Joyce

**From:** Dianne Smith
**Sent:** Monday, March 10, 2008 10:30 AM
**To:** Joyce Penney
**Subject:** FW: Revised Paper ER/PR Briefing Note Feb 29, 2008 - NLCHI Databse
**Attachments:** ERPR Note Feb 29Draft.doc; ERPR Note Feb 28Draft.doc

Joyce,

Pat and Kara (and I believe Wayne Miller participated also) in a conference call on Friday past in which they verbally provided feedback to Robert Thompson on the technical brief.

From the Coordinating meeting this morning, Pat indicated Robert Thompson has been provided our feedback and was going to be working over the weekend to do a major rewrite of the technical brief. Pat advised Mr. Thompson indicated we would receive a copy of the technical brief but did not indicate whether or not an opportunity to provide feedback on the revised report would be provided.

Pat also advised Mr. Thompson would be preparing a report on contacts next.

Dianne

Dianne Smith, CPS
Executive Assistant to the COO of
Cancer Care, Quality and Risk Management
Eastern Health
Room 1345, Level I, Health Sciences Centre
St. John's, NL A1B 3V6
Telephone: 709-777-1318
Facsimile: 709-777-1347
E-Mail: dianne.smith@easternhealth.ca

Eastern Health

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**From:** Joyce Penney
**Sent:** Sunday, March 09, 2008 11:31 AM
**To:** Dianne Smith
**Cc:** Pat Pilgrim; Joyce Penney
**Subject:** FW: Revised Paper ER/PR Briefing Note Feb 29, 2008 - NLCHI Databse

I know your office has been working on this one!
Just give me a one liner update on Monday for Louise
Thanks
Joyce

**From:** Dianne Smith
**Sent:** Tuesday, March 04, 2008 12:02 PM
**To:** Wayne Miller
**Cc:** Joyce Penney; Pat Pilgrim
**Subject:** FW: Revised Paper ER/PR Briefing Note Feb 29, 2008 - NLCHI Databse

Wayne,

Forwarding in Pat's absence – in response to your E-mail that you did not receive the revised document, I believe the attached is what you are looking for.

Joyce, I've also copied you on this as the report I sent over to you yesterday was the draft prepared earlier. This is an updated version which Louise may prefer.

Dianne

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Telephone: 709-777-1318
Facsimile: 709-777-1347
E-Mail: dianne.smith@easternhealth.ca

Eastern Health

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**From:** Thompson, Robert [mailto:rthompson@gov.nl.ca]
**Sent:** Friday, February 29, 2008 2:22 PM
**To:** Pat Pilgrim; Gregory, Deborah
**Subject:** Revised Paper

Pat:

Thanks to you and your colleagues for the feedback during yesterday's meeting.

I thought it would be helpful to give you a revised draft today, as you indicated the oncologists would be providing comments on Monday. Rather than having them provide comments on itmes which may already be revised, this draft may make the job easier.

I am attaching two versions: 1) with the revisions highlighted (Feb 28); and 2) a clean draft (Feb 29).

Look forward to getting the additional feedback.

Robert

"This email and any attached files are intended for the sole use of the primary and copied addressee(s) and may contain privileged and/or confidential information. Any distribution, use or copying by any means of this information is strictly prohibited. If you received this email in error, please delete it immediately and notify the sender."

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**To:** Pat Pilgrim; Gregory, Deborah

**Subject:** Revised Paper

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Technical Brief on Statistical Tables from Estrogen Receptor/Progesterone Receptor (ER/PR) Database

DRAFT: February 29, 2008

## 1. Introduction

This note provides a summary interpretation of the statistical tables from the NLCHI ER/PR Database. The tables address clinical issues only. Communications data will be forthcoming.

Throughout this report, references are made to original data from the Eastern Regional Health Authority. It is important to bear in mind that the data represents patients from all regions of the province and that not all of the steps in ER/PR testing take place in the Eastern Health laboratory. For example, tissue extraction and fixation occur at many sites throughout the province before transport to the laboratory, and post-laboratory interpretation and reporting by pathologists occur at many sites as well. Eastern Health collected and reported data on the retesting process for all patients starting in 2005, and therefore the data against which the NLCHI database can be compared was produced by Eastern Health.

Throughout this paper, the terms "case" and "patient" are used interchangeably and mean the same things. The term "tests" refers to ER/PR tests, with the distinction that some "cases" and "patients" had more than one "test" included in the database. The term "original test" refers to a test at the Health Sciences Centre laboratory between 1997 and 2005. A "Mount Sinai test" or "retest" refers to a new test conducted at Mount Sinai Hospital between 2005 and 2008 on a tissue sample that was the subject of an original test.

A statement about database methodology is contained in Appendix 3.

## 2. Total Cases

Eastern Health reported to the public on December 11, 2006 that there were 939 ER negative patients retested at Mount Sinai. This number was also reported to the Minister of Health and Community Services on November 23, 2006, to the court in affidavits, and to the media and public throughout the period in 2007 leading up to the appointment of the Commission of Inquiry.

The 939 total was explained by Eastern Health as containing all patients who had an ER negative test result performed at Eastern Health between 1997 and August 2005 and subsequently sent to Mount Sinai for retesting. The 939 total included 18 patients with original ER-positive results, meaning that they were ER positive before being sent to Mount Sinai. This is a small anomaly, attributable to specific requests from physicians to have these original ER positive results retested.

Using the same time period and inclusion criteria, NLCHI found 1013 patients, or 74 greater than the number reported by Eastern Health. It is not possible to explain completely the difference between the original 939 total and the new 1013 total because, as part of the tracking and data management process within Eastern Health, the spreadsheet which originally contained the 939 count was overwritten with updates. Therefore, it cannot be known with certainty how many cases, or which cases, were present or absent from the older Eastern Health spreadsheets. However, the general explanations for the new, higher total are:

- Some cases were identified by Eastern Health or self-identified by patients after the initial reporting of 939;
- Some cases of deceased individuals were not initially forwarded for testing because of a perception in some RHAs that only living patients need be identified;
- The challenges faced by Eastern Health (e.g., multiple information systems from which to identify original ER/PR tests and original test scores; multiple channels for submitting retests to Mount Sinai; lack of an overarching information system to integrate records for all unique patients) made it difficult to identify every case.

Within the 1013 patients, or cases, there are 18 original ER positives that were sent to Mount Sinai for retesting. Removing these cases for analytical purposes, there were 995 ER-negative cases for which tissue samples were retested at Mount Sinai.

3. Comparison of Eastern Health's November 23, 2006 Briefing for the Minister with New Database Results.

The briefing by Eastern Health for the Minister of Health and Community Services on November 23, 2006 identified 939 cases of which 763 were living and 176 deceased. While some of the 176 deceased cases had been retested at Mount Sinai, they were not included in the detailed results as the focus was on the results and treatment recommendations for living patients.

If Eastern Health had captured all of the cases that are in the new database, and had it been linked to the Provincial Mortality Database (through NLCHI), 295 people would have been identified as deceased at that time instead of 176.[1]

In the briefing for the Minister, 104 patients were identified as requiring a treatment change. A matching number in the new database is not available for "treatment change". Such a comparator could be identified by examining additional records which identify treatment recommendations, a step that was not within the scope of this project.

[1] A year later, in November 2007, the number of deceased was 323 people.

4. Time frame for Retesting

The date that samples were sent to Mount Sinai can be determined for most of the cases. There are 52 cases where the date of testing cannot be determined from existing records. Out of the remaining xxx cases, 85% were sent in 2005, 4% were sent in 2006, 11% were sent in 2007 and xx% were sent in 2008.

The reason why there was an increase in cases in 2007 over 2006 was the identification of some deceased that had been originally omitted due to uncertainty over "inclusion criteria", the inclusion of cases between January and May 1997 over which it was initially unclear whether they were supposed to be retested, and the identification of additional cases that should have been sent in 2005.

5. Number of Cases and Tests by Year of Original Test

Table A in Appendix 1 displays the number of original ER-negative cases by year which were subsequently retested at Mount Sinai Hospital. Out of the total 995 patients, the volume of testing was highest between 1998 and 2002. There were 202 patients tested in the peak year of 2000. The volume of negative cases declined substantially in 2004 after the automated Ventana testing system was utilized. Breast tissue samples from all surgical locations in the province were sent to Eastern Health throughout this period, with the exception of Clarenville which has been sending samples for testing outside the province since 1998.

6. Positivity Rates and Change Rates

a. Data Issues

The following are some methodological points about the data used to calculate positivity rates and change rates:

1. The calculations (in the attached tables) refer to tests rather than patients because the positivity rate measures a characteristic of a group of tests, not a characteristic of a group of patients. The number of original negative tests (the numerator in the positivity rate) was gathered by NLCHI using criteria which ensured the exclusion of ER/PR tests performed for a reason other than breast cancer, duplicate records and data entry errors.
2. The total number of ER/PR tests performed by Eastern Health (which is used as the denominator in the positivity rate) was provided by Eastern Health. This number excludes the "non-breast" ER/PR tests in St. John's (about 4-5% of total tests), but data was not readily available to identify and exclude the non-breast cases from outside St. John's. This data could be requested from the regional health authorities, but such an effort was outside the scope of this project. It is estimated that this factor has a small upward impact on the overall positivity rate, and is likely

to be less than the 4-5% of samples in St. John's because sites outside St. John's have fewer non-breast tissue samples that require ER/PR testing.

3. Some of the retest samples were not the same paraffin blocks that were used to produce the original slides. The number of instances where this happened is believed to be about 5-10%, and it is uncertain whether the impact of this factor is to increase, decrease or cause no change in the positivity rate.
4. Between 1997 and 2005 there were 49 ER negative cases (57 tests) [Check] which were subsequently identified as DCIS. For purposes of calculating the original positivity rate, these tests have been retained even though DCIS patients are not normally sent for ER/PR testing.[2] They have been retained because these tests were part of the original set of tests that Eastern Health performed.
5. Depending on the cutoff point used in the statistical tables, some tests could not be interpreted as negative or positive (the number of such tests varies between cutoff points), and therefore have been excluded from the calculations.
6. The original purpose of the retesting process was patient care, not controlled research. Nonetheless, the retest group represents the complete set of negative ER-negative cases between 1997 and 2005 and therefore is unbiased for Newfoundland and Labrador. The characteristics of the Newfoundland and Labrador population could vary from the characteristics of study groups in the literature, but this issue has not been assessed.

b. Interpretation Issues

The interpretation of the ER/PR database is complex because of the changes over time in clinical cutoff points to define positivity, the uncertainty over whether all pathologists and oncologists were using the same cutoff points, and the distinction between "technical positivity" used in the laboratory environment and "clinical positivity" used in the treatment environment. The following discussion explains how these issues have been addressed in the presentation of data from the ER/PR database.

Changes in Clinical Cutoff Point

An single required standard for classifying positive and negative ER/PR tests is not used in Newfoundland and Labrador, and much disagreement exists throughout the world on the appropriate standards. While there are alternative methods for scoring ER and PR tests, most of the current literature suggests that positivity occurs at the 1% or 10% threshold. In Newfoundland and Labrador, since 2001, oncologists have generally regarded the 10% threshold as the appropriate threshold, and they used 30% between 1997 and 2000, though it is uncertain whether there was uniform compliance with these cutoffs. All practitioners agree that, while there is professional disagreement about the right cutoff points, the final determination on a case by case basis, taking into account other patient-related factors, is based on the oncologist's professional

[2] DCIS cases are not normally tested for hormone receptivity because they are not normally prescribed tamoxifen in Canada. An ER/PR test would only be done for the purpose of determining whether a person might be a candidate for taking tamoxifen.

opinion. Therefore, for presentation purposes, data from the ER/PR database is presented several ways: 1) a 30%/10% split before and after January 1, 2001 to reflect the clinical environment as practiced in this province; 2) a 10% cutoff for all years and a 1% cutoff for all years to allow for comparisons with the scientific literature and to allow for a consistent cutoff over the whole testing period. The 1% cutoff is comparable to a "technical" measure of positivity, and is discussed further below.

Uncertainty over Usage of Cutoff Points

The pathology reports show various descriptors used to report positivity and negativity. For example, some reports may say "0/0", which is a clear indication there is 0% staining and therefore a negative tissue sample. Other reports may include less precise descriptors such as "N", or "Neg/Neg", or "Weak Pos". The exact meanings of descriptors have not been determined with each reporting pathologist as part of the database exercise. Therefore, interpretation is necessary, and brings with it the possibility of a small amount of error. It is understood that the approach in interpreting the descriptors was consistent with the approach used by oncologists.

"Technical Positivity" and "Clinical Positivity"

In the laboratory environment the concept of technical positivity means that there is evidence of staining on an ER or PR slide. Even though the amount of staining may be less than 10%, and therefore in the region which oncologists may say the result is negative, the laboratory regards the test as positive because it has picked up the signal that some receptors exist in the cells.

Clinical positivity is the concept used by oncologists to make treatment decisions. As noted above, the consensus cutoff currently in use, though not necessarily uniformly, is 10%.

The database presentation noted above using several cutoff points can address the distinction of technical versus clinical positivity. Clinical is best reflected in the 30%/10% presentation, while the technical positivity is best reflected in the 1% presentation.

Analyzing PR

In pathology and oncology, ER and PR are reported and considered together as they both provide information for treatment decisions. Interpretation is straightforward for three of the four possible ER/PR combinations: ER+/PR+ is clearly positive; ER-/PR- is clearly negative; and ER+/PR- can be deemed positive based on the clinical significance of the ER test. The approach to ER-/PR+ requires some discussion.

Oncologists at Eastern Health have advised that ER-/PR+ is a result they see periodically and a PR+ can be a determining factor in prescribing tamoxifen.

This opinion is confirmed by Rhodes (date), but he identifies a possible technical problem that may accompany a high number of ER-/PR+ results:

> In addition to ER, it is possible to demonstrate elevated progesterone receptor (PR) levels in a proportion of breast cancers, although PR alone is not a particularly strong independent indicator of tumour response to hormonal therapy. However, its presence does indicate a functioning hormone receptor pathway and is useful when unexpected results are obtained with the ER assay. For example, only approximately 3% of breast tumours are ER-negative and PR-positive. Therefore, the reporting of a relatively high number of ER-negative, PR-positive cases by a laboratory might indicate a technical problem resulting in false-negative results for ER.[3]

Another opinion by Moshin, et. al. (date):

> …many clinicians depend on ER status alone to select patients for hormonal therapy.
> …as compared to ER, PR adds only a limited amount of additional predictive information for response to hormonal therapy.

In assessing the degree of significance of PR in the database, it is also important to explain the use of PR in the retesting process by Eastern Health starting in 2005. One of the criteria used by Eastern Health to identify samples for retesting was ER negativity. The positivity or negativity of PR was not a factor. Therefore, samples that originally had ER-/PR+ results, and which may have been regarded as positive by oncologists at the time of a patient's initial treatment recommendation, were also gathered for retesting. Eastern Health has explained this approach as "casting a wider net" because it was not known whether ER-/PR+ patients were normally being prescribed Tamoxifen, and retesting might result in additional benefit for them.

A potentially confusing issue is Eastern Health's court affidavit in which it reports the number of clinically negative patients based on "ER/PR tests", yet in another affidavit the number of false negatives is reported as based on "ER test" cutoff points. The variance is explained by the fact that, in the latter, the court directed Eastern Health to identify all patients which converted from ER-negative to ER-positive, without consideration of PR.

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[3] The use of scientific literature in assessing the ER/PR database results must be done with care to ensure that conclusions based on comparisons with the literature employ studies that were available before the date of the comparison.

To accommodate both perspectives, positivity rates and change rates (e.g., false negatives) are reported for ER-negative alone as well as ER/PR together, and both are presented at clinical cutoffs (30%/10%) and the technical cutoff (1%).

Understanding the Change Rate

Given that the results of the pathology reports are normally reported as a quantitative score between 0 and 100, it is possible to calculate the rate of change from negative to positive for the whole retest group. This approach is a mathematical approach, not a clinical one, and is not to be regarded as a substitute for the work of the tumour panel or other clinical judgments in the retesting process. In particular, the change rate in the test results is not an indicator of the proportion of patients who should have received alternate treatment. It is important to bear in mind that out of 317 patients who had "changed results" as reported by Eastern Health to the Minister on November 23, 2006, 117 needed a change in treatment.

c. Results:

The database results are presented below with respect to positivity rates, the ratio of ER/PR combinations to total tests, and change rates (i.e., false negatives). The 1997-2005 averages are presented, though the associated tables display considerable variability of annual results. In particular, the results begin to move much closer to the results expected in the literature starting in 2003, and strongly so in 2004-2005. The 1998 results are anomalous without apparent explanation.

Positivity (see Tables B to E)

Summary of Original ER/PR Test Data and Positivity Rates, 1997-2005, by Cutoff Point

| Cutoff Point (%) | ER- | Total Tests (ER Adjusted) | ER-/PR- | ER-/PR+ | Total Tests (HR Adjusted) | ER Positivity Rate | HR Positivity Rate | ER-/PR- % of Total Tests (HR Adjusted) | ER-/PR+ % of Total Tests (HR Adjusted) |
|---|---|---|---|---|---|---|---|---|---|
| 30/10 | 1089 | 2533 | 871 | 207 | 2522 | 57.0 | 65.5 | 34.5 | 8.2 |
| 10 | 1030 | 2527 | 803 | 215 | 2514 | 59.2 | 68.1 | 31.9 | 8.6 |
| 1 | 815 | 2551 | 597 | 217 | 2550 | 68.1 | 76.6 | 23.4 | 8.5 |

Using a clinical cutoff of 30%/10%, there were 1089 original ER-negative tests between 1997 and 2005 which were retested at Mount Sinai Hospital. These original ER-negative tests comprised 43% of total tests, which means there was a

57% positivity rate for the whole period. Removing the ER-/PR+ tests from this group, and assigning them as ER/PR positive, the hormone receptor (HR) positivity rate is 66%.

Using a 10% cutoff point for the whole period, the number of ER-negative tests was 1030, the ER-positivity rate was 59% and the HR-positivity rate was 68%. Using a technical 1% cutoff, which is closely aligned with the way positivity is defined in the laboratory environment, the number of ER-negative tests was 815, the ER-positivity rate was 68% and the HR-positivity rate was 77%.

Table J presents a list of studies may be helpful in placing these results in context.

Ratio of ER/PR Results to Total Tests (see Tables B to I)

Original ERHA Tests: Using a clinical cutoff of 30%/10%, the ratio of ER-/PR- tests to total tests was 35% and the ratio of ER-/PR+ tests to total tests was 8%. Using a 10% cutoff point, the ratio of ER-/PR- tests to total tests was 32% and the ratio of ER-/PR+ tests to total tests was 9%. Using a 1% cutoff point, the ratio of ER-/PR- tests to total tests was 23% and the ratio of ER-/PR+ tests to total tests was 9%.

Mount Sinai Hospital Re-tests: Using a clinical cutoff of 30%/10%, the ratio of ER-/PR- tests to total tests was 24% and the ratio of ER-/PR+ tests to total tests was 2%. Using a 10% cutoff point, the ratio of ER-/PR- tests to total tests was 22% and the ratio of ER-/PR+ tests to total tests was 1%. Using a 1% cutoff point, the ratio of ER-/PR- tests to total tests was 19% and the ratio of ER-/PR+ tests to total tests was less than 1%.

Table J presents a list of studies may be helpful in placing these results in context.

Change Rates (False Negatives) - (see Tables F to I)

| Summary of ER/PR Mount Sinai Retest Data and Change Rates, 1997-2005, by Cutoff Point | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Cutoff Points (%) | ER- Tests | ER-/PR- Tests | ER - | HR and DCIS Adjusted Total Tests | ER Negative Change Rate | ER-/PR- Change Rate | ER-/PR+ Change Rate | ER-/PR- % of HR- Adjusted Total tests | ER-/PR+ % of HR- Adjusted Total tests |
| 30/10 | 623 | 584 | 39 | 2465 | 42.8 | 33.0 | 81.2 | 23.7 | 1.6 |
| 10 | 560 | 535 | 25 | 2457 | 45.6 | 33.4 | 88.4 | 21.8 | 1.0 |
| 1 | 491 | 480 | 11 | 2493 | 39.8 | 19.6 | 94.9 | 19.3 | 0.4 |

Using a clinical cutoff of 30%/10%, the number of original ER-negative tests between 1997 and 2005 dropped from 1089 to 623 after being retested at Mount Sinai Hospital. Thus, the change rate was 43% of total ER-negative tests for the whole period. Removing the ER-/PR+ tests from this group, and assigning them as ER/PR positive, the change rate was 33%. In other words, even though the proportion of false ER negatives was 43%, a more inclusive definition of positive, incorporating ER-/PR+ tests, means that the false negative rate from a clinical perspective was 33%.

Using a 10% cutoff point for the whole period, the total number of ER-negative tests dropped from 1030 to 560, for a change rate of 46%. Removing the ER-/PR+ tests from this group, and assigning them as ER/PR-positive, the change rate was 33%.

Using a 1% cutoff point for the whole period, the total number of ER-negative tests dropped from 815 to 491, for a change rate of 40%. Removing the ER-/PR+ tests from this group, and assigning them as ER/PR positive, the change rate was 20%.

Table K presents a list of studies may be helpful in placing these results in context.

## Appendix 1: Results Tables (based on NLCHI Database results)

**Table A: Number and Percentage of Original Negative ER Tests and Cases by year.**

| Year | Number of Tests with Negative ER | Percentage | Number of Cases | Percentage |
|---|---|---|---|---|
| 1997 | 66 | 5.9 | 61 | 6.1 |
| 1998 | 161 | 14.5 | 140 | 14.1 |
| 1999 | 168 | 15.1 | 149 | 15.0 |
| 2000 | 202 | 18.2 | 181 | 18.2 |
| 2001 | 152 | 13.7 | 141 | 14.2 |
| 2002 | 160 | 14.4 | 147 | 14.8 |
| 2003 | 111 | 10.0 | 98 | 9.8 |
| 2004 | 64 | 5.8 | 54 | 5.4 |
| 2005 | 28 | 2.5 | 24 | 2.4 |
| Total | 1112 | 100.0 | 995 | 100.0 |

1. Some patients had more than one ER/PR test. Some tests for a single patient may have occurred in different years, but the patient appears only in a single year.
2. Between 1997 and 2000 ER negative is ≤30% and between 2001 and 2005 ER negative is ≤10%. This definition is based on a clinical guideline and was used to determine which tests would be retested at Mount Sinai Hospital.

Table B: **Original ER/PR Test Results at ERHA and Positivity Rates, 1997-2005 (Cutoff: 1997-2000: 30%; 2001-2005: 10%)**

| Year | ER- Tests | Total ER/PR Tests (ER Adjusted) | ER-/PR- Tests | ER-/PR+ Tests | Total Tests (HR Adjusted) | ER Positivity Rate | HR Positivity Rate | ER-/PR- % of Total Tests (HR Adjusted) | ER-/PR+ % of Total Tests (HR Adjusted) |
|---|---|---|---|---|---|---|---|---|---|
| 1997 | 64 | 135 | 49 | 12 | 132 | 52.6 | 62.9 | 37.1 | 9.1 |
| 1998 | 159 | 216 | 125 | 31 | 213 | 26.4 | 41.3 | 58.7 | 14.6 |
| 1999 | 165 | 358 | 132 | 32 | 357 | 53.9 | 63.0 | 37.0 | 9.0 |
| 2000 | 199 | 329 | 170 | 29 | 329 | 39.5 | 48.3 | 51.7 | 8.8 |
| 2001 | 148 | 338 | 113 | 34 | 337 | 56.2 | 66.5 | 33.5 | 10.1 |
| 2002 | 159 | 319 | 122 | 36 | 318 | 50.2 | 61.6 | 38.4 | 11.3 |
| 2003 | 108 | 316 | 89 | 17 | 314 | 65.8 | 71.7 | 28.3 | 5.4 |
| 2004 | 62 | 327 | 51 | 11 | 327 | 81.0 | 84.4 | 15.6 | 3.4 |
| 2005 | 25 | 195 | 20 | 5 | 195 | 87.2 | 89.7 | 10.3 | 2.6 |
| Total | 1089 | 2533 | 871 | 207 | 2522 | 57.0 | 65.5 | 34.5 | 8.2 |

1. All data are from the NLCHI database except Total ER/PR Tests which is based on Eastern Health's count of all ER/PR tests performed between 1997-2005.
2. ER Adjusted – means that results for which the ER score could not be interpreted for making a positive or negative classification have been removed. HR (hormone receptor) Adjusted – means that results for which the ER/PR score could not be interpreted for making a positive or negative classification have been removed.
3. Positivity Rate = ([Total Tests] – [ER or HR Tests]) / Total Tests

**Table C: Original ER/PR Test Results at ERHA and Positivity Rates, 1997-2000 (Cutoff: 1997-2000: 30%)**

| Year | ER- Tests | Total ER/PR Tests (ER Adjusted) | ER-/PR- Tests | ER-/PR+ Tests | Total Tests (HR Adjusted) | ER Positivity Rate | HR Positivity Rate | ER-/PR- % of Total Tests (HR Adjusted) | ER-/PR+ % of Total Tests (HR Adjusted) |
|---|---|---|---|---|---|---|---|---|---|
| 1997 | 64 | 135 | 49 | 12 | 132 | 52.6 | 62.9 | 37.1 | 9.1 |
| 1998 | 159 | 216 | 125 | 31 | 213 | 26.4 | 41.3 | 58.7 | 14.6 |
| 1999 | 165 | 358 | 132 | 32 | 357 | 53.9 | 63.0 | 37.0 | 9.0 |
| 2000 | 199 | 329 | 170 | 29 | 329 | 39.5 | 48.3 | 51.7 | 8.8 |
| Total | 587 | 1038 | 476 | 104 | 1031 | 43.4 | 53.8 | 46.2 | 10.1 |

Notes: Same as above.

**Table D: Original ER/PR Test Results at ERHA and Positivity Rates, 1997-2005 (Cutoff: 1997-2005: 10%)**

| Year | ER- Tests | Total ER/PR Tests (ER Adjusted) | ER-/PR- Tests | ER-/PR+ Tests | Total Tests (HR Adjusted) | ER Positivity Rate | HR Positivity Rate | ER-/PR- % of Total Tests (HR Adjusted) | ER-/PR+ % of Total Tests (HR Adjusted) |
|---|---|---|---|---|---|---|---|---|---|
| 1997 | 64 | 135 | 47 | 14 | 132 | 52.6 | 64.4 | 35.6 | 10.6 |
| 1998 | 143 | 215 | 101 | 39 | 211 | 33.5 | 52.1 | 47.9 | 18.5 |
| 1999 | 145 | 356 | 114 | 30 | 355 | 59.3 | 67.9 | 32.1 | 8.5 |
| 2000 | 176 | 326 | 146 | 29 | 325 | 46.0 | 55.1 | 44.9 | 8.9 |
| 2001 | 148 | 338 | 113 | 34 | 337 | 56.2 | 66.5 | 33.5 | 10.1 |
| 2002 | 159 | 319 | 122 | 36 | 318 | 50.2 | 61.6 | 38.4 | 11.3 |
| 2003 | 108 | 316 | 89 | 17 | 314 | 65.8 | 71.7 | 28.3 | 5.4 |
| 2004 | 62 | 327 | 51 | 11 | 327 | 81.0 | 84.4 | 15.6 | 3.4 |
| 2005 | 25 | 195 | 20 | 5 | 195 | 87.2 | 89.7 | 10.3 | 2.6 |
| Total | 1030 | 2527 | 803 | 215 | 2514 | 59.2 | 68.1 | 31.9 | 8.6 |

Notes: same as above.

**Table E: Original ER/PR Test Results at ERHA and Positivity Rates, 1997-2005 (Cutoff: 1997-2005: 1%)**

| Year | ER- Tests | Total ER/PR Tests (ER Adjusted) | ER-/PR- Tests | ER-/PR+ Tests | Total Tests (HR Adjusted) | ER Positivity Rate | HR Positivity Rate | ER-/PR- % of Total Tests (HR Adjusted) | ER-/PR+ % of Total Tests (HR Adjusted) |
|---|---|---|---|---|---|---|---|---|---|
| 1997 | 52 | 137 | 36 | 16 | 137 | 62.0 | 73.7 | 26.3 | 11.7 |
| 1998 | 118 | 218 | 77 | 41 | 218 | 45.9 | 64.7 | 35.3 | 18.8 |
| 1999 | 109 | 360 | 80 | 29 | 360 | 69.7 | 77.8 | 22.2 | 8.1 |
| 2000 | 136 | 332 | 110 | 25 | 331 | 59.0 | 66.8 | 33.2 | 7.6 |
| 2001 | 119 | 342 | 83 | 36 | 342 | 65.2 | 75.7 | 24.3 | 10.5 |
| 2002 | 128 | 320 | 87 | 41 | 320 | 60.0 | 72.8 | 27.2 | 12.8 |
| 2003 | 78 | 318 | 64 | 14 | 318 | 75.5 | 79.9 | 20.1 | 4.4 |
| 2004 | 54 | 328 | 42 | 12 | 328 | 83.5 | 87.2 | 12.8 | 3.7 |
| 2005 | 21 | 196 | 18 | 3 | 196 | 89.3 | 90.8 | 9.2 | 1.5 |
| Total | 815 | 2551 | 597 | 217 | 2550 | 68.1 | 76.6 | 23.4 | 8.5 |

Notes: same as above.

**Table F: ER/PR Re-test Results at Mount Sinai Hospital and Change Rates, 1997-2005 (Cutoff: 1997-2000: 30%; 2001-2005: 10%)**

| Year | ER- Tests | ER-/PR- Tests | ER-/PR+ Tests | Total Tests (HR and DCIS Adjusted) | ER Negative Change Rate | ER-/PR- Change Rate | ER-/PR+ Change Rate | ER-/PR- % of HR and DCIS Adjusted Total tests | ER-/PR+ % of HR and DCIS Adjusted Total tests |
|---|---|---|---|---|---|---|---|---|---|
| 1997 | 42 | 40 | 2 | 129 | 34.4 | 18.4 | 83.3 | 31.0 | 1.6 |
| 1998 | 91 | 83 | 8 | 203 | 42.8 | 33.6 | 74.2 | 40.9 | 3.9 |
| 1999 | 93 | 80 | 13 | 349 | 43.6 | 39.4 | 59.4 | 22.9 | 3.7 |
| 2000 | 117 | 111 | 6 | 316 | 41.2 | 34.7 | 79.3 | 35.1 | 1.9 |
| 2001 | 67 | 64 | 3 | 329 | 54.7 | 43.4 | 91.2 | 19.5 | 0.9 |
| 2002 | 73 | 69 | 4 | 313 | 54.1 | 43.4 | 88.9 | 22.0 | 1.3 |
| 2003 | 64 | 63 | 1 | 307 | 40.7 | 29.2 | 94.1 | 20.5 | 0.3 |
| 2004 | 52 | 50 | 2 | 326 | 16.1 | 2.0 | 81.8 | 15.3 | 0.6 |
| 2005 | 24 | 24 | 0 | 193 | 4.0 | -20.0 | 100.0 | 12.4 | 0.0 |
| Total | 623 | 584 | 39 | 2465 | 42.8 | 33.0 | 81.2 | 23.7 | 1.6 |

1. All data are from the NLCHI database except Total ER/PR Tests which is based on Eastern Health's count of all ER/PR tests performed from 1997-2005.
2. HR (hormone receptor) and DCIS Adjusted – means that tests classified as DCIS, and tests results for which the ER/PR score could not be interpreted for making a positive or negative classification, have been removed.
3. Change Rate = ([Original Tests] – [Mount Sinai Tests]) / Original Tests

**Table G: ER/PR Re-test Results at Mount Sinai Hospital and Change Rates, 1997-2005 (Cutoff: 1997-2000: 30%)**

| Year | ER- Tests | ER-/PR- Tests | ER-/PR+ Tests | Total Tests (HR and DCIS Adjusted) | ER Negative Change Rate | ER-/PR- Change Rate | ER-/PR+ Change Rate | ER-/PR- % of HR and DCIS Adjusted Total tests | ER-/PR+ % of HR and DCIS Adjusted Total tests |
|---|---|---|---|---|---|---|---|---|---|
| 1997 | 42 | 40 | 2 | 129 | 34.4 | 18.4 | 83.3 | 31.0 | 1.6 |
| 1998 | 91 | 83 | 8 | 203 | 42.8 | 33.6 | 74.2 | 40.9 | 3.9 |
| 1999 | 93 | 80 | 13 | 349 | 43.6 | 39.4 | 59.4 | 22.9 | 3.7 |
| 2000 | 117 | 111 | 6 | 316 | 41.2 | 34.7 | 79.3 | 35.1 | 1.9 |
| Total | 343 | 314 | 29 | 997 | 41.6 | 34.0 | 72.1 | 31.5 | 2.9 |

Notes: same as above.

**Table H: ER/PR Re-test Results at Mount Sinai Hospital and Change Rates, 1997-2005 (Cutoff: 1997-2005: 10%)**

| Year | ER- Tests | ER-/PR- Tests | ER-/PR+ Tests | Total Tests (HR and DCIS Adjusted) | ER Negative Change Rate | ER-/PR- Change Rate | ER-/PR+ Change Rate | ER-/PR- % of HR and DCIS Adjusted Total tests | ER-/PR+ % of HR and DCIS Adjusted Total tests |
|---|---|---|---|---|---|---|---|---|---|
| 1997 | 38 | 37 | 1 | 129 | 40.6 | 21.3 | 92.9 | 28.7 | 0.8 |
| 1998 | 77 | 72 | 5 | 201 | 46.2 | 28.7 | 87.2 | 35.8 | 2.5 |
| 1999 | 66 | 63 | 3 | 347 | 54.5 | 44.7 | 90.0 | 18.2 | 0.9 |
| 2000 | 99 | 93 | 6 | 312 | 43.8 | 36.3 | 79.3 | 29.8 | 1.9 |
| 2001 | 67 | 64 | 3 | 329 | 54.7 | 43.4 | 91.2 | 19.5 | 0.9 |
| 2002 | 73 | 69 | 4 | 313 | 54.1 | 43.4 | 88.9 | 22.0 | 1.3 |
| 2003 | 64 | 63 | 1 | 307 | 40.7 | 29.2 | 94.1 | 20.5 | 0.3 |
| 2004 | 52 | 50 | 2 | 326 | 16.1 | 2.0 | 81.8 | 15.3 | 0.6 |
| 2005 | 24 | 24 | 0 | 193 | 4.0 | -20.0 | 100.0 | 12.4 | 0.0 |
| Total | 560 | 535 | 25 | 2457 | 45.6 | 33.4 | 88.4 | 21.8 | 1.0 |

Notes: same as above.

**Table I: ER/PR Re-test Results at Mount Sinai Hospital and Change Rates, 1997-2005 (Cutoff: 1997-2005: 1%)**

| Year | ER- Tests | ER-/PR- Tests | ER-/PR+ Tests | Total Tests (HR and DCIS Adjusted) | ER Negative Change Rate | ER-/PR- Change Rate | ER-/PR+ Change Rate | ER-/PR- % of HR and DCIS Adjusted Total tests | ER-/PR+ % of HR and DCIS Adjusted Total tests |
|---|---|---|---|---|---|---|---|---|---|
| 1997 | 36 | 36 | 0 | 134 | 30.8 | 0.0 | 100.0 | 26.9 | 0.0 |
| 1998 | 67 | 66 | 1 | 208 | 43.2 | 14.3 | 97.6 | 31.7 | 0.5 |
| 1999 | 57 | 56 | 1 | 352 | 47.7 | 30.0 | 96.6 | 15.9 | 0.3 |
| 2000 | 86 | 82 | 4 | 318 | 36.8 | 25.5 | 84.0 | 25.8 | 1.3 |
| 2001 | 61 | 57 | 4 | 334 | 48.7 | 31.3 | 88.9 | 17.1 | 1.2 |
| 2002 | 59 | 59 | 0 | 315 | 53.9 | 32.2 | 100.0 | 18.7 | 0.0 |
| 2003 | 55 | 54 | 1 | 311 | 29.5 | 15.6 | 92.9 | 17.4 | 0.3 |
| 2004 | 49 | 49 | 0 | 327 | 9.3 | -16.7 | 100.0 | 15.0 | 0.0 |
| 2005 | 21 | 21 | 0 | 194 | 0.0 | -16.7 | 100.0 | 10.8 | 0.0 |
| Total | 491 | 480 | 11 | 2493 | 39.8 | 19.6 | 94.9 | 19.3 | 0.4 |

Notes: same as above.

**Table J: List of studies which identify positivity rates in samples of ER/PR test, and the cutoff points used**

| Year of Publication | Cutoff point | Number of cases | ER+/PR+ (%) | ER+/PR- (%) | ER-/PR+ (%) | ER-/PR- (%) | ER Positivity rate | HR Positivity rate (excludes ER-PR-) |
|---|---|---|---|---|---|---|---|---|
| *Harvey et al (1999) | IHC score of > 2 (corresponding to as few as 1% to 10% weakly positive cells) was used to define ER positivity) | 1,982 | 70.5% | | 29.5% | | 70.5% | --- |
| Rhodes et al (2000) | 10% receptor positive threshold | 2,222 | 54.8 | 19.8 | 3.2 | 22.1 | 74.6% | 77.85 |
| Anderson (2001) | National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) has no standard definition or centralized laboratory to determine HR expression. Depending on the assay used, each SEER site codes ER and pr expression as presence – positive or absence-negative | 19,541 | 66 | 12.5 | 3.4 | 18.6 | 78.5% | 81.9% |
| Dako Manual **N.D. | Allred score which incorporates not only the proportion of cells staining but also the intensity of those cells. | | 58 | 23 | 4 | 15 | 81% | 85% |
| Huang (2005) | H score for ER and PR, a negative result was defined as a score of < 50, weakly positive as 51-100, moderately positive as 101-200, and strongly positive as > 200. | 1,362 | 62.6 | 18.5 | 1.6 | 17.3 | 81.1% | 82.7% |
| Killeen (2006) | Tumors considered positive if nuclear staining was detected by Image Analysis in ≥ 5% of tumor cells. | 667 | 62.4 | 16.9 | 1.3 | 19.3 | 79.3% | 80.6% |
| Francis et al (2006a) | Scoring system used a modified quickscore system, which utilized a combination of percentage of cells and intensity of staining. | 591 | 69.4 | 10.7 | 2.5 | 17.4 | 80.1% | 82.6% |
| Francis et al (2006b) | Participating labs used their own cutoffs 1-5%, 5-9%, 10% 22% of the labs did not provide an answer to the cutoff level used | 8,128 | 59 | 15.9 | 2.4 | 22.7 | 74.9% | 77.3% |
| Collins et al (2008) | Any positivity (nuclear positivity in > 1% of tumor cell nuclei) on Tissue Microarrray<br><br>10% positivity (nuclear positivity in > 10% of tumor cell nuclei) on Tissue Microarrray | 336 | Any positivity 73.5<br><br>10% positivity 66.4 | Any positivity 2.7<br><br>10% positivity 9.8 | Any positivity 5.1<br><br>10% positivity 4.8 | Any positivity 18.7<br><br>10% positivity 19.0 | Any positivity 76.2%<br><br>10% positivity 76.2% | Any positivity 81.3%<br><br>10% positivity 81% |

*Harvey et al. study only refers to ER positivity. PR is not addressed.
**2004 - last cited reference in the Dako Manual

**Table K: List of Studies/Expert Opinion Addressing False Negative/False Positive Rates, Intra- and Interlaboratory Variation in IHC Assessment of Hormone Receptors.**

| Authors | Cutoff | Findings |
|---|---|---|
| Rűdiger et al (2002) | Unknown | 11% false negative rate |
| Layfield et al (2003) | Variable cutoffs | Arbitrary cut point - 26% disagreement between labs<br>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**<br>False positive rate was 0% and the false negative rate was 1%.<br>**Stained slides**<br>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.<br>**ER** (14%, 95% CI , 7.9% to 23.4%)<br>**PR** (15%, 95% CI , 7.6% to 24.7%)<br>**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**<br>21.3% false negative rate as a % of negatives and 5.1% false negative rate as a percentage of total tests.<br>3.5% false positive rate as a % of positives and 2.7% false positive rate as a percentage of total tests.<br>**10% cutoff**<br>20.0% false negative rate as a % of negatives and 4.7% false negative rate as a percentage of total tests.<br>12.9% false positive rate as a % of positives and 9.8% false positive rate as a percentage of total tests |
| **Expert Opinion** | | |
| Allred (2004) | | Community data - 30% false negative rate<br>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 |

Eastern Health

## Appendix 2: NLCHI Database additional tables

| Table 1: Database Contents | |
|---|---|
| Total Cases | 1209 |
| Total Patient Cases | 1044 |
| Less: Cases with original results before January 1997 | --- |
| Less: Cases with original results that were positive, and not known/included in Eastern Health spreadsheet August 1, 2006 (e.g., were retested after December 2006) | 15 |
| Less: Cases without original tests at Eastern Health. | 16 |
| Other??? | --- |
| Total A – Retested Cases consistent with December 2006 EH Report | 1013 |
| Less Original Positives up to December 2006*** | 18 |
| Total B – Retested Cases with Original Negatives | 995 |

Note: Total A includes:

-Any original positives that were identified in the August 1 Excel file
-Only those with original scores
-Cases with an original test done between January 1997 and August 2005

Total B includes

-Only those with original ***negative*** scores
-Cases with an original test done between January 1997 and August 2005

| Table 3: Deceased (Using Total A) | |
|---|---|
| EH Reported as Deceased November 23, 2006 | 176 |
| EH Reported as Deceased August 1, 2007 | 195 |
| NLCHI Confirmed Deceased as of October 2005 | 238 |
| NLCHI Confirmed Deceased as of November 23, 2006 | 294 |
| NLCHI Confirmed Deceased August 1, 2007 | 315 |
| NLCHI Confirmed Deceased November 26, 2007 | 322 |

Note: The vital status of any individuals from St. Pierre, or have since moved from the province are not captured.

| Time Period of Original Test | Table 5: Number of Cases and Tests by Time Period of Original Test | |
|---|---|---|
| | Database (Total B) | Database (Total Original negative tests) |
| | # Cases sent for Retests* | # Tests sent for Retests* |
| 1997 | 61 | 66 |
| 1998 | 140 | 161 |
| 1999 | 149 | 168 |
| 2000 | 181 | 202 |
| 2001 | 141 | 152 |
| 2002 | 147 | 160 |
| 2003 | 98 | 111 |
| 2004 | 54 | 64 |
| 2005 (August) | 24 | 28 |
| Total | 995 | 1112 |

*Note: Excludes positives; negative defined as: ≤ 30 from 1997-2000, and ≤ 10 from 2001-2005. Includes tests with unclear original scores (i.e. weak positive, equivocal, etc.)

Appendix 3

**Estrogen and Progesterone Receptor (ER/PR)**
**Breast Cancer Testing Communication Event Database**

***Interim Report***

Submitted by:
Research and Evaluation Department
Newfoundland and Labrador Centre for Health Information

October 23, 2007

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**Project Background**

Estrogen and progesterone receptor (ER/PR) testing takes place after a diagnosis of breast cancer and is used to determine whether cancer cells have estrogen and progesterone receptors. Breast cancers that are either ER-positive or PR-positive (or both) may respond to hormone therapy such as Tamoxifen. Hormonal therapy, chemotherapy and radiation are potential treatments given after surgery.

In July 2007, the Department of Health and Community Services requested that the Centre for Health Information develop a database that would identify all breast cancer patients who received ER/PR testing in Newfoundland and Labrador (NL) (prior to August 2005) and were subsequently retested at Mount Sinai Hospital (Toronto). A second phase of this work involved the documentation of relevant communication events related to the retesting. While the main focus of the database is on: 1) when and how patients were contacted to inform them of the retesting, and 2) when and how patients were informed of the subsequent test results, it was recognized early in the process that the foundation of the database would be an accurate patient list. Given this, the approach taken to develop the database had two components, the patient listing and communications events surrounding the patient. For the purpose of this report the resulting database is called the "*ER/PR Patient Listing and Communication Events Database*". The aim of this report is to describe the methodology used to develop the database, and present a description of the variables within the database. It should be noted that this document serves as an interim report as of October 24, 2007. The database will continue to be enhanced as additional information becomes available.

**Selection Criteria**

The following criteria were initially used to develop the *ER/PR Patient Listing and Communication Events database*:

- Both male and female breast cancer patients;
- Original ER testing in NL within time frame: between January 1997 and August 2005;

- Original ER testing (either negative or positive) done in NL **AND** retested at Mount Sinai;
- Include tissue other than breast (e.g., lymph node, chest etc);
- Include DCIS (ductal carcinoma in situ) patients (originally sent for retesting but at Mount Sinai diagnosed as DCIS and were not retested for ER);
- Insufficient tumor/tissue for ER testing at Mount Sinai;
- Include deceased patients who have recently been sent for retesting at Mount Sinai;
- Include all originally negative ER done in NL BUT not retested at Mount Sinai;
- Include all ER tested at Mount Sinai BUT no original ER testing in NL;
- Those patients who called in and asked to be tested at Mount Sinai BUT did not meet the eligibility criteria.

On September 11, 2007, a meeting between the Department of Health and Community Services and the Centre resulted in the original criteria being revised.

**Revised Criteria**

1. Had original ER test in NL;
2. Had original ER test for sample related to breast cancer (e.g., breast, lymph node, chest etc);
3. Had original ER test between January 1997 and August 2005 (inclusive) **OR** had original ER test prior to January 1997 **AND** sent to Mount Sinai for re-testing;
4. Had negative original ER test result **OR** had positive original ER test result **AND** sent to Mount Sinai for re-testing.

**OR**

1. Had sample taken in NL related to breast cancer (e.g., breast, lymph node, chest etc);
2. Had sample taken between January 1997 and August 2005 (inclusive) **OR** had sample taken prior to January 1997 **AND** sent to Mount Sinai for testing;
3. Had no original ER test in NL **BUT** sample sent to Mount Sinai for testing.

In addition, if an individual met the above criteria, he/she would not be excluded based on any of the following criteria:

1. Sample not retested at Mount Sinai due to DCIS;
2. Sample not retested at Mount Sinai due to insufficient tumor for ER testing;
3. Patient is deceased.

But would be excluded if the following applied:

1. Original ER test done outside of NL and sample retested at Mount Sinai.

**Description of Data Sources**

The following data sources (electronic and hard copy) were used in the development of the *ER/PR Patient Listing and Communication Events* database:

**I) Patient Clinical/Demographic Data Sources**

a) ***Eastern Health Quality and Risk Management August 1st Excel File***

The Centre received this data file in electronic format (Excel) on August 1st, 2007. The data included 1032 records. The data file originally did not contain MCP numbers. An extensive effort was made to capture MCP number for each patient using the MCP registry file (primary source) as well as Meditech (secondary source). As a result, a total number of 924 unique patients were identified in the Eastern Health Quality and Risk Management August 1st file based on MCP number. The data included demographic and clinical information regarding ER/PR scoring, the Tumor Board recommendations, and communication events for most patients' records. It should be noted that prior to the Centre receiving a copy of this data file on August 1st it was modified over time with no documentation on previous changes.

b) ***Eastern Health Quality and Risk Management August 3rd Excel File***

The Centre received this file in electronic format (Excel) on August 20th, 2007. This file was an updated version of the Eastern Health Quality and Risk Management

August 1st Excel file. The data included 1055 records. This database was used only for identifying newly added cases since the August 1st file – the foundation for developing the *ER/PR Patient Listing and Communication Events database* was the August 1st file.

c) ***Eastern Health Laboratory Written Lists***

The Centre received a hard copy of the following lists developed by the Laboratory Department at Eastern Health. The lists were electronically entered into the Statistical Package for the Social Sciences (SPSS) software by the Centre.

a) A list of breast cancer patients with ER negative and/or weakly positive [as defined by Eastern Health] for the St. John's region (Health Sciences Centre, St. Clair's Mercy Hospital, and Grace Hospital) - This list included demographic information (name, MCP, surgical number) as well as original ER/PR scoring and contained 652 records.

b) A list of breast cancer patients with ER negative for other Regional Health Authorities (Central, Western, Labrador/Grenfell, Clarenville [former Peninsulas Institutional Board] and Carbonear [former Avalon Institutional Board]) - This included demographic information (name, MCP, surgical number, Health Care Facilities within each Regional Health Authority) as well as original ER/PR scoring and contained 464 records.

c) A list of deceased breast cancer patients who were ER negative, as well as those individuals who called (or their family called) inquiring about ER retesting at Mount Sinai - This included demographic information (name, MCP, surgical number, Regional Health Authority) as well as original ER/PR scoring and contained 111 of records.

***d) Mount Sinai ER/PR Retesting File***

On July 18, 2007, the Department of Health and Community Services requested from Mount Sinai Hospital a list of all breast cancer patients who had been sent for retesting. This file was received by the Centre on August 17, 2007 and contains demographic information (name, surgical number, block number, site/region [health care facility], Mount Sinai reference number [RS#]) as well as ER/PR retest scores.

*e) Mount Sinai Pathology Consultations*

In some cases, tumor tissues for breast cancer patients were individually sent to Mount Sinai for ER/PR retesting which resulted in a full pathology report being generated for each patient. Eastern Health's Laboratory provided the Centre with a copy of these pathology consultation reports. In addition, Eastern Health's Quality and Risk Management Division provided the Centre with a number of Mount Sinai consultation reports which were reviewed by Eastern Health's Laboratory staff. Consultations from both the Eastern Health Laboratory and the Health Quality and Risk Management Division were reviewed to identify unique consults that met the inclusion criteria for the database. The resulting data file contained demographic information including name, surgical number and block number, as well as ER/PR retest scores.

*f) Regional Health Authority Pathology Reports*

At the request of the Department of Health and Community Services, the other Regional Health Authorities (Central, Western, Labrador/Grenfell, Clarenville [part of the former Peninsulas Institutional Board] and Carbonear [part of the former Avalon Institutional Board]) provided the Centre with original pathology reports for all breast cancer patients (1997-2005) that had ER/PR testing. These included both original negative and/or positive ER scoring. The reports contained demographic information (name, MCP, surgical and block number) and, where available, original and retest scores. The name of the pathologist who reported the original ER/PR scores was available from most reports.

*g) Meditech System*

The pathology module of the Meditech system at Eastern Health was used to obtain demographic (e.g. MCP, surgical number, name of the pathologist who reported the original ER/PR only for the St. John's region etc) and clinical information (ER/PR testing and/or retesting scores) to supplement existing sources.

*h) Medical Care Plan (MCP) File*

The MCP registry and Meditech were used to obtain the MCP number for each breast cancer patient.

***i) Mortality System***

Using the mortality system, vital status and date of death were obtained. Causes of death are to be obtained at a later date.

***II) Communication Events***

a) Eastern Health Sources

The following sources were used to identify and document communication events surrounding the ER/PR testing process:

i. *Quality and Risk Management Communication Documents* - used to identify whether an individual was initially contacted regarding the ER/PR retesting process. Information includes the name of the employee who placed the call, the employer, and the date of contact. In addition, information on re-contacting the patient regarding the Mount Sinai results was obtained.

ii. *Panel Letters issued by the Expert Review Panel (Tumor Board)* - The Expert Review Panel consisted of oncologists and pathologists and the Eastern Health's Quality and Risk Management official who reviewed the Mount Sinai ER/PR retest results for those patients whose ER/PR test scores required a clinical review (i.e. changed from negative to positive). The Panel reviewed the results and made recommendations for treatment. A letter was sent to the most responsible physicians (e.g., oncologist, family physician, surgeon) summarizing the Panel's recommendation. The Panel letter includes demographic and clinical information, as well as the date that the Panel reviewed the patients' results and the date that the letter was issued.

iii. *Patient Relations Database (Quality and Risk Management Division)* - a hard copy list compiled and maintained by the Patient Relations Officer at Eastern Health. This list includes information on those individuals who contacted Eastern Health regarding the ER/PR recall process. A summary of the conversation, the dates and suggestions were documented. Demographic information on the caller was also collected.

b) Regional Health Authorities Sources

The Western Regional Health Authority provided the Centre with written documentation on communication events surrounding ER/PR retesting for each individual from their region. The Central Regional Health Authority provided the Centre with similar information in an electronic format (Excel) for both Central East and Central West (former Institutional Boards). The Labrador/Grenfell Regional Health Authority provided the Centre with information on communication events through email communication.

**Database Development Methodology**

In order to develop and create the *ER/PR Patient Listing and Communication Events database*, data standardization, linkages, cross-referencing between various data sources and categorization were carried out:

**Step 1**: Standardization - All variables in each data source (electronic) were standardized in order to ensure proper data linkages (e.g. name, MCP, etc).

**Step 2**: Data Linkage and Cross Referencing – Various data sources were linked via MCP number or name where applicable; discrepancies were investigated using secondary data sources.

*Step 2.1*: Eastern Health Quality and Risk Management August 1st Data and Mount Sinai Data linkage. Since the Mount Sinai file was considered to be a "core source", the purpose of this linkage was to identify potential missing patients/records in the Eastern Health Quality and Risk Management August 1st

file through cross referencing. Any missing cases/records were investigated and documented.

*Step 2.2*: Eastern Health Quality and Risk Management August 1st Data and Mount Sinai Consultations File Linkage. The Mount Sinai Consultations file was considered to be the second "core source"; therefore, this linkage was carried out to identify potential missing patients/records in the Eastern Health Quality and Risk Management August 1st file through cross referencing. Any missing patients/records were investigated and documented.

*Step 2.3*: Eastern Health Quality and Risk Management August 1st Data and Eastern Health Laboratory Written List (A list of deceased breast cancer patients who were ER negative, as well as those individuals who called (or their family called) inquiring about ER retesting at Mount Sinai). This was performed to identify deceased patients who were not on the Eastern Health August 1st Data file and sent to Mount Sinai for retesting. These patients were documented and listed to be added to the final database if they met the inclusion criteria.

*Step 2.4*: Eastern Health Quality and Risk Management August 1st Data and Eastern Health Laboratory Written List (A list of breast cancer patients with ER negative and/or weakly positive [as defined by Eastern Health] for the St. John's region; A list of breast cancer patients with ER negative for other Regional Health Authorities). This linkage was carried out to capture those breast cancer patients who were identified by Eastern Health's Laboratory but were not found in Eastern Health's August 1st Data. In addition, cross referencing between the above linked data files and the Mount Sinai file and Mount Sinai Consultations file was performed in order to identify those who were in the Eastern Health Laboratory file and were not sent to Mount Sinai. These patients were listed and documented to be added to the final database if they met the inclusion criteria.

*Step 2.5*: Eastern Health Quality and Risk Management August 1st and August 3rd Files. The purpose of this linkage was to identify any differences in records/patients between the two files. Any differences were resolved with the use of the other data sources (Meditech, MCP, Mount Sinai file, and Mount Sinai consultations) and documented to be added to the final database if they met the inclusion criteria.

*Step 2.6*: Eastern Health Quality and Risk Management August 1st File and Regional Health Authority Pathology Reports. The pathology reports were reviewed and cross-referenced with Eastern Health's Quality and Risk Management August 1st File. Information (e.g., name of the pathologist, original ER/PR scores etc) was added from the reports and any missing/inaccurate information was addressed and corrected. Any reports that were received by the Centre from the Regional Health Authorities that were not included in Eastern Health's Quality and Risk Management August 1st File were documented and added to the final database if they met the inclusion criteria.

*Step 2.7*: Eastern Health Quality and Risk Management August 1st File and Communications Data. The Communication data for each patient was linked to the demographic and clinical data.

*Step 2.8*: Eastern Health Quality and Risk Management August 1st File and the Centre's Mortality System. This linkage identified the vital status of patients that were in the Centre's Mortality System up to June 2007.

**Database Maintenance**

The Centre is currently maintaining the *ER/PR Patient Listing and Communication Events Database* on behalf of the Department of Health and Community Services. It is recognized that the database will require ongoing maintenance and updating for several months as more data

becomes available. The database is currently in SPSS (Statistical Package for the Social Sciences), which the Centre will use to maintain as the Master File.

Table 1 presents description of variables in the *ER/PR Patient Listing and Communication Events database*.

**Table 1.** Description of the *ER/PR Patient Listing and Communication Events database* variables

| Variable Name | Label | Values |
|---|---|---|
| id | ID | Number given to identify record |
| Name | Patient Name | Patient Name |
| MCP | MCP Number | MCP Number |
| duplicate | Duplicate | To select unique patients (0=duplicate, 1=unique) |
| dob | Date of Birth | Date of Birth (mm/dd/yyyy) |
| gender | Gender | Gender (1=Male; 2=Female) |
| region | RHA | Health Care Facility (1=St. John's; 2=Carbonear; 3=G.B. Cross; 4=Grand Falls; 5=Gander; 6=Western Memorial; 7=Lab/Grenfell; 99=Missing/Unknown) |
| specimen | Specimen # | Specimen (surgical) number assigned by the Health Care Facility |
| Year_spec | Year Specimen Taken | This is the year that the Specimen was taken, based on the Surgical Number |
| RE_Num | Referral number | RE# assigned by Eastern Health to each specimen/block from the regions before being sent for retesting at Mt. Sinai |

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|---|---|---|
| pathol | Name of Pathologist | Name of Pathologist who reported the original ER/PR (categorized) |
| Source | Source of Case | Source of each record (1=Eastern Health August 1 File, 2=Mount Sinai file, 3=Mount Sinai Consultation, 4=Eastern Health Laboratory Lists, 5=Region Reports) |
| date_ms | Date sample sent Mt. Sinai | Date sample sent Mt. Sinai for retesting |
| Date_sent | Date sample sent to Mt. Sinai | Categorized date sample sent to Mount Sinai (1=2005, 2=July 2005, 3=August 2005, 4=September 2005, 5=October 2005, 6=November 2005, 7=December 2005, 8=January 2006, 9=March 2006, 10=April 2006, 11=May 2006, 12=June 2006, 13=July 2006 14=August 2006, 15=July 2007, 16=September 2007, 17=October 2007, 99=Missing/Not Available) |
| date_ent | Date result Mt. Sinai entered Meditech | Date Mt. Sinai results entered in Meditech |
| Entry_date | Date results entered in Meditech | Categorized date entered in Meditech (1=August 2005, 2=September 2005, 3=October 2005, 4=November 2005, 5=December 2005, 6=January 2006, 7=February 2006, 8=March 2006, 9=April 2006, 10=May 2006, 11=June 2006, 12=July 2006 13=August 2006, 14=September 2006, 15=March 2007, 16=May 2007, 17=July 2007, 18=August 2007, 99=Missing/Not Available) |
| Note | Notes | Comments/Notes regarding specimen numbers, ER/PR scores etc |
| num_samples | Number Samples | Did patient have more than one sample tested/retested (1=Yes, 2=No, 99=Unknown) |
| test_NL | Tested in NL | Was sample originally tested in NL (1=Yes, 2=No, 99=Unknown) |
| ORI_ER_results | Categorized Original ER results based on Clinical Practice Guidelines | 1=≤30 for 1997-2000, 2=≤10 for 2001-2005, 9=Questionable, 50=No Ori test, 99=Missing/Unknown |

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|---|---|---|
| ER_ORI_30 | ER-Ori with 30 as Cut-Off | 1=≤30, 2>30, 9=Questionable, 50=No Ori test, 99=Missing/Unknown |
| ER_ORI_10 | ER-Ori with 10 as cut-off | 1=≤10, 2>10, 9=Questionable, 50=No Ori test, 99=Missing/Unknown |
| ori_er | Original ER | Original ER score as reported by Meditech or in Regional Pathology Reports |
| ori_pr | Original PR | Original PR score as reported by Meditech or in Regional Pathology Reports |
| MS_ER_results | Categorized Mt. Sinai ER results based on Clinical Practice Guidelines | 1=≤30 for 1997-2000, 2=≤10 for 2001-2005, 9=Questionable, 10=Pending, 20=DCIS, 30=NT, 40=Other, 99=Missing/Unknown |
| ER_MS_30 | ER-MS with 30 as Cut-Off | 1=≤30, 2>30, 9=Questionable, 10=Pending, 20=DCIS, 30=NT, 99=Missing/Unknown |
| ER_MS_10 | ER-MS with 10 as cut-off | 1=≤10, 2>10, 9=Questionable, 10=Pending, 20=DCIS, 30=NT, 99=Missing/Unknown |
| ms_er | MS ER | Mount Sinai ER score |
| ms_pr | MS PR | Mount Sinai PR score |
| blocks | Block | Pathology block # retested at Mount Sinai |
| rs# | RS # | Mount Sinai research number (assigned number to each specimen submitted for retesting) |
| ms_tumor | MS Tumour | Mount Sinai tumor diagnosis: D-ductal, DL-ductal with lobular features, DT-ductal with tubular features, L-lobular, PAP papillary, DCIS-ductal carcinoma in situ, DCIS/M-ductal carcinoma in situ with microinvasion (<1mm), C-colloid, T-tubular, MCa-metastatic CA,EPAP-encysted papillary in situ carcinoma, DA-ductal carcinoma with apocrine features, EIC-extensive DCIS (>25%), M-metaplastic carcinoma, AC-adenoid cystic carcinoma, CaNOS-unclassified carcinoma, PU-pickup with tumour adherent to tissue and NT-no tumour |
| retest | Retest | Is the Specimen retested? (1=Yes, 2=No, |

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|---|---|---|
| | | 99=Unknown) |
| type_test | Type of test/retest | Categorization base don type of test (1=Ori test neg and retested, 2=Ori test pos and retested, 3=No ori Test/Test at MS only) |
| comm_a | Comment | Comment regarding patient vital status, communication, etc from the Eastern Health Quality and Risk Management August 1st file |
| treatment | Treatment | Categorization based on treatment from comm._a |
| change | Treatment Change | This has been further categorized using the information from comm._a (1=change, 2=no change, 9=Other, 99=Not Applicable) |
| comment | comment | Comment regarding paneling from the Eastern Health Quality and Risk Management August 1st file |
| res_con | Results Contact | Variable from the Eastern Health Quality and Risk Management August 1st file |
| ori_con | Original Contact | Variable from the Eastern Health Quality and Risk Management August 1st file |
| other_is | Other issues | Variable from Eastern Health Quality and Risk Management August 1st file |
| Con_retesting | Contact re retesting | Whether the patient was initially contacted regarding the ER/PR retesting process (Yes/No) |
| Date_Con_Retest | Date patients informed Retesting | The date of contact if the initial contact was made with the patient regarding the ER/PR retesting process |
| Person_Con_Retest | Person informed patient retesting | Person who made the initial contact with the patient regarding the ER/PR retesting process |
| Employer | Employer | Employer of the person who made the initial contact with the patient regarding the ER/PR retesting process |
| panel | Panel | Was patient paneled (1=Yes, 2=No, 99=Unknown) |

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| letter | Letter | Is there a panel letter? (1=Yes, 2=No) |
| Date_panel | Date Panel Review | The date that patient was paneled (note: not all patients were paneled) |
| Date_panel_letter | Date panel letter sent to physician | The date the panel letter was issued and sent |
| Contact | Contact | Was patient contacted before receiving results (1=Yes, 2=No, 99=Unknown) |
| Date_Con_Pt | Date patients (no conversion) contacted re results | Date patient was contacted regarding the Mount Sinai results (mostly for those whose their ER/PR results were changed) |
| Comment_Communication | Comments/Notes on Communications | Extra communication information regarding the processing and/or results (e.g., patient/family called in etc) |
| Verification | Verification | Verification that doctor reviewed results with patient |
| vital_stat | Vital status | 1=Deceased, 2=Alive |
| dod | Date of death | Date of death |
| year_death | Year of Death | Year of Death |