

ABSTRACT

Background: Colorectal cancer (CRC) is the second most frequent (12.2%) cancer and the second leading cause of death (13.5%) among women in Puerto Rico (PR). Between 1987 and 2012, secondary malignancies comprised 14.8% of all female cancer cases in PR; of those, 3.0% were CRC. The propose of this study is to estimate the risk of developing CRC among women who had survived 2 months or longer after the diagnosis of primary breast, ovary, cervix uteri, or corpus and uterus between 1987 and 2012. **Methods:** Standardized incidence ratios (SIR) and excess absolute risk (EAR) were calculated for CRC using SEER*Stat 8.2.1 MP-SIR. **Results:** A total of 511 secondary CRC were identified after diagnosis of primary cancer of the breast (64.2%), corpus and uterus (19.4%), cervix uteri (9.0%), or ovary (8.0%). Overall, for all primary sites, the risk of developing secondary CRC is significantly higher after 10 years of follow-up. The risk of developing secondary CRC was significantly higher for ovarian cancer (SIR=6.5, EAR=43.8) followed by corpus and uterus (SIR=4.0, EAR=31.5), cervix (SIR=3.6, EAR=19.1), and breast (SIR=2.5, EAR=14.2). Overall, for ovary and cervix, the risk is higher for women <40 years old; but for breast and corpus and uterus, the risk is higher for women 40-59 years old. Women aged <40 years who survived ovarian cancer between 2 months to 1 year had a higher risk of secondary CRC compared with age groups; women aged 60+ years who survived breast cancer between 2 months to 1 year had a higher risk of secondary CRC compared with other age groups. **Conclusions:** Women with primary ovarian cancer had a significant higher risk of developing CRC than women with primary breast, cervix, and corpus and uterus. Women in PR with an initial cancer diagnosis of ovary, breast, corpus and uterus, and cervix should be monitored carefully for the occurrence of a secondary CRC.

INTRODUCTION AND AIM

- The population of cancer survivors has increased as a result of early detection and advances in treatments.
- A major medical concern for cancer survivors is the risk of developing a new primary cancer (secondary primary cancer).
- In Puerto Rico, between 1987 and 2012, secondary malignancies comprised 15% of all female cancer cases; of those, 3% were CRC.
- CRC is the second most frequent (12.2%) cancer and the second leading cause of death (13.5%) among women in Puerto Rico.
- The purpose of this study is to estimate the risk of developing CRC among women who had survived 2 months or longer after the diagnosis of a primary breast or gynecological cancers (corpus and uterus, ovary, or cervix uteri) (BGC) between 1987 and 2012.

DATA AND METHODS

First primary BGC diagnosed during 1987-2012 from the Puerto Rico Central Cancer Registry (PRCCR) were included (N=47,261). Cases with unknown age and unknown diagnostic confirmation were excluded. Secondary colorectal cancers (SCRC) were defined as those reported after 2 months of surviving a primary BGC. Standardized incidence ratios (SIR) and excess absolute risk (EAR) were calculated for CRC using SEER*Stat 8.2.1 MP-SIR. SIR (observed/expected) is a measure of the risk of developing a second cancer relative to the general population. Statistical significance was set at $p < 0.05$.

RESULTS

Risk of SCRC among Survivors* of a BGC Cancer in Puerto Rico, 1987-2012

| Follow-up → Age ↓ | <1 year | | 1 - 4 year | | 5 – 9 year | | 10 + year | | Total | |
|----------------------|----------------|------|----------------|------|----------------|------|-----------------|------|----------------|------|
| | SIR (95%CI) | EAR | SIR (95%CI) | EAR | SIR (95%CI) | EAR | SIR (95%CI) | EAR | SIR (95%CI) | EAR |
| Breast | | | | | | | | | | |
| <40 | 0.0 – | -0.3 | 0.0 – | -0.7 | 0.0 – | -1.4 | 5.0# (1.0-14.6) | 14.8 | 2.3 (0.5-6.6) | 1.6 |
| 40-59 | 1.9 (0.7-3.8) | 3.2 | 2.5# (1.8-3.5) | 8.1 | 2.4# (1.6-3.4) | 11.5 | 3.7# (3.0-5.0) | 32.2 | 2.7# (2.3-3.3) | 12.0 |
| 60+ | 1.9# (1.3-2.8) | 12.7 | 2.1# (1.7-2.6) | 14.7 | 2.5# (1.9-3.2) | 21.2 | 3.4# (2.4-4.7) | 34.8 | 2.3# (2.0-2.7) | 18.5 |
| Overall | 1.9# (1.3-2.6) | 7.5 | 2.2# (1.8-2.6) | 10.6 | 2.4# (2.0-3.0) | 15.2 | 3.6# (2.9-4.4) | 31.8 | 2.5# (2.2-2.7) | 14.2 |

| | | | | | | | | | | |
|-------------------------------|----------------|------|-----------------|------|-----------------|------|-----------------|------|----------------|------|
| Corpus and Uterus, NOS | | | | | | | | | | |
| <40 | 0.0 – | -0.3 | 0.0 – | -1.0 | 15.4 (0.4-86.0) | 18.0 | 0.0 – | -3.2 | 4.0 (0.1-22.3) | 4.0 |
| 40-59 | 3.5 (0.4-12.7) | 10.8 | 6.2# (3.4-10.4) | 32.0 | 3.1# (1.3-6.4) | 19.9 | 8.1# (4.9-12.7) | 92.0 | 5.7# (4.1-7.7) | 37.6 |
| 60+ | 2.0 (0.8-4.4) | 14.2 | 3.3# (2.2-4.9) | 31.8 | 3.4# (1.8-5.7) | 33.2 | 4.3# (2.2-7.7) | 48.1 | 3.3# (2.5-4.2) | 31.4 |
| Overall | 2.3 (1.0-4.5) | 11.9 | 4.0# (2.8-5.4) | 29.3 | 3.4# (2.1-5.2) | 26.4 | 6.0# (4.0-8.5) | 63.1 | 4.0# (3.2-4.9) | 31.5 |

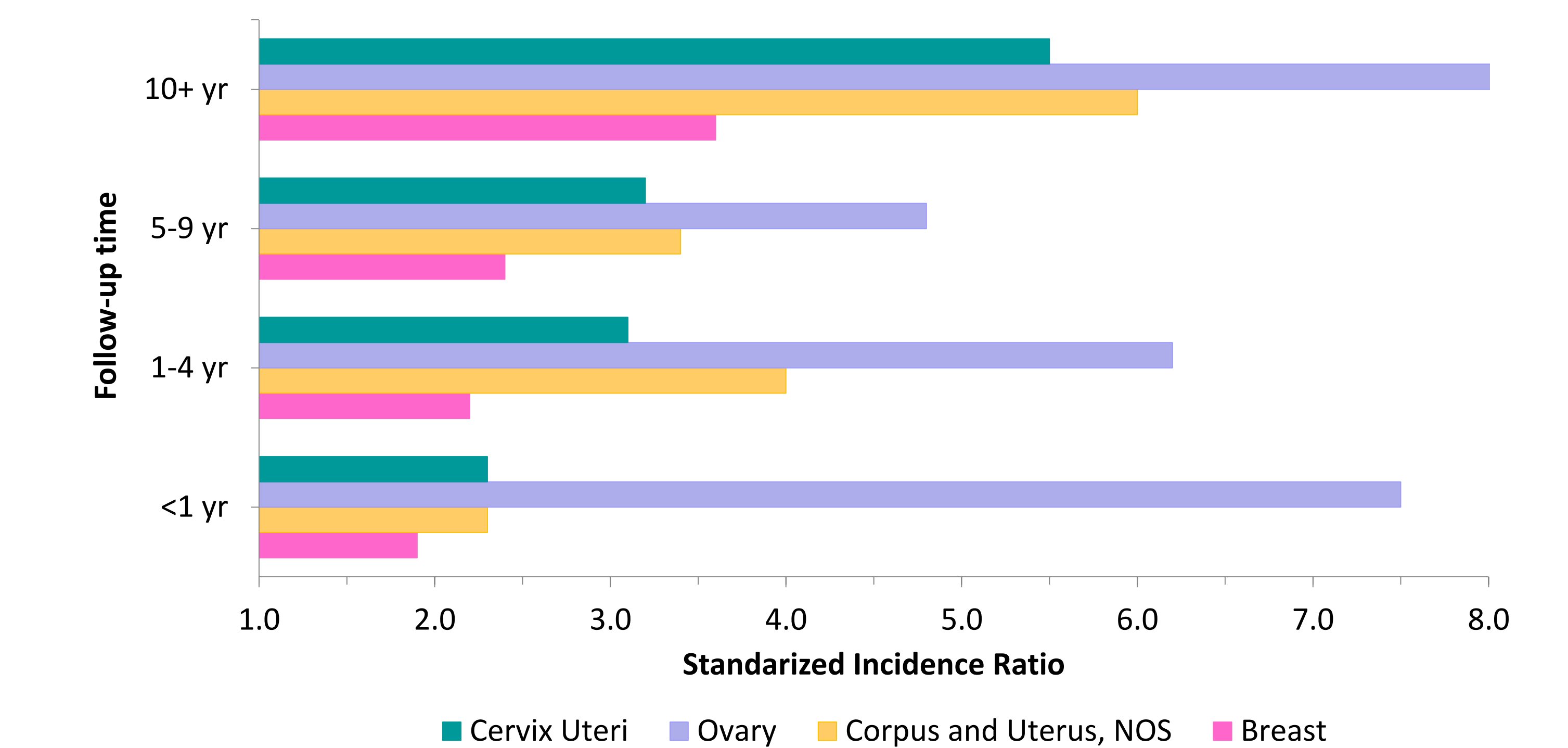
| | | | | | | | | | | |
|--------------|-----------------------|-------|------------------|------|------------------|------|------------------|-------|------------------|------|
| Ovary | | | | | | | | | | |
| <40 | 551.5# (113.7-1611.7) | 123.8 | 0.0 – | -0.4 | 33.1 (0.8-184.1) | 23.0 | 0.0 – | -1.8 | 34.2# (9.3-87.5) | 23.5 |
| 40-59 | 13.3# (2.7-38.8) | 47.7 | 13.6# (6.5-25.1) | 64.7 | 4.1 (0.5-14.9) | 23.3 | 13.3# (4.9-28.9) | 141.0 | 11.1# (6.9-16.9) | 62.5 |
| 60+ | 3.1 (0.6-9.0) | 28.1 | 3.5# (1.4-7.2) | 34.2 | 4.1 (0.8-12.0) | 43.1 | 4.6 (0.6-16.6) | 52.3 | 3.6# (2.0-6.0) | 36.1 |
| Overall | 7.5# (3.4-14.2) | 50.5 | 6.2# (3.6-9.9) | 39.6 | 4.8# (1.8-10.5) | 29.7 | 8.5# (3.7-16.8) | 72.1 | 6.5# (4.7-8.9) | 43.8 |

| | | | | | | | | | | |
|---------------------|----------------|------|-----------------|------|----------------|------|------------------|------|------------------|------|
| Cervix Uteri | | | | | | | | | | |
| <40 | 0.0 – | -0.3 | 10.4 (0.3-57.9) | 5.7 | 9.7 (0.3-54.1) | 10.5 | 25.0# (6.8-63.9) | 71.4 | 16.0# (5.8-34.6) | 15.3 |
| 40-59 | 2.5 (0.1-13.7) | 4.7 | 5.2# (2.1-10.7) | 18.4 | 3.6# (1.2-8.5) | 19.6 | 5.1# (2.2-10.0) | 46.8 | 4.5# (2.8-6.8) | 21.6 |
| 60+ | 2.3 (0.5-6.8) | 17.5 | 1.9 (0.7-4.2) | 12.5 | 2.4 (0.6-6.0) | 18.6 | 3.5 (0.9-8.8) | 35.4 | 2.4# (1.4-3.8) | 18.3 |
| Overall | 2.3 (0.6-6.0) | 7.8 | 3.1# (1.7-5.2) | 13.6 | 3.2# (1.5-5.8) | 17.3 | 5.5# (3.2-9.0) | 48.3 | 3.6# (2.6-4.8) | 19.1 |

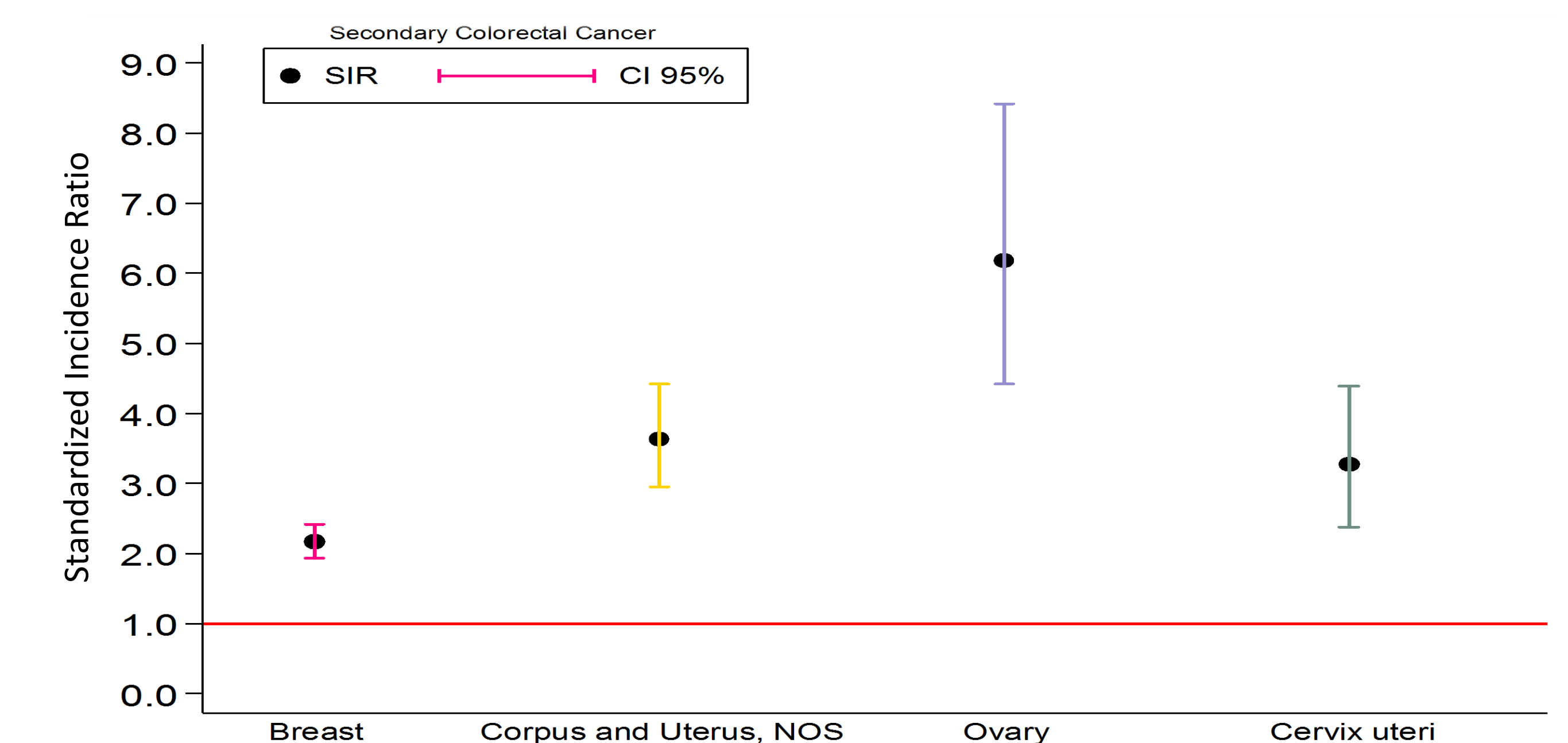
*Females diagnosed with first primary cancer who survived 2 months or longer following diagnosis. SIR: O/E = observed number of subsequent primary cancers/expected number of subsequent primary cancer; # $p < 0.05$, O/E is statistically significant. Excess absolute risk (EAR) = (O-E)*10,000/person-years at risk.

- A total of 511 SCRC were identified after diagnosis of primary cancer of the breast (64.2%), corpus and uterus (19.4%), cervix uteri (9.0%), or ovary (8.0%).
- Overall, for all primary sites, the risk of developing SCRC is significantly higher after 10 years of follow-up.
- The risk of developing SCRC was significantly higher for ovarian cancer (SIR=6.5, EAR=43.8) followed by corpus and uterus (SIR=4.0, EAR=31.5), cervix (SIR=3.6, EAR=19.1), and breast (SIR=2.5, EAR=14.2).
- Overall, for ovary (SIR=34.2, EAR=23.5) and cervix (SIR=16.0, EAR=15.3) the risk is higher for women aged <40 years old, but for breast (SIR=2.7, EAR=12.0) and corpus and uterus (SIR=5.7, EAR=37.6), the risk is higher for women aged 40-59 years old.
- Women aged <40 years who survived ovarian cancer between 2 months to 1 year had a higher risk (SIR=551.5, EAR=123.8) of SCRC compared with other age groups; however women aged 60+ years who survived breast cancer between 2 months to 1 year had a higher risk (SIR=1.9, EAR=7.5) of SCRC compared with other age groups.
- The EAR of SCRC among breast and cervix uteri increased over time. While for corpus and uterus, and ovary there was some variations over time.

Standardized Incidence Ratio by Follow-up Time of SCRC among Survivors of BGC in Puerto Rico, 1987-2012



Standardized Incidence Ratio of SCRC after a BGC Diagnosis in Puerto Rico, 1987-2012



CONCLUSIONS

Women with primary ovarian cancer had a significant higher risk of developing CRC than women with primary cancer of breast, cervix, and corpus and uterus ($p < 0.05$). For breast cancer there is a significant risk of SCRC in all age groups after one year of follow up. This risk (EAR) increased in magnitude with length of follow-up. Women in PR with an initial cancer diagnosis of BGC should be monitored carefully for the occurrence of a SCRC. Future research is needed to identify the patients at highest risk of developing a secondary malignancies to aim prevention and screening efforts, and planning for future healthcare needs among cancer survivors. Understanding survivors' health status and behaviors is also important.