BEYOND LIFE AND DEATH

Measuring recurrence, progression and functional outcomes in patients with cancer

WE ARE MACMILLAN. CANCER SUPPORT

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Background and methods

Cancer pathways are increasingly complex, but important information on individual post-diagnosis pathways is often not routinely collected as part of cancer registration. Disease progression, including the date and type, is an important event for cancer patients, their families, medical staff and health services with implications for quality of care, quality of life and cost, but we cannot currently measure the incidence or prevalence of progressive disease, nor the impact of multiple lines of treatment.

Here we aim to frame this important area. We review and distinguish some conceptual issues – loco-regional recurrence, metastasis and (second or) subsequent primary cancers. We review definitions and language, and consider the impacts of different forms of progression on patients. Clear definitions, limitations and assumptions should help to interpret the available data and allow studies to explore different areas of progression in more detail.

Results and discussion

Defining progressive cancers

Current literature is inconsistent in the description and definition of recurrence, metastasis and subsequent primary cancers, thus hampering our ability to measure and distinguish different types of cancer progression in the various datasets. Our working definition of progression is designed to encompass all significant cancer events which occur after an individual's first cancer diagnosis.

Figure 1 maps events which indicate the three different groups of progressive disease – recurrence, metastasis and subsequent primary cancers – and the different progression events of interest which may occur across a cancer pathway.

Figure 1: Map to identify progressive cancers, by events of interest
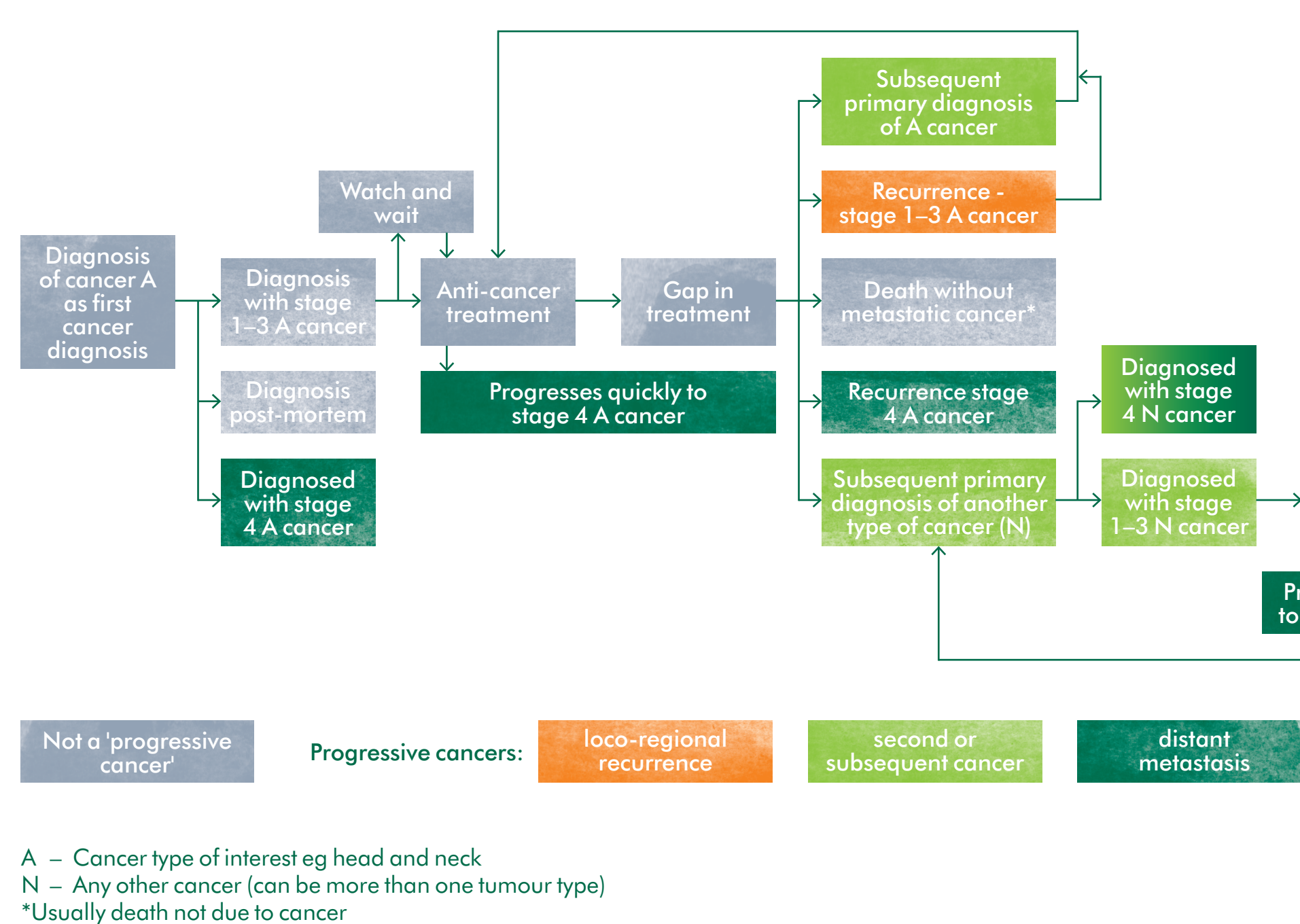
A – Cancer type of interest eg head and neck
N – Any other cancer (can be more than one tumour type)
*Usually death not due to cancer

Recurrence in its simplest definition is when cancer returns after anti-cancer treatment. It can develop in the same area or a different part of the body to the initial cancer.[1] A recurrence may be 'local', 'regional' or 'distant' (see below), but in the literature, 'recurrence' sometimes includes only loco-regional recurrence even when it is not the first episode, which can cause confusion. The prognosis of recurrent cancers depends on the type of cancer, the previous treatment and the stage of recurrence. Local recurrent cancers can sometimes be cured.

Metastatic cancer (metastatic disease, secondary cancer or *distant recurrence*) is cancer that has spread from the original (or primary) cancer site to another part of the body. In a few cases, metastatic disease can be eradicated (eg liver metastasis from colorectal cancer), but generally these patients ultimately die of their primary disease. However, some may live many years and can be considered as 'incurable but treatable'. Metastasis may already be present at initial diagnosis, developing gradually following unsuccessful treatment, or may only appear some years later. The bones, lungs, liver and brain are the most common locations for metastases from solid tumours.[2]

A subsequent primary cancer is the occurrence of a new cancer that is biologically distinct from the original primary cancer.[3] We have included this group as we believe that, for many people living with cancer, this is considered as a new cancer event comparable to the other two types of progression. For some sites, eg in the literature on breast cancer, there have been debates as to how loco-regional recurrence and new primary cancer should be distinguished. New primary cancers may be independent of the initial diagnosis or related to the initial cancer or its treatment. The risk of being diagnosed with second primary cancers differs according to treatment received, previous cancer and other factors.[4]

What do we know about progressive disease?

The prevalence of cancer is increasing year on year, and so the population at risk of recurrence, metastasis or subsequent cancers is bigger than ever. The Cancer Taskforce report[5] has identified that for some people, their cancer has a complex trajectory and may be similar to a long-term condition which may need to be managed and monitored over many years, including acute interventions, self-management and chronic illness management.[6]

The Cancer Outcomes and Services Dataset (COSD) now includes a recurrence field. Data are starting to be collected and analysed to assess consistency across provider trusts and completeness, but no data are yet in the public domain. It will be sometime before these data will allow understanding of the pattern of recurrence over time and in long-term follow-up.

Previous work on recurrent breast cancer, led by the then National Cancer Intelligence Network and supported by Breast Cancer Care, the Association for Breast Surgery and the former West Midlands Cancer Intelligence Unit, piloted the collection of recurrence data. While 94% of those identified in breast units were found in the National Cancer Waiting Times Dataset, cancer registry data, or both, there were still deficits in the depth and accuracy of information available.[7] Comparison with clinical trials datasets may allow the challenge of identifying disease progression to be defined more clearly.

The National Cancer Survivorship Initiative identified the need to understand progressive illness. Work carried out by Macmillan estimated the number of people potentially living with metastatic disease and not in their last year of life for the top four most commonly diagnosed cancers (Figure 2). People in the progressive and end of life care segments are an estimate of the number of people with metastatic disease amounting to more than 150,000 people living with advanced and incurable breast, prostate, colorectal and lung cancer across the UK in 2010.[8] As highlighted in the Cancer Taskforce report,[5] people with metastatic cancer have unique needs:

'These patients' cancers may ultimately be terminal. But they may live for many years and metastases may appear some years after the initial tumour. We should strive for the same significant improvements in survival for patients with secondary cancers as seen for many primary cancers.'[5]

Studies in the UK,[9] US[10] and Australia[4] suggest that between 5% and 12% of cancer patients may get a second or subsequent primary cancer, however the studies also demonstrate the difficulty in comparing studies, as cohorts of patients and follow-up times differ. For example, 5% of patients diagnosed with cancer between 2000-04 in West of Scotland were diagnosed with a further primary cancer within five years of diagnosis; whilst in Queensland their study reported 12% of adult residents diagnosed with a first cancer between 1982 and 2001 (and survived for a minimum of two months), followed up to 2006, developed a second primary cancer.

Why does progressive disease matter?

- **A patient priority:** We know that patients' hope for survival does not differ when diagnosed with a recurrent or new cancer.[11,12] In one study of nearly 5,000 breast, colorectal, prostate and non-Hodgkin's lymphoma survivors one to five years from diagnosis, 47% of respondents reported fear of recurrence.[13]
- **As a Care Quality indicator:** The timing and the pattern of recurrence (loco-regional versus distant) may tell us something about the quality of the care that was delivered.
- **Identifying curable disease:** Some patients who develop progressive disease may still be curable (eg isolated liver metastases in colorectal cancer).
- **Treatment-related consequences:** Patients who have previously been diagnosed and treated for cancer are more likely to develop a second primary cancer many years after treatment or to have a recurrence. It is therefore essential that healthcare professionals, in particular GPs, are aware of possible signs and symptoms in these patients.[5]
- **As a research platform:** Reliable, routinely collected data, recording date of recurrence and outcome after subsequent treatments, would enable routine data to be used as a substitute for expensive stand-alone research datasets for treatment of progressive disease, and would ensure that when new drugs are introduced, the difference between trial populations and non-trial populations is clearly described.
- **Support for decision-making:** The addition of Patient Reported Outcome Measures and quality of life data after treatment episodes would enable more appropriate decision-making and targeting of early palliative care in addition to anti-cancer treatment. Additionally, as well curative treatment for loco-regional recurrence, progression towards end of life (metastases) for cancer patients, is often more stable and predictable than other conditions allowing cancer to be a unique test bed for end of life care.[5]
- **Poorer patient experience:** The 2014 National Cancer Patient Experience Survey in England found that patients with a recurrence were less likely to report that their care and treatment had been good compared to experience reported by those being treated for the first time.[14]
- **Costs:** A large proportion of current NHS cancer costs relate to treating people who have completed initial treatment.[15] More tailored care in the survivorship phase has the potential to reduce costs through reducing recurrences, better managing side effects and supporting people to live well.[5] The development of progressive disease itself also represents a considerable expense for health services, with the majority of the Cancer Drugs Fund being used in this phase.

Conclusions

The number of people living with cancer is increasing year on year. Some live well with no cancer-related problems, some have consequences of cancer and its treatment, and some have cancer progression. The perceptions and needs of people with cancer, as well as their quality of life and outcomes, may change considerably with disease progression. Progression therefore represents an opportunity for healthcare professionals to discuss these issues, and so identification of these points of progression is essential.

Figure 2: Cancer care pathway – estimating the number of people by cancer type, UK, 2010

Here we aim to stimulate debate in the area and to raise awareness of the need to understand this complex population. We believe that there are great opportunities to improve the outcomes and experience for people with progressive cancers, with identification and quantification of the population as a key first step. Macmillan and Public Health England's National Cancer Registration and Analysis Service are working together, using patient-level national datasets, to build understanding of progressive cancer.

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June 2016

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