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Technical Briefing
ER/PR Database

DRAFT

February 21, 2008

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Introduction

- Technical briefing on the conclusion of the ER/PR database project.
- Participants: Robert Thompson (Secretary to Cabinet – Health Issues); Don MacDonald (Director, Research and Evaluation, NLCHI); Dr. Reza Aleghehbandan (Consultant, NLCHI); Dr. Deborah Gregory (Senior Researcher, Office of the Secretary to Cabinet, Health Issues)
- No clinical opinions; no evaluations of ER/PR testing performance.

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Background

- June 2007 – questions asked about patient contact. Was everyone contacted?
- Department asked Newfoundland and Labrador Centre for Health Information (NLCHI) to prepare database on communications and clinical information. Eastern Health endorsed and provided cooperation.
- Will assist work of Commission.
- July 2007 – work commences (2 full time staff)

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Content and Methodology

- Content
  - Original scores/Mount Sinai scores
  - Dates of testing/retesting
  - Region
  - Gender
  - Type of contact/date of contact
- Methodology
  - Data linked to source documents where available
  - Multiple sources cross-checked
  - All four RHAs involved

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Database Limitations

- Multiple sources of data needed reconciliation
- Many paper-based systems still in use
- Information systems did not always “talk” to each other
- Data up to ten years old
- Some retests were done on different samples than original tests

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Number of Patients

- 2006-11-23 – Eastern Health reported 939 patients were retested.
- ER-negative was main criterion for retesting.
- 2007-11-02 – Ministerial update – approximately 1000
- Database Result – 1013 people were retested at Mount Sinai; 995 of which were ER-negative.
- 995 patients had 1112 ER/PR tests

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Number of Deceased

- 2006-11-23 (and 2007-05-17) Eastern Health reported 176 deceased out of the 939 patients sent to Mount Sinai.
- Did not use Provincial Mortality Database (PMD) to identify deceased patients.
- PMD measures “all source” mortality
- Database result - 293 patients were deceased on 2006-11-23 (321 one year later)
- This issue is one of data.

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Contact with Families of Deceased

- Some families of deceased have already obtained results.
- In May 2007 Eastern committed to test all deceased and make results available.
- Eastern will announce that data is now ready for families to access.

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What is a Change Rate?

- The proportion of negative tests that changed to positive after retesting
- E.g., conversion rate; false negatives

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Cutoff Points

- Clinical context:
  - 1997-2000: less than or equal to 30% staining is negative; greater than 30% is positive.
  - 2001-2005: less than or equal to 10% staining is negative; greater than 10% is positive
- Technical Context:
  - Any staining is positive (e.g., greater than 1%)

Studies which address issue of false negatives in IHC Testing

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Authors	Cutoff	Findings
Rüdiger et al (2002)	Unknown	11% false negative rate
Layfield et al (2003)	Variable cutoffs	Arbitrary cut point - 26% disagreement between labs Uniform cut points used – 28% disagreement between labs
Allred (2005)	1%	Approximately 20% for Estrogen Receptor
Rhodes et al (2001)	10%	Reliable assays found in only 36% of labs (24/66).
Regitnig et al (2002)	10%	**Unstained slides** False positive rate was 0% and the false negative rate was 1%. **Stained slides** False positive was 3% and the false negative rate was 2%.
Viale et al (2007)	10%	False negative rate as a percentage of negatives was 70% (73/105 tumors locally ER negative were positive i.e., > 10%); 7.6% or 8/105 had 1% to 9% positive cells.
Mann et al (2005)	0, <10% and ≥ 10%	False negative rate for core biopsies. **ER** (14%, 95% CI , 7.9% to 23.4%) **PR** (15%, 95% CI , 7.6% to 24.7%) **HR** (10%, 95% CI , 4.7% to 18.1%)
Rhodes et al (2000)	1% and 10%	Only 37% scored adequately on low expressing tumors
Collins et al (2008)	1% and 10%	**1% cutoff** 21.3% false negative rate as a % of negatives and 5.1% false negative rate as a percentage of total tests. 3.5% false positive rate as a % of positives and 2.7% false positive rate as a percentage of total tests. **10% cutoff** 20.0% false negative rate as a % of negatives and 4.7% false negative rate as a percentage of total tests. 12.9% false positive rate as a % of positives and 9.8% false positive rate as a percentage of total tests

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Expert Opinions which address false negatives in IHC testing

Allred (2004)	Community data - 30% false negative rate Repeat ER testing in difficult cases - conversion rate from negative to positive is 20-30%
Moshin (2004)	30% false negative rate
Magliocco (2005)	20% false negative rate

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Database Change Rate, 1997-2005

Cutoff Points (%)	ER Negative Change Rate (%)	ER-/PR- Change Rate (%)
30%: 1997-2000 10%: 2001-2005	42.8	33.0
10%: 19972005	45.6	33.4
1%: 1997-2005	39.8	19.6

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Contact with Patients

- Large scale patient contact regarding retesting started in October 2005
- Followed by contact regarding test results
- Various channels used

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Communications

- [34] people were not contacted (by a Health Authority) or it is uncertain if they were contacted.

- RHAs have been asked to contact these people ASAP.

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Questions