



# **Examining Subsequent Occurrence and Outcomes of Estrogen-related Cancers (Breast and Thyroid) in Missouri Women**

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# Background

- Both breast and thyroid cancers occur primarily in females and both are estrogen-related
- Females diagnosed with either breast or thyroid cancer are more likely to develop the other cancer
- Because thyroid cancer has a relatively low mortality and breast cancer survival is high, follow up and treatment for this growing group of survivors is particularly important



# Background cont.

- Association between synchronous neoplasms of breast cancer and thyroid cancer in 1966

(Chalstrey LJ, Benjamin B. High incidence of breast cancer in thyroid cancer patients. Br J Cancer. 1966;20:670–675.)

- SEER reported a significant increased risk of developing breast cancer for premenopausal females (age 20-49) with a history of thyroid cancer

(Chen AY, Levy L, Goepfert H, et al. The development of breast carcinoma in women with thyroid carcinoma. Cancer. 2001;92:225–231)

- Breast was reported as the most common site of secondary cancers following a primary thyroid cancer

(Kim C, Bi X, Pan D, et al. The risk of second cancers after diagnosis of primary thyroid cancer is elevated in thyroid microcarcinomas. Thyroid. 2013;23:575–582)



# Background cont.

- Curtis RE, Freedman DM, Ron E, Ries LAG, Hacker DG, Edwards BK, Tucker MA, Fraumeni JF Jr. (eds). **New Malignancies Among Cancer Survivors: SEER Cancer Registries, 1973-2000**. National Cancer Institute, NIH Publ. No. 05-5302. Bethesda, MD, 2006.
- American Cancer Society. **Cancer Facts & Figures 2009**. Atlanta: American Cancer Society; 2009.
  - Special Section: Multiple Primary Cancers, Cancer Facts and Figures 2009



# Purpose

- Evaluate the risk of developing:
  - Thyroid (& breast) cancer after being diagnosed with breast cancer
  - Breast (& thyroid) cancer after being diagnosed with thyroid cancer
- Evaluate survival outcomes of these subsequent cancers



# Methods

- We examined demographic (age at diagnosis, race, county of residence) and tumor-related characteristics (stage, time between diagnoses) of females with both thyroid and breast cancer in the central cancer registry database
- All female patients with breast cancer, thyroid cancer or both breast and thyroid cancer from 2005 to 2014 are included



# Methods – SIRs

- Standardized Incidence Ratios (SIRs) calculated via SEER\*Stat
- Case selection:
  - Female
  - Breast or thyroid
  - Malignant
  - Diagnosed 2005-2014
  - Known age, county, race
  - Exclude DCO/autopsy
- Follow-up through 2015, excluding 1<sup>st</sup> 2 months



# Methods – SIRs

- Expected counts based on rates by
  - Age (20 groups in 5-year spans)
  - Sex (female only)
  - Race (WBO)
  - ACS 2008-2012 county % persons below poverty (<10, 10-<20, 20+)
  - Rural-Urban Continuum Code 2013 (Metro, Urban non-metro, completely rural or small urban)
  - Year of diagnosis (2005-2009, 2010-2014)





# Methods – survival

- Cox proportional hazards (all-cause)
- 4 analyses:
  - Survival of *subsequent* breast cancer (after an initial breast cancer) vs breast cancer in general
    - (breast → breast) vs breast
  - Survival of a subsequent thyroid cancer after breast cancer vs thyroid cancer in general
    - (breast → thyroid) vs thyroid
  - Survival of *subsequent* thyroid cancer (after an initial thyroid cancer) vs thyroid cancer in general
    - (thyroid → thyroid) vs thyroid
  - Survival of a subsequent breast cancer after thyroid cancer vs breast cancer in general
    - (thyroid → breast) vs breast



# Methods – survival

- Controlling for (based on subsequent tumor for the group of interest):
  - Year of diagnosis
  - Age at diagnosis (5-year spans, but <39 & 85+)
  - Race (WBO)
  - Stage at diagnosis (LRDU)
  - County % persons in poverty / MUR2013 in 7 groups:
    - <10% / Metro
    - 10 - <20% / Metro
    - ≥20% / Metro
    - 10 - <20% / Urban, non-metro
    - ≥20% / Urban, non-metro
    - 10 - <20% / Rural or small urban
    - ≥20% / Rural or small urban
  - ER/PR status (only for breast cancer survival)



# Methods – survival (time-varying)

- Alternatively, Cox models with time-varying were also examined
- Same covariates (but based on the first tumor)
- For both subsequent breast & subsequent thyroid cancers: A time-varying covariate is introduced to indicate when (if ever) the patient was diagnosed with it
- 4 runs in proc phreg:
  - Initial **breast** cancer cohort with subsequent **breast** indicator
  - Initial **breast** cancer cohort with subsequent **thyroid** indicator
  - Initial **thyroid** cancer cohort with subsequent **breast** indicator
  - Initial **thyroid** cancer cohort with subsequent **thyroid** indicator



# Results – SIRs, breast

	Cohort	Subsequent breast SIR	Subsequent thyroid SIR
	<b>All breast</b>	<b>1.09 (1.01, 1.17)</b>	<b>1.76 (1.42, 2.15)</b>
Race	White	1.00 (0.93, 1.09)	<b>1.78 (1.43, 2.21)</b>
	Black	<b>1.82 (1.5, 2.18)</b>	1.39 (0.51, 3.02)
Year of dx	2005-2009	<b>1.19 (1.09, 1.29)</b>	<b>1.59 (1.20, 2.07)</b>
	2010-2014	0.88 (0.76, 1.01)	<b>2.09 (1.46, 2.89)</b>
Age at dx	00-39	<b>4.57 (3.24, 6.38)</b>	1.96 (0.64, 4.57)
	40-49	<b>1.40 (1.13, 1.72)</b>	<b>2.04 (1.27, 3.13)</b>
	50-69	1.01 (0.91, 1.11)	<b>1.63 (1.21, 2.16)</b>
	70+	1.00 (0.88, 1.14)	<b>1.78 (1.03, 2.84)</b>
Stage	Localized	1.05 (0.96, 1.15)	<b>1.53 (1.14, 2.01)</b>
	Regional	<b>1.15 (1.01, 1.31)</b>	<b>2.19 (1.53, 3.03)</b>
	Distant	1.29 (0.81, 1.95)	2.13 (0.44, 6.23)



# Results – SIRs, breast

	Cohort	Subsequent breast SIR	Subsequent thyroid SIR
Latency	<1 year	<b>1.20 (1.01, 1.43)</b>	<b>2.58 (1.64, 3.87)</b>
	1 - <5 years	<b>0.82 (0.73, 0.91)</b>	<b>1.85 (1.40, 2.41)</b>
	5 - <10 years	<b>1.58 (1.40, 1.77)</b>	1.00 (0.53, 1.71)
Poverty %	<10	1.16 (0.95, 1.41)	1.31 (0.65, 2.34)
	10 - <20	1.05 (0.96, 1.14)	<b>1.86 (1.45, 2.34)</b>
	20+	<b>1.23 (1.00, 1.18)</b>	1.71 (0.78, 3.25)
RUCC2013	Metro	<b>1.06 (1.00, 1.18)</b>	<b>1.71 (1.33 2.17)</b>
	Urban, non-metro	1.06 (0.90, 1.25)	<b>1.90 (1.16, 2.94)</b>
	Rural or small urban	1.11 (0.74, 1.61)	1.90 (0.52, 4.87)



# Results – SIRs, thyroid

	Cohort	Subsequent breast SIR	Subsequent thyroid SIR
	<b>All thyroid</b>	1.14 (0.90, 1.43)	1.67 (0.89, 2.86)
Race	White	1.17 (0.91, 1.49)	1.69 (0.87, 2.95)
	Black	0.89 (0.29, 2.08)	^
Year of dx	2005-2009	1.13 (0.84, 1.49)	1.32 (0.53, 2.73)
	2010-2014	1.16 (0.73, 1.74)	2.41 (0.88, 5.24)
Age at dx	00-39	1.09 (0.35, 2.53)	^
	40-49	<b>1.65 (1.02, 2.53)</b>	1.8 (0.86, 3.31)
	50-69	0.91 (0.63, 1.28)	^
	70+	1.33 (0.75, 2.20)	^
Stage	Localized	1.17 (0.89, 1.51)	1.68 (0.81, 3.09)
	Regional	1.12 (0.61, 1.88)	^
	Distant	^	^



# Results – SIRs, thyroid

	Cohort	Subsequent breast SIR	Subsequent thyroid SIR
Latency	<1 year	0.87 (0.38, 1.71)	<b>6.64 (2.86, 13.07)</b>
	1 - <5 years	1.19 (0.86, 1.60)	^
	5 - <10 years	1.15 (0.72, 1.74)	^
Poverty %	<10	<b>1.80 (1.10, 2.79)</b>	^
	10 - <20	0.99 (0.73, 1.31)	1.8 (0.86, 3.31)
	20+	1.13 (0.46, 2.33)	^
RUCC2013	Metro	1.17 (0.89, 1.51)	1.33 (0.57, 2.62)
	Urban, non-metro	1.09 (0.59, 1.82)	^
	Rural or small urban	^	^



# Results – survival

- (breast → breast) vs breast
  - HR 1.57 (p-val <.0001); 605 cases in group of interest
- (breast → thyroid) vs thyroid
  - HR 1.36 (p-val .3491); 78 cases in group of interest
- (thyroid → thyroid) vs thyroid
  - HR 0.73 (p-val .6650); 13 cases in group of interest
- (thyroid → breast) vs breast
  - HR 2.24 (p-val .0075); 61 cases in group of interest





# Results – survival (time-varying)

- Initially diagnosed with **breast** cancer
  - Subsequent **breast** indicator: HR 1.88 (p-val <.0001)
  - Subsequent **thyroid** indicator: HR .69 (p-val .2362)
- Initially diagnosed with **thyroid** cancer
  - Subsequent **breast** indicator: 3.82 (p-val <.0001)
  - Subsequent **thyroid** indicator: HR .76 (p-val .7014)



# Conclusion

- Increase of developing either breast or thyroid cancer as a second malignancy after a diagnosis with one of the cancers
- For breast→breast cancer, the risk begins to increase after about the first 5 years after diagnosis
- Targeted follow up of patients with either breast or thyroid cancer can be beneficial for outcomes
- Survival for subsequent breast tumors is worse; not statistically significantly different for thyroid (small number of cases)



Questions ?



# Contact & acknowledgments

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# Revisions since presenting

- ❖ rev06, 2018-07-05:
  - ❖ Title slide (#1): Typo corrected in JJT's degrees (MSPH, not MPH).
- ❖ rev05:
  - ❖ Presented at the 2018 NAACCR conference in Pittsburgh, PA on 13 June 2018.