Applying Risk Management Principles to QA in Surgical Pathology: From Principles to Practice

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Disclosure Statement

I do not have any financial interest or affiliation with any organization that may cause conflict of interest pertaining to content of this presentation.
Objectives

1. To introduce concepts of Risk Management to errors in pathology
2. Using Risk Management principle to explore the causes of error
3. Use published literature to make assumptions about probability of error
4. To introduce Evidence based medicine tools such as number needed to treat
5. To consider the concept of uncertainty of measurement and relate it to pathology confidence
• What errors or hazards can occur?
• How severe can they be?
• How frequent can they be?
• What precautions should be taken for reducing the risk?
Risk management techniques present us with systematic ways to search for the error-prone processes.
Risk Management

- Present systematic ways to search for the error-prone processes
- Focuses on potential and observed adverse events
- Determine
  - The weak points in the processes
  - Their probability of causing errors
  - The estimating the impact of the error
- Final aim is to identify risky situations and giving prioritization to prevent occurrence of the adverse events
Risk Assessment

Risk Monitoring

Risk Evaluation (Severity of harm, probability of harm)

Risk Control

Risk Reduction
Process Mapping

RCA
(Root Cause Analysis)

FMEA
(Failure Mode and Effects Analysis)

FMECA
(Failure Mode, Effects and Criticality Analysis)

Preliminary Hazard Analysis

FTA
(Fault Tree Analysis)

“To address this mistake we must use root-cause analysis. I’ll begin by saying it’s not my fault.”
Steps in a RCA Investigation

- Definition of the problem
- Identification of the critical steps
- Identification of root causes
- Evidences for root causes
- Identification of solutions
- Development of recommendations
Can we develop a risk management tool for the selection of pathology cases that need to be sent for second review?
Methodology 1

Literature was critically reviewed for assessment of:

1. Error rates
2. Causes of errors (focus was on interpretation of errors)
Methodology 2

1. Error Rates:

• Journal articles presenting error rates in surgical pathology based on second opinion were selected.

• Errors were re-classified as catastrophic, major, moderate and minor.

• Articles containing incomplete information for this re-classification were excluded from the study.

• Discrepancy frequency was calculated for the aggregate data (100* number of discrepancy/ total number of cases)

2. Causes of Errors (focus was on interpretation errors)
Variables could affect published error rates

- Research designs
- Definition of discrepancy/error
- Method of case selection
- Tissue type
Error detection methods in Pathology

Single institution studies
- Second opinion:
  - Double reader no specialized skills
  - Double reader specialized skills
  - Conference review
  - Institutional review
- Correlation review
  - Cytology- histology correlation
  - Frozen section - histology correlation
- Virtual microscopy

Multi-institutional studies
- Surveys
- Databases

Virtual microscopy
External quality assessment
Sources of Errors

- Accessioning errors
- Grossing errors
- Histology tissue processing
- Transcription errors
- Ancillary testing errors
- Interpretation errors
- Reporting errors

Heterogeneity of research designs and error classification

- Lack of gold standard for error detection
- Selection of cases
- Error detection methods
- Type of second opinion
- Classification of errors

Heterogeneity of research designs and error classification

- Lack of gold standard for error detection
  - Second reviewer’s diagnosis is assumed to be gold standard
  - Clinical and pathologic outcome (most studies do not include)

- Selection of cases
  - Random
  - Pseudo random

- Error detection methods
  - Blind review
  - Focused review
  - Review of referral cases
  - Cytology histology correlation
  - Clinician driven review
  - Amended report review

- Type of second opinion
  - Expert
  - Non-expert
  - Expert center
  - Consultation
  - Conference (e.g. tumour board, subspecialty, difficult case conferences)

- Classification of errors
  (Lack of standard way of reporting errors makes it difficult to compare results from different studies.)
  - False positive, false negative
  - Threshold (differences in opinion), differences in grade and type
  - Major and minor
  - Pre-analytiic, analytic and post-analytic

# Definitions of errors and their severity

<table>
<thead>
<tr>
<th>Category</th>
<th>Definitions</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Catastrophic</td>
<td>Multiple, consistent (precise) major harm</td>
<td>All end result IHC (like FISH or oestrogen receptor) results are false negative or false positive because of systematic error</td>
</tr>
<tr>
<td>Major</td>
<td>Irreversible major clinical harm</td>
<td>Erroneous patient management leading to loss of life, limb, or organ</td>
</tr>
<tr>
<td>Moderate</td>
<td>Moderate clinical harm, correction is not easy but possible Unnecessary invasive intervention or follow up</td>
<td>Tumour grading errors which affects treatment</td>
</tr>
<tr>
<td></td>
<td>Tumour grading errors which affects treatment</td>
<td>Mixing up atrophic cervicitis with high grade squamous intraepithelial lesion</td>
</tr>
<tr>
<td>Minor</td>
<td>Minor harm, easily amendable</td>
<td>Same treatment, different prognosis or Pertinent information not included</td>
</tr>
<tr>
<td>Near Miss</td>
<td>Near misses (system or guideline has stop and control points, harm is easily avoidable)</td>
<td>Evaluating more than one specimen from same patient can correct possible error</td>
</tr>
</tbody>
</table>
### Error rates (referral cases)

<table>
<thead>
<tr>
<th>No. of Journal Articles</th>
<th>Total No. of Cases</th>
<th>Median Discrepancy % (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Total</td>
</tr>
<tr>
<td>30</td>
<td>22340</td>
<td>22.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(5.4–53.5)</td>
</tr>
</tbody>
</table>
## Relationship between discrepancy rates and type of second opinion

<table>
<thead>
<tr>
<th>Second Opinion</th>
<th>Total No. of Cases</th>
<th>Total D*</th>
<th>Major D*</th>
<th>Moderate D*</th>
<th>Minor D*</th>
<th>No D*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expert (n=14)</td>
<td>11090</td>
<td>23.9</td>
<td>6.9</td>
<td>6.2</td>
<td>10.4</td>
<td>76.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(10.9–43.8)</td>
<td>(0.6–24.4)</td>
<td>(0.0–20.4)</td>
<td>(0.0–34.7)</td>
<td>(56.2–89.1)</td>
</tr>
<tr>
<td>Academic/Cancer Center (n=8)</td>
<td>3436</td>
<td>19.5</td>
<td>4.3</td>
<td>5.5</td>
<td>4.3</td>
<td>80.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(6.6–53.3)</td>
<td>(0.0–9.9)</td>
<td>(0.0–27.7)</td>
<td>(0.1–53.3)</td>
<td>(46.7–93.4)</td>
</tr>
<tr>
<td>Non-expert (n=8)</td>
<td>7814</td>
<td>23.4</td>
<td>3.4</td>
<td>5.6</td>
<td>10.0</td>
<td>76.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(5.4–34.0)</td>
<td>(0.7–11.5)</td>
<td>(1.1–17.0)</td>
<td>(0.7–17.8)</td>
<td>(66.0–94.6)</td>
</tr>
<tr>
<td>Total</td>
<td>22340</td>
<td>22.8</td>
<td>4.4</td>
<td>6.2</td>
<td>8.5</td>
<td>77.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(5.4–53.5)</td>
<td>(0–24.4)</td>
<td>(0–27.7)</td>
<td>(0–53.3)</td>
<td>(46.7–94.6)</td>
</tr>
</tbody>
</table>

* Discrepancy P values: >0.05

Mann-Whitney U-test were used for the comparison of median values obtained in subgroups
Blinded Review

Advantages

• Free from bias

• It can be applied all cases (consultation rarely applied on negative cases, so false negative cases are rarely recognized)

Disadvantages

• For some types of tissues, impossible to diagnose without knowing clinical presentation (e.g. bone biopsies)

• Review is generally performed faster than initial examination, sensitivity does not 100%

Renshaw AA, Blinded Review as a Method for Quality Improvement in Surgical Pathology, Arch Pathol Lab Med—Vol 126, August 2002
## Blinded Review

<table>
<thead>
<tr>
<th>Total No. of Cases</th>
<th>Total D* (%)</th>
<th>False negatives (%)</th>
<th>Amendments and/or clinically significant D* (%)</th>
<th>Agreement (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>23220</td>
<td>7.38</td>
<td>0.24</td>
<td>0.44</td>
<td>92.62</td>
</tr>
</tbody>
</table>

* Discrepancy

Renshaw 2002
Renshaw 2006
Renshaw 2003
Renshaw 2006
Trotter 2003
Review of literature indicates

- Risk of major error in referral cases: 4.4%
- Risk of occurrence of major or moderate errors in referral cases: 10.6%
- Risk of false negative errors in blinded reviews: 0.24%.
Evidence Based Medicine

- Number needed to treat (NNT)
- Can we use the same methodology for Number needed to review (NNR)
- 2 Path Sign out versus 1
- Disagreements and amendments
Review of literature indicates…

416 cases should be reviewed for identification of one false negative error.

It is necessary to develop a strategy for selection of cases that need to be sent for second review.
Value of Second Review

<table>
<thead>
<tr>
<th>No. of Pathologist on First Report</th>
<th>No. of Cases</th>
<th>Disagreements (%)</th>
<th>Amendments (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7276</td>
<td>7.2</td>
<td>0.5</td>
</tr>
<tr>
<td>≥2</td>
<td>1087</td>
<td>4.8</td>
<td>0.0</td>
</tr>
<tr>
<td>Total</td>
<td>8363</td>
<td>6.9</td>
<td>0.4</td>
</tr>
<tr>
<td>p</td>
<td></td>
<td>0.004</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Intra-departmental second review of cases lower disagreement in subsequent blinded review.

Q: How do we determine cases that need to be sent for a second opinion?

**One option**

Sending all neoplasia cases to second review.

**But**

- Some neoplasia can be easily diagnosed – second opinion is not necessary.
- False negatives cannot be identified.
- Non-neoplastic difficult cases, such as infection and atypia are not reviewed.

Renshaw proposed to review “all cases that appear to be difficult.”

## Root causes of discrepancies (errors)

<table>
<thead>
<tr>
<th>No fault</th>
<th>Systemic</th>
<th>Cognitive</th>
</tr>
</thead>
<tbody>
<tr>
<td>• New tumour classification or different grading system</td>
<td>• Systematic errors in ancillary tests (e.g. IHC)</td>
<td>• Data interpretation</td>
</tr>
<tr>
<td>• New diagnostic criteria</td>
<td>• Problems associated with histological stain or technique</td>
<td>• Reasoning</td>
</tr>
<tr>
<td>• Unexpected presentation</td>
<td>• No system to confirm patient ID or sample</td>
<td>• Knowledge related</td>
</tr>
<tr>
<td>• Tissue or cytological sample is not representative for a lesion</td>
<td>• Long turnaround times</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Software errors</td>
<td></td>
</tr>
</tbody>
</table>
No fault – as a discrepancy cause

Murphy et. al. (2002) evaluated

- Inter-observer discrepancy
- WHO/International Society of Urologic Pathology Classification of Urothelial Neoplasms
No fault – as a discrepancy cause

Discrimination of:

Low malignant potential papillary uroepithelial neoplasm
AND
Low grade papillary uroepithelial carcinoma

Discrepancy rate:
before education: 50%
after education: 39%

Papillary urothelial neoplasm of low malignant potential
AND
High grade carcinoma or carcinoma in situ.

No discrepancies

After eliminating categories with poor reproducibility

Discrepancy rate: 10%

No fault – as a discrepancy cause

- Diagnostic and prognostic classifications affects discrimination rates
- Morphological similarity among categories increases the interpretive discrepancy

Cognitive Error Types

- Anchoring
- Confirmation bias
- Expectation bias
- Semmelweis effect
- Availability of heuristics
- Premature closure
- Over confidence
- Change blindness
Overconfidence

“Miscalibration of one’s own sense of accuracy”

• 1% of drivers rate their skills below that of the average driver.

• 94% of academic professionals rate themselves in the top half of their profession.

Overconfidence

- Physicians’ confidence levels in case scenarios
  - **Medical students**: least accurate and least confident
  - **Attending physicians**: most accurate and highly confident
  - **Residents**: more confident, but less accurate

- Board certified radiologists
  - Confidence level of the worst performers were higher than the best performers

Pathology interpretation errors may arise from multiple causes

1. Lack of knowledge
2. Cognitive Errors
3. Lack of well established diagnostic criteria
4. Inter- and intra-observer discrepancy
5. Lack of adequate clinical information
6. Clinician’s interpretation
7. Lack of expertise
8. Lack of experience
9. (New methods are riskier than older methods)
Suggestion 1:
Use of Sign-out Checklist
Use of sign-out checklist

- Filled by the pathologist just before sending out the reports
- This checklist prepared based on previously published literature on causes of discrepancies in pathology laboratories and misdiagnosis in medicine general.
Conscious review of subconscious processing may prevent biases and errors.

- Medical decisions are made in the “adaptive unconscious”
- Cognitive errors arise in “synthesis step of diagnostic process”
- Synthesis step is mainly unconscious and habitual

Berner ES et al., Overconfidence as a cause of diagnostic error in medicine, Am J Med 2008;121:5A-S2-S23
Patient ID #: Specimen ID #: Specimen type:

How would you rate your confidence level as a Pathologists for this specific case
3. Confident 2. Diagnosis seems likely 1. Need second opinion

Intra-observer variability for specific type of specimen or diagnosis comparing with the general practice.
3. Low 2. Same 1. High

Inter-observer reproducibility for specific type of specimen or diagnosis comparing with the general practice
3. Low 2. Same 1. High

Diagnostic criteria’s for this specific type of specimen
3. Well established 2. In progress 1. Cloudy

If well established, how many out of total number of criteria does this particular specimen have?
3. More than 80% 2. 20-80% 1. Less than 20%

Pathologists’ experience
3. > 5 years 2. < 5 years 1. Resident

Pathologists’ expertise

Did pathologist previously see the all spectrum of pathologies seen in this organ/ tissue type?
3. Most of it 2. Enough to have a confidence 1. Not enough

Average number of cases reviewed by pathologist in this organ system in a year
3. More than 100 2. 10-100 1. Less than 10

Were ancillary tests necessary for this particular diagnosis?
3. Yes and it’s available to your practice 2. Yes but it’s not available to your practice 1. No

Is this specimen meeting the specimen adequacy criteria (quality of the slides, representativeness, obscuring factors, amount of tumor present)?
3. Yes 2. No 1. Not evaluated
Benefits of checklists

1. Provide tool for selection of the cases for second opinion.
2. Help pathologist to evaluate her/his risk of making incorrect decision in a particular specimen, and select cases for second review.
3. Give pathologist a chance to self assesses her/his decision making process, just before sending the report.
4. Might be a tool for improving the match between pathologists self-claimed confidence levels and actual errors in long term.
Suggestion 2: Disclosing Uncertainty
• Measurement uncertainty concept is introduced in medical testing, but not interpretive tests like surgical pathology.

• Not because pathology tests results does not bear uncertainty, but lack of method for determination of uncertainty.

Bryant SJ and Davies DJ, Diagnostic error in anatomical pathology: the uncertainty of its measurement? Pathology (December 2006) 38(6), pp. 487–9
## Uncertainty – Clinical Chemistry

<table>
<thead>
<tr>
<th>Measured HbA1c (%)</th>
<th>Uncertainty of Measurement range for and analytical CV of 3% (95% confidence levels)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.5</td>
<td>6.1 - 6.9</td>
</tr>
<tr>
<td>7.0</td>
<td>6.6 - 7.4</td>
</tr>
<tr>
<td>7.5</td>
<td>7.1 - 8.0</td>
</tr>
</tbody>
</table>

Uncertainty

- In current practice, histopathology results are considered as absolute truth.
- Introducing “measurement uncertainty” in histopathology decreases unrealistic expectations, and protects pathologist from excessive demands.

Bryant SJ and Davies DJ, Diagnostic error in anatomical pathology: the uncertainty of its measurement? Pathology (December 2006) 38(6), pp. 487–9
Reporting risk of malignancy

Renshaw: Reporting a quantitative risk for malignancy or dysplasia for cytological screening tests

Risk values can be obtain from:
• Literature,
• Individual laboratory and
• Individual cytologist
Reporting Uncertainty

University of Colorado Health Sciences Center adds a note to the report:

“This is a difficult case.”

• This approach

  ▪ Inform physician and patients about necessity of considering other differential diagnosis.

Reporting diagnostic certainty in a scale of 1–5

1. Uncertain
2. Somewhat uncertain
3. Neither certain nor uncertain
4. Somewhat certain
5. Certain

Drazen MJ et al., Clinical examination and validation of primary diagnosis in anatomic pathology using whole slide digital images. Arch Pathol Lab Med-2011 (135):372-78
Sign-out checklist and published literature can be used in determining uncertainty.
Acknowledgement

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