **The searches identified 6,783 abstracts (from initial search and literature refreshes) and ultimately, 224 papers met the selection criteria.**

High Level Systematic Review and Recommendation Development Overview



Data extraction and quality assessment conducted by librarian and unbiased expert methodologist, other functions fulfilled by expert panel and advisory panel

Considered Judgement – a formal process for Interpretation of the Evidence



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Clinical practice guidelines (CPGs) reflect the best available evidence supported in practice. They are intended to assist physicians and patients in clinical decision-making and to identify questions and settings for further research. With the rapid flow of scientific information, new evidence may emerge between the time a CPG is developed and when it is published or read. CPGs are not continually updated and may not reflect the most recent evidence. CPGs address only the topics specifically identified therein and are not applicable to other interventions, diseases, or stages of diseases. Furthermore, guidelines cannot account for individual variation among patients and cannot be considered inclusive of all proper methods of care or exclusive of other treatments. It is the responsibility of the treating physician or other health care provider, relying on independent experience and knowledge, to determine the best course of treatment for the patient. Accordingly, adherence to any CPG is voluntary, with the ultimate determination regarding its application to be made by the physician considering each patient's individual circumstances and preferences. The ASCP and CAP organizations make no warranty, express or implied, regarding CPGs and specifically excludes any warranties of merchantability and fitness for a particular use or purpose. The ASCP and CAP organizations assume no responsibility for any injury or damage to persons or property arising out of or related to any use of this statement or for any errors or omissions.

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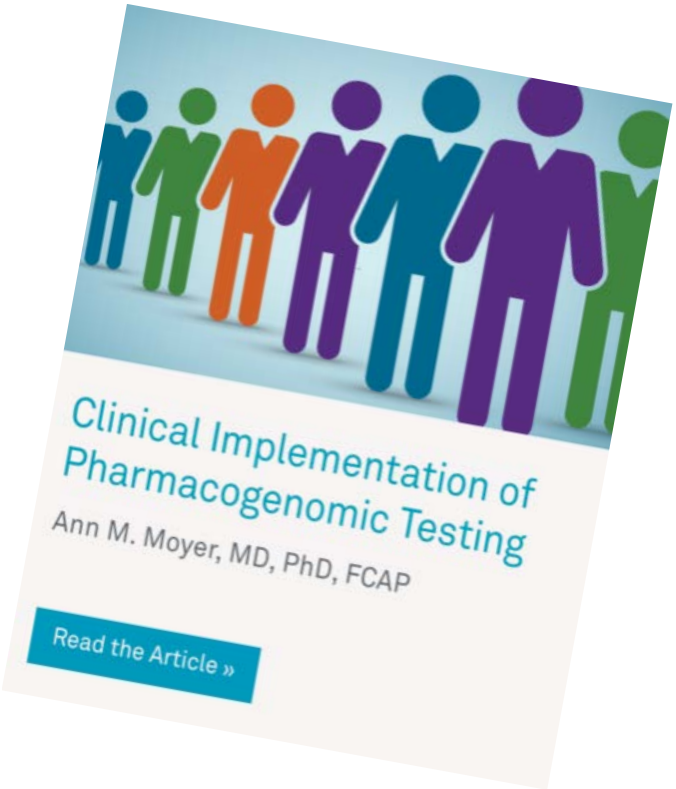
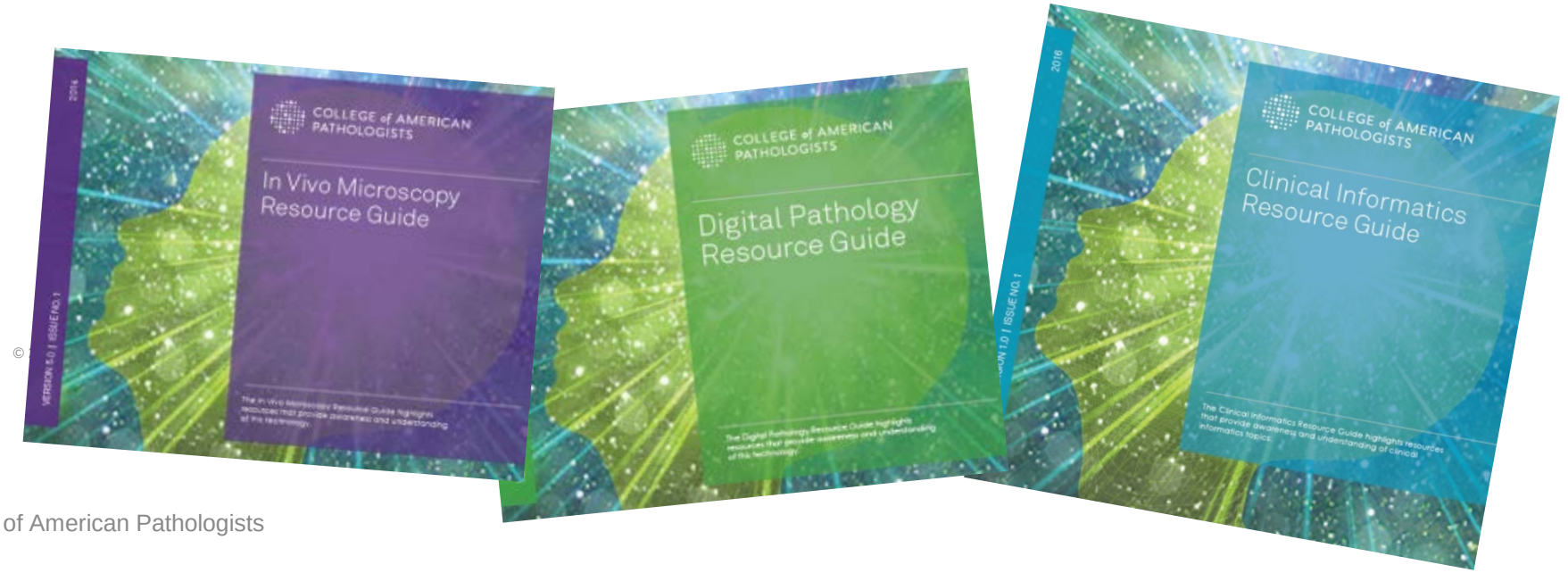
- **The webpage includes brief, relevant articles by CAP members that enable the reader to gain a better understanding of a particular area of precision medicine.**
  - **Examples include pharmacogenetics, immune response genes, and the latest in the molecular drivers of cancer.**
  - **Access them www.cap.org >**

    Member Resources > Precision Medicine



CAP's Pathology Resource Guide: Precision Medicine

- **The CAP has created the Pathology Resource Guides to assist pathologists in understanding key emerging technologies.**
  - **Printed guides are now available for members ($39) and non-members ($69)**
  - **The digital copy of the Resource Guides are a complimentary member benefit**
  - **Access them www.cap.org > Resources and Publications**



THANK YOU!

Thank you for attending our webinar,

“Laboratory Work-up of Lymphoma in Adults”

by Cordelia Sever MD, FCAP and Matthew Cheung SM, MD, FRCP(C)

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