Quality Assurance/Quality Control – Cervical Cytology and Histopathology

Brenda Smith
Dr. Jasenka Matisic
Dr. Malcolm Hayes
BC Cancer Agency
Vancouver, BC, Canada

20 May 2016
Quality Management

Quality Assurance

Quality Control

Collection of processes and techniques (bench level) → detect, reduce, and correct deficiencies in the Pap test

Continuous Quality Improvement (CQI):
Systematic activities that are organized and implemented to monitor, assess, improve

Systematic monitoring of QC results to ensure all systems are functioning at desired level of quality
Quality Control in Cervical Cytology

**Objective**: to improve the performance of the Pap test to minimize False Positive + False Negative results

- **Pre-analytic**
  - Adequate sampling, handling and staining

- **Analytic**
  - Adequate screening and interpretation

- **Post-analytic**
  - Adequate reporting of results

Dependent on

- Identify potential errors that can occur
- Evaluate the steps where failures may occur
Pre-analytic QC

• Smear taking
  - Adequate training for all smear takers, including access to written, illustrated guidelines

  Monitor:

  - Collect data on rates of adequacy and transformation zone sampling
    - Feedback improves the performance of Pap smear providers

• Receipt of sample in lab
  - Written criteria for rejection of specimens
    • i.e. unlabeled slides, broken slides, mislabeled specimen (slide)

  Monitor:

  - Log of rejected specimens (include submitting clinician, reason for rejection)
    - Monitor for increases in incidence
Pre-analytic QC cont’d

• Data entry
  – Cross-check multiple patient identifiers to ensure slide and requisition match
  – Regular monitoring of possible data entry errors
    • i.e. unlikely date of birth, sample date is later than received date

  Monitor:
  □ Log of discrepancies in data entry
  □ Number of cases requiring troubleshooting (i.e. clarification, verification, confirmation of patient demographics or clinical history)

• Specimen staining
  – Daily monitoring of stain quality

  Monitor:
  □ Log of QC stain procedures (include date, # of times stain is filtered/changed, record of stain evaluation, any problems)
Analytic QC

• Workload records of individual cytotechnologists

  Monitor:
  • Productivity Report = data on individual screening and re-screening workload
    • Use QC re-screens and other correlation data to determine workload limit

• Specimen acceptance and adequacy

  Monitor:
  • Volume of unsatisfactory specimens
  • Submitting clinicians/clinics (track for need of education if in excess)
  • Individual rates of unsatisfactory specimens
Analytic QC cont’d

• Screening and interpretation
  – Practices such as second screenings in women with atypical histories, ASC-US+ smears, or AGC+
  – Standard method of reporting used

Monitor:

- Report percentages of main categories of cytologic findings (i.e. unsatisfactory, ASC-US, LSIL, ASC-H, HSIL, AGC+) for individual screeners and cytopathologists
  - Compare with lab as a whole, also against national standard (if exists)

- Performance evaluations
  - Identify those under-performing or patterns of poor performance
Analytic QC cont’d

• Review of abnormal cases
  – 2nd opinion or peer review
    • i.e. significant discrepancy between screener and pathologist, difficult diagnostic cases

Monitor:

- Documentation of peer review
- ASC:SIL ratio
  – monitor to identify any potential problems with diagnostic criteria for ASC
Analytic QC cont’d

- Re-screening of negative cases

**Random 10% re-screening**
- Full re-screen of entire slide
- Cannot identify all FN smears
- Statistically unlikely to detect a poor performance (low rate of abnormal smears)
- Has however been proven to be effective for improving performance
- Suitable for higher volume labs

**Rapid re-screen**
- 100% of slides get a low power stepwise review/scan (~30-60 secs)
- Potential to detect more false negative smears in same amount of time
- Dependent on skill and experience of the reviewer
- Good for lower volume labs

Monitor:
- Plot findings of screener vs. final call
- Regular evaluations
## Analytic QC cont’d

### Rapid pre-screen
- Partial inspection of a slide (max 120 secs) before full routine screen
- All slides, not just NILM
- Rapidly identifies most abnormal cases
- Sensitivity gain comparable to rapid re-screen

### Targeted re-screen
- Smears from patients with a higher risk of having cytological atypia
- Previous abnormal smears, abnormal appearance of cervix, abnormal bleeding, recurrent infections, etc
- No data on comparison with other methods, but could help to reduce screening errors
- Can also be used to monitor screeners with screening issues (ie increase QC quota)

### Monitor:
- Plot findings of screener vs. final call
- Regular evaluations
Sample re-screen tracking form
QUARTERLY QUALITY CONTROL EVALUATION FORM

Cytotechnologist ID #:    Signature:          Date:

<table>
<thead>
<tr>
<th>Quarter</th>
<th># of Hold-outs</th>
<th># of QC’s</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Meets Expectation</th>
<th>Needs Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smear quality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of incorrect recommendations (expectation of 10 or less per 3 months)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of inattention to details (expectation of 10 or less per 3 months)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Comments on performance:

Suggestions for improvement:

Evaluated by Monitor/Senior:    Date:
Post-analytic QC

- Report generation
  - Follow a consistent language in reporting
  - Accurate reporting keeping

  Monitor:
  - Daily audit of reports (if automatic, or electronic distribution)

- Response time (Turnaround time [TAT])
  - Establish a mutually agreed upon turnaround time from the date the smear is received in the laboratory to the date of the finalized report

  Monitor:
  - Weekly tracking of specimen sign-out dates compared to date of receipt
Post-analytic QC cont’d

- Cytology-histology correlation
  - If Pap NILM or LSIL, and biopsy is high grade → review cytology
  - If Pap HSIL, and biopsy is normal → review cytology

**NOTE** • Inherent errors:
- Colposcopic technique
- Colposcopic sampling
- Biopsy interpretation

Pap test may at times better represent cervical pathology than the biopsy

Monitor:
- **Positive Predictive Value (PPV) reports** = % of positive Pap tests that have a histological confirmation of significant cervical dysplasia
  - monitor rates of lab and individual pathologists
### AGC neoplastic+ and HSIL+ Positive Predictive Value 2011-2015

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>3377</td>
<td>643</td>
<td>4038</td>
<td>1342</td>
<td>3574</td>
<td>1751</td>
<td>2373</td>
<td>755</td>
<td>2070</td>
<td>952</td>
</tr>
<tr>
<td>CIN 2 or higher</td>
<td>1960</td>
<td>385</td>
<td>2243</td>
<td>752</td>
<td>1983</td>
<td>1026</td>
<td>1504</td>
<td>494</td>
<td>1316</td>
<td>626</td>
</tr>
<tr>
<td>CIN 1 or lower</td>
<td>934</td>
<td>175</td>
<td>1176</td>
<td>384</td>
<td>1009</td>
<td>467</td>
<td>553</td>
<td>176</td>
<td>467</td>
<td>201</td>
</tr>
<tr>
<td>no pathology</td>
<td>483</td>
<td>83</td>
<td>619</td>
<td>206</td>
<td>582</td>
<td>258</td>
<td>316</td>
<td>85</td>
<td>287</td>
<td>125</td>
</tr>
</tbody>
</table>

**BC Cancer Agency**

CARE + RESEARCH

An agency of the Provincial Health Services Authority
Post-analytic QA

- Targeted retrospective review = NILM Pap smears within last 5 years are retrieved for re-screening when current Pap is HSIL+
  - Biases due to knowledge of current result should be kept in mind

Monitor:
- Internal documentation of result of re-screen
- Discrepancy report = statistical data on minor and major discrepancies in retrospective reviews and re-screened cases
Laboratory (Internal) QA/CQI

Pre-analytic

Analytic

Post-analytic

Adequate sampling, handling and staining

Adequate screening and interpretation

Adequate reporting of results
External QA

• Accreditation by a certified regulatory body to determine if pre-determined standards are met

  – BCCA Cervical Cancer Screening Lab is accredited by:
    • The College of Physicians and Surgeons of British Columbia Diagnostic Accreditation Program (DAP)
    • The College of American Pathologists (CAP)
      – an internationally recognized leader in laboratory quality assurance and accreditation programs
      – Incorporates ISO:15189
External QA cont’d

- **Proficiency Testing**
  - Circulation of Pap smears (good examples) from an outside facility; results submitted and inter-laboratory comparisons made

- **BCCA CCSL currently subscribes with:**
  - College of American Pathologists (CAP) – 2x/year
  - American Society for Clinical Pathology (ASCP) – 2x/year
Maintenance of Competence

• On-going education is a requirement for proficiency in cytology

• Fulfilled by:
  – Cyto-morphological group discussions
  – Internal education forums
  – Attending webinars, teleconferences
  – Access to journals
  – Online education activities
  – Proficiency testing participation
  – Attending workshops and symposia
Screening Program Performance Indicators

External QA/CQI

Laboratory (Internal) QA/CQI

- Pre-analytic: Adequate sampling, handling and staining
- Analytic: Adequate screening and interpretation
- Post-analytic: Adequate reporting of results

Recruitment of women
System for re-calling women

Patient management (i.e., screening intervals, colposcopy referrals)
Cancer incidence rates
## Screening Program Performance Indicators - Canada

<table>
<thead>
<tr>
<th>Coverage</th>
<th>Follow-up</th>
<th>Outcome Indicators</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Participation rate</td>
<td>7) Histological investigation</td>
<td>9) Pre-cancer incidence rate</td>
</tr>
<tr>
<td>2) Retention rate</td>
<td>8) Cyto-Histo agreement</td>
<td>10) Cancer incidence rate</td>
</tr>
<tr>
<td><strong>Cytology Performance Indicator</strong></td>
<td></td>
<td>11) Cancers diagnosed at Stage 1</td>
</tr>
<tr>
<td>3) Specimen adequacy</td>
<td></td>
<td>12) Screening history in cases of invasive cancer</td>
</tr>
<tr>
<td>4) Screening test results</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>System Capacity Indicators</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5) Cytology TAT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6) Time to colposcopy</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

See Appendix for definitions & targets
QA Topics in Histopathology

• Establish a nomenclature that is uniformly accepted

• Constant/consistent use of terminology
  – enable data to be extracted and analyzed

• Correlate histology findings with cytology
  – Patient history is viewable
  – Cytology slides are present when signing out biopsies
QA Topics in Histopathology QA cont’d

- If pathology has diagnosis of normal/benign, and cytology was HSIL/AGC+ → review cytology

- If requested, document a review in cases of ASC-H when no high grade lesion is found on biopsy
Appendix:
Cervical Cancer Screening Indicators - Canada

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Definition</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Participation rate</td>
<td>% of eligible women in the target population who had at least one Pap test in a 3-year period.</td>
<td>≥ 80 percent for women aged 21 to 69 should be screened within the recommended screening interval plus six months (i.e. 3 years plus 6 months)</td>
</tr>
<tr>
<td>2) Retention rate</td>
<td>% of eligible women who were re-screened within 3 years after a negative Pap test. Retention reflects the ability to screen women repeatedly over time as well as the acceptability of the test</td>
<td></td>
</tr>
<tr>
<td>3) Specimen adequacy</td>
<td>% of test results reported as unsatisfactory in a 12 month period</td>
<td>0.5 to ≤ 2.0% of tests should be reported as unsatisfactory</td>
</tr>
<tr>
<td>4) Screening test results</td>
<td>Categorize women by their most severe cytology result in a 12-month period</td>
<td></td>
</tr>
<tr>
<td>5) Cytology turnaround time</td>
<td>Median number of days from the date of specimen collection to the date the laboratory issues the Pap test report</td>
<td>90 percent of Pap tests should be reported within 14 calendar days (or 10 working days)</td>
</tr>
</tbody>
</table>
## Appendix: Screening Indicators (Canada) cont’d

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Definition</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>6) Time to colposcopy</td>
<td>% of women with a high-grade abnormal Pap test result (AGC, ASC-H or HSIL+) who had a colposcopy within three, six, nine and 12 months</td>
<td>90 percent of women with a high-grade Pap test result should have a colposcopy examination within six weeks from the Pap test report date or four weeks from the colposcopy referral date</td>
</tr>
<tr>
<td>7) Histological investigation</td>
<td>% of women with a high-grade abnormal Pap test result (ASC-H or HSIL+) who had a colposcopy, histological investigation, or both</td>
<td></td>
</tr>
<tr>
<td>8) Cytology histology agreement</td>
<td>% of high-grade abnormal Pap test results (ASC-H or HSIL+) that had histological confirmation of CIN 2+</td>
<td>Target: ≥ 65 percent of high-grade Pap tests (HSIL+ cytology result) should have a pre-cancerous or an invasive cancer histological outcome</td>
</tr>
<tr>
<td>9) Pre-cancer incidence rate</td>
<td>The number of pre-cancerous lesions detected per 1,000 women screened in a 12-month period</td>
<td></td>
</tr>
</tbody>
</table>
## Appendix: Screening Indicators (Canada) cont’d

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Definition</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>10) Cancer incidence rate</td>
<td>The number of new cases of invasive cervical cancer per 100,000 women</td>
<td></td>
</tr>
<tr>
<td>11) Cancers diagnosed at Stage 1</td>
<td>% of invasive cervical cancer cases detected at Stage 1 according to the International Federation of Gynaecology and Obstetrics (FIGO) classification system.</td>
<td></td>
</tr>
<tr>
<td>12) Screening history in cases of invasive cancer</td>
<td>Screening history in cases of invasive cancer is a retrospective summary of screening prior to diagnosis and is measured as the percentage of women diagnosed with invasive cervical cancer since their last Pap test</td>
<td></td>
</tr>
</tbody>
</table>

References

American Society of Cytopathology Quality Control and Quality Assurance Practices

Cervical Cancer Screening in Canada – Program Performance Results Report


European guidelines for quality assurance in cervical cancer screening