

## **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 on line. 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 Pathologist's *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:
  - o Does this article address or contribute to the scope?
    - Directly = 2
    - Partially= 1
  - o 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<sup>1</sup>.

From 18 studies, eight studies were included and 10 studies were excluded. Another study (Coffin et al 2007)<sup>2</sup> 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**

Study	Type of study/ Design	Include	Exclude	Reasons of exclusion
Coffin 2007 <sup>2</sup>	Survey	Yes		
Clayton 2006 <sup>3</sup>	Survey	-	Yes	Abstract, Duplicate of Pereira 2006 <sup>10</sup>
Hanna 2005 <sup>4</sup>	Recommendations	-	Yes	Recommendations
Huang 2009 <sup>5</sup>	Time Series	Yes	-	
Kuperman 1999 <sup>6</sup>	Randomized controlled trial	Yes	-	
Myers 2010 <sup>7</sup>	Slides	-	Yes	Not a study
Nakhleh 2009 <sup>8</sup>	Survey	Yes	-	
Pereira 2008 <sup>9</sup>	Survey	Yes	-	
Pereira 2006 <sup>10</sup>	Survey	Yes	-	
Pereira 2004 <sup>11</sup>	Survey	Yes	-	
Pereira 2008 <sup>9</sup>	Survey	-	Yes	Abstract, Duplicate of

				Pereira 2008 <sup>9</sup>
Piva 2010 <sup>12</sup>	Letter	-	Yes	Letter
Sarewitz 2009 <sup>13</sup>	Editorial	-	Yes	Editorial
Silverman 2006 <sup>14</sup>	Special article	-	Yes	Review
Steindel 1994 <sup>15</sup>	Lab values	-	Yes	Lab values
Tazelaar <sup>16</sup>	Survey	-	Yes	Abstract
The Joint Commission report 2010 <sup>17</sup>	Recommendations	-	Yes	Recommendations
Wager 2007 <sup>18</sup>	Time Series	Yes	-	
Wager 2007 <sup>19</sup>	Survey	Yes	-	

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**

<b>Section Number</b>	<b>Internal Validity: In A Well Conducted Randomized Control Trial</b>	<b>Kuperman et al 1999<sup>6</sup></b>
1.1	The study addresses an appropriate and clearly focused question.	Yes
1.2	The assignment of subjects to treatment groups is randomized	No
1.3	An adequate concealment method is used	No
1.4	Subjects and investigators are kept 'blind' about treatment allocation	No
1.5	The treatment and control groups are similar at the start of the trial	No
1.6	The only difference between groups is the treatment under investigation	Yes
1.7	All relevant outcomes are measured in a standard, valid and reliable way	Yes
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	No
1.9	All the subjects are analyzed in the groups to which they were randomly allocated (often referred to as intention to treat analysis)	No
1.10	Where the study is carried out at more than one site, results are comparable for all sites	NA
<b>Overall Assessment Of The Study</b>		
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.

Modified with permission from <sup>20</sup> from the Scottish Intercollegiate Guidelines Network (SIGN); Copyright 2004. Copyright of the material in table 2 is retained by SIGN. For specific information regarding terms and conditions of the use of this material, go to <http://www.sign.ac.uk/guidelines/published/licence/.html>. The reference column was added Aug 2011.

**Table 3: Quality Assessment of Time Series**

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

<sup>21</sup>Ramsay CR, Matowe L, Grilli R, Grimshaw JM, Thomas RE. Interrupted time series designs in health technology assessment: lessons from two systematic reviews of behavior change strategies. *Int J Technol Assess Health Care*.19(4):613-623, 2003, reproduced with permission.

**Table 4: Body of Evidence Matrix Component**

	A	B	C	D
	Excellent	Good	Satisfactory	Poor
<b>Evidence base</b>	several level I or	one or two level	level III studies with	level IV studies, or



	level II studies with low risk of bias	II studies with low risk of bias or a SR/multiple level III studies with low risk of bias	low risk of bias, or level I or II studies with moderate risk of bias	level I to III studies with high risk of bias
<b>Consistency</b>	all studies consistent	most studies consistent and inconsistency may be explained	some inconsistency reflecting genuine uncertainty around clinical question	evidence is inconsistent
<b>Clinical impact</b>	very large	substantial	moderate	slight or restricted
<b>Generalizability</b>	population/s studied in body of evidence are the same as the target population for the guideline	population/s studied in the body of evidence are similar to the target population for the guideline	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	population/s studied in body of evidence differ from target population and hard to judge whether it is sensible to generalise to target population
<b>Applicability</b>	directly applicable to American healthcare	applicable to American healthcare context with few	probably applicable to American healthcare context	not applicable to American healthcare context

	context	caveats	with some caveats	
--	---------	---------	-------------------	--

Reprinted with permission from <sup>22</sup>Hillier S, Grimmer-Somers K, Merlin T, et al. *BMC Med Res Methodol.* 2011;11(1):23.

**Table 5: Definition of grades of recommendations**

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

Reprinted with permission from <sup>22</sup>Hillier S, Grimmer-Somers K, Merlin T, et al. *BMC Med Res Methodol.* 2011;11(1):23.

**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 <sup>2,5,8,18</sup> partially supported the recommendation. Two of these studies <sup>5,18</sup> are uncontrolled Time series studies and one <sup>5</sup> of which assessed the program instead of policy. Two studies <sup>2,8</sup> are on survey.
Evidence base: C
Consistency: D
Clinical impact: C

Generalizability: A
Applicability: A
Overall Grade: C

<p>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.</p>
Evidence base: No Evidence
Consistency: Not Applicable
Clinical impact: Not Applicable
Generalizability: Not Applicable
Applicability: Not Applicable
Overall Grade: D
<p>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.</p>
<p>Three studies<sup>6,9,10</sup> supported the recommendation. One<sup>6</sup> of these is a poor quality randomized controlled trial. Two studies<sup>9,10</sup> are on survey.</p>
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 <sup>2,6,9,10</sup> partially supported the recommendation. Three <sup>2,9,10</sup> of these are on survey and one <sup>6</sup> is a poor quality randomized controlled trial. Another survey <sup>11</sup> 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

Applicability: A
Overall Grade: C

<p>5. Pathologists should communicate verbally and directly with physicians, but other satisfactory methods of communication may be established and validated by each institution. Back up communication plans should be developed for those circumstances in which a physician is not available.</p>
<p>Three studies<sup>2,9,10</sup> supported the recommendation, whereas one study<sup>11</sup> mentioned that stat phone call be made in 20% of the Critical Value reports.</p>
Evidence base: C
Consistency: D
Clinical impact: C
Generalizability: A
Applicability: A
Overall Grade: C

<p>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.</p> <p>Documentation should include the person with whom the case was discussed, the time and date and when appropriate, the means of communication.</p>
<p>Four studies<sup>2,5,9,10</sup> supported the recommendation. Three<sup>2,9,10</sup> of these are on survey and one is Time series<sup>5</sup>. Another survey<sup>11</sup> mentioned that a documentation of phone call was found in 30% of the Critical Value reports.</p>
Evidence base: C
Consistency: D

Clinical impact: C
Generalizability: A
Applicability: A
Overall Grade: C

#### **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:

1. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.* 2009;6(7):e1000097.
2. Coffin CM, Spilker K, Lowichik A, et al. Critical values in pediatric surgical pathology: definition, implementation, and reporting in a children's hospital. *Am J Clin Pathol.* 2007;128(6):1035-1040.
3. Clayton ACP, T.C.; Tazelaar, H.D.; Liu, Y.L.; Leon, M.E.; Silverman, J.F. The prevalence of critical values in cytopathology. *95th Annual Meeting of the United States and Canadian Academy of Pathology.* Hyatt Regency Atlanta, Atlanta, Georgia (USA) 2006.
4. Hanna D, Griswold P, Leape LL, Bates DW. Communicating critical test results: safe practice recommendations. *Jt Comm J Qual Patient Saf.* 2005;31(2):68-80.
5. Huang EC, Kuo FC, Fletcher CD, Nose V. Critical diagnoses in surgical pathology: a retrospective single-institution study to monitor guidelines for communication of urgent results. *Am J Surg Pathol.* 2009;33(7):1098-1102.
6. Kuperman GJ, Teich JM, Tanasijevic MJ, et al. Improving response to critical laboratory results with automation: results of a randomized controlled trial. *J Am Med Inform Assoc.* 1999;6(6):512-522.
7. Myers JL. Critical values and persistent challenges in communicating pathology results. *CAP Companion Meeting at USCAP 2010 Quality and Patient Safety in Anatomic Pathology: Practical Solutions.* Marriott Wardman Park Hotel, Washington, DC (USA) 2010.

8. Nakhleh RE, Souers R, Brown RW. Significant and unexpected, and critical diagnoses in surgical pathology: a College of American Pathologists' survey of 1130 laboratories. *Arch Pathol Lab Med.* 2009;133(9):1375-1378.
9. Pereira TC, Silverman JF, LiVolsi V, et al. A multi-institutional survey of critical diagnoses (critical values) in surgical pathology and cytology. *Am J Clin Pathol.* 2008;130(5):731-735.
10. Pereira TC, Clayton AC, Tazelaar HD, Liu Y, Leon M, Silverman JF. Critical values in cytology. *Diagn Cytopathol.* 2006;34(6):447-451.
11. Pereira TC, Liu Y, Silverman JF. Critical values in surgical pathology. *Am J Clin Pathol.* 2004;122(2):201-205.
12. Piva E, Lippi G, Plebani M. Notification of abnormal and critical values: the road ahead. *Am J Med.* 2010;123(10):e19; author reply e21.
13. Sarewitz SJ, Williams RB. Significant and unexpected versus critical results in surgical pathology. *Arch Pathol Lab Med.* 2009;133(9):1366.
14. Silverman JF, Pereira TC. Critical values in anatomic pathology. *Arch Pathol Lab Med.* 2006;130(5):638-640.
15. Steindel SJ. Critical values: When they're reported, how they're used. *CAP Today.* 1994;94(3):22-25.
16. Tazelaar HD, Pereira TC, Clayton AC, Liu YL, Leon ME, Silverman JF. The perception of clinicians and pathologists about critical values in cytopathology. *95th Annual Meeting of the United States and Canadian Academy of Pathology.* Hyatt Regency Atlanta, Atlanta, Georgia (USA) 2006.
17. Joint Commission. 2011 National patient safety goals, laboratory services program (NPSGs). [http://www.jointcommission.org/lab\\_2011\\_npsgs](http://www.jointcommission.org/lab_2011_npsgs). Accessed May 3, 2011.
18. Wagar EA, Stankovic AK, Wilkinson DS, Walsh M, Souers RJ. Assessment monitoring of laboratory critical values: a College of American Pathologists Q-Tracks study of 180 institutions. *Arch Pathol Lab Med.* 2007;131(1):44-49.



19. Wagar EA, Friedberg RC, Souers R, Stankovic AK. Critical values comparison: a College of American Pathologists Q-Probes survey of 163 clinical laboratories. *Arch Pathol Lab Med*. 2007;131(12):1769-1775.
20. Scottish Intercollegiate Guidelines Network. SIGN 50. A guideline developers' handbook. Methodology checklist 2: Randomized controlled trials. Edinburgh: Scottish Intercollegiate Guidelines Network; 2008: <http://www.sign.ac.uk/guidelines/fulltext/50/checklist2.html>. Accessed June 16, 2011.
21. Ramsay CR, Matowe L, Grilli R, Grimshaw JM, Thomas RE. Interrupted time series designs in health technology assessment: lessons from two systematic reviews of behavior change strategies. *Int J Technol Assess Health Care*. 2003;19(4):613-623.
22. Hillier S, Grimmer-Somers K, Merlin T, et al. FORM: An Australian method for formulating and grading recommendations in evidence-based clinical guidelines. *BMC Med Res Methodol*. 2011;11(1):23.