

# BREAST CANCER

**Table 10.1: Characteristics of the cohort**

	Females
First primary cancer	49,441
Age at diagnosis	
Mean	60.2
<65 years	30,632
=>65 years	18,809
Total person-years	335,061
Mean follow-up (years)	6.8
Histological confirmation (%)	96.6
Adenocarcinoma	92.5
Other specific carcinoma	0.1
Unspecified carcinoma	3.5
Other specified types	0.4
No histological confirmation	3.4
Second primary cancers	
Non-simultaneous	4707
Simultaneous	1024

**Table 10.2: Cumulative risk (%) of the most common second primary cancers**

	Sex	Follow-up years					
		1	5	10	15	20	23
All cancers	F	1.0	5.2	10.2	13.8	16.7	17.9
Colon	F	0.1	0.5	1.0	1.4	1.7	2.2
Melanoma	F	0.1	0.3	0.6	0.7	1.0	1.0
Breast	F	0.4	2.2	4.3	5.7	6.9	7.1
Uterus	F	0.1	0.3	0.8	1.1	1.3	1.3

*All other cancers have 10-year cumulative risk of less than 0.5 %.*

## Common second cancers

From Table 10.2 a woman's 10-year cumulative risk of contracting a second cancer following breast cancer is seen to be 1 in 10. Cancers with a 10 year cumulative risk of greater than 0.5% are breast, colon, uterus and melanoma.

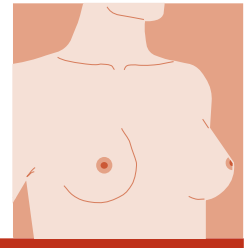
## Age-specific Incidence

The principal feature of Figure 10.1 is that the age incidence curves for the second primary cancers are orders of magnitude higher at all ages though the curves begin to converge in old age.

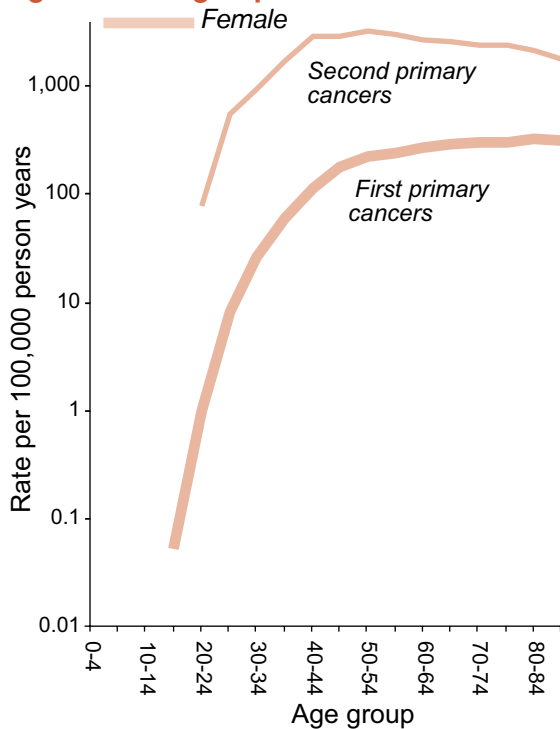
## Trends in the SIRs

The trends in Figure 10.2 show increased SIRs following a diagnosis of breast cancer up to 10 years following diagnosis and that this decreases thereafter with each year of follow-up.

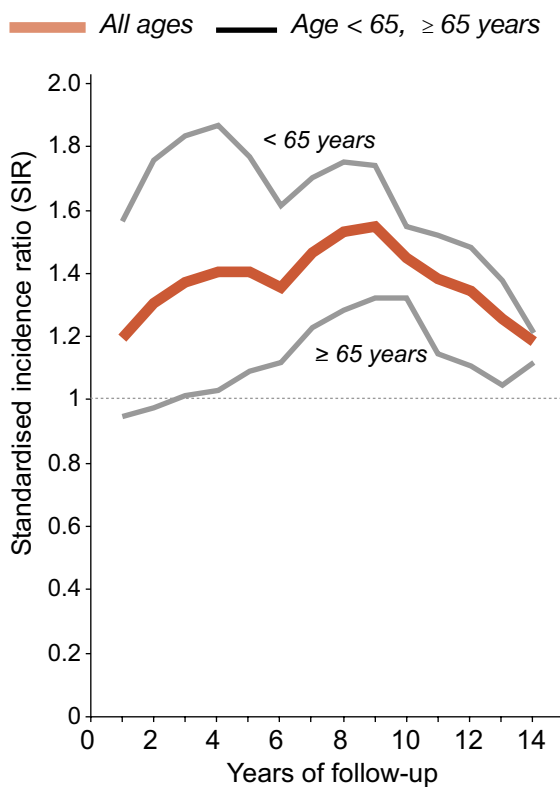
Trends in SIRs for specific cancer types by period of follow-up can be found in Table 10.4 (page 78) and overall 23-year SIRs are given in Table 1.3 (pages 58-61). The overall 23-year SIR for all cancer is 1.33. The highest, statistically significant SIRs for women include uterus 2.24, breast 1.97, AML 1.69, soft tissue 1.66, ovary 1.59, stomach 1.30, melanoma 1.14 and other cancers 1.20.



**Figure 10.1: Age-specific rates**



**Figure 10.2: Trends in the annual SIR for all second primary cancers**



**Trends in SIRs with age**

In Figure 10.2 the general pattern is of increasing SIRs with increasing follow-up to about 10 years for older women. The under 65 year age group consistently shows higher risks, though decreasing over time, than older people at any time during follow-up.

Estimates of overall 23-year SIRs by age group are to be found in Table 10.5 (page 79). The younger age group has a SIR 50% higher than the older age group. The SIRs are 1.61 for women first diagnosed before 65 years of age compared with 1.06 for those diagnosed at an older age (both statistically significant).

For women under age 65 the highest SIRs are soft tissue 2.48, AML 2.42, breast cancer 2.38, uterus 2.05, ovary 2.00, stomach 1.50, rectum 1.35 and colorectum 1.21. For older women only the risk of breast and uterine cancers are elevated.

**Comments**

Women diagnosed with breast cancer are at relatively high risk of a second cancer and their risk is greater if diagnosed at an earlier age.

Various genetic conditions and mutations are associated with increased cancer risks:

Li-Fraumeni syndrome (tp53), a rare autosomal dominant hereditary disorder - increased risk of soft tissue sarcoma, breast cancer, leukaemia, osteosarcoma, melanoma and cancers of the colon, pancreas, adrenal cortex and brain.

BRCA1 mutation - increased risk of breast, ovarian and prostate cancers.

BRCA2 mutation - increased risk of cancers of the breast, ovary, colon, pancreas, larynx, oesophagus, stomach, gallbladder, bile ducts and of haematopoietic neoplasms and melanoma.

Breast cancer also shares obesity and reproductive risk factors, such as number of pregnancies, age at menarche and menopause, with cancers of the ovary and uterus.

The above mutations and shared risk factors may account for some of the elevated risks of second primary cancers following breast cancer.

# CERVICAL CANCER

**Table 11.1: Characteristics of the cohort**

	Females
First primary cancer	4,855
Age at diagnosis	
Mean	51.7
<65 years	3,649
=>65 years	1,206
Total person-years	41,417
Mean follow-up (years)	8.5
Histological confirmation (%)	98.6
Squamous and transitional	72.2
Adenocarcinoma	18.3
Other specific carcinoma	4.8
Unspecified carcinoma	2.7
Other specified types	0.6
No histological confirmation	1.4
Second primary cancers	
Non-simultaneous	364
Simultaneous	38

**Table 11.2: Cumulative risk (%) of the most common second primary cancers**

	Sex	Follow-up years					
		1	5	10	15	20	23
All cancers	F	0.8	3.1	6.0	8.6	11.1	12.8
Colon	F	0.0	0.2	0.5	0.8	0.9	1.2
Lung	F	0.1	0.7	1.5	2.0	2.2	2.4
Breast	F	0.1	0.6	1.3	1.8	2.1	2.4

*All other cancers have 10-year cumulative risk of less than 0.5 %.*

## Common second cancers

From Table 11.2 a woman's 10-year cumulative risk of contracting a second cancer following cervical cancer is seen to be 1 in 17 with cumulative risk at 10 years of > 0.5% in colon, lung and breast cancers.

## Age-specific Incidence

The principal feature of Figure 11.1 is that the age incidence curves for the second primary cancers are orders of magnitude higher than for first primaries and remaining parallel over time.

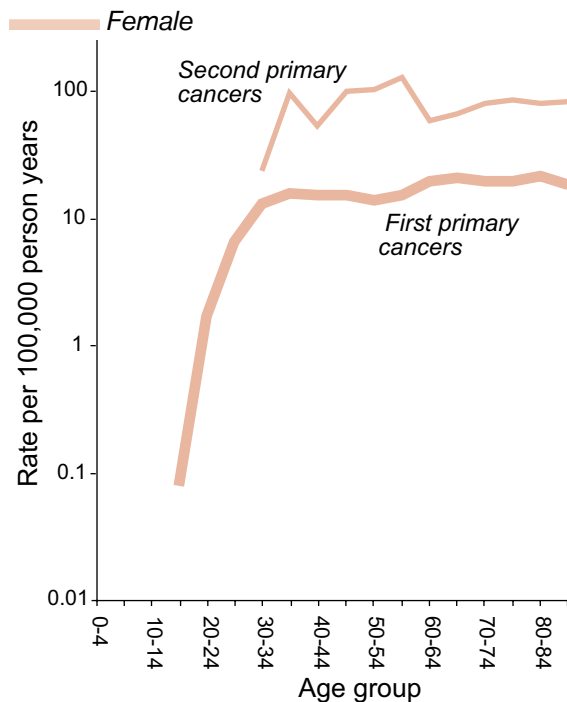
## Trends in the SIRs

The trends in Figure 11.2 show slightly increased SIRs following a diagnosis of cervical cancer and that these risks fluctuate over years of follow-up.

Trends in SIRs for specific cancer types by period of follow-up can be found in Table 11.4 (page 80). Overall 23-year SIRs are given in Table 1.3 (pages 58-61). The overall SIR at 23-years of follow-up is 1.24. The highest, statistically significant SIRs include; renal pelvis 4.26, bladder 2.64, lung 3.51, oesophagus 2.91, pancreas 2.50, stomach 2.14 and other 1.94.



**Figure 11.1: Age-specific rates**



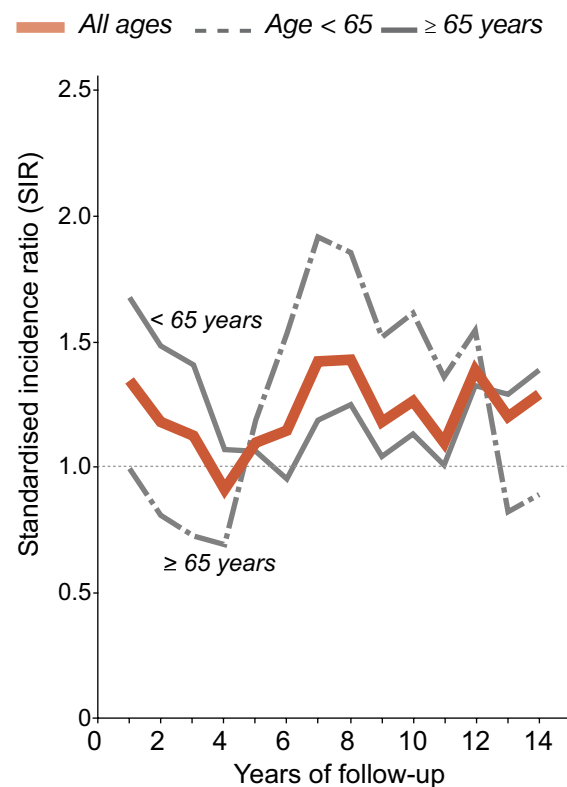
**Trends in SIRs with age**

In Figure 11.2 the general pattern of SIRs with increasing follow-up is unstable for both age groups. Unusually, the older age group has higher SIRs than younger people during the period 4-12 years after diagnosis, with younger women having a fairly stable SIR around 1 during this time.

Estimates of overall 23-year SIRs by age group are to be found in Table 11.5 (page 81). The younger age group has a slightly higher SIR than the older age group. The SIRs were 1.27 for women first diagnosed before 65 years of age compared with 1.17 for those diagnosed at an older age.

For women under age 65 the highest SIRs are renal pelvis 8.27, bladder 4.10, lung 4.01, pancreas 2.85, stomach 2.63 and other 2.08.

**Figure 11.2: Trends in the annual SIR for all second primary cancers**



**Comments**

Almost all cervical cancer is caused by human papilloma virus (HPV). Smoking does increase the risk of cervical cancer and would explain some of the excess risk for cancers such as those of the renal pelvis, bladder, lung, oesophagus, stomach and pancreas.

Cervical cancer is unusual in that the SIRs for second cancers are not substantially greater for women diagnosed at an earlier age.

# UTERINE CANCER

**Table 12.1: Characteristics of the cohort**

	Females
First primary cancer	7,371
Age at diagnosis	
Mean	64
<65 years	3,930
=>65 years	3,441
Total person-years	53,177
Mean follow-up (years)	7.2
Histological confirmation (%)	97.8
Squamous and transitional	0.4
Adenocarcinoma	82.2
Other specific carcinoma	4.3
Unspecified carcinoma	2.0
Sarcomas and soft tissue	3.3
Other specified types	5.7
No histological confirmation	2.2
Second primary cancers	
Non-simultaneous	649
Simultaneous	98

**Table 12.2: Cumulative risk (%) of the most common second primary cancers**

	Sex	Follow-up years					
		1	5	10	15	20	23
All cancers	F	1.0	4.3	8.4	12.2	15.4	16.9
Colon	F	0.1	0.7	1.3	2.0	2.5	2.5
Rectum	F	0.1	0.4	0.7	1.0	1.3	1.3
Lung	F	0.1	0.5	1.0	1.2	1.5	1.5
Melanoma	F	0.1	0.3	0.5	0.9	1.2	1.4
Breast	F	0.3	1.1	2.1	3.0	3.3	3.6

*All other cancers have 10-year cumulative risk of less than 0.5 %.*

## Common second cancers

From Table 12.2 a woman's 10-year cumulative risk of contracting a second cancer following uterine cancer is seen to be 1 in 12 with 10-year cumulative risks > 0.5% for cancers of the colon, rectum, lung, breast and melanoma.

## Age-specific Incidence

Figure 12.1 shows that the age incidence curves for the second primary cancers are orders of magnitude higher at early ages and that both stabilise after the age of 50.

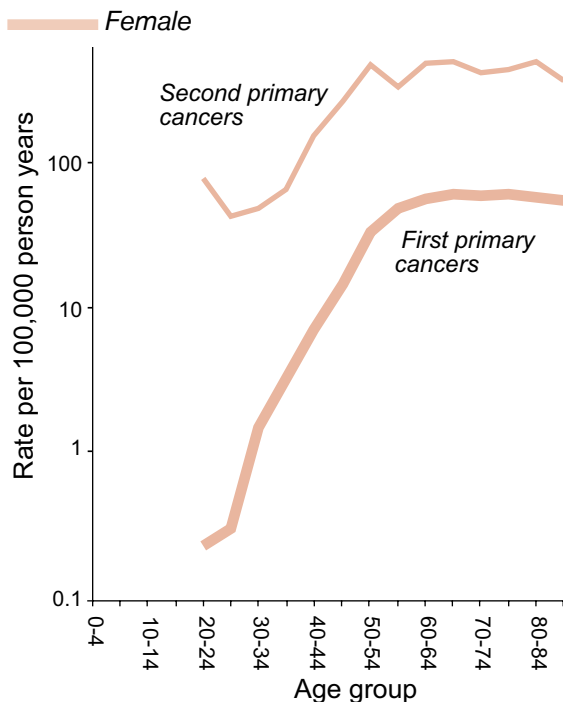
## Trends in the SIRs

The trends in Figure 12.2 show increased SIRs following a diagnosis of uterine cancer only 8-10 years after first cancer diagnosis.

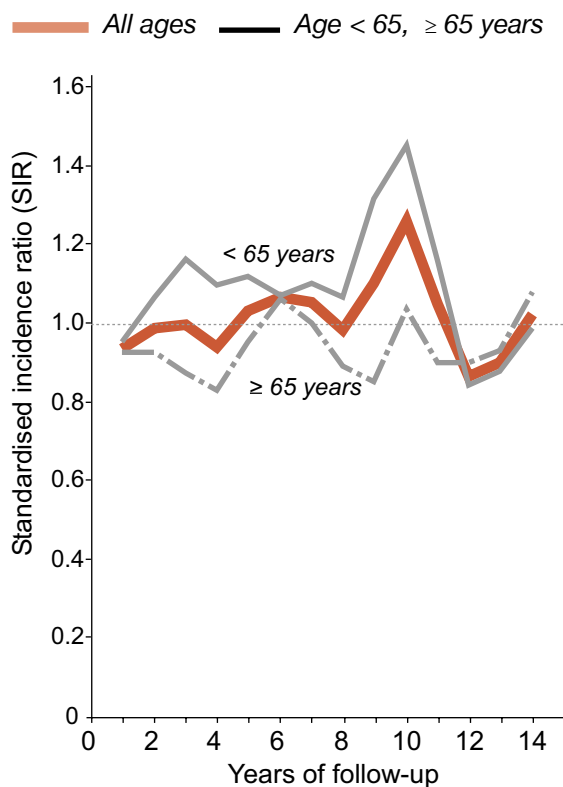
Trends in SIRs for specific cancer types by period of follow-up can be found in Table 12.4 (page 82) and overall 23-year SIRs are given in Table 1.3 (pages 58-61). The overall SIR at 23-years of follow-up is not significantly greater than 1. The statistically significant SIRs are colon 1.30, rectum 1.51 and colorectum 1.35.



**Figure 12.1: Age-specific rates**



**Figure 12.2: Trends in the annual SIR for all second primary cancers**



### Trends in SIRs with age

In Figure 12.2 the general pattern of SIRs for the under 65 year age group shows risks > 1 with a peak about 10 years after first diagnosis and decreases thereafter. For older women SIRs fluctuate just below 1 during the whole period of follow-up.

Estimates of overall 23-year SIRs by age group and sex are to be found in Table 12.5 (page 83). The younger age group has slightly higher risk compared with the older age group. The SIRs are 1.09 for women first diagnosed before 65 years of age compared with 0.93 for those diagnosed at an older age (neither is significantly different to 1).

For women under age 65 the highest SIRs are bladder 2.44, colon 1.68, colorectum 1.53 and other 1.93.

### Comments

An inherited form of colorectal cancer (Lynch syndrome) is also associated with high risks for some other cancers, including cancers of the small bowel, uterus, renal pelvis, ureter, stomach, gallbladder, liver, intrahepatic bile ducts and other biliary tract, pancreas, ovary, brain and some skin cancers. Thus, Lynch syndrome might explain part of the association between uterine cancer and colorectal cancer.

Obesity is a strong risk factor for uterine cancer and might also explain part of the association with colorectal cancer and kidney cancer, both of which are also obesity-related cancers.

Radiotherapy might have contributed to the excess of bladder cancers for younger women treated for uterine cancer.

# OVARIAN CANCER

**Table 131: Characteristics of the cohort**

	Females
First primary cancer	5,202
Age at diagnosis	
Mean	61
<65 years	2,939
=>65 years	2,263
Total person-years	22,930
Mean follow-up (years)	4.4
Histological confirmation (%)	93.8
Squamous and transitional	0.3
Adenocarcinoma	80.8
Other specific carcinoma	2.2
Unspecified carcinoma	4.0
Sarcomas and soft tissue	0.2
Other specified types	6.2
No histological confirmation	6.3
Second primary cancers	
Non-simultaneous	254
Simultaneous	57

**Table 13.2: Cumulative risk (%) of the most common second primary cancers**

	Sex	Follow-up years					
		1	5	10	15	20	23
All cancers	F	1.0	2.7	4.3	6.1	7.8	8.1
Colon	F	0.3	0.5	0.7	1.0	1.2	1.2
Breast	F	0.1	0.7	1.3	2.0	2.6	2.6

*All other cancers have 10-year cumulative risk of less than 0.5 %.*

## Common second cancers

From Table 13.2 a woman's 10-year cumulative risk of contracting a second cancer following ovarian cancer is seen to be 1 in 23 with cumulative risks of > 0.5% for colon and breast cancer.

## Age-specific Incidence

The principal feature of Figure 13.1 is that the age incidence curves for the second primary cancers are orders of magnitude higher at all ages. Whilst first primary rates rise steadily across all age groups, the rates for second primary cancers stabilise and then decrease after the age of fifty years.

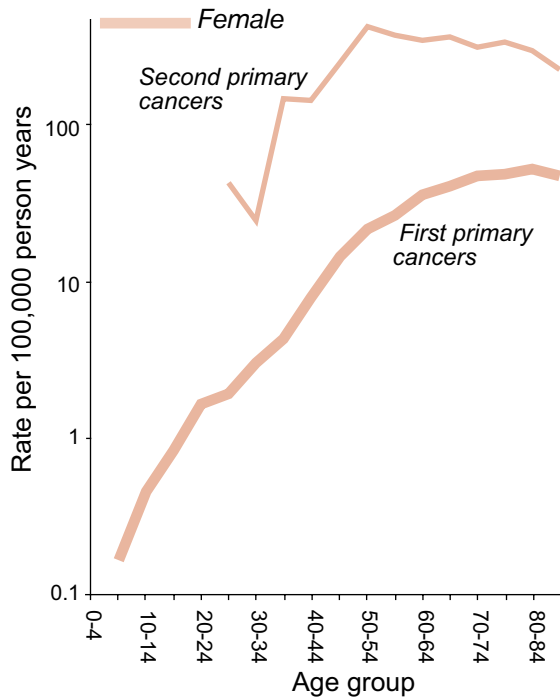
## Trends in the SIRs

The trends in Figure 13.2 show only slightly increased SIRs following a diagnosis of ovarian cancer until ten years after initial diagnosis and that these risks increase over the next five years of follow-up.

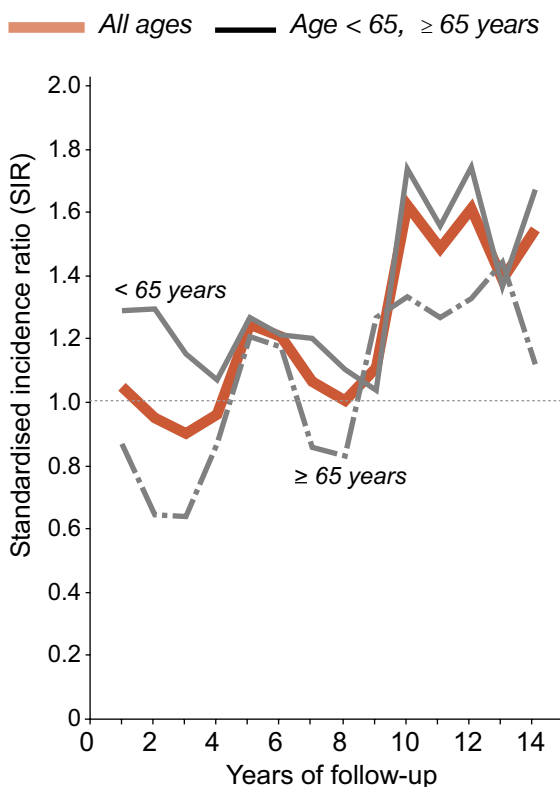
Trends in SIRs for specific cancer types by period of follow-up can be found in Table 13.4 (page 84) and overall 23-year SIRs are given in Table 1.3 (pages 58-61). The overall 23-year SIR is 1.19 (significantly greater than 1). Statistically significant SIRs are seen for cancers of the colon 1.75, colorectum 1.59 and AML 3.99.



**Figure 13.1: Age-specific rates**



**Figure 13.2: Trends in the annual SIR for all second primary cancers**



**Trends in SIRs with age**

In Figure 13.2 the general pattern of increasing SIRs with increasing follow-up is observed for both age groups from about 8 years after initial diagnosis.

Estimates of overall 23-year SIRs by age group and sex are to be found in Table 13.5 (page 85). The younger age group has higher SIRs than the older age group. The SIRs are 1.40 for women first diagnosed before 65 years of age compared with 0.95 for those diagnosed at an older age.

For the under 65 year age group the highest SIRs are for cancers of the renal pelvis 9.17, AML 5.89, bladder 4.23, colon 1.96, colorectum 1.75, and breast 1.45. For older women the only significant SIR is for colon cancer 1.60.

**Comments**

Various genetic conditions and mutations are associated with increased cancer risks including:

BRCA1 mutation - increased risk of breast, ovarian and prostate cancers.

BRCA2 mutation - increased risk of cancers of the breast, ovary, colon, pancreas, larynx, oesophagus, stomach, gallbladder, bile ducts and of haematopoietic neoplasms and melanoma.

Ovarian cancer also shares obesity and reproductive risk factors, such as number of pregnancies, age at menarche and menopause, with cancers of the breast and uterus.

The above mutations and shared risk factors may account for some of the elevated risks of second primary cancers following ovarian cancer.