

Adherence to Human Epidermal Growth Factor Receptor-2 (HER2) Testing & Adjuvant Treatment Guidelines in Ontario

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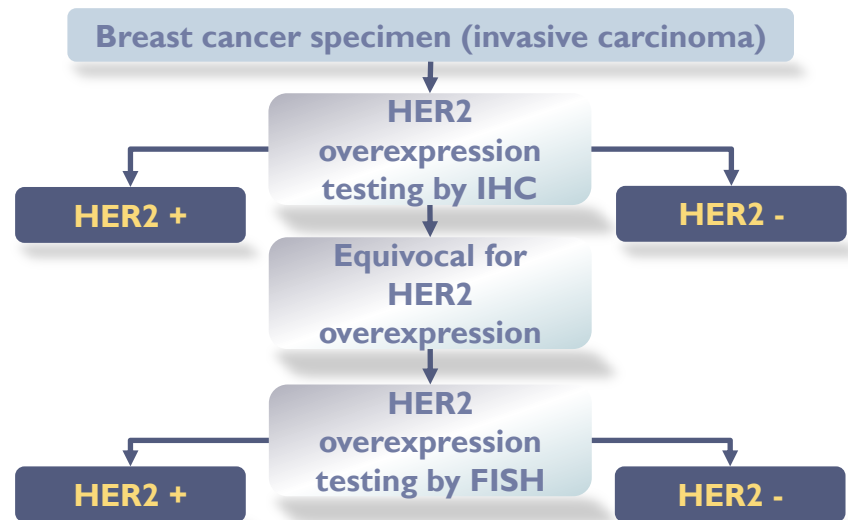
Background on HER2 Testing

HER2 Testing

- ▶ Alternative tests available for human epidermal growth factor receptor-2 (HER2) diagnosis:
 1. **Immunohistochemistry (IHC)**
 - ▶ Easiest to perform, least cost alternative
 2. **Fluorescence in situ hybridisation (FISH)**
 - ▶ Gold standard but 3-4 time the cost of IHC
- ▶ Trastuzumab (Herceptin) indicated for HER2 positive early-stage and metastatic breast cancer (BC)

Canadian Guidelines

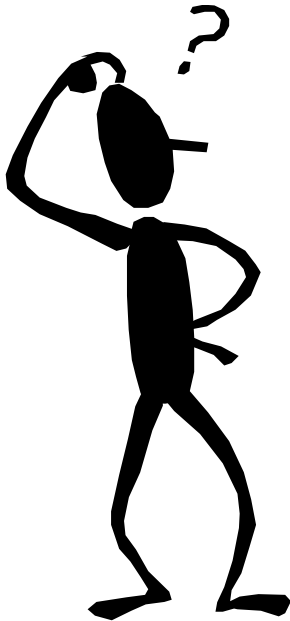
(all early BC invasive carcinomas)



- ▶ Ontario has provincial HER2 testing validation program
- ▶ Trastuzumab only reimbursed with evidence of positive HER2 test (NDFP)

HER2 Testing in Practice

- ▶ Older patients with smaller tumours were less likely to have a HER2 test in Nova Scotia chart review
- ▶ US-based payor studies demonstrate HER2 test rates ranging from 32% to 97% of incident BC patients had a documented test



- ▶ **Much remains unknown in Canada:**

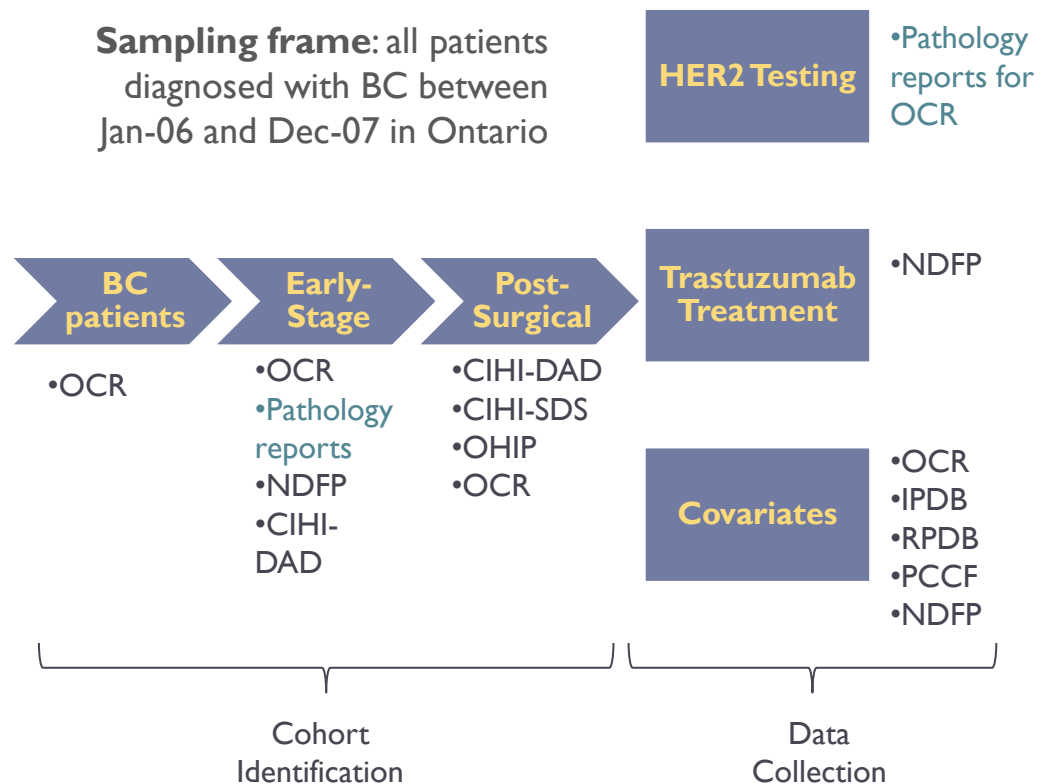
- ▶ *Do all early-stage BC patients get tested at diagnosis?*
- ▶ *What tests are used?*
- ▶ *Is confirmatory testing provided to all equivocal cases?*
- ▶ *How is TRA used given test results?*

Study Rationale & Design: Ontario

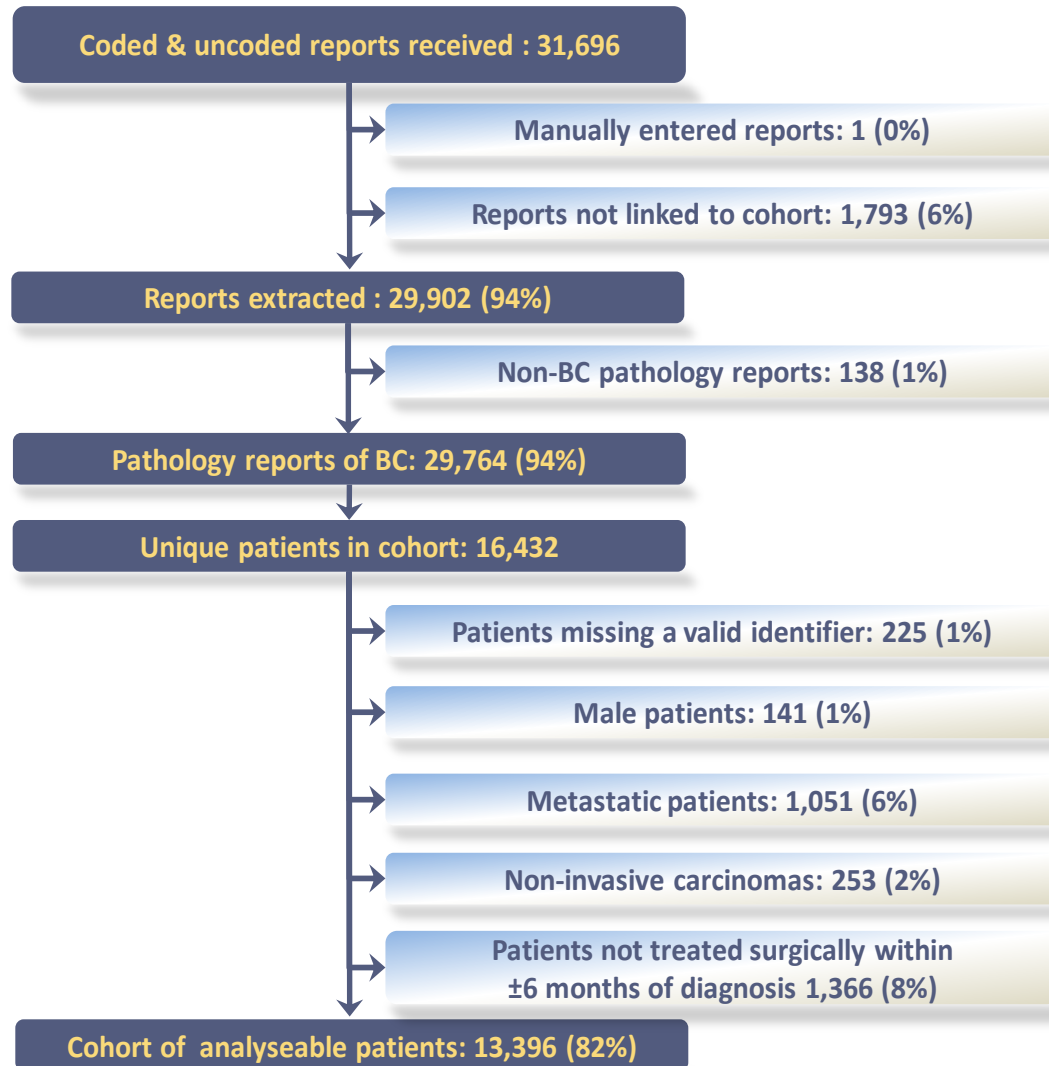
Research Objectives

1. Document HER2 testing & treatment practices for early-stage BC patients
2. Assess adherence to testing & trastuzumab treatment guidelines in Ontario
 - 2.1 Testing:
 - 2.1.1 All patients should receive a HER2 test
 - 2.1.2 All IHC equivocal patients should be retested with FISH
 - 2.2 Treatment : only patients with evidence of a positive HER2 test should get trastuzumab

Retrospective Cohort Data Creation Plan



Results: Cohort & Pathology Review



Results: Cohort Descriptives (1)

Descriptive		Percent of Cohort (n=13,396)
Age at Diagnosis, Mean (SD)		61 y (14 y)
	0-39	5% (628)
	40-49	18% (2,406)
	50-59	25% (3,376)
	60-69	24% (3,149)
	70-79	18% (2,449)
	80+	10% (1,388)
Diagnosis Year		
	2006	49% (6,622)
	2007	51% (6,774)
Vital Status		
	Alive at end of follow-up	95% (12,704)
Laterality		
	Left	44% (5,835)
	Right	47% (6,250)
	Bilateral	2% (302)

- ▶ Age at diagnosis, laterality representative of an Ontario BC population
- ▶ Follow-up data to March 2009

Results: Cohort Descriptives (2)

Descriptive	Percent of Cohort (n)
Stage at Diagnosis	
I	35% (4,712)
II	32% (4,319)
III	10% (1,358)
Unknown	22% (3,007)
Urbanicity	
Urban	87% (11,706)
Rural	13% (1,688)
Breast Conserving Surgery	60% (8,048)
Radiation Treatment	67% (8,966)
Prior Comorbidity	7% (988)
HER2 Test Documented	66% (8,854)

- ▶ Stage at diagnosis, breast conserving surgery representative of an Ontario BC population
- ▶ Significant missing proportion in centrally-reported pathology
- ▶ Inconclusive results for Research Objective 2.1.1 (test access)
 - ▶ HER2 not a mandatory registry reporting element in 06-07

Results: Research Objective 2.1.2

Confirmation of IHC Equivocal (2+) Results with FISH

Covariate	Adjusted ^a OR of 2 nd FISH Test
1st HER2 test result	
equivocal vs. positive	115.8*
negative vs. positive	0.6*
unknown vs. positive	0.1*
Prior Comorbidity (Charlson)	
≥1 vs. 0	1.19
Age (years)	
50-69 vs. <50	1.0
≥70 vs. <50	0.9
Stage at Diagnosis	
II vs. I	1.2
III vs. I	1.5*
OR: odds ratio	
^a adjusted for variation in practice by LHIN	
*significant, p<0.05	
Number of observations = 7,069	

Results: Research Objective 2.2

TRA Usage

Covariate		Adjusted ^a OR of TRA Treatment
HER2 Status		
	equivocal vs. positive	0.1*
	negative vs. positive	0.002*
	unknown vs. positive	0.1*
Age (years)		
	50-69 vs. <50	0.9
	≥70 vs. <50	0.5*
Grade		
	2 vs. 1	2.5*
	3 vs. 1	3.4*
Hormone Receptor Status		
	negative vs. positive	1.6*
	unknown vs. positive	1.5*
Breast Conserving Surgery		
	conserving vs. non-conserving	0.75*
Physician Specialty		
	GP/FP vs. medical oncologist	1.2
	other vs. medical oncologist	0.1*

OR: odds ratio, *significant, p<0.05

^a adjusted for LHIN, urbanicity, socioeconomic status, prior comorbidity, stage

Number of observations = 3,586

Interpretation & Discussion

- 1. Despite challenges in assessing access to HER2 testing, we identified a cohort of almost 9,000 early-stage BC patients with centrally-reported HER2 documentation.*
- 2. We have observed a high degree of adherence to HER2 testing and trastuzumab treatment guidelines in Ontario.*
- 3. Socioeconomic factors did not predict confirmatory testing or trastuzumab utilisation, as expected in the publicly funded Ontario environment.*
- 4. Clinical indicators of lower trastuzumab utilisation are generally reflective of chemotherapy utilisation in general.*

Thank you

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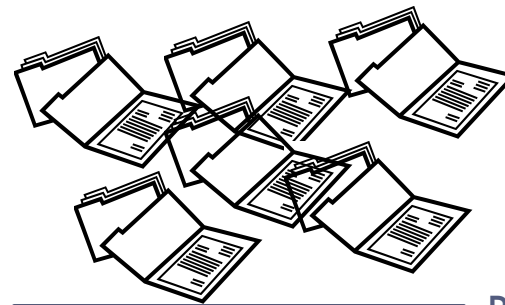
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Extra Slides

Pathology Report Challenges

Data Sought:

- HER2 test(s) provided
- HER2 test type(s)
- HER2 status
- Hormone receptor status
- Staging
- Histology



Electronic & faxed surgical & laboratory pathology reports

OCR Case Resolution Filter (PIMs)

Reportable Elements

- Invasive
- Incident
- Tissue type
- ICD
- Vital status

HER2 is not a reportable element for OCR



Linkage

OCR group no.

“Coded” pathology reports

- 27,051 rec'd & reviewed
- 2,070 “manually entered”
- Searchable by HIN, registry group #, ICD code

“Un-coded” pathology reports

- OHIN (~90%)
- identified by HER2 keyword search, HIN
- Received 4,645; 1,793 not in cohort

HER2 & TRA Utilisation Descriptives

- ▶ **HER2 test types among tested patients (8,854):**
 - ▶ 69% received IHC alone
 - ▶ 3% received FISH alone
 - ▶ 14% received IHC & FISH
 - ▶ 4% unclear test method reported
 - ▶ 90% other test combinations, >2 tests
- ▶ **HER2 prevalence at 13% of tested patients in cohort**
- ▶ **Trastuzumab utilisation:**
 - ▶ 61% of HER2+ treated with TRA
 - ▶ 29% of TRA treated lacked H2N documentation

Additional Results: Research Objective 2

Confirmation of IHC Negative (0,1+) Results with FISH

Covariate		Adjusted ^a OR of 2 nd FISH Test Among IHC Negative
Age (years)		
	50-69 vs. <50	0.8
	≥70 vs. <50	0.7
Stage at Diagnosis		
	II vs. I	1.3
	III vs. I	1.7*
OR: odds ratio ^a adjusted for variation in practice by LHIN *significant, p<0.05 Number of observations = 4,228		

HER2 Testing in Ontario

- ▶ Alternative tests available for human epidermal growth factor receptor-2 (HER2) diagnosis:

	IHC (immunohistochemistry)	FISH (fluorescence <i>in-situ</i> hybridisation)
Cost	<\$100	\$300 - \$400
Sensitivity	-	+
Specificity	-	+
Ease of Conduct	Can be performed in majority of diagnostic labs	Requires specially trained personnel & often performed at centralized laboratory

- ▶ Trastuzumab (Herceptin) indicated for HER2 positive early-stage and metastatic breast cancer (BC)