The College of American Pathologists (CAP) and Association of Directors of Anatomic and Surgical Pathology (ADASP): Effective Communication of Urgent and Significant Unexpected Diagnoses in Surgical Pathology and Cytopathology

Supplemental Material

The College of American Pathologists (CAP) developed the Pathology and Laboratory Quality Center (CAP Center) as a forum to author and maintain evidence-based guidelines and consensus statements. Practice guidelines and consensus statements reflect the best available evidence and majority expert agreement 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 throughout medicine and especially in pathology and laboratory medicine, new evidence may emerge between the time an updated guideline was submitted for publication and when it is read or appears in print or online. These documents are reviewed periodically and following the publication of substantive and high-quality medical evidence that could potentially alter the original guideline recommendations. This manuscript and its recommendations are meant only to address the topics within the scope of the guideline or consensus statement. They are not applicable to interventions, diseases, or stages of diseases not specifically identified.

A. Panel Composition

The CAP center and the Association for Directors of Anatomic and Surgical Pathology (ADASP) convened a Work Group (WG) consisting of experts in anatomic pathology relevant to their efforts and interpretations of what constitutes a ‘critical value’ and communication thereof. Members included representatives from both organizations. Both organizations utilized their
respective organization’s approval processes in formal review and appointment of the project, chair and work group members.

B. Management of Conflict of Interest (COI)

All members of the WG complied with the CAP conflicts of interest policy, dated April 2010, which required disclosure of financial or other interests that may have an actual, potential or apparent conflict. No authors had any conflicts to disclose. The CAP Center uses the following criteria:

Nominees who have the following conflicts may be excused from the panel:

a. Stock or equity interest in a commercial entity that would likely be affected by the guideline or white paper
b. Royalties or licensing fees from products that would likely be affected by the guideline or white paper
c. Employee of a commercial entity that would likely be affected by the guideline or white paper

Nominees who have the following potentially manageable direct conflicts may be appointed to the panel:

a. Patents for products covered by the guideline or white paper
b. Member of an advisory board of a commercial entity that would be affected by the guideline or white paper
c. Payments to cover costs of clinical trials, including travel expenses associated directly with the trial
d. Reimbursement from commercial entity for travel to scientific or educational meetings
All WG members were required to disclose new conflicts continuously and throughout the entire project’s timeline. ADASP and the CAP Center covered the cost of developing this project in equal parts.

C. Evidence –

1. Information Sources and Search

We conducted a computerized search during the period of May 2010 to February 2011 of the following electronic databases: OVID MEDLINE, CSA Illumina Conference Papers Index, Google Scholar, and the College of American Pathologists’ Archives of Pathology and Laboratory Medicine, for English language only articles from 1990 through February 2011. All study designs and publication types were included. The search utilized the following terms:

- Anatomic pathology OR Surgical pathology OR Cytopathology OR Radiology OR Cardiology
- (Critical OR Significant OR unexpected) AND (values OR diagnosis OR results)

Reference lists from identified articles were scrutinized for articles not identified in the above search.

The scope of the project was defined as:

- To devise sound communication strategies for urgent or significant unexpected findings in anatomic pathology
- To review other communication efforts of “critical” values in comparable clinical settings such as clinical pathology, cardiology or radiology

2. Study Selection
128 studies met the search term requirements (see Appendix A). Each study underwent an inclusion-exclusion, independent review conducted by one co-chair and one WG member with a third member referee utilized when chair/WG member review did not achieve unanimous agreement on inclusion/exclusion. Studies were selected for full text review based upon the following criteria: (1) the title/abstract referred to pathology (except autopsy or forensic-exclusions), cardiology or radiology (2) the terms critical, panic values, urgent, significant unexpected (or implied) and (3) communication or reporting (or implied) were in the title or abstract. Studies that did not address the scope of the project were also excluded. The initial title/abstract review eliminated 24 studies. Dual independent WG members reviewed the remaining 104 articles in full with the following criteria:

Does this article pertain to the scope of our white paper?

1. No, discard article

2. Yes:
   - Does this article address or contribute to the scope?
     - Directly = 2
     - Partially = 1
   - Does this article?
     - Provide consensus recommendations by an authoritative organization = 3
     - Represent results of a single institutional review of experience = 2
     - Classify as an editorial or represent opinion of a single group = 1

Composite scoring by both reviewers to include the article for grading by the methodologist was determined as eight or above. The WG members unanimously eliminated nine articles from the full text review and the chair eliminated 38 for discordance. Eighteen articles received a strong enough score to be considered for review by the contracted
methodologist. The remaining relevant articles were available as discussion or background references.

From 18 studies, eight studies were included and 10 studies were excluded. Another study (Coffin et al 2007) suggested by the experts (but only scored a 7 on the original review) was included, making a total of 9 studies. Of these studies, one was a randomized controlled trial, two were Time Series, and six were on Survey of laboratories, pathologists or physicians. The inclusion and exclusion of the studies and the different reasons of exclusion are listed in Table 1.

Table 1: Study Selection for Effective Communication

<table>
<thead>
<tr>
<th>Study</th>
<th>Type of study/ Design</th>
<th>Include</th>
<th>Exclude</th>
<th>Reasons of exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coffin 2007</td>
<td>Survey</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clayton 2006</td>
<td>Survey</td>
<td>-</td>
<td>Yes</td>
<td>Abstract, Duplicate of Pereira 2006</td>
</tr>
<tr>
<td>Hanna 2005</td>
<td>Recommendations</td>
<td>-</td>
<td>Yes</td>
<td>Recommendations</td>
</tr>
<tr>
<td>Huang 2009</td>
<td>Time Series</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kupeman 1999</td>
<td>Randomized controlled trial</td>
<td>Yes</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Myers 2010</td>
<td>Slides</td>
<td>-</td>
<td>Yes</td>
<td>Not a study</td>
</tr>
<tr>
<td>Nakhleh 2009</td>
<td>Survey</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pereira 2008</td>
<td>Survey</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pereira 2006</td>
<td>Survey</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pereira 2004</td>
<td>Survey</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pereira 2008</td>
<td>Survey</td>
<td>-</td>
<td>Yes</td>
<td>Abstract, Duplicate of Pereira 2008</td>
</tr>
</tbody>
</table>
The scientific quality of randomized controlled trial data was assessed using the SIGN 50 instrument (Scottish Intercollegiate Guidelines Network, Edinburgh) and its quality was poor (Table 2). The scientific quality of Time Series data was measured using the Ramsay et al. instrument and the quality of both studies were good (Table 3); however, both Time Series studies lacked comparative control groups.

Nine studies underwent data extraction to capture evidence in support of the recommendations. Each study was assessed for strength of evidence, which consists of level of evidence, quantity, size of the effect, statistical precision and, quality assessment (risk of bias) of included studies. Also taken into account were the study components of consistency, clinical impact, generalizability, and applicability to anatomic pathology when determining the strength of evidence score for individual studies. The studies individual components' scores,
derived at from predetermined criteria, generated the overall grade for the strength of evidence (Tables 4, 5, 6).

**Table 2: Quality Assessment of Randomized Controlled Trial**

<table>
<thead>
<tr>
<th>Section Number</th>
<th>Internal Validity: In A Well Conducted Randomized Control Trial</th>
<th>Kuperman et al 1999⁶</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1</td>
<td>The study addresses an appropriate and clearly focused question.</td>
<td>Yes</td>
</tr>
<tr>
<td>1.2</td>
<td>The assignment of subjects to treatment groups is randomized</td>
<td>No</td>
</tr>
<tr>
<td>1.3</td>
<td>An adequate concealment method is used</td>
<td>No</td>
</tr>
<tr>
<td>1.4</td>
<td>Subjects and investigators are kept ‘blind’ about treatment allocation</td>
<td>No</td>
</tr>
<tr>
<td>1.5</td>
<td>The treatment and control groups are similar at the start of the trial</td>
<td>No</td>
</tr>
<tr>
<td>1.6</td>
<td>The only difference between groups is the treatment under investigation</td>
<td>Yes</td>
</tr>
<tr>
<td>1.7</td>
<td>All relevant outcomes are measured in a standard, valid and reliable way</td>
<td>Yes</td>
</tr>
<tr>
<td>1.8</td>
<td>What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?</td>
<td>No</td>
</tr>
<tr>
<td>1.9</td>
<td>All the subjects are analyzed in the groups to which they were randomly allocated (often referred to as intention to treat analysis)</td>
<td>No</td>
</tr>
<tr>
<td>1.10</td>
<td>Where the study is carried out at more than one site, results are comparable for all sites</td>
<td>NA</td>
</tr>
</tbody>
</table>

**Overall Assessment Of The Study**

| 2.1 | How well was the study done to minimize bias? Code ++, +, or - | Poor |

++ All or most of the criteria have been fulfilled. Where they have not been fulfilled the conclusions of the study or review are thought very unlikely to alter.

+ Some of the criteria have been fulfilled. Those criteria that have not been fulfilled or not adequately described are thought unlikely to alter the conclusions.

- Few or no criteria fulfilled. The conclusions of the study are thought likely or very likely to alter.

NA indicates not available.
Table 3: Quality Assessment of Time Series

<table>
<thead>
<tr>
<th>Items of Quality Assessment</th>
<th>Huang et al 2009\textsuperscript{5}</th>
<th>Wager et al 2007\textsuperscript{18}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Intervention occurred independently of other changes over time</td>
<td>Done</td>
<td>Done</td>
</tr>
<tr>
<td>2 Intervention was unlikely to affect data collection</td>
<td>Done</td>
<td>Done</td>
</tr>
<tr>
<td>3 The primary outcome was assessed blindly or was measured objectively</td>
<td>Done</td>
<td>Done</td>
</tr>
<tr>
<td>4 The primary outcome was reliable or was measured objectively</td>
<td>Done</td>
<td>Done</td>
</tr>
<tr>
<td>5 The composition of data at each time point covered at least 80% of the total number of participants in the study</td>
<td>Done</td>
<td>Done</td>
</tr>
<tr>
<td>6 The shape of the intervention effect was pre-specified</td>
<td>Done</td>
<td>Done</td>
</tr>
<tr>
<td>7 A rationale for the number and spacing of data points was described</td>
<td>Not done</td>
<td>Not done</td>
</tr>
<tr>
<td>8 The study was analyzed appropriately using time series technique</td>
<td>Not done</td>
<td>Not done</td>
</tr>
<tr>
<td>Overall Quality</td>
<td>Good</td>
<td>Good</td>
</tr>
</tbody>
</table>


Table 4: Body of Evidence Matrix Component

<table>
<thead>
<tr>
<th>Evidence base</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Excellent</td>
<td>Good</td>
<td>Satisfactory</td>
<td>Poor</td>
</tr>
<tr>
<td>Evidence base</td>
<td>several level I</td>
<td>one or two level</td>
<td>level III studies with</td>
<td>level IV studies, or</td>
</tr>
<tr>
<td><strong>Consistency</strong></td>
<td>level II studies with low risk of bias</td>
<td>II studies with low risk of bias or a SR/multiple level III studies with low risk of bias</td>
<td>low risk of bias, or level I or II studies with moderate risk of bias</td>
<td>level I to III studies with high risk of bias</td>
</tr>
<tr>
<td>-----------------------</td>
<td>----------------------------------------</td>
<td>---------------------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>all studies consistent</td>
<td>all studies consistent</td>
<td>most studies consistent and inconsistency may be explained</td>
<td>some inconsistency reflecting genuine uncertainty around clinical question</td>
<td>evidence is inconsistent</td>
</tr>
<tr>
<td><strong>Clinical impact</strong></td>
<td>very large</td>
<td>substantial</td>
<td>moderate</td>
<td>slight or restricted</td>
</tr>
<tr>
<td><strong>Generalizability</strong></td>
<td>population/s studied in body of evidence are the same as the target population for the guideline</td>
<td>population/s studied in the body of evidence are similar to the target population for the guideline</td>
<td>population/s studied in body of evidence differ from target population for guideline but it is clinically sensible to apply this evidence to target population</td>
<td>population/s studied in body of evidence differ from target population and hard to judge whether it is sensible to generalise to target population</td>
</tr>
<tr>
<td><strong>Applicability</strong></td>
<td>directly applicable to American healthcare</td>
<td>applicable to American healthcare context with few</td>
<td>probably applicable to American healthcare context</td>
<td>not applicable to American healthcare context</td>
</tr>
</tbody>
</table>
Table 5: Definition of grades of recommendations

<table>
<thead>
<tr>
<th>Grade of recommendation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Body of evidence can be trusted to guide practice</td>
</tr>
<tr>
<td>B</td>
<td>Body of evidence can be trusted to guide practice in most situations</td>
</tr>
<tr>
<td>C</td>
<td>Body of evidence provides some support for recommendation(s) but care should be taken in its application</td>
</tr>
<tr>
<td>D</td>
<td>Body of evidence is weak and recommendation must be applied with caution</td>
</tr>
</tbody>
</table>

Table 6: Recommendation Grade

1. Each institution should create its own policy regarding URGENT DIAGNOSES and SIGNIFICANT UNEXPECTED DIAGNOSES in ANATOMIC PATHOLOGY. This policy should be separate from critical result/panic value policies in clinical pathology with the expectation of a different timeframe for communication.

Four studies\(^2\,5\,8\,18\) partially supported the recommendation. Two of these studies\(^6\,18\) are uncontrolled Time series studies and one\(^5\) of which assessed the program instead of policy. Two studies\(^2\,8\) are on survey.

Evidence base: C

Consistency: D

Clinical impact: C
2. A. Pathology departments should determine specific urgent diagnoses in collaboration with the clinical staff. Pathologists, however, should use their experience and judgment to communicate any diagnoses, even if not included in the policy. In hospital practice, approval by the appropriate institutional governing body is recommended.

Evidence base: No Evidence

Consistency: Not Applicable

Clinical impact: Not Applicable

Generalizability: Not Applicable

Applicability: Not Applicable

Overall Grade: D

B. These urgent diagnoses should include situations where urgently conveying the information may directly affect patient care. An example of an urgent diagnosis is an unknown life threatening infection in an immune compromised patient.

Three studies\textsuperscript{6,9,10} supported the recommendation. One\textsuperscript{6} of these is a poor quality randomized controlled trial. Two studies\textsuperscript{9,10} are on survey.

Evidence base: C

Consistency: D

Clinical impact: D

Generalizability: A

Applicability: A

Overall Grade: C
3. Determination of a significant unexpected diagnosis is heavily dependent on the pathologist's judgment as a physician. By their nature, significant unexpected diagnoses cannot always be anticipated. Examples such as a frozen section permanent section discordance that affects patient care or a clinically unsuspected malignancy may be listed in the policy.

Evidence base: No Evidence
Consistency: Not Applicable
Clinical impact: Not Applicable
Generalizability: Not Applicable
Applicability: Not Applicable
Overall Grade: D

4. Pathologists should communicate urgent diagnoses as soon as possible as it may directly impact patient care, but each institution should establish a reasonable time frame. We recommend no longer than the same day on which the diagnosis is made. Communication of significant unexpected diagnoses should occur as soon as is practical; pathologists may exercise their judgment as to the appropriate timing of communication.

Four studies\textsuperscript{2,6,9,10} partially supported the recommendation. Three\textsuperscript{2,9,10} of these are on survey and one\textsuperscript{6} is a poor quality randomized controlled trial. Another survey\textsuperscript{11} mentioned that a stat call should be made in 20\% of the Critical Value reports and the opinion of the pathologists and clinicians varied for other diagnoses.

Evidence base: C
Consistency: D
Clinical impact: B
Generalizability: A
5. Pathologists should communicate verbally and directly with physicians, but other satisfactory methods of communication may be established and validated by each institution. Backup communication plans should be developed for those circumstances in which a physician is not available.

Three studies\textsuperscript{2,9,10} supported the recommendation, whereas one study\textsuperscript{11} mentioned that stat phone call be made in 20\% of the Critical Value reports.

Evidence base: C
Consistency: D
Clinical impact: C
Generalizability: A
Applicability: A
Overall Grade: C

6. Pathologists should document the communication. This can be done in the original pathology report, as an addendum, in the electronic medical record, or by another mechanism.

Documentation should include the person with whom the case was discussed, the time and date and when appropriate, the means of communication.

Four studies\textsuperscript{2,5,9,10} supported the recommendation. Three\textsuperscript{2,9,10} of these are on survey and one is Time series\textsuperscript{5}. Another survey\textsuperscript{11} mentioned that a documentation of phone call was found in 30\% of the Critical Value reports.

Evidence base: C
Consistency: D
D. Methods used to produce guideline/consensus statements

The WG members obtained expert consensus on the statements. The chair sent out 10 communication statements and requested all members to respond with Agree, Disagree, or needs further discussion during a face-face meeting. Resolution was obtained by majority consensus.

The WG met in September 2010; additional work on the project was completed through teleconference webinars, collaboration site access (Oracle WebCenter Spaces v11.1.1.2.0, Oracle Corp, Redwood Shores, CA) and electronic mail. The purpose of the panel meeting was to refine the literature search, and approach the situation from multiple aspects of laboratory service. All members of the WG participated in the draft of consensus statements and manuscript, which was then disseminated for review by the entire work group.

A public comment period was held from March 11 through April 10, 2011. An announcement was sent to the following societies: College of American Pathologists (CAP), Association of Directors of Anatomic and Surgical Pathology (ADASP), American Society of Clinical Pathology (ASCP), American Society of Cytopathology (ASC), Arthur Purdy Stout Society (APSS), and Papanicolaou Society of Cytopathology (PSC). The website received 599 visits with 441 comments in total. The chair reviewed and documented according to whether the comment was in agreement, disagreement or neutral. The response was documented as maintain original recommendation; revise with minor language change, or considered major recommendation change. One consensus statement was removed (major recommendation
change) based upon the feedback received and several were revised with minor language changes by the work group.

The CAP Center Subcommittee and the ADASP officers provided final review and approval of the manuscript.

References:


