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Public Health Scotland

Scottish Routes from Diagnosis: Multiple cancers and metastatic disease

MACMILLAN CANCER SUPPORT

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Acknowledgements

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Thank you to the Macmillan-ISD Steering Group and to the Scottish Routes from Diagnosis Clinical Advisory Group for clinical and research support and advice in relation to the Scottish Routes from Diagnosis project.

Background

Scottish Routes from Diagnosis (SRfD) was a project between Public Health Scotland and Macmillan, which investigated survivorship outcomes and experiences of residents of Scotland with the four most common types of cancer found in Scotland: breast, prostate, colorectal and lung, using national datasets from 2007 and 2012.

The project developed survivorship Outcome Groups (OGs), which capture the survivorship experiences in four different groups and allows comparisons across (as well as within) cancer types. Reporting patient factors, pathways, and outcomes using these outcome groups allows for investigation into the very different experiences people can have following a cancer diagnosis, both within a particular cancer type and across different types.

For a full explanation of the methodology of SRfD, please refer to the SRfD Context and Methodology publication. The technical notes, limitations and assumptions covering methods specific to this chapter are presented in the technical appendix.

Please note that this publication is based on data relating to cancer prior to the COVID-19 pandemic. Consequently, caution may be required in generalising these results to later time periods.

Multiple cancers, metastatic disease

This chapter focusses on a specific group of people from the SRfD cohorts who have more than one cancer diagnosis, and on those with metastatic disease[1] (which may be treatable but is less likely to be curable). Macmillan have previously published on Treatable but not curable cancer in England. As continued experience of cancer forms part of the definition of the outcome groups in the SRfD framework, the focus of this chapter is primarily people in Outcome group 3 (People likely to be living with a continued presence of cancer), and Outcome Group 4 (Limited survival). However, we also explore cancer diagnoses before the cohort cancer, and this includes people in all outcome groups.

People with an ongoing or repeated experience of cancer will potentially have a quite different experience of cancer compared to those who are treated successfully and experience no further cancer diagnoses.

This chapter reports on:

- People with multiple cancers of the same cancer type
- People with more than one cancer, in different sites (e.g. a breast cancer and a colorectal cancer).

[1] Cancer that has spread to other parts of the body

- People with metastatic disease, i.e. cancer that has spread to other parts of the body.

A Supplementary Report on survival in people with a previous cancer diagnosis is included at the end of this document.

Results

1. An Overview of Any Multiple Cancer Diagnosis

During the 20-year period covering the lookback and follow-up periods in the 2007 cohorts (1997-2017: 10 year lookback, 10 year follow-up), more than 1 in 10 people had a second cancer diagnosis (this includes multiple tumours of the cohort cancer as well as cancers at other sites) (Figure 1). For the **prostate** and **colorectal** cohorts, this was 17% (around 1 in 6) of people.

In the 2012 cohorts, in the total 15-year period (2002-2017: 10 year lookback, 5 year follow-up), more than 1 in 8 people in the **prostate**, **lung** and **colorectal** cancer cohorts had at least one other tumour. Just under 1 in 10 of the 2012 **breast** cancer cohort had an additional cancer diagnosis (Figure 1).

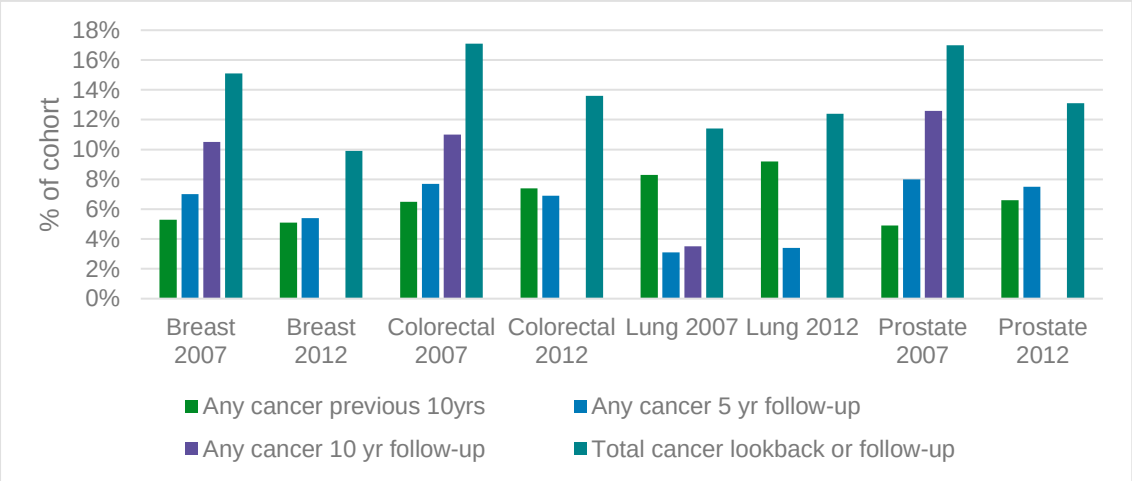

Figure 1: Proportion of people in the cohort with another cancer diagnosis in look-back or follow-up[2], and the total time period[3,4], including multiple primaries of cohort cancer.

In both the 2012 and 2007 cohorts, the **lung** cancer cohorts had the highest proportion of individuals with a previous cancer of any sort before the cohort diagnosis (more than 1 in 12 people). However, just 3% of the **lung** cancer cohorts had a further tumour in follow-up, this was likely linked to short survival, which was highlighted in the SRfD Context and Methodology Report and is explored further in the 'Supplementary Report

[2] Maximum follow-up is 5-years for 2012 cohort, 10 years for 2007 cohort.
[3] Therefore, the total lookback plus follow-up periods are 20 years for the 2007 cohorts and 15 years for the 2012 cohorts
[4] The total time period bar does not necessarily equal the sum of the previous period and longest follow-up periods as a small number of people had cancer diagnoses both in the lookback period and in the follow-up period.

on Survival in People with a Previous Cancer Diagnosis'. In contrast, only around 1 in 20 people in the **breast** and **prostate** cancer cohorts had experienced a previous cancer diagnosis (Figure 1). However, in the 10-year follow-up period for the 2007 cohorts, more than 1 in 10 of the **prostate** and **breast** cancer cohorts had a further cancer diagnosis at some point. Differences between the cohorts may reflect differences in the average age of people in the cohorts, differences in cancer aetiology or differences in common risk factors in the cohorts.

Note, this will be an underestimate of the true proportion of people with previous cancer diagnoses, as we are looking back 10 years only – any cancers diagnosed prior to 2002 (for the 2012 cohort) or 1997 (for the 2007 cohort) are not included.

This includes cancers of the same tumour site as well as cancers of a different cancer site (detailed later in the chapter). Some of these 'same tumour site' diagnoses were diagnosed around the same time as the cohort cancer. For this reason, analysis beyond this section will look at multiple tumours of the same cancer (Section 2) and tumours of other cancer types (Section 3) separately.

Results are for the 2012 cohorts; the equivalent 2007 cohort results are only presented where there has been a noticeable change or to provide additional information from the longer (ten year) follow up period. Tables and figures referred to in the report can be found in the data appendix.

1.1. Types of Cancers Diagnosed

1.1.1. Cancers diagnosed prior to cohort cancer

In the **breast** cancer 2012 cohort there were a total of 226 women diagnosed with a tumour previously, almost half (89) had other breast cancer tumours[5]. The next most common cancer sites by frequency, were colorectal cancer, corpus uteri, lung cancer and malignant melanoma (Figure 2).

The order of frequency of previous cancer sites was broadly similar to the order of the most common cancer in the general female population (Data appendix

Table A13). The major exception was lung cancer, which was fourth most common in the 2012 cohort, compared to being the second most common in the general female population in Scotland in 2012.

[5] A few people had more than one additional cancer at different sites, therefore the total number of persons with any other cancer in the text may be lower than the sum of the numbers in the figures in this section.

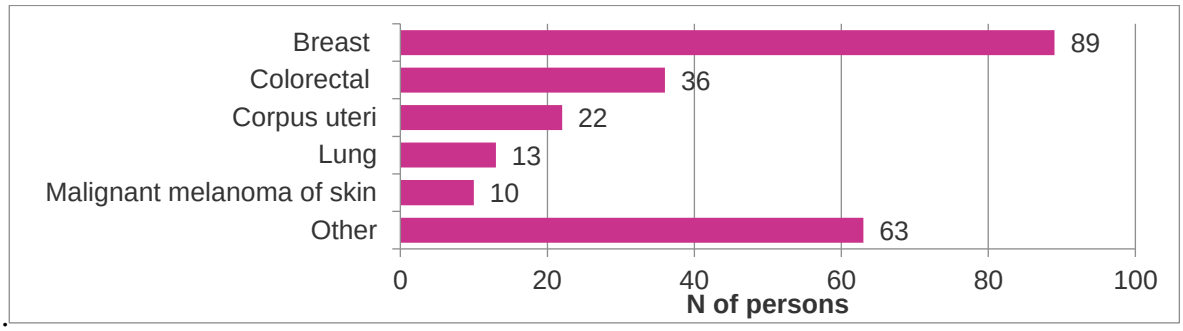

Figure 2: Frequency of the most common cancer sites diagnosed before the cohort cancer in the breast cancer 2012 cohort

In the **colorectal** cohort 284 people were diagnosed with a previous cancer, 63 people had previous diagnoses of colorectal cancer. Other common previous diagnoses were prostate and breast cancers. Numbers of people diagnosed with other cancers were low.

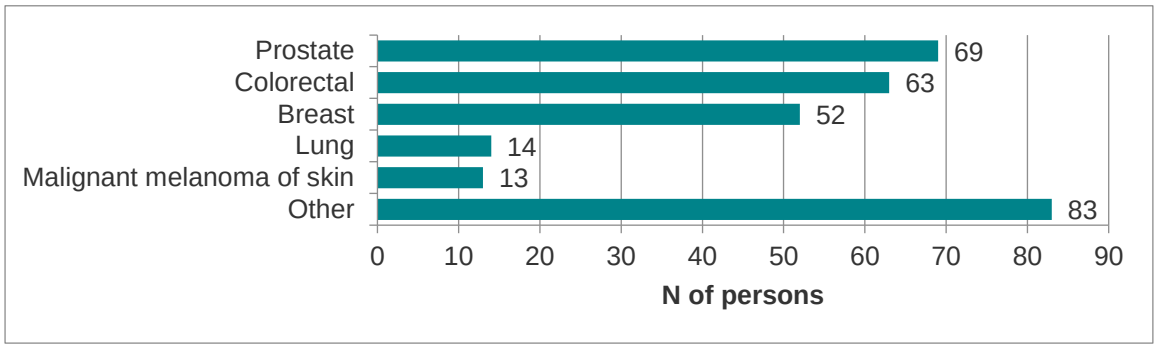

Figure 3: Frequency of the most common cancer sites diagnosed in the 2012 colorectal cancer cohort prior to their cohort diagnosis

In the **lung** cohort 479 people had been diagnosed with another cancer before their lung cancer diagnosis in 2012. The most common previously diagnosed cancer in the 2012 lung cancer cohort was head and neck cancer while similar numbers of people were diagnosed with breast and colorectal cancers. Head and neck cancer was the fifth most common in the general population (Figure 4, Data appendix Table A12).

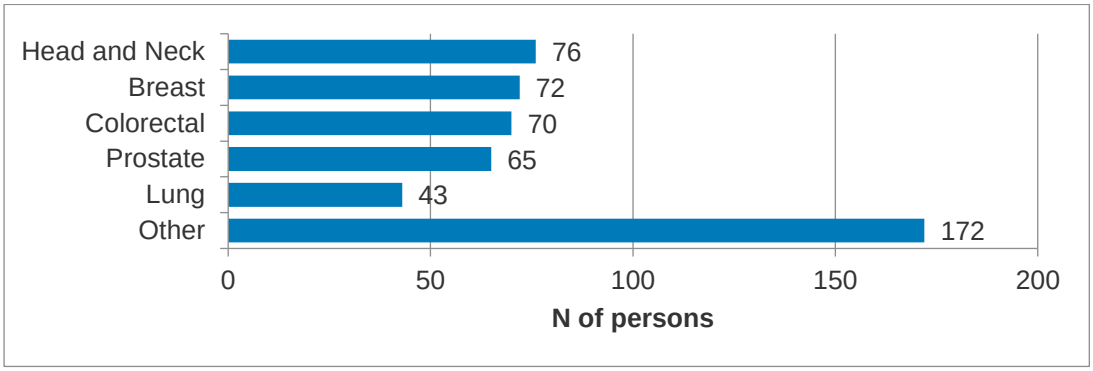

Figure 4: Number of people diagnosed with the most common cancer sites in the lung cancer 2012 cohort before the cohort diagnosis

Lung cancer itself is underrepresented as a previous diagnosis in all cohorts compared to its frequency in the general population (9.4% of previous diagnoses in the 2012 cohort) as a result of its low survival.

In the **prostate** cancer cohort 205 men had a previous cancer diagnosis. The most common previous cancer diagnoses were colorectal and bladder cancers. Bladder cancer is a less common cancer, its relatively high numbers here are also documented elsewhere suggesting an increased risk following prostate cancer[6]. Other cancer diagnoses were spread across a number of sites.

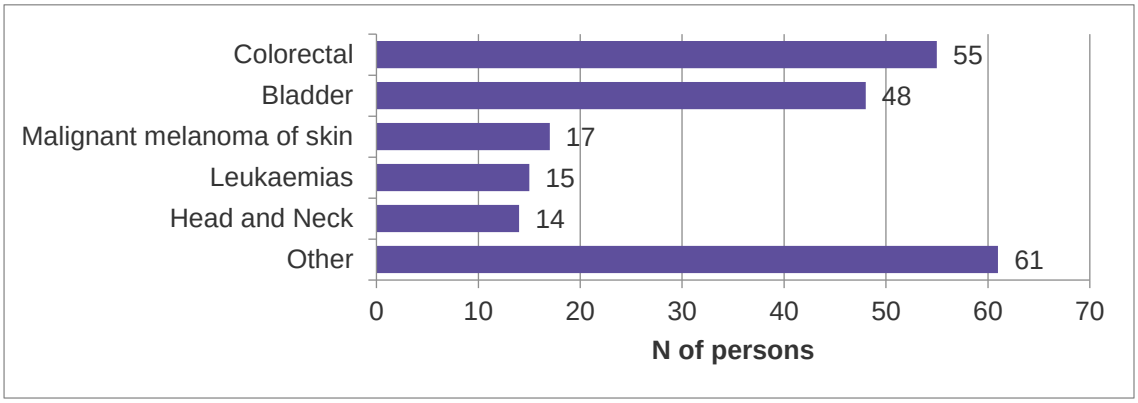

Figure 5: Number of men diagnosed with the most common cancers occurring before the cohort cancer in the prostate cancer 2012 cohort

[6] https://www.cancer.org/cancer/prostate-cancer/after-treatment/second-cancers.html

1.1.1. Further cancers diagnosed around the same time or in follow-up

In the 2012 **breast** cancer cohort, 170 of the 346 women diagnosed with another cancer had a further breast cancer. The next most common diagnoses were lung and colorectal cancers, then cancer of the corpus uteri and kidney cancer (Figure 6).

Common cancers diagnosed after the cohort cancer broadly follow the frequency of cancers in the general female population (Data Appendix

Table A13).

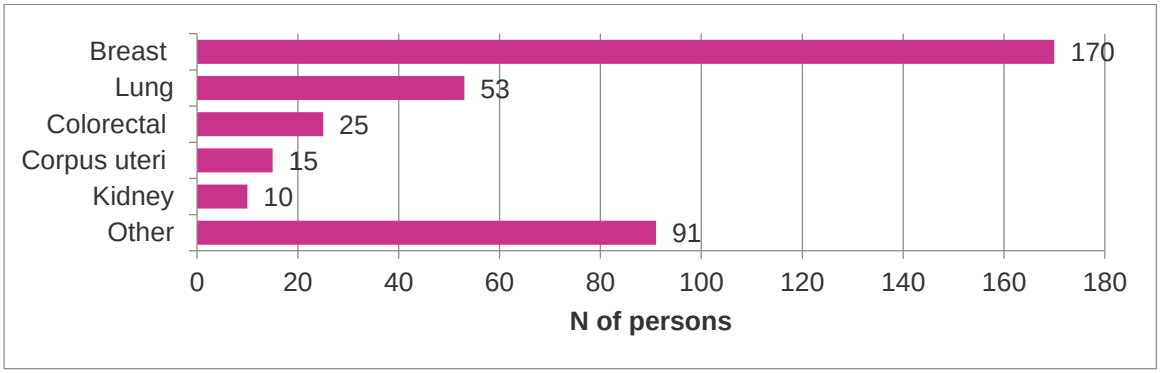

Figure 6: Number of women with the most common cancer sites diagnosed after the cohort cancer in the breast cancer 2012 cohort

In the **colorectal** cohort, a further tumour of colorectal cancer was the most common cancer in follow-up (95 people) (**Error! Reference source not found.**). With the e xception of a further colorectal cancer diagnosis, the frequency of cancer of other sites in follow-up broadly follows that in the general population (Data appendix Table A12) with prostate, lung and breast cancers the most common.

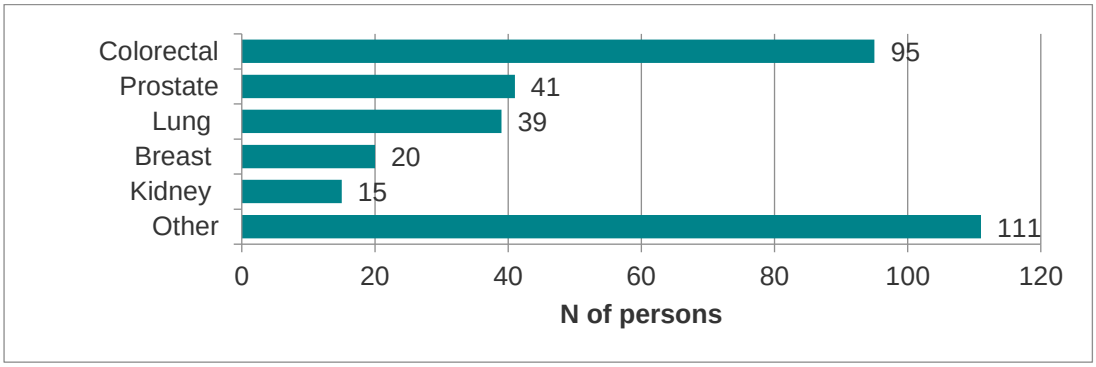

Figure 7: Frequency of the most common cancer sites diagnosed in the 2012 colorectal cancer cohort after their cohort diagnosis

In the **lung** cancer cohort, 235 people were diagnosed with a subsequent cancer after their cohort cancer diagnosis, with a further lung cancer being the most commonly diagnosed site (106 people). People in the cohort had diagnoses from a wide range of other sites but few people were diagnosed with any particular cancer: 21 people were diagnosed with a head and neck cancer, and 14 each with a breast, colorectal or prostate cancer (Figure 8).

Head and neck cancer was higher than might be expected from its presence in the general population (Data appendix Table A12), as the most common cancer (other than lung cancer) diagnosed in the 2012 cohort. This is similar to the commonly diagnosed previous cancers in this cohort (Figure 8).

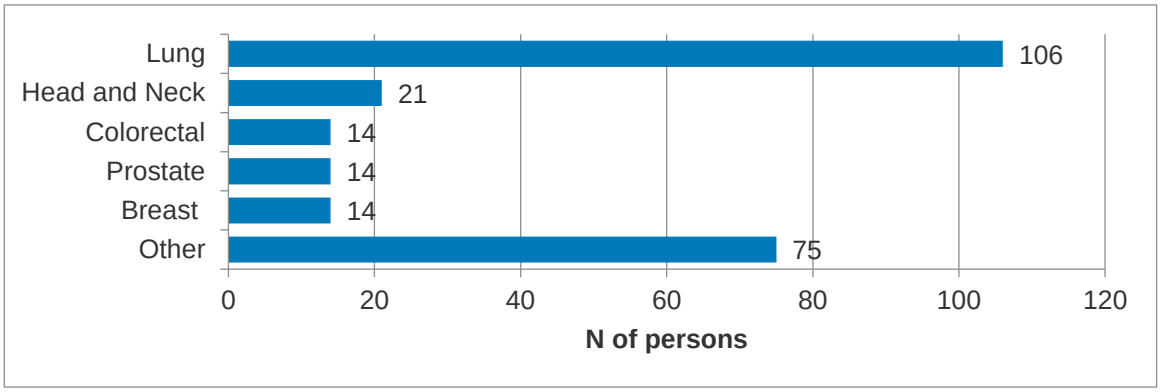

Figure 8 Number of people diagnosed with the most common cancers occurring after the cohort cancer in the lung cancer 2012 cohort

In the 2012 **prostate** cancer cohort 222 people were diagnosed with another tumour after their prostate cancer. Colorectal and lung cancers were the most common cancer diagnoses in the 5-year follow-up. These two sites are the most common (after prostate cancer[7]) in the general male population (Figure 9, Data appendix

Table A14).

[7] A second primary cancer of the prostate is extremely rare, so although prostate cancer is common in the general male population we do not expect to see it as a second cancer diagnosis in the prostate cancer cohort.

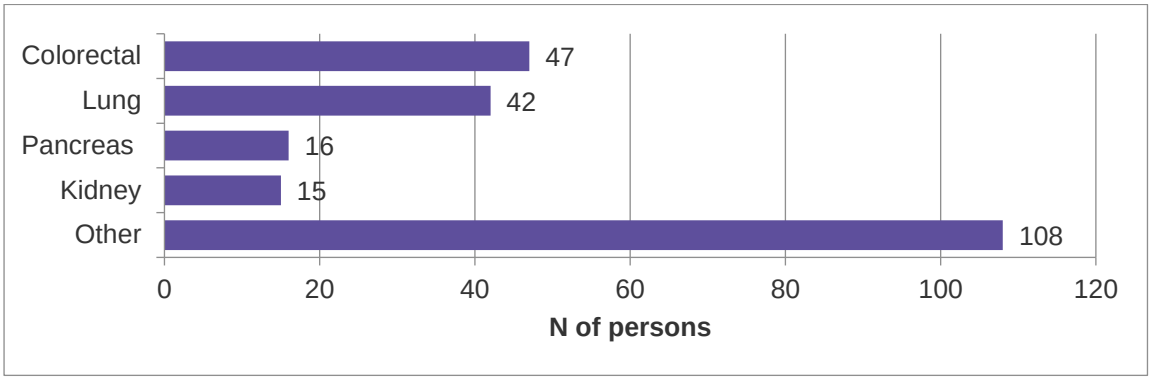

Figure 9: Number of men diagnosed with the most common cancers occurring after the cohort cancer in the prostate cancer 2012 cohort

Summary

- In the 2012 cohorts, in the total 15-year period (10 year lookback, 5 year follow-up), more than 1 in 8 people in the **prostate**, **lung** and **colorectal** cancer cohorts had at least one other tumour. Just under 1 in 10 of the 2012 **breast** cancer cohort had an additional cancer diagnosis.

- In the **breast** and **colorectal** cohorts, breast and colorectal cancer themselves are common as previous diagnoses.

- In **breast**, **colorectal** and **lung** cancer the most common diagnosis in follow-up was another tumour of the cohort site.

- For cancers of non-cohort sites, frequency of other cancer sites diagnosed tends to follow that in the general population, as far as can be told with sometimes low numbers involved. There are a few notable exceptions:
    - Head and neck cancer was overrepresented in the **lung** cancer cohort both as a previous tumour and a follow-on diagnosis.
    - Bladder cancer was similarly overrepresented in the **prostate** cancer cohort, more so as a previous diagnosis.
    - Lung cancer was generally underrepresented as a previous cancer, due to low survival rates.

2. Multiple cancers of the same type

As shown above, some people diagnosed with lung, colorectal or breast cancer in 2012 also had a previous or later diagnosis of the same cancer type either before or after the cohort cancer diagnosis in 2012 (between 2002-2017); this section looks at these people in further detail. No statistics for the prostate cancer cohort are presented here as multiple primaries of prostate cancer were very rare.

2.1. Timing

Women in the **breast** cancer cohort were most likely to have another diagnosis of breast cancer either before or after their cohort cancer – amounting to 259 (5.8%) of the cohort in 2012. 156 people (4%) in the **colorectal** cohort had another primary of colorectal cancer diagnosed before or after their cohort cancer. While 148 people (2%) of people in the **lung** cancer cohort had another diagnosis of lung cancer in the time before or after the cohort cancer (Figure 10).

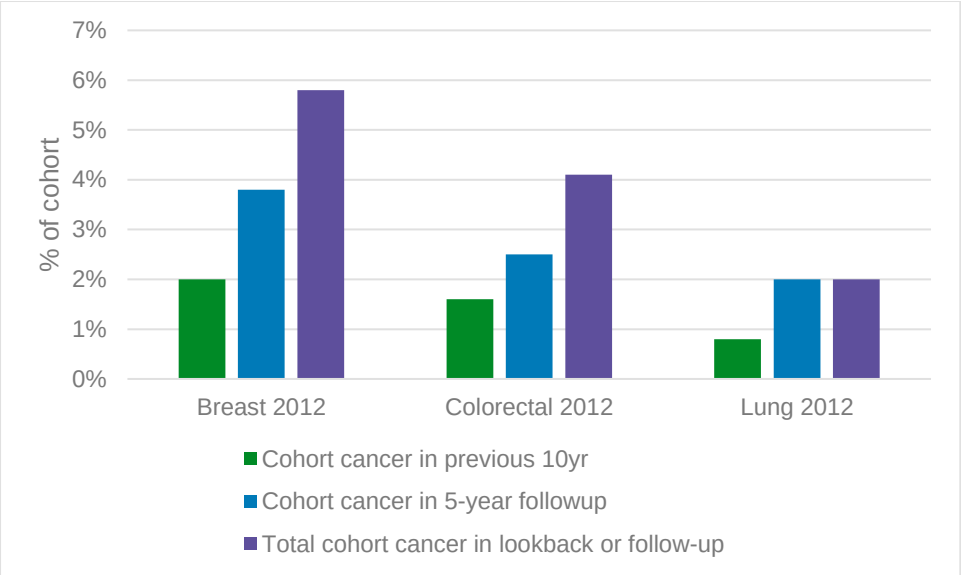

Figure 10 Proportion of people in the cohort with multiple primaries of the cohort cancer diagnosed in look-back or follow-up periods.

2.2. Prior cancer diagnoses

Very small numbers of people had received a previous diagnosis of the same cancer type in the preceding 10 years (Table 1).

Table 1: Proportion of people with previous cancer diagnosis of the same type by 2012 cohort, 10-year look back

	N of people		
Cohort	No previous cancer	Previous cancer	% with previous cancer diagnosis
Breast 2012	4379	89	2.0%
Colorectal 2012	3762	63	1.6%
Lung 2012	5139	43	0.8%

This varied from 2% of the **breast** cancer cohort to <1% of the **lung** cancer cohort.

2.2.1. Characteristics

There are limitations in the conclusions that can be made about the characteristics of these people due to the small numbers involved. However, those people who had a previous diagnosis of colorectal cancer were on average, slightly older when their cohort cancer was diagnosed than those who did not. There was no significant difference in age in the breast and lung cancer cohorts.

Table 2: Age at diagnosis of people with previous cancer registrations of the cohort cancer

Cohort	Previous cancer	Mean age	LCI	UCI
Breast 2012	No	63.6	63.2	64.0
	Yes	64.2	61.5	67.0
Colorectal 2012	No	70.6	70.2	71.0
	Yes	76.3	73.7	78.9
Lung 2012	No	70.6	72.1	72.7
	Yes	74.1	71.6	76.5

There was no notable difference detected in the proportion of males and females in the **colorectal** and **lung** cohorts with a previous cancer. Location (measured by deprivation and rurality) was not associated with previous cancers. See Data Appendix p34 for details.

2.3. Further cancer diagnoses around the same time or in follow-up

In the 2012 cohort 170 (3.8%) women had a further diagnosis of **breast** cancer, most of whom (n=119, 70%) had an additional tumour diagnosed on the same day as the cohort cancer. Tumours of the same cancer type diagnosed on the same day, while considered as separate cancers medically, may be considered by the person as part of the same cancer 'experience'.

Table 3: Number of people diagnosed with cohort cancers in 5 year follow up period

Cohort	No diagnoses in follow-up	Other diagnoses in 5 years of follow-up
Breast 2012	4298	170 (3.8%)
Colorectal 2012	3730	95 (2.5%)
Lung 2012	5076	106 (2.1%)

In the **colorectal** cohort, 95 (2.5%) people had a further diagnosis of colorectal cancer; around half (57) had at least one other tumour diagnosed on the same day as their cohort cancer. 106 people (2%) of the **lung** cancer cohort had another tumour in follow-up; 62 of these were on the same day.

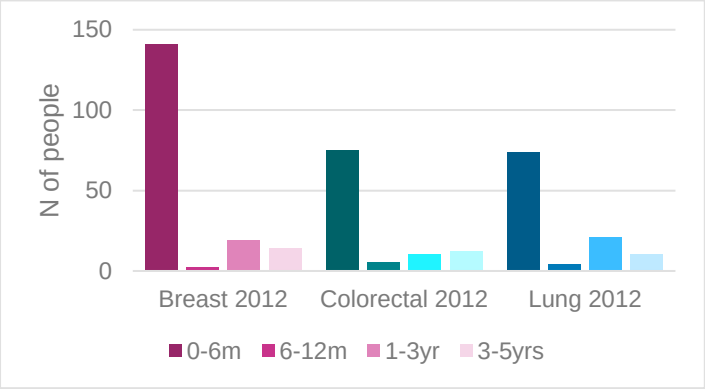

Figure 11: Additional diagnoses of cohort tumours by 2012 cohort and follow-up period. Shading indicates time period, darkest shade = closest to cohort diagnosis (0-6 months), lightest shade = furthers from cohort diagnosis (3 – 5 years).

The majority of additional tumours of the cohort cancer across all three cancers were diagnosed within the first 6 months after the cohort cancer diagnosis.

2.3.1. Characteristics

There was no significant difference in the average age of people who went on to have another cohort cancer diagnosis and no difference in the proportion of males and females in the **colorectal** and **lung** cohorts. No trends were apparent by deprivation or rurality. As the total number of people with a further cohort cancer was small, slight differences according to demographics would be difficult to detect. See Data appendix p36 for further details.

Summary

- The number of people diagnosed with more than one cancer of the same site is relatively small. It is most common in the **breast** cancer cohort, with 1 in 18 women diagnosed with a second tumour at some point in the lookback and follow-up periods.

- Many of the multiple tumours of the same type in the **breast**, **colorectal** and **lung** cohorts were diagnosed on the same day or within a few months of the cohort cancer diagnosis.

- People in the **colorectal** cohorts with a previous colorectal cancer diagnosis were, on average, older than those who did not have a previous diagnosis.

3. Multiple cancers of different types

This section considers people in the lung, colorectal, breast or prostate cohorts who also had other types of cancer diagnoses (non-cohort cancers) either before or after the cohort cancer diagnosis in 2012 (between 2002-2017).

3.1. Timing of Diagnosis

Men in the **prostate** cancer cohort were most likely to have another diagnosis of a different cancer type either before or after their cohort cancer – amounting to 408 (13%) of the cohort. 424 (11%) people in the **colorectal** cohort and 566 (11%) people in the **lung** cancer cohort also had a previous or subsequent cancer diagnosis of a different site/type. Seven percent (319) of women in the 2012 **breast** cancer cohort experienced another cancer of a different type in the 10 year look-back and/or 5 year follow-up periods (Data Appendix (p30)).

Survival time following the cohort cancer affects the likelihood of being diagnosed with another cancer in the follow-up period: i.e. someone who survives for a long period of time after cancer diagnosis has a greater chance of another cancer developing and being diagnosed before death compared to someone with short survival. This needs to be borne in mind when comparing the rates of new tumours in different cohorts. Consequently, rates per 1000 person years at risk (PYAR) are presented throughout the chapter. These rates are age standardised to take account of differences in the age profile of the different cancer types.

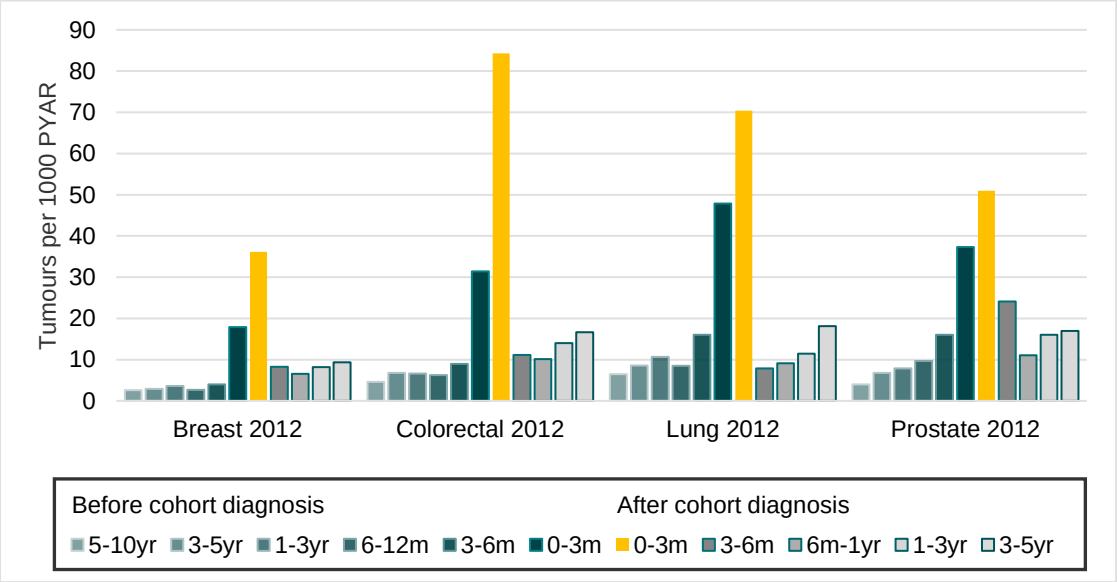

Figure 12: Rate of tumours diagnosed (per PYAR), in relation to the cohort diagnosis date.

When looking at the rate of non-cohort tumour diagnoses (per 1000 person years at risk (PYAR)), there was a general pattern across the cohorts of diagnoses increasing 3-6 months prior to the cohort cancer diagnosis (Figure 12). There continues to be a relatively high rate of other cancer diagnoses in the first 3 months after the cohort diagnosis, likely reflecting diagnoses made as a result of investigations and work up for

the cohort cancer. This was followed by a drop in diagnoses in the following months and then a gradual rise in the rate in the years thereafter (Figure 12).

Women with **breast** cancer consistently had the lowest risk of being diagnosed with a tumour at another site. The **colorectal** cancer cohorts had a higher risk than the other groups in the first 6 months, but this becomes more comparable with the **lung** and **prostate** cancer cohorts in later time periods. The diagnosis rate per PYAR remains higher 1 year or more post cohort diagnosis compared to 1 year or more before the diagnosis date across all cohorts. This may be due to the consequences of the initial diagnosis, for example increased medical investigations in treatment/follow-up or increased risk of cancer due to treatments such as radiotherapy. However, it should also be borne in mind that the surviving members of the cohorts are aging over the time period and this will also be playing a role in the increased rate of cancer diagnoses over time.

3.2. Prior Cancer Diagnoses

Of the people who had a cancer prior to the cohort cancer in 2012, the **breast** cancer cohort were the least likely to have had a non-cohort cancer diagnosis previously, with 3.2% having had another cancer diagnosis in the preceding 10 years. The **lung** cancer cohorts had the highest proportion of people with a previous diagnosis: 8.5% of the 2012 cohort (Table 4).

Table 4: Proportion of people with previous cancer diagnoses by 2012 cohort (excluding previous primaries of the cohort cancer site), 10-year look back

	N of people		
Cohort	No previous cancer	Previous cancer	% with previous cancer diagnosis
Breast 2012	4327	141	3.2%
Colorectal 2012	3604	221	5.8%
Lung 2012	4740	442	8.5%
Prostate 2012	2902	205	6.6%

The difference between cohorts partially reflects the younger age profile of the breast cancer cohort and conversely the older age of the lung cancer cohort (see the SRfD Results Chapter). However, age-standardised rates were still significantly lower for the breast cancer cohort compared to the others and higher for the lung cancer 2012 cohort compared to any of the other cohorts in 2012 (Table 5). Lifestyle risk factors will also play a role between cohort differences.

Table 5: Truncated (at 45) age-standardised incidence rates of other cancers per 1000 PYAR (person years at risk) diagnosed in the 10 years before the cohort cancer. Standardisation based on age at cohort diagnosis.

Cohort	EASR45 (per 1000 PYAR)	LCI	UCI
Breast 2012	3.24	2.72	3.81
Colorectal 2012	4.52	3.88	5.20
Lung 2012	8.13	6.87	9.48
Prostate 2012	5.20	4.35	6.13

EASR=European Age Standardised rate, LCI/UCI=Lower/Upper Confidence Interval

3.2.1. Characteristics

Age

Across all cohorts the mean age of people who have had a previous cancer diagnosis was older than those who hadn't. The difference was largest for **breast** cancer where the mean age of the 2012 cohort without any previous cancer was 62.9 (CI 62.5 – 63.4) and for those with it was 69.7 (CI 67.6-71.8) (6.8 years older) and least for **lung** cancer (1.3 years older) (Figure 13).

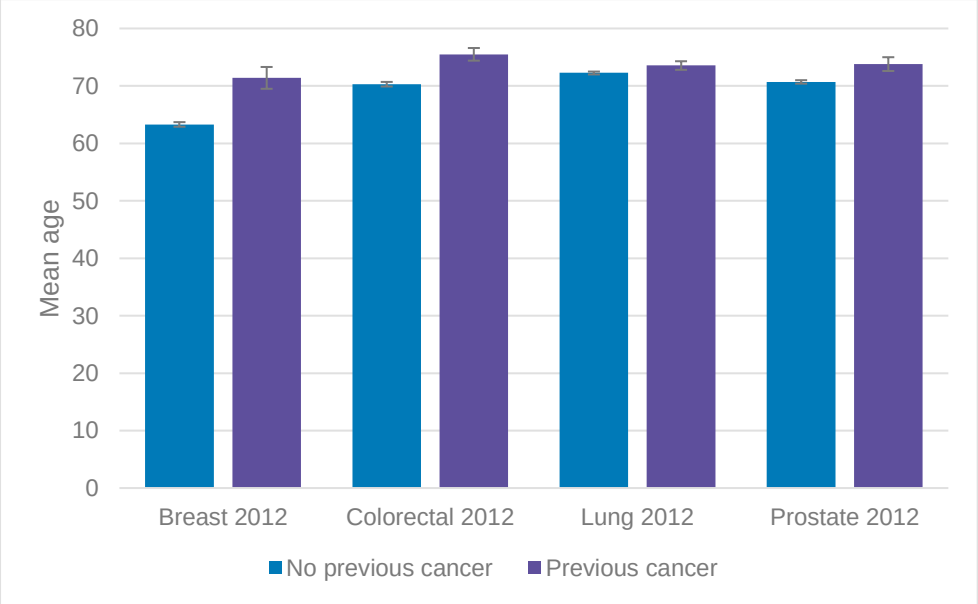

Figure 13: Mean age of those with previous non-cohort cancer recorded vs. rest of the cohort.

Other characteristics

There were no significant differences in the rates of previous diagnoses by SIMD, urban rural index, or sex (for lung and colorectal only). See Data Appendix (p38) for results.

3.3. Further cancer diagnoses around the same time or in follow-up

The proportion of people who experience a further cancer diagnosis in the 5 year follow-up period was relatively small, but varies by cancer site. It was highest in the **prostate** cancer cohort (7%, n=222) and **lowest** in the lung cancer cohort (under 3%, n=134) (Table 6).

Table 6: Number of people diagnosed with non-cohort cancers in 5 year follow up period

Cohort	No diagnoses in follow-up	Other diagnoses in 5 years of follow-up
Breast 2012	4280	188 (4.2%)
Colorectal 2012	3610	215 (5.6%)
Lung 2012	5048	134 (2.6%)
Prostate 2012	2885	222 (7.1%)

The **breast** cancer cohort had the lowest overall risk of a further cancer in the following 5 years compared to the other cohorts (Figure 14), significantly lower than the colorectal and lung cohorts. The **lung** cancer cohort had the highest age-standardised rate, although this was not significantly higher than the prostate and colorectal cancer cohorts.

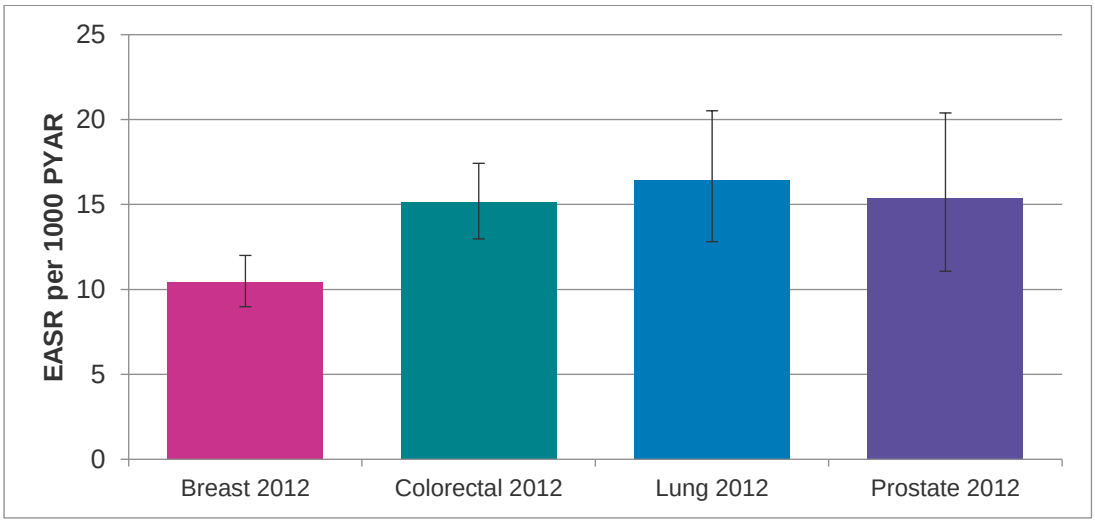

Figure 14 Non cohort diagnoses in follow up, EASR per 1000 PYAR in the 5 year follow-up period.

3.3.1. Characteristics

Age

Further cancer diagnoses in follow-up were, broadly speaking, more common in older people. In the **prostate** cancer cohort, the percentage of people diagnosed with a new cancer in follow-up increases steadily with age (Figure 15). However, in the other cohorts although the proportion developing another cancer in follow-up was notably higher in over 65s compared to under 65s, the increase is not continuous into older age.

When converting to rates per PYAR, to account for survival, the increase in diagnosis rate still increases with age but there was no marked peak in any cohort. Wide confidence intervals mean that, although rates are clearly higher in the oldest people compared to the youngest, it is not possible to say for certain whether the rate is truly ever-increasing with age, or whether it levels off after a certain point, as appears to be the case in over 65s in the **breast** cancer cohort (Figure 15, Figure 16).

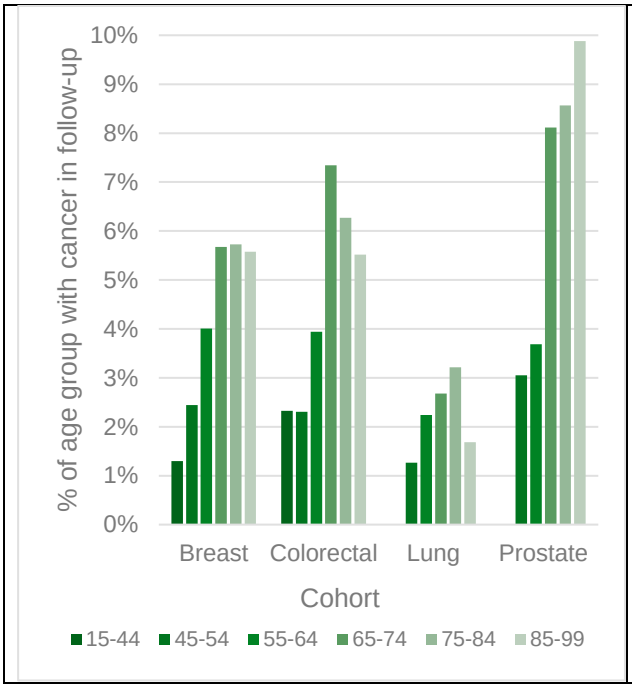

Figure 15: Percentage of people diagnosed in 2012 who had a non-cohort cancer diagnosis in the 5-year follow-up period, by age group

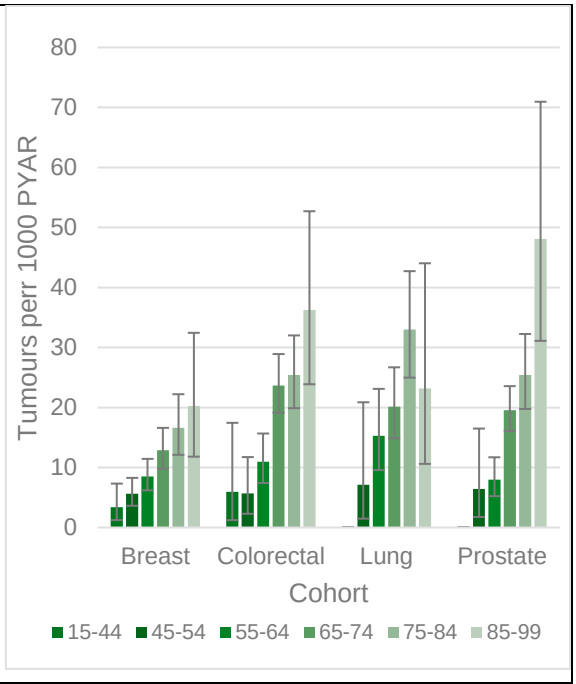

Figure 16: Rates of non-cohort cancer diagnoses per 1000 PYAR in the 5-year follow-up period in the 2012 cohorts

Other characteristics

In the **lung** and **colorecta**l 2012 cohorts a slightly higher proportion of males were diagnosed with another cancer in follow-up compared to females (Table 7).

Table 7: Proportion of males and females with further non-cohort cancer diagnoses.

Cohort	Sex	Further cancer diagnosed (%)
Colorectal 2012	Males	131 (6.3%)
Colorectal 2012	Females	84 (4.8%)
Lung 2012	Males	75 (2.9%)
Lung 2012	Females	59 (2.3%)

Differences in the rate of new cancer diagnoses in follow-up by deprivation (SIMD quintile) and by rurality were tested for. There was no evidence of any trend in the rate of new diagnoses by either rurality or deprivation. Results can be found in the Data appendix (p41).

Summary

- Diagnoses of cancers of other types tend to cluster in time, investigations for one cancer or set of symptoms are likely to uncover multiple tumours if present.
    - Before the cohort diagnosis, other diagnosis rates rise in the preceding 3-6 months.
    - Post-cohort diagnosis the rates of further cancer diagnosis remain high in the first 3-month period and are still elevated for prostate cancer in 3-6m time.
    - New tumour diagnosis rates start to increase again 1 year after diagnosis.

- Around 1 in 12 people in the **lung** cancer cohort had a previous diagnosis of a cancer of another site.

- The **breast** cancer cohort had the lowest proportion experiencing another cancer in the previous 10 years – possibly reflecting the younger age and general better health profile of this cohort.

- In general, multiple cancer diagnoses were more common in those over 65 at cohort diagnosis. This is probably because age is a risk factor for many cancers.

- The number of persons diagnosed with another cancer after the cohort cancer diagnosis broadly reflects survival differences, groups with generally short survival have few further cancers diagnosed.

- When converted to tumours per person year at risk (i.e. accounting for survival differences) it can be seen that:
    - The **breast** cancer cohorts have the lowest overall risk of a further (non-breast) cancer.
    - Conversely, the **lung** cancer cohorts have the highest risk.

- The rate of other cancer diagnoses increases with age at diagnosis.

4. Metastatic disease

Metastatic cancer (sometimes known as secondary cancer) is cancer that has spread from its original site to form a new tumour elsewhere[8]. In this chapter we include metastatic disease from any cancer, not just metastases originating from the cohort cancer.

Taking into account the whole follow-up period, the **prostate** cancer 2012 cohort (28%) has the lowest incidence of metastasis and the 2012 **lung** cancer cohort the highest (62%) (Table 8). Across all cohorts, a high proportion of all metastatic diagnoses are made within 6 months of the cohort cancer (Figure 17).

Table 8: Proportion of cohort with metastasis in the follow-up period.

Cohort	No	Yes	% with metastasis
Breast 2012	2953	1515	33.9%
Colorectal 2012	2166	1659	43.4%
Lung 2012	1987	3195	61.7%
Prostate 2012	2226	881	28.4%

4.1. Timing of metastasis

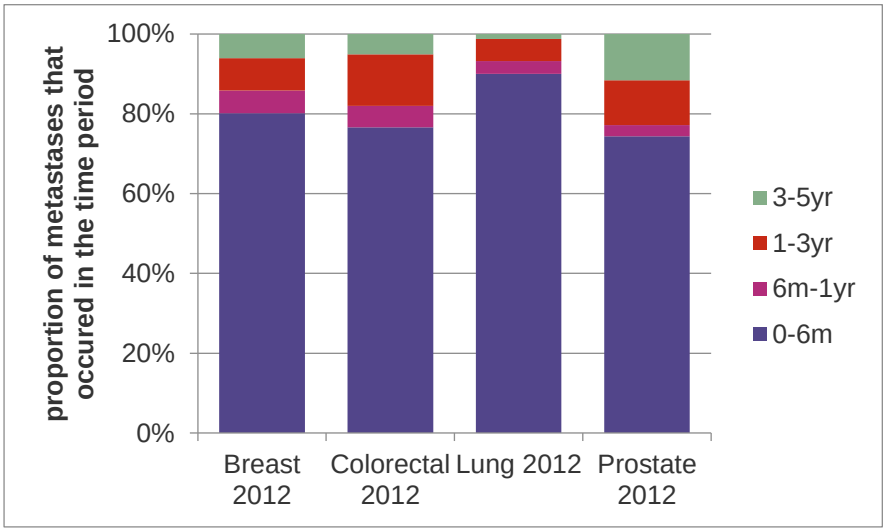

Figure 17: Timing of first evidence of metastatic disease in follow-up

Being diagnosed with a metastasis more than one year from the initial diagnosis is very rare in lung cancer (Figure 17,

Table 9), this is probably linked to the fact that a high proportion of people already have metastatic disease at diagnosis (see SRfD Results chapter), and to limited survival. The prostate cancer 2012 cohort had a relatively large number of people with their first evidence of metastatic disease occurring late in follow-up – 102 people were diagnosed

[8] For more information on what metastatic disease is, see https://www.macmillan.org.uk/cancer-information-and-support/secondary-cancer

with metastases over 3 years from their initial cancer diagnosis. (Figure 17). The **prostate** cancer cohort also had a relatively large number of people with additional cancers, and some metastatic disease is likely to be from these other cancers.

Table 9: Number and percentage of cohorts with metastasis recorded within 6 months of cohort diagnosis or later in follow-up

Cohort	0-6m metastases	Later metastases	No metastases
Breast 2012	1214 (27%)	301 (7%)	2953 (66%)
Colorectal 2012	1271 (33%)	388 (10%)	2166 (57%)
Lung 2012	2875 (55%)	320 (6%)	1987 (38%)
Prostate 2012	655 (21%)	226 (7%)	2226 (72%)

4.2. Characteristics

Age

In the **breast**, **colorectal** and **lung** cancer cohorts, a higher proportion of younger people have evidence of metastases compared to older people. However, a greater proportion of older people have unknown stage recorded, so we can't be certain that this gradient is real, rather than an artefact of data quality (see SRfD Results chapter).

The opposite trend occurs in the prostate cohort, with more metastases in older people. This is despite the fact that there is poorer recording of staging information in the elderly, so the true gradient may be steeper.

Table 10: The numbers and percentage of each age group with metastases recorded

Cohort	Age group	N (%) with metastasis	N(%) without metastasis
Breast 2012	15-44	184 (47.8%)	201 (52.2%)
	45-54	369 (39.2%)	572 (60.8%)
	55-64	335 (30.5%)	764 (69.5%)
	65-74	305 (30.3%)	700 (69.7%)
	75-84	244 (33.3%)	489 (66.7%)
	85-99	78 (25.6%)	227 (74.4%)
CRC 2012	15-44	63 (48.8%)	66 (51.2%)
	45-54	152 (50.0%)	152 (50.0%)
	55-64	330 (46.4%)	381 (53.6%)
	65-74	499 (43.6%)	645 (56.4%)
	75-84	448 (41.3%)	636 (58.7%)
	85-99	167 (36.9%)	286 (63.1%)
Lung 2012	15-44	30 (78.9%)	8 (21.1%)
	45-54	185 (78.1%)	52 (21.9%)
	55-64	658 (70.2%)	279 (29.8%)
	65-74	1131 (64.4%)	624 (35.6%)
	75-84	938 (55.8%)	743 (44.2%)
	85-99	253 (47.4%)	281 (52.6%)
Prostate 2012	15-54	20 (15.3%)	112 (85.5%)
	55-64	146 (20.7%)	560 (79.3%)
	65-74	289 (22.8%)	980 (77.2%)
	75-84	299 (40.0%)	448 (60.0%)
	85-99	127 (50.2%)	126 (49.8%)

Other characteristics

There was no difference in the proportion of males and females with metastases in the lung and colorectal cancer cohorts. There were no significant trends evident in the proportion of people with metastases by deprivation (SIMD) and rurality (urban-rural index). (See Data appendix p41 for full results).

4.3. Metastases and other cancers

If a person has another primary cancer diagnosis in addition to the primary cohort cancer it is not possible to determine for certain from the available data whether the metastasis arises from the cohort cancer or another cancer (see technical appendix for further details). Out of people with metastases recorded in follow-up, the proportion that have a non-cohort tumour diagnosed before the metastasis ranges from 7% to 17% (Table 11). In the **breast**, **colorectal** and **lung** cancer cohorts, the proportion of people with metastases *and* another cancer diagnosis broadly reflects the proportion of people in the cohorts with another diagnosis at any point. In the **prostate** cancer cohort, a slightly higher proportion of the men with metastases also had another cancer diagnosis, compared to the rest of the cohort.

When broken down by the timing of metastases, it is notable that a much higher proportion of those with metastases diagnosed after 6 months have another non-cohort cancer present before the metastases is diagnosed. This is highest in the **prostate** cancer cohorts, where up to 40% of those developing metastases more than 6 months after their cohort diagnosis also have another primary cancer in addition to their prostate cancer (see Data appendix Table A31).

Table 11: Number and percentage of people with metastases who had another tumour diagnosed on or before the date the metastases was first recorded.

Cohort	No other cancer	Other cancer (%)
Breast 2012	1409 (93.0%)	106 (7.0%)
Colorectal 2012	1482 (89.3%)	177 (10.7%)
Lung 2012	2882 (90.2%)	313 (9.8%)
Prostate 2012	728 (82.6%)	153 (17.4%)

Summary

- The **lung** cancer cohort had the highest proportion of people with metastatic disease, and the **prostate** cancer cohort the lowest.

- Most metastatic disease was diagnosed within 0-6 months of the cohort diagnosis. However, there are a minority diagnosed with metastatic disease years later, this proportion is highest in cohorts with higher long-term survival. Some of these late metastatic diagnoses will be related to other cancers, not the cohort cancer.

- Trends in recording of more metastases in younger people in the **breast**, **colorectal** and **lung** cohorts may be due to more missing data in older people's records.

- In **prostate** cancer cohorts, there was more metastatic disease in older people, despite more missing staging data.

Further Information

Further information on the Scottish Routes from Diagnosis project, or other work resulting from our partnership, can be found on the Macmillan or the Public Health Scotland websites or by contacting us at phs.macmillan@phs.scot or HealthData@macmillan.org.uk.

Technical appendix

Technical notes & Assumptions

The SRfD project focused on 8 cohorts of people diagnosed with cancer. Each cohort was divided into four "outcome groups", depending on factors such as survival time, evidence of continued cancer (treatment) beyond the first year and long term use of hospital services (see SRfD previous chapters for more details of these groups*)*. In other chapters the focus was on the different experiences of each outcome group in this chapter there is more limited exploration of differences between outcome groups, as having evidence of further cancers is part of the definition for OG3, and by definition, OG1 and 2 should not have any evidence of further cancer related hospital activity between 1 and 5 years after the cancer diagnosis. However, cancer diagnoses before the cohort cancer date do not determine which OG a person is in, so for previous cancers, between group differences are addressed.

Data sources

Cancer registrations were retrieved from the Scottish Cancer registry (SMR06) for the follow-up periods for each cohort (5 years for the 2012 cohorts, 10 years for the 2007 cohorts) and for 10 years before the cohort diagnosis date.

For the section of the chapter that deals with metastatic disease (when the cancer has spread beyond its original site), evidence of metastasis was also taken from the cancer registry. Metastases are not recorded separately on the registry, cancer records include information on the cancer stage at diagnosis, including whether metastases are known to be present at that time. Acute hospital records were also searched for diagnosis codes relating to metastases.

Definitions

Metastasis– metastatic disease is defined as when a cancer has spread from its original site and started new tumour(s) in another organ or organs in the body. Otherwise known as secondary or stage IV cancer. Metastatic cancer is much less likely to be curable, although it may still be treatable. If a cancer is not noted to be metastatic at diagnosis, but the person later has metastatic disease, this is an indication that the disease has either progressed (treatment was unsuccessful), or recurred (treatment was apparently or initially successful, but the cancer has returned at a later date, at a different site).

Recurrence - When a cancer has become clinically undetectable but then a new tumour grows from the same cells. If a biopsy is taken, it is possible to determine if the new tumour is formed of cells from the original cancer or is a new, independent growth. It can be clinically difficult to determine whether a cancer is a genuinely new tumour or a recurrence. Tumours determined to be a recurrence are not recorded in the cancer

registry, nor are they specifically noted to be recurrences in other datasets, so we do not have any data on recurrence to analyse.

Abbreviations – please see Appendix A in the SRfD Context and Methodology chapter for a full list of useful terms and abbreviations

SRfD - Scottish Routes from Diagnosis

PHS – Public Health Scotland

PYAR – Person year at risk. i.e. the total number of people alive times the time period. One person for one year = 1 PYAR, 2 people for 6 months each = 1PYAR.

PLWC – People/Person living with cancer

Methods

Multiple primary tumours of the same cancer site are not infrequently diagnosed for some cancer sites, due to cancer aetiology e.g. for breast cancer, bilateral occurrence or repeat occurrences are not uncommon. Therefore, the chances of developing another cancer of the same site compared to another cancer site are often determined by different factors. For this reason, we report statistics on multiple tumours of the same site and multiple tumours of different sites separately.

Some PLWC have more than one additional tumour diagnosed in the follow-up period or look back period. Most measures in this chapter focus on the number of people affected by multiple cancers, rather than the total number of tumours diagnosed per cohort. The exceptions to this are clearly noted in the text.

It should be noted that in follow-up, death is a competing factor with risk of another tumour i.e. those with short survival do not have much time to develop/ be diagnosed with another tumour. The number of tumour diagnoses is therefore converted to a rate **per person year at risk (PYAR);** this allows exploration of the relative risks of developing another tumour according to cohort, whilst accounting for differences in survival time. Any use of rates per PYAR *do* include multiple tumours per person in the calculation of these rates.

Age-sex-standardised rates allow for differences in the age/sex structure of populations and allow valid comparisons to be made between geographical areas and through time. They do this by applying the age-specific rates for the area being studied to a theoretical European standard population. Age-standardised rates in this publication are usually expressed in terms of rate per 1000 PYAR, see above. The standardised rates presented are truncated (age 45 and over) European age-sex-standardised rates (EASR) for colorectal and lung cancer and truncated European age-standardised rates (EASR) for breast and prostate cancer; as such they differ from national rates published elsewhere.

Defining and dating evidence of metastasis*:* Evidence of metastatic disease was taken from:

1. Linked hospital admission (SMR01) records which contained a diagnosis of metastatic disease or
2. Any cancer registration in SMR06 that indicate the presence of metastases, (including evidence of radiotherapy to metastases or histology of metastasis).
3. In SMR06, cancers recorded as 'cancers of unknown primary' (i.e. metastases for which the original cancer is not known) are also included in the analysis.

The date of metastasis was taken to be the date of diagnosis on an SMR06 record, or the date of discharge from SMR01, with the following exceptions:

- Where the evidence of metastasis was based on pathology (pathology M, Duke's D stage, and histology of metastasis) the date of metastasis was taken to be the date of surgery (if present). If no date of surgery was present, the date was taken to be the date of diagnosis.
- If radiotherapy to metastasis was indicated and clinical M stage was not 1, the date of metastasis was taken to be the first radiotherapy date.

Where there is more than one record that indicates metastases, the earliest date is taken to be the date of first evidence of metastases.

Cox regression

Cox regression was used to calculate the impact of a previous cancer on the risk of death compared to not having a previous cancer diagnosis. Cox regression is a commonly used method to analyse survival date to investigate the impact of specific variables on survival. The output of the model is a hazard ratio or ratios, a ratio of more than one means that the risk, or hazard of death for the individuals in the group it refers to is increased at any point in the time period, compared to the comparison group. A hazard ratio of less than one means that the risk is reduced. The output of Cox regression does not tell you anything about the absolute risk of death (how many people are expected to die), only about the relative risk of death in one group compared to another.

Limitations (general)

Metastasis

If a person has known metastatic disease at the time a primary tumour is diagnosed (or within 4 months), the information in the cancer registry will include this information as part of the cancer stage at diagnosis. However, staging information is not always completed or is recorded as "unknown stage" if investigations for metastases have not taken place or not been completed. This may lead to an underestimate of the true total number of people with metastatic disease. Incompleteness can also lead to bias; stage at diagnosis is more often recorded as "not known" in older people for example. Later

diagnoses of metastatic disease can be picked up from acute hospital records. Metastasis that are detected at a later date determined by pathology may be recorded if surgery takes place at a later date (this is unlikely except in case of prostate cancer initially treated by watch and wait but then later progressing to surgery).

We do not attempt to attribute the metastasis to the cohort cancer or another cancer in the analysis. This decision was made partially in order to include the experiences of those that have a metastasis originating from another tumour, but also because if a person has been diagnosed with more than one primary cancer, there is inherent uncertainty about the origin of any metastatic disease. If a biopsy is taken of the metastasis it would usually be possible to determine the origin with some certainty, however in some cases a biopsy is not taken – e.g. often in the case of brain metastases – and under this scenario any attribution of the origin contains some uncertainty. The datasets that we use in this analysis do not include information on how the origin of metastasis was determined. We include all records of metastases in our analysis, including those that are specifically recorded as cancers of unknown primary.

Recurrence

We were not able to address the question of recurrent disease in the analysis as data on recurrence is available in the datasets used. This is a major limitation of the study, as we do not have any information on the proportion of the cohort experiencing recurrence, or any information on the time which was spent "cancer free" between treatment and recurrence.

Data appendix

SIMD 2012 and URI6 2011-12 were used for the 2012 cohorts.

Where standardised rates are shown (EASR45) these are European age standardised rates truncated at age 45. UCI = upper 95% confidence interval. LCI = Lower 95% confidence interval. Rates/CI are blank where they can't be calculated due to low numbers.

Table A12: Incidence of cancers in Scotland 2012 - total population[6]

Cancer site	Incidence
Trachea; bronchus and lung	5292
Breast	4659
Colorectal cancer	3919
Prostate	3135
Head and neck	1330
Malignant melanoma of the skin	1188
Non-Hodgkin lymphoma	1102
Kidney	913

Oesophagus	895
Bladder	854

Table A13: Cancer incidence in Scotland 2012: Top ten for females[9]

Cancer site	Incidence
Breast	4631
Trachea; bronchus and lung	2635
Colorectal cancer	1787
Corpus uteri	683
Malignant melanoma of the skin	635
Ovary	626
Non-Hodgkin lymphoma	545
Head and neck	427
Pancreas	396
Kidney	388

Table A14: Cancer incidence in Scotland 2012: Top ten cancers in males[6]

	Males
Cancer site	**Incidence**
Prostate	3135
Trachea; bronchus and lung	2657
Colorectal cancer	2132
Head and neck	903
Oesophagus	584
Bladder	572
Non-Hodgkin lymphoma	557
Malignant melanoma of the skin	553
Kidney	525
Stomach	451

Multiple cancers of the same type

Previous cancers

Table A15: Proportion of males and females with a previous cohort cancer diagnoses.

Cohort	Sex	Further cancer diagnosed (%)
Colorectal 2012	Males	40 (1.9%)
Colorectal 2012	Females	23 (1.3%)
Lung 2012	Males	21 (0.8%)
Lung 2012	Females	22 (0.9%)

[9] From ISD Cancer Statistics https://www.isdscotland.org/Health-Topics/Cancer/Publications/2019-04-30/visualisation.asp

Table A16 Number of people with a previous cohort cancer diagnosis, by cohort and SIMD quintile (SIMD 2012 was used for the 2012 cohorts).

		Previous cohort cancer		
Cohort	SIMD	No	Yes	% with previous cohort cancer
Breast 2012	1 - Most deprived	768	21	2.7%
	2	834	15	1.8%
	3	901	18	2.0%
	4	909	16	1.7%
	5 - Least deprived	967	19	1.9%
Colorectal 2012	1 - Most deprived	754	9	1.2%
	2	798	15	1.8%
	3	698	12	1.7%
	4	798	16	2.0%
	5 - Least deprived	714	11	1.5%
Lung 2012	1 - Most deprived	1600	15	0.9%
	2	1216	10	0.8%
	3	1007	11	1.1%
	4	757	5	0.7%
	5 - Least deprived	559	2	0.4%

Table A17: Number of people with a previous cohort cancer diagnosis, by cohort and urban rural index (UR 6 2011-12 was used for the 2012 cohorts).

Cohort	Urban rural index	Previous cohort cancer		Total	%
		No	Yes		
Breast 2012	Large Urban Areas	1648	30	1678	1.8%
	Other Urban Areas	1247	31	1278	2.4%
	Accessible Small Towns	405	6	411	1.5%
	Remote Small Towns	177	1	178	0.6%
	Accessible Rural	555	15	570	2.6%
	Remote Rural	346	5	351	1.4%
	Missing index	1	1	2	
Colorectal 2012	Large Urban Areas	1380	15	1395	1.1%
	Other Urban Areas	1100	26	1126	2.3%
	Accessible Small Towns	337	5	342	1.5%
	Remote Small Towns	188	4	192	2.1%
	Accessible Rural	473	9	482	1.9%
	Remote Rural	283	4	287	1.4%
	Missing Index	1	0	1	
Lung 2012	Large Urban Areas	2181	21	2202	1.0%
	Other Urban Areas	1530	15	1545	1.0%
	Accessible Small Towns	436	1	437	0.2%
	Remote Small Towns	203	1	204	0.5%
	Accessible Rural	494	4	498	0.8%
	Remote Rural	292	1	293	0.3%
	Missing index	3	0	3	

Cohort cancer diagnosis in follow-up

Table A18: Proportion of males and females with a cohort site tumours after cohort diagnosis.

Cohort	Sex	Further cancer diagnosed (%)
Colorectal 2012	Males	58 (2.8%)
Colorectal 2012	Females	37 (2.1%)
Lung 2012	Males	47 (1.8%)
Lung 2012	Females	59 (2.3%)

Table A19: The numbers and percentage of each age group with a cohort site tumours after cohort diagnosis.

Cohort	Age band	N with cohort tumour afte cohort diagnosis (%)
Breast 2012	15-44	11 (2.9%)
	45-54	39 (4.1%)
	55-64	29 (2.6%)
	65-74	47 (4.7%)
	75-84	32 (4.4%)
	85-99	12 (3.9%)
Colorectal 2012	15-44	2 (1.6%)
	45-54	3 (1.0%)
	55-64	23 (3.2%)
	65-74	31 (2.7%)
	75-84	32 (3.0%)
	85-99	4 (0.9%)
Lung 2012	15-44	2 (5.3%)
	45-54	8 (3.4%)
	55-64	23 (2.5%)
	65-74	39 (2.2%)
	75-84	27 (1.6%)
	85-99	7 (1.3%)

Table A20: number of people with cohort site tumours after cohort diagnosis, by SIMD quintile (SIMD 2012 was used for the 2012 cohorts).

Cohort	SIMD	Multiple primaries		Total	% with multiple primaries
		No	Yes		
Breast 2012	1 - Most deprived	758	31	789	3.9%
	2	813	36	849	4.2%
	3	880	39	919	4.2%
	4	895	30	925	3.2%
	5 - Least deprived	952	34	986	3.4%
Colorectal 2012	1 - Most deprived	744	19	763	2.5%
	2	800	13	813	1.6%
	3	695	15	710	2.1%
	4	783	31	814	3.8%
	5 - Least deprived	708	17	725	2.3%
Lung 2012	1 - Most deprived	1583	32	1615	2.0%
	2	1206	20	1226	1.6%
	3	993	25	1018	2.5%
	4	742	20	762	2.6%
	5 - Least deprived	552	9	561	1.6%

Table A21: number of people with cohort site tumours in follow-up, by urban rural index

Cohort	UR index	no	yes	total	%
Breast 2012	Large Urban Areas	1608	70	1678	4.2%
	Other Urban Areas	1231	47	1278	3.7%
	Accessible Small Towns	398	13	411	3.2%
	Remote Small Towns	171	7	178	3.9%
	Accessible Rural	551	19	570	3.3%
	Remote Rural	337	14	351	4.0%
	Missing	2	0	2	-
Colorectal 2012	Large Urban Areas	1363	32	1395	2.3%
	Other Urban Areas	1090	36	1126	3.2%
	Accessible Small Towns	334	8	342	2.3%
	Remote Small Towns	186	6	192	3.1%
	Accessible Rural	474	8	482	1.7%
	Remote Rural	282	5	287	1.7%
	Missing	1	0	1	
Lung 2012	Large Urban Areas	2152	50	2202	2.3%
	Other Urban Areas	1506	39	1545	2.5%
	Accessible Small Towns	427	10	437	2.3%
	Remote Small Towns	203	1	204	0.5%
	Accessible Rural	492	6	498	1.2%
	Remote Rural	293	0	293	0.0%
	Missing	3	0	3	0

Multiple cancers of different types

Table A22: Proportion of people with a non-cohort site tumour either prior to cohort diagnosis or in follow-up.

Cohort	Number (%)
Breast 2012	319 (7.1%)
Colorectal 2012	424 (11.1%)
Lung 2012	566 (10.9%)
Prostate 2012	408 (13.1%)

Previous non-cohort cancers

Table A23: Proportion of males and females with a non-cohort site tumour prior to cohort diagnosis.

Cohort	Sex	Further cancer diagnosed (%)
Colorectal 2012	Males	120 (5.8%)
Colorectal 2012	Females	101 (5.8%)
Lung 2012	Males	249 (9.6%)

Lung 2012	Females	193 (7.5%)

Table A24 Number of people with a previous non-cohort cancer diagnosis, by cohort and SIMD quintile (SIMD 2012 was used for the 2012 cohorts).

Cohort	SIMD	Number	% with non-cohort cancer in follow-up
Breast 2012	1 - Most deprived	34	4.3%
	2	24	2.8%
	3	30	3.3%
	4	24	2.6%
	5 - Least deprived	29	2.9%
Colorectal 2012	1 - Most deprived	39	5.1%
	2	38	4.7%
	3	40	5.6%
	4	47	5.8%
	5 - Least deprived	57	7.9%
Lung 2012	1 - Most deprived	134	8.3%
	2	112	9.1%
	3	87	8.5%
	4	55	7.2%
	5 - Least deprived	54	9.6%
Prostate 2012	1 - Most deprived	26	5.7%
	2	43	7.2%
	3	47	7.4%
	4	37	5.2%
	5 - Least deprived	52	7.4%

Table A25 Number of people with a previous non-cohort cancer diagnosis, by cohort and urban rural index

		Previous non-cohort diagnosis		
Cohort	**Urban rural index**	**No**	**Yes**	**% with non-cohort cancer**
Breast 2012	Large Urban Areas	1622	56	3.3%
	Other Urban Areas	1242	36	2.8%
	Accessible Small Towns	395	16	3.9%
	Remote Small Towns	172	6	3.4%
	Accessible Rural	550	20	3.5%
	Remote Rural	344	7	2.0%
	Missing Index	2	0	0.0%
Colorectal 2012	Large Urban Areas	1310	85	6.1%
	Other Urban Areas	1065	61	5.4%
	Accessible Small Towns	323	19	5.6%
	Remote Small Towns	179	13	6.8%
	Accessible Rural	449	33	6.8%
	Remote Rural	277	10	3.5%
	Missing Index	1	0	0.0%
Lung 2012	Large Urban Areas	1998	204	9.3%
	Other Urban Areas	1413	132	8.5%
	Accessible Small Towns	409	28	6.4%
	Remote Small Towns	187	17	8.3%
	Accessible Rural	460	38	7.6%
	Remote Rural	270	23	7.8%
	Missing Index	3	0	0.0%
Prostate 2012	Large Urban Areas	1005	64	6.0%
	Other Urban Areas	811	60	6.9%
	Accessible Small Towns	275	22	7.4%
	Remote Small Towns	104	11	9.6%
	Accessible Rural	464	27	5.5%
	Remote Rural	241	21	8.0%
	Missing Index	2	0	0.0%

Non-cohort cancers diagnosis in follow-up

Table A26: Crude incidence rates of other cancers per 1000 PYAR (person years at risk) diagnosed in the 10 years before the cohort cancer.

Cohort	Crude rate (per 1000 PYAR)	LCI	UCI
Breast 2012	3.27	2.76	3.84
Colorectal 2012	6.35	5.58	7.20
Lung 2012	9.01	8.21	9.87
Prostate 2012	6.86	5.97	7.84

Table A27 Number of people with a non-cohort cancer diagnosis in follow-up, by cohort and SIMD quintile (SIMD 2012 was used for the 2012 cohorts).

Cohort	SIMD	Number	% with non-cohort cancer in follow-up
Breast 2012	1 - Most deprived	44	5.6%
	2	26	3.1%
	3	49	5.3%
	4	27	2.9%
	5 - Least deprived	42	4.3%
Colorectal 2012	1 - Most deprived	38	5.0%
	2	47	5.8%
	3	44	6.2%
	4	45	5.5%
	5 - Least deprived	41	5.7%
Lung 2012	1 - Most deprived	53	3.3%
	2	30	2.4%
	3	26	2.6%
	4	12	1.6%
	5 - Least deprived	13	2.3%
Prostate 2012	1 - Most deprived	43	9.4%
	2	40	6.7%
	3	44	6.9%
	4	49	6.9%
	5 - Least deprived	46	6.5%

Table A28 Number of people with a non-cohort cancer diagnosis in follow-up, by cohort and urban rural index.

Cohort	SIMD	Number	% with non-cohort cancer in follow-up
Breast 2012	Large Urban Areas	58	3.9%
	Other Urban Areas	76	4.9%
	Accessible Small Towns	15	3.9%
	Remote Small Towns	8	4.5%
	Accessible Rural	26	3.7%
	Remote Rural	5	3.2%
Colorectal 2012	Large Urban Areas	79	6.4%
	Other Urban Areas	67	4.9%
	Accessible Small Towns	23	6.6%
	Remote Small Towns	9	5.0%
	Accessible Rural	28	4.8%
	Remote Rural	9	7.1%
Lung 2012	Large Urban Areas	54	2.7%
	Other Urban Areas	50	2.7%
	Accessible Small Towns	10	2.4%
	Remote Small Towns	1	0.5%
	Accessible Rural	15	2.4%
	Remote Rural	4	2.9%
Prostate 2012	Large Urban Areas	76	7.9%
	Other Urban Areas	70	6.8%
	Accessible Small Towns	19	6.8%
	Remote Small Towns	10	8.6%
	Accessible Rural	42	7.0%
	Remote Rural	5	4.2%

Metastatic disease

Table A29 Number and truncated (at 45) age-standardised rates per 1000 people with metastases in follow-up by SIMD quintile (SIMD 2012 was used for the 2012 cohorts). EASR45 = European age standardised rates truncated at 45. UCI = upper 95% confidence interval. LCI = Lower 95% confidence interval

		Metastasis								
Cohort	**SIMD2009**	no	yes	**Total**	**Percentage**	**LCI**	**UCI**	**EASR45**	**LCI**	**UCI**
Breast 2012	1 - Most deprived	516	273	789	34.6%	30.6	39.0	35.4	31.0	40.2
	2	554	295	849	34.7%	30.9	38.9	34.7	30.4	39.3
	3	586	333	919	36.2%	32.4	40.3	36.6	32.4	41.1
	4	627	298	925	32.2%	28.7	36.1	32.0	28.2	36.0
	5 - Least deprived	670	316	986	32.0%	28.6	35.8	30.4	26.8	34.3
Colorectal 2012	1 - Most deprived	434	329	763	43.1%	38.6	48.0	47.2	40.3	54.6
	2	464	349	813	42.9%	38.5	47.7	44.6	38.2	51.4
	3	383	327	710	46.1%	41.2	51.3	48.5	40.2	57.5
	4	474	340	814	41.8%	37.4	46.5	45.8	38.5	53.7
	5 - Least deprived	411	314	725	43.3%	38.7	48.4	44.3	37.6	51.6
Lung 2012	1 - Most deprived	642	973	1615	60.2%	56.5	64.2	64.2	64.2	64.2
	2	467	759	1226	61.9%	57.6	66.5	66.5	66.5	66.5
	3	371	647	1018	63.6%	58.8	68.6	68.6	68.6	68.6
	4	290	472	762	61.9%	56.5	67.8	67.8	67.8	67.8
	5 - Least deprived	217	344	561	61.3%	55.0	68.2	68.2	68.2	68.2
Prostate 2012	1 - Most deprived	304	152	456	33.3%	28.2	39.1	31.6	21.1	44.2
	2	437	158	595	26.6%	22.6	31.0	22.6	15.1	31.5
	3	446	192	638	30.1%	26.0	34.7	24.1	19.9	28.8
	4	505	209	714	29.3%	25.4	33.5	22.4	18.6	26.6
	5 - Least deprived	534	170	704	24.1%	20.7	28.1	18.2	15.2	21.5

Urban rural index

Table A30: Number and truncated (at age 45) age-standardised rates per 1000 people with metastases in follow-up by urban rural index (2011-12 URI index was used for the 2012 cohorts) EASR45 = European age standardised rates truncated at 45. UCI = upper 95% confidence interval. LCI = Lower 95% confidence interval

		Metastasis								
Cohort	**Urban rural index**	No	Yes	**Total**	**Percentage**	**LCI**	**UCI**	**EASR45**	**LCI**	**UCI**
Breast 2012	Large Urban Areas	1104	574	1678	34.2%	31.5	37.1	33.3	30.4	36.4
	Other Urban Areas	849	429	1278	33.6%	30.5	36.9	32.9	29.5	36.4
	Accessible Small Towns	274	137	411	33.3%	28.0	39.4	36.1	29.8	42.9
	Remote Small Towns	106	72	178	40.4%	31.6	50.9	41.5	31.6	52.8
	Accessible Rural	378	192	570	33.7%	29.1	38.8	33.3	28.4	38.7
	Remote Rural	242	109	351	31.1%	25.5	37.5	32.4	25.6	39.9
	Missing	0	2	2	100.0%	-	-	-	-	-
Colorectal 2012	Large Urban Areas	800	595	1395	42.7%	39.3	46.2	44.1	39.0	49.5
	Other Urban Areas	640	486	1126	43.2%	39.4	47.2	46.1	40.3	52.1
	Accessible Small Towns	189	153	342	44.7%	37.9	52.4	46.3	34.9	59.2
	Remote Small Towns	106	86	192	44.8%	35.8	55.3	56.0	39.8	75.0
	Accessible Rural	274	208	482	43.2%	37.5	49.4	44.1	35.6	53.5
	Remote Rural	156	131	287	45.6%	38.2	54.2	48.1	32.0	67.5
	Missing	1	0	1	0.0%	-	-	-	-	-
Lung 2012	Large Urban Areas	859	1343	2202	61.0%	57.8	64.3	68.1	61.9	74.7
	Other Urban Areas	587	958	1545	62.0%	58.1	66.1	67.5	59.7	75.8
	Accessible Small Towns	187	250	437	57.2%	50.3	64.8	60.6	43.7	80.4
	Remote Small Towns	81	123	204	60.3%	50.1	71.9	55.9	43.8	69.4
	Accessible Rural	176	322	498	64.7%	57.8	72.1	64.9	51.3	80.1
	Remote Rural	95	198	293	67.6%	58.5	77.7	73.7	54.4	95.9
	Missing	2	1	3	66.6%	-	-	-	-	-
Prostate 2012	Large Urban Areas	767	302	1069	28.3%	25.2	31.6	23.9	19.6	28.6
	Other Urban Areas	613	258	871	29.6%	26.1	33.5	28.4	18.5	40.4
	Accessible Small Towns	225	72	297	24.2%	19.0	30.5	18.4	12.9	25.0
	Remote Small Towns	81	34	115	29.6%	20.5	41.3			
	Accessible Rural	351	140	491	28.5%	24.0	33.6	21.5	17.5	26.0
	Remote Rural	187	75	262	28.6%	22.5	35.9	22.6	15.8	30.5
	Missing	2	0	2	0.0%	-	-	-	-	-

Metastases and other cancers

Table A31: Number of people with metastases who also have a non-cohort primary cancer that was diagnosed before the metastasis was diagnosed.

		People with metastases within 6m of cohort diagnosis			People with metastases diagnosed more than 6m after cohort diagnosis		
Cohort	N of people with no metastases	No pre-existing non-cohort cancer	Pre-existing non-cohort cancer	% with other cancer	No pre-existing non-cohort cancer	Pre-existing non-cohort cancer	% with other cancer
Breast 2012	2953	1172	42	3%	237	64	21%
Colorectal 2012	2166	1170	101	8%	312	76	20%
Lung 2012	1987	2623	252	9%	259	61	19%
Prostate 2012	2226	594	61	9%	134	92	41%

Supplementary Report on survival in people with a previous cancer diagnosis

Introduction

It was hypothesised that people who had a previous (non-cohort) cancer diagnosis would have lower survival and poorer outcomes due to increased burden of illness, and possibly increased burden of treatment. It was expected that the effect would be stronger if the previous cancer diagnosis was more recent, as treatments might therefore be concurrent, or second treatment / illness occur before full recovery from the previous cancer.

The look back period was divided into the periods: 0 to <1 year, 1 year to <3y ears, 3 to <5 years, and 5 to <10 years and grouped people according to which period they had received a previous diagnosis (in the case that a person had more than one record of a previous cancer, persons were assigned to the most recent time category in which they had a diagnosis). Cox regression was used to compare survival times of persons with no history of cancer in the last 10 years with those who had a history of cancer (in the time categories above)[10]. The models were stratified by age band to account for age differences between the groups. Results are shown and discussed below.

Method

Cox regression was used to calculate the impact of a previous cancer on the risk of death compared to not having a previous cancer diagnosis. Cox regression is a commonly used method to analyse survival date to investigate the impact of specific variables on survival. The output of the model is a hazard ratio or ratios, a ratio of more than one means that the risk, or hazard of death for the individuals in the group it refers to is increased at any point in the time period, compared to the comparison group. A hazard ratio of less than one means that the risk is reduced. The output of Cox regression does not tell you anything about the absolute risk of death (how many people are expected to die), only about the relative risk of death in one group compared to another.

[10] See technical appendix for details of method.

Results

Breast cancer

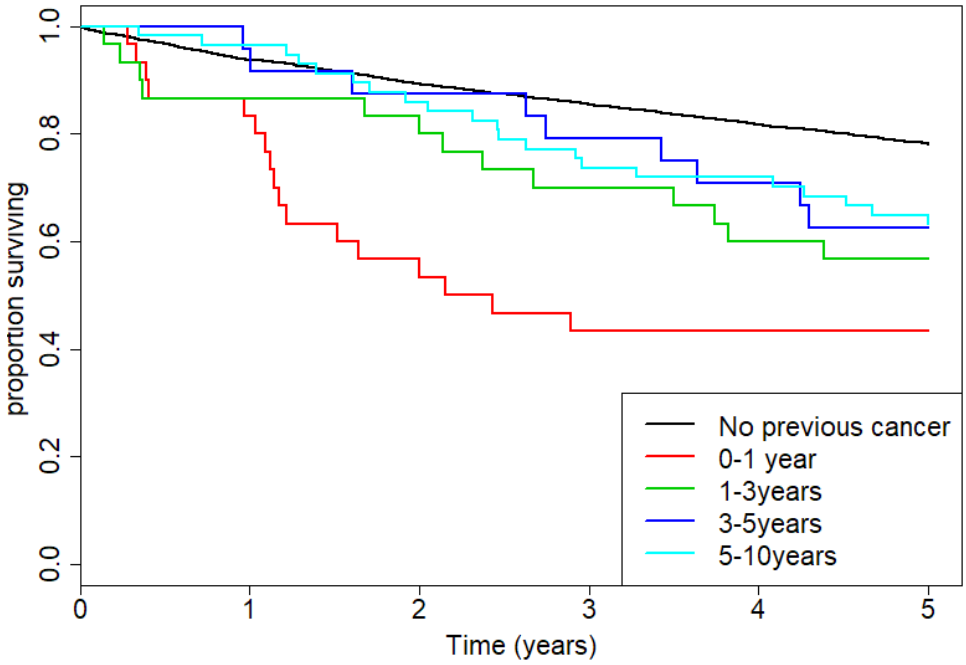

Figure 18 Kaplan-Meier plot of survival in Breast cancer 2012 cohort, divided according to presence and timing of a previous cancer diagnosis.

Table 32: Cox regression results for the age stratified model, Breast 2012 cohort.

Timing of previous cancer	N in group	Hazard ratio	p-value
<1 year	30	2.4	**<0.001**
1-3 year	30	1.6	0.111
3-5 year	24	1.3	0.504
5-10 years	57	1.3	0.198
None in last 10 years	4327		

In the 2012 **breast** cancer cohort, reduced survival was seen in persons with a previous cancer history (Figure 18), this was significant only for persons with a previous diagnosis within 1 year (Table 32). Results from the 2007 cohort were similar.

Colorectal cancer

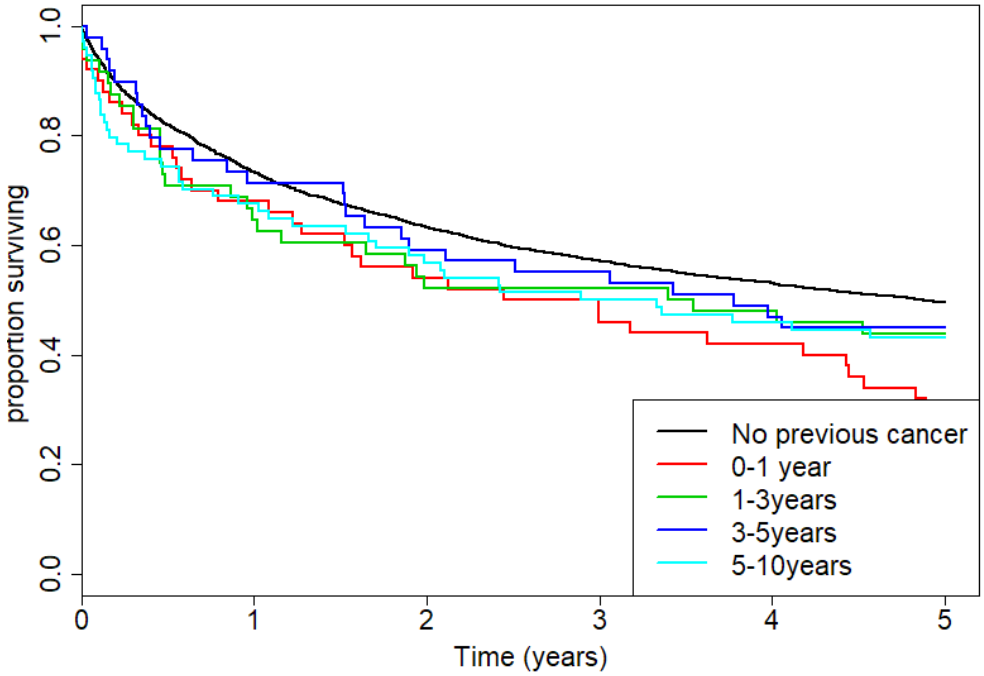

Figure 19 Kaplan-Meier plot of survival in Colorectal cancer 2012 cohort, by presence and timing of a previous cancer diagnosis.

Table 33: Cox regression results Colorectal cancer 2012

Timing of previous cancer	N in group	Hazard ratio	p-value
<1 year	50	1.4	0.066
1-<3 year	48	1.1	0.792
3-<5 year	49	1.0	0.824
5-<10 years	74	0.99	0.968
None in last 10 years	3604		

There was no evidence that a prior diagnosis had a significant impact on survival in the **colorectal** cancer cohort (Figure 19), hazard ratios were above 1 for most groups with previous cancers compared to those with no cancer history, however, this was not statistically significant (Table 33). Again, the results for the 2007 cohort were similar.

Lung cancer

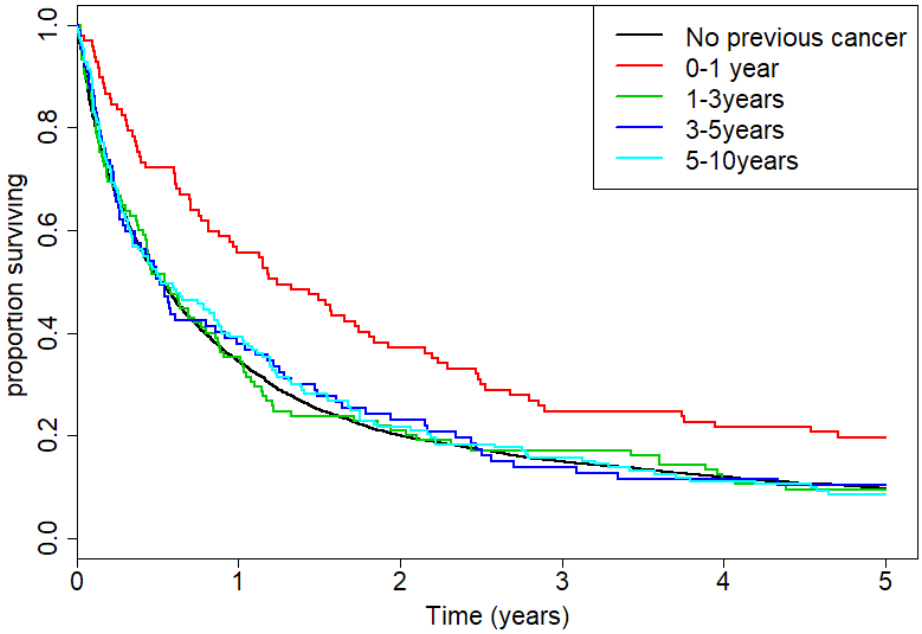

Figure 20: Kaplan-Meier plot of survival in the Lung cancer 2012 cohort by presence and timing of previous cancer diagnosis

Table 34: Cox regression results Lung 2012

Timing of previous cancer	N in group	Hazard ratio	**p-value**
<1 year	97	0.6	<0.001
1-<3 year	105	1.0	0.866
3-<5 year	87	0.9	0.620
5-<10 years	153	0.9	0.354
None in last 10 years	4740		

Counterintuitively, having a recent previous diagnosis of another cancer (<1 year previously) was associated with significantly higher survival rates in the 2012 **lung** cancer cohort (Figure 20). There was no effect if the previous diagnosis occurred longer than a year before the lung cancer diagnosis (Table 34).

There was a larger proportion of persons diagnosed at an early stage in the group with a cancer diagnosis in the previous year compared to other groups (Figure 21). It is possible that investigations for a recent previous cancer increased the chances of early diagnosis.

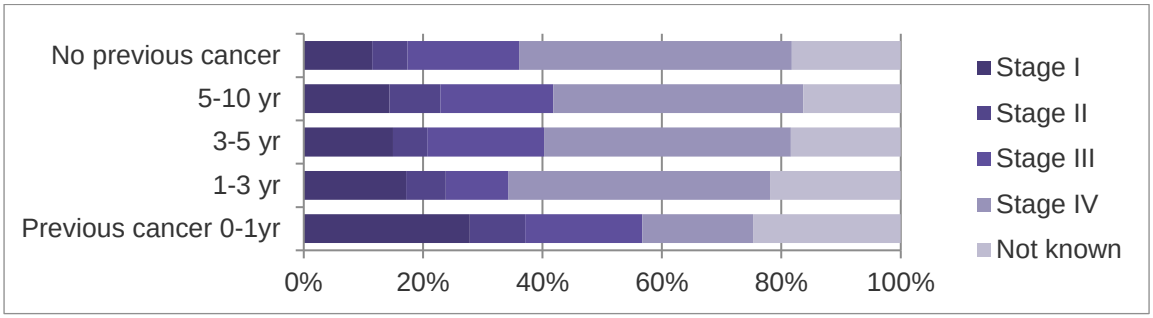

Figure 21: Lung cancer stage at diagnosis according to previous cancer diagnosis (2012 cohort).

Prostate cancer

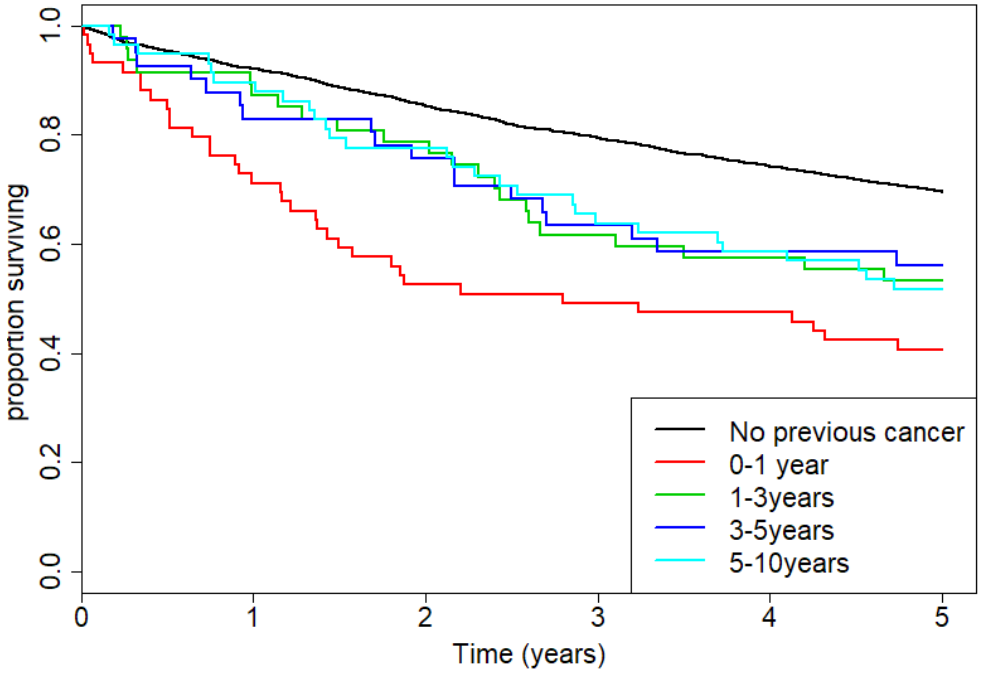

Figure 22 Kaplan-Meier plot of survival in the Prostate cancer 2012 cohort by presence and timing of previous cancer diagnosis

Table 35: Cox regression results Prostate 2012

Timing of previous cancer	N in group	Hazard ratio	p-value
<1 year	59	2.5	<0.001
1-<3 year	47	1.5	0.047
3-<5 year	41	1.4	0.138
5-<10 years	58	1.3	0.135
None in last 10 years	2902		

Previous cancer diagnosis was associated with decreased survival in follow-up in the 2012 **prostate** cancer cohort (Figure 22). This was significant for a previous cancer up to three years ago. The hazard ratio was highest for more recent diagnoses (Table 35).

Summary

A recent previous cancer diagnosis was related to poorer prognosis in **prostate** and **breast** cancer.

- The increase in risk of death was significant for the breast cancer cohorts only for those with a recent (<1-year age) diagnosis.
- In the prostate cancer cohorts, the risk was increased for those with a previous cancer up to three years prior to the cohort diagnosis
- Poorer survival may be due to treatment complications, greater disease burden, or simply because the other cancer is likely one with a poorer prognosis than the breast/prostate cancer, and therefore the course of the other cancer determines survival.

In the **lung** cancer cohorts survival was better in those who had another cancer diagnosed in the year prior to the lung cancer diagnosis

- Earlier presentation of the lung cancer due to investigations for other tumours may be a partial explanation.

People living with cancer in the **colorectal** cancer cohorts had a modestly increased risk if they had experienced a previous diagnosis in the previous year, however this was not statistically significant.

For Further Information

More information on this can be found on this poster presented at NCRI 2019.