Department of Health

The impact of patient age on clinical decision-making in oncology

February 2012

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Pharmaceutical Oncology Initiative

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Policy	Clinical	Estates
HR / Workforce	Commissioner Development	IM & T
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Planning / Performance	Improvement and Efficiency	Social Care / Partnership Working

Document Purpose	For Information
Gateway Reference	17160
Title	The impact of patient age on clinical decision-making in oncology
Author	National Cancer Equality Initiative/Pharmaceutical Oncology Initiative
Publication Date	February 2012
Target Audience	PCT Cluster CEs, NHS Trust CEs, SHA Cluster CEs, Foundation Trust CEs, Medical Directors, Directors of Nursing, PCT Cluster Chairs, NHS Trust Board Chairs
Circulation List	Directors of Finance, GPs, Voluntary Organisations/NDPBs
Description	This report sets out the results of a study investigating the extent to which age is a factor in oncology treatment decisions. The result suggests that clinicians may over rely on chronological age as a proxy for other factors which are often but not necessarily associated with age, e.g. comorbidities, frailty.
Cross Ref	Reducing cancer inequality: evidence, progress and making it happen (NCEI, March 2010)
Superseded Docs	N/A
Action Required	N/A
Timing	N/A
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For Recipient's Use	

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Foreword

Cancer incidence increases with age and, as the population ages, it will affect greater numbers of older people. If we are to improve cancer outcomes, it is therefore important that we do all that we can to ensure that older people are able to benefit from the most appropriate treatment, care and support.

In cancer, more intense treatment is often associated with better, and longer term, clinical outcomes. However, it can also be associated with more significant side effects which can damage a patient's quality of life and their health.

There is emerging evidence that older people are offered less intensive treatment. Age is often associated with other clinical factors, such as frailty and comorbidities – which can reduce the ability of a patient to withstand cancer treatment - so it is perhaps unsurprising to find this decline in intensive treatment. At the same time, life expectancy continues to increase and many older people are enjoying healthy ageing, allowing us to speak of biological age and not chronological age alone.

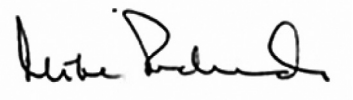
The study detailed in this report set out to investigate the extent to which age is a factor in treatment decisions. The results suggest that clinicians may over rely on chronological age as a proxy for other factors which are often but not necessarily associated with age, such as comorbidities or frailty. This finding is in contrast to the perceptions of clinicians which is that factors such as comorbidity or frailty are more important than age itself.

A similar pattern is emerging across different countries, suggesting that a concerted international effort is required to support clinicians in ensuring that the individual characteristics of each patient are considered in making recommendations about appropriate treatment. We would also welcome co-ordinated international studies of the tolerability of individual treatments.

Ensuring that this personalised approach to treatment is a reality for all patients will require action from health services, the professions, charities, researchers and the pharmaceutical industry and this report identifies a series of next steps. All have a role to play in overcoming the barriers to appropriate treatment.

We hope that all those with a commitment to improving cancer outcomes will examine the evidence presented in this report and consider what more they can do to ensure that older people affected by cancer are offered the most appropriate treatment and care.

Professor Sir Mike Richards **Joanne Rule**



Co-chairs, National Cancer Equality Initiative

Acknowledgements

This report based on research undertaken by Kantar Health was made possible through a partnership between the National Cancer Equality Initiative and the Pharmaceutical Oncology Initiative, a group of pharmaceutical companies, all members of the ABPI (Association of the British Pharmaceutical Industry), coming together to work with and support the NHS in improving the delivery of cancer services.

The project steering group comprised:

- Joanne Rule, NCEI (project steering group chair)
- Sir Mike Richards, National Cancer Director
- Mike Birtwistle, NCEI
- Robert Day, POI
- Jackie Holding, POI
- Ana Matarredona, POI
- Nicola Redfern, POI

We are most grateful for the time and expertise of the clinical advisers to the project, who are listed in Annex 2.

The market research was funded by a grant from 11 member companies of the POI;

- Bristol-Myers Squibb
- Celgene
- GlaxoSmithKline
- Janssen
- Lilly
- Merck Serono
- Napp
- Novartis
- Pfizer
- Sanofi
- Takeda

Executive Summary

Cancer is a condition which affects all age groups but where incidence increases with age. As the population ages, the number of older people diagnosed with cancer will increase and it is important that the NHS does everything it can to ensure that their needs are met. This is the ambition of the National Cancer Equality Initiative (NCEI).

Providing all patients with high quality, timely treatment is a vital part of improving cancer outcomes. However, stakeholders continue to report concerns that the general needs of older people in relation to cancer are not being fully met and that, in particular, there may be under treatment of older people. This perception is supported by evidence generated by the National Cancer Intelligence Network (NCIN) and others. The evidence is summarised in Chapter 2.

It is important to stress that there may be good reasons why older people are offered less intensive cancer treatment. Treatment for cancer is often invasive and can cause significant side effects. Age is associated with the development of comorbidities and older people may well be less able to withstand the toxicities which can be associated with cancer treatment. It is therefore to be expected that treatment rates, as well as the intensity of treatment provided, will decline with age.

The intensity of treatment provided to all cancer patients can be a key determinant of both outcomes and quality of life. More intense treatment is often associated with a greater clinical response, but is also associated with greater side effects. It is therefore important that clinicians take a range of characteristics into account when recommending a treatment approach. This will need to balance the significant benefits which can be gained from more intense treatment with the negative impact which can be caused.

There are important differences between chronological age (the length of time a person has been alive) and biological age (the condition of their body). There is a concern that chronological age alone may be used as a proxy for wider biological factors, resulting in some patients being provided with less intense treatment than might be appropriate. It is, however, important to note that estimating a person's biological age is a subjective process, although there are a variety of approaches for assessing a person's fitness for treatment. As part of wider efforts to improve the quality of services provided to older people, the NCEI has entered into a partnership with the Pharmaceutical Oncology Initiative (POI). The POI is a group of pharmaceutical companies, all members of the Association of the British Pharmaceutical Industry, which have joined together to work with the NHS to ensure that cancer patients get access to services and treatments in the UK that are comparable to the best in Europe.

The aims of the partnership between the NCEI and the POI are to:

- Explore the extent to which a patient's age is a factor in clinical decision-making;
- Examine the interplay between age and other influences on clinical decision-making;
- Assess whether similar patterns are observed across different types of cancer and different stages of cancer; and
- Investigate whether clinical approaches to the treatment of older people vary in different countries.

This report sets out the key findings from this study. The study explored:

- Clinical attitudes to age as a factor in approaches to cancer treatment. This was investigated through asking 301 oncologists and haematologists a series of direct questions relating to the factors they thought influenced their treatment decisions;
- The extent to which age influences clinical recommendations about the intensity of treatment which should be offered to patients, for both early stage and advanced disease, across a range of cancers (breast cancer, chronic myeloid leukaemia, colorectal cancer, Non-Hodgkin's lymphoma and renal cell carcinoma) and across a range of countries (England, Canada, Sweden, Germany, Denmark and Spain). This was investigated by asking clinicians to state how they would treat a series of patient scenarios with alternating variables (age, cancer stage, comorbidity and social support). A predictive model was then developed to enable an assessment of the impact of the different variables on clinical decision-making.

The research was undertaken in a qualitative phase (10 in-depth interviews with oncologists and haematologists used to test the research questions for the quantitative phase) and a quantitative phase (30 minute online questionnaires used to explore clinicians' beliefs and behaviour). Further detail on the methodology is set out in Chapter 3.

The study found a high level of consistency in the clinical attitudes observed in England and other countries. Clinicians do feel that age is an important factor to consider in patient decision-making alongside issues such as performance status, number and severity of comorbidities, stage of cancer and the potential toxicity of treatment.

In relation to treating older people, clinicians perceive that the major challenge is patients' ability to tolerate the side effects that may be associated with treatment. Other notable challenges identified relate to the relative lack of data on the efficacy of treatments in older patients. However, when asked to rank the importance of age in determining how intensively a patient can be treated, clinicians saw it as significantly less influential than other factors. Biological age – rather than chronological age – was seen as a more significant factor. Further details on the findings in relation to clinical attitudes are included in Chapter 4.

The attitudes reported by clinicians were in contrast with the factors observed as being significant in the patient scenarios exercise. It is important to stress that there is no optimum level of intensity of treatment according to age, comorbidity or social support. Therefore the findings should be used to consider the relative impact of these factors, as well as their influence on intensity of treatment, rather than to assess whether the proportion of patients offered a particular intensity of treatment is appropriate.

Chronological age alone was found to be a significantly bigger factor than either comorbidities or social support in determining the intensity of the treatment they would recommend, as set out in Chapter 5. Again, there was a high level of consistency in response, with few differences being observed between clinicians in England and those in other countries.

The prominence of age as a factor translates into an impact on the level of treatment intensity which would be recommended by clinicians. There were statistically significant reductions observed in the proportion of patients in their 70s and 80s with early stage cancer who would be offered high intensity treatment, when compared with the earlier age group. For advanced cancers, there was a statistically significant reduction for patients in their 80s and a downward – although not statistically significant trend – for patients in their 70s.

The findings from the patient scenarios suggest that, contrary to the approach towards clinical decision-making that clinicians report, chronological age is a significant factor in determining the intensity of treatment that would be recommended to patients. If the approach observed in response to the patient scenarios was replicated in clinical practice, then age would indeed play a significant role in determining the nature of treatment offered to cancer patients. For example, analysis of the results from the patient scenarios suggest that, for a patient in their 70s with advanced cancer, a decade of healthy ageing would have the same impact on the likelihood of their clinician to prescribe more intensive cancer therapy, as if they were to develop a severe comorbidity that affected their everyday life.

This study suggests that age may be used as a proxy for other factors (such as comorbidities) in making recommendations on treatment and that this may lead to some patients receiving less intensive treatment, solely on the basis of their chronological age. This pattern is observed for a range of both early stage and advanced forms of cancer. It is not a phenomenon which is limited to certain countries, with a high degree of consistency being observed across six different countries.

The research findings will be relevant to a range of stakeholders committed to improving cancer outcomes, both in England and elsewhere, and place greater emphasis upon the need to assess fitness for treatment of individual patients and to support informed decision making for older people themselves. The work will be of particular relevance to the clinical community, commissioners and providers of cancer services, the pharmaceutical industry, cancer charities and older people's organisations. Chapter 6 suggests some actions which different groups may wish to consider in responding to this report.

1. Introduction

1.1 For the vast majority of cancers, incidence increases with age. Over a third (36%) of all cancers are diagnosed in people who are 75 or over and a further 17% are diagnosed in people between 65 and 74[1]. As the population ages, these figures are set to increase. It is therefore important that the NHS, public health and social care services do everything they can to ensure that older people are offered the best possible cancer services.

1.2 Unsurprisingly, cancer mortality rates also increase with age and are therefore highest amongst the over 85s[2]. In 2007, over 50% of all cancer deaths occurred in patients aged over 75. There has been good progress in reducing mortality amongst younger patients, although there is much more to do. However, improvements in the outcomes achieved for the under 75s have not been matched by that in the over 75s, where reductions in mortality have been much lower.

1.3 The Government has set out ambitious plans to improve cancer outcomes in *Improving Outcomes: a Strategy for Cancer,* including saving an additional 5,000 lives by 2014/15. If this objective is to be achieved, then further action will be required to improve outcomes in older people. The reasons for poorer outcomes in older people are complex. Efforts are required to improve prevention, early diagnosis and the treatment of cancer in older people if outcomes are to be improved.

1.4 A significant focus for the National Cancer Equality Initiative (NCEI) has been to examine ways in which older people can be better supported. The NCEI aims to:

- Bring together experts in the field to identify problems and areas of good practice, facilitating the spread of what works;
- Work across the wider national cancer programme to ensure inequalities are both identified and addressed within individual initiatives and fully integrated within work programmes to support improvement;
- Identify areas, in collaboration with the National Cancer Intelligence Network (NCIN), where data collection can be improved within the NHS and ensuring that data are analysed and published to support service providers to make improvements;
- Uncover gaps in research and work with stakeholders and academic institutions to improve knowledge and evidence around cancer inequalities.

1.5 In developing *Improving Outcomes: a Strategy for Cancer* it became clear that there was strong interest in cancer equality issues, with over 35 submissions directly relating to the

subject[3]. Within these, a clear theme emerged that stakeholders are concerned that under-treatment may be occurring in older people and that more needs to be done to explore the extent and causes of this, as well as to better support healthcare professionals in making decisions about appropriate treatment options for older people.

1.6 It is important to stress that there may be good reasons why older people are offered less intensive cancer treatment. Age is associated with the development of comorbidities and older people may well be less able to withstand the toxicities which can be associated with cancer treatment. Nonetheless, there is a concern that chronological age alone may be used as a proxy for wider biological factors, such as comorbidity, which may have an impact on the ability to achieve a positive outcome for a patient. This may be in part because there is no objective way of assessing biological age, when there clearly is for chronological age.

1.7 In order to help address this, the NCEI is undertaking a number of initiatives to explore how cancer services can best support older people. As part of this, the NCEI has entered into a partnership with the Pharmaceutical Oncology Initiative (POI). The POI is a group of pharmaceutical companies, all members of the ABPI, coming together to work with the NHS to support improving the delivery of cancer services and to ensure that cancer patients get access to services and treatments in the UK that are comparable to the best in Europe.

1.8 The purpose of the partnership is to:

- Explore the extent to which a patient's age is a factor in clinical decision-making;
- Examine the interplay between age and other influences on clinical decision-making;
- Assess whether similar patterns are observed across different forms of cancer, different stages of cancer and different countries; and
- Investigate whether clinical approaches to the treatment of older people vary in different countries.

1.9 This report details the headline findings from the study, particularly its use of patient scenarios to understand clinical decision-making. The full data set is available to bone fide researchers. The report is intended to promote discussion and further research into how clinicians might best be supported in managing the treatment of older people, as well as the wider steps that NHS organisations might take to ensure that everything possible is done to ensure that older people affected by cancer receive the best possible treatment and care.

2. Background

2.1 Tackling health inequalities and promoting equality of outcome in England is essential to improving outcomes and achieving cancer survival rates which match the best performing countries in the world. *Equity and Excellence: Liberating the NHS* makes clear the Government's ambition to reduce health inequalities and improve the health of those with the poorest outcomes, an ambition which is reiterated in *Improving Outcomes: a Strategy for Cancer*[4,5].

2.2 In relation to cancer, the National Cancer Equality Initiative (NCEI) has been leading efforts to reduce inequality and promote equality. The approach to achieving this was set out in *Reducing cancer inequality: evidence, progress and making it happen,* including the national and local actions required on data collection, analysis and publication; targeted interventions; training, development and research; evaluation and monitoring; and embedding equality[6]. The work of the NCEI was recognised at the 2010 Civil Service Diversity and Equality Awards, where the NCEI won the award for Leading Change in Diversity and Equality.

2.3 This chapter summarises:

- The imperative to improve services for older people affected by cancer;
- Recent developments in the evidence on the treatment of cancer in older people; and
- Some of the action underway to address the issues highlighted in this chapter.

The imperative of improving cancer services for older people

2.4 The *NHS Constitution* makes clear that a core duty of the NHS is to promote equality for all groups in society, including older people[7]:

> *"The NHS provides a comprehensive service, available to all irrespective of gender, race, disability, age, sexual orientation, religion or belief. It has a duty to each and every individual that it serves and must respect their human rights. At the same time, it has a wider social duty to promote equality through the services it provides and to pay particular attention to groups or sections of society where improvements in health and life expectancy are not keeping pace with the rest of the population."*

2.5 In addition, the ban on age discrimination in NHS services and social care will take effect from 2012, meaning that NHS services will need to do everything they can to ensure that services do not unwittingly discriminate against older people.

2.6 There is also a clear outcomes case for improving services for older people. Without doing so, it will be difficult for the NHS to achieve its wider cancer outcomes objectives. Research has shown that cancer outcomes in older people (those over the age of 75) are poorer in the UK than they are in other comparable countries. It is estimated that if UK survival rates matched the highest performers in Western Europe for 75-84 year olds and outcomes in the USA for those aged 85 and over, then there would be 15,000 fewer cancer deaths every year[8].

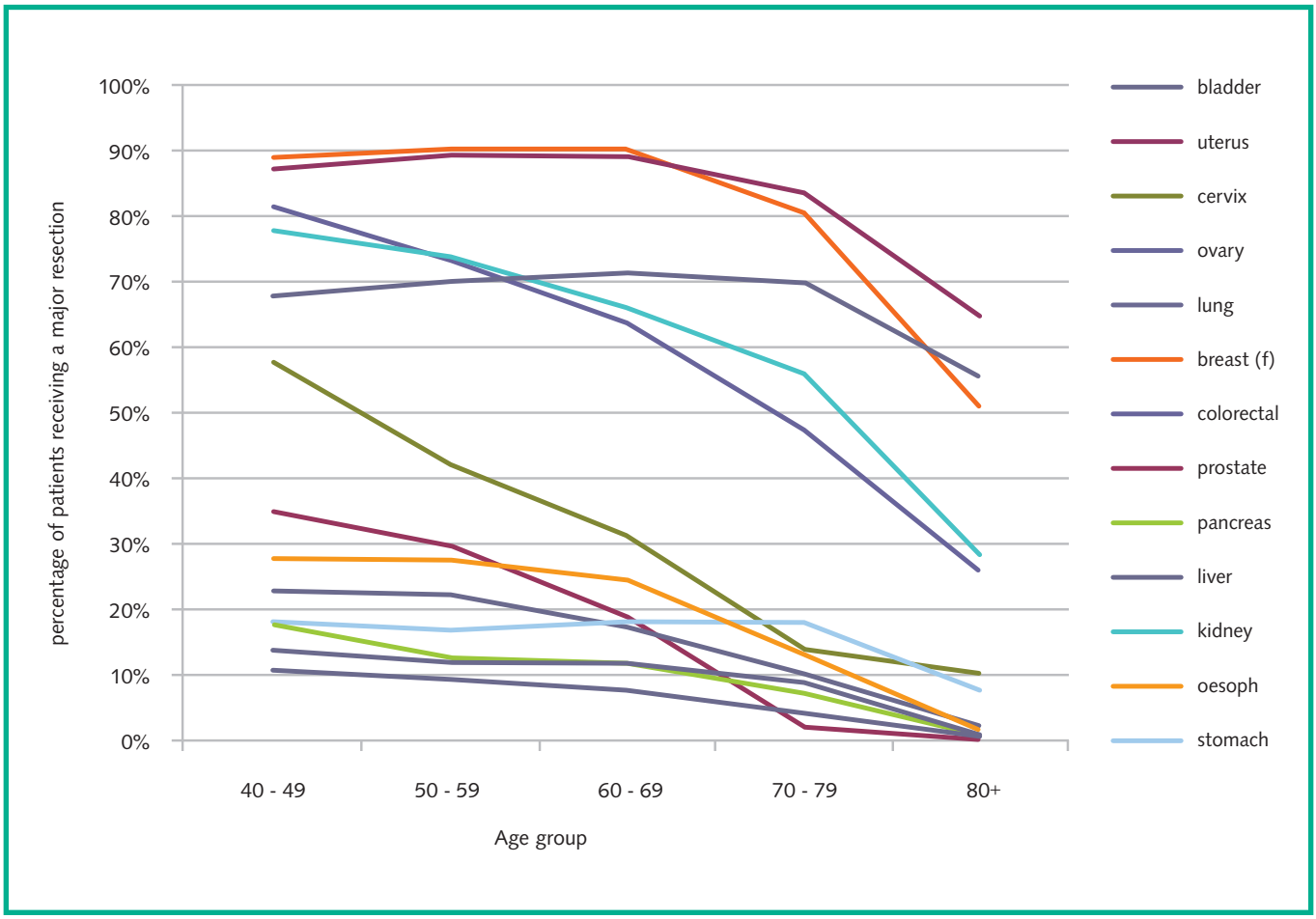
2.7 The reasons for this disparity are complex and are likely to include prevention issues, delays in diagnosis and treatment rates.

Evidence on the treatment of cancer in older people

2.8 There have been many advances in cancer treatment in recent years, resulting in more effective, targeted and less invasive interventions. This has increased the efficacy and tolerability of many treatments. Nonetheless, cancer treatment is still often associated with side effects which can diminish quality of life and impact on wider health. It is therefore important for clinicians to balance expected benefits and side effects when considering what treatment to recommend.

2.9 In general, older people with cancer receive less intensive/radical treatment than younger people[9]. An analysis by the NCIN has revealed the extent to which access to surgery drops off with age, as set out in Figure 1. It is notable that the age at which resection rates begin to fall is relatively young. For example, over 80% of ovarian cancer patients between the age of 40 and 49 have a record of a major resection, whereas less than 50% of patients in their 70s have a record of one.

Figure 1: Percentage of patients with a record of a major resection, by age and cancer site, patients diagnosed 2004-2006, followed up to 2007



2.10 The issue is whether or not this is appropriate for their condition. Older people may be frailer than younger people and thus less able to withstand intensive treatment. For example, percentage volume of haematopoietic marrow usually decreases progressively with age and there is a corresponding increase in fatty marrow, which is a factor in patients' ability to withstand some forms of chemotherapy[10,11]. Older people may also present with more advanced disease, for which some treatments may not be appropriate (e.g. surgery)[12]. It is therefore to be expected that overall treatments rates would decline.

2.11 However, there is a danger that chronological age can be confused with biological factors which may be associated with ageing. Older people are not uniformly frail and may enjoy good biological health and many years' life expectancy. For example, the life expectancy of a 70 year old woman is 16.1 years and a 70 year old man is 13.7 years. At the age of 80, life expectancy is 9.2 and 7.7 years respectively[13]. Therefore, for many older people, intensive cancer treatment – and its associated side effects – may be justified.

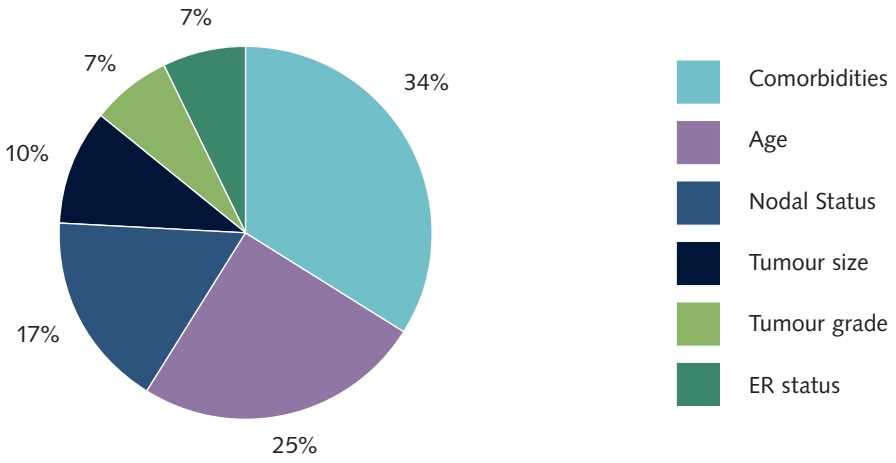
2.12 It follows that age alone should not be used as a determinant of treatment decision. The Government has made clear that the only acceptable criteria for not giving a clinically appropriate and cost effective treatment should be poor patient health or a patient themselves making a choice not to receive further treatment[14].

2.13 Despite this, there is some evidence that older people are offered less intensive treatment, irrespective of their other characteristics:

- Detailed research studies have been undertaken on the treatment given to older women with breast cancer in the North West. These have shown that older women are investigated less intensively and are less likely to receive potentially curative surgery. Older age was shown to be the major factor determining treatment even when tumour characteristics had been accounted for[15]; and

- A small scale study on the use of chemotherapy and biologic treatment in early stage breast cancer found that age is a major factor in influencing clinical judgement, irrespective of other factors such as comorbidities and tumour size, as set out in Figure 2[16];

Figure 2: Overall importance of the patient characteristics considered in the treatment of early stage HER2-positive breast cancer



2.14 Comorbidities or patient choice alone are unlikely to explain why older people receive less intensive treatment. Potential contributory factors include:

- Healthcare professionals may make assumptions about an older person's preferences about treatment and a decision that an older person will not be able to cope with treatment can be made without fully assessing their overall physical health[17];
- Evidence about the efficacy and side effects of treatments in older people may be lacking, with older people less likely to be included in clinical trials, in part because most trial protocols require full treatment doses, which may not be appropriate for some older patients [18, 19];
- Healthcare professionals may feel less confident about how to manage treatment in older people[20]; and
- Gaps in appropriate community support for older cancer patients may mean that healthcare professionals are less willing to offer intensive treatment[21, 22].

Action to improve cancer services for older people

2.15 This project forms part of a wider work programme being coordinated by the NCEI on cancer and older people. A range of actions are already underway to improve the support available to older patients at every stage of the cancer pathway, including:

- The National Awareness and Early Diagnosis Initiative is developing tailored messages about risk, signs and symptoms of breast cancer for women over the age of 70, as evidence suggests that awareness levels are particularly low in this group, despite elevated risk;

- A partnership project between the Department of Health and Macmillan Cancer Support is identifying, testing and evaluating simpler ways to assess an older person's suitability for different forms of cancer treatment, as well as how best practical support and information to support patient/practitioner decision-making. Such approaches have been found to have an outcomes benefit in other conditions, as set out in Box 1;

- The National Cancer Intelligence Network has analysed responses to the National Cancer Patient Experience Survey 2010 according to age, identifying areas in which older people may require additional support. The main findings from this are set out in Box 2; and

- The NCEI is supporting Macmillan Cancer Support's Values Standard, which aims to provide a framework for commissioners and providers of cancer services to ensure that every patient is treated with dignity and respect, according to their own personal preferences and circumstances. This project will be particularly important in supporting improvements in the way older people are treated.

Box 1

Impact of tailored assessment on health outcomes in older people

A recent systematic review has found that older patients who were given a tailored assessment of their health needs – known as a comprehensive geriatric assessment – after admission to hospital were significantly less likely to die or experience functional deterioration and were also more likely to be alive in their own homes at longer-term follow-up[23]. This approach is now being tested for cancer in a variety of pilots.

Box 2

Variations in cancer patient experience according to age

The 2010 National Cancer Patient Experience Survey enables an analysis of how the reported experience of different aspects of treatment and care varies according to age[24]. Analysis by the NCEI and the NCIN suggests that important variations do occur according to age group, suggesting that cancer services may wish to target additional support at various parts of the cancer pathway at different age groups. For example:

- Younger people (16-25) were more likely to experience difficulties in receiving a prompt referral from primary care, were less likely to have tests explained to them in a way which they could easily understand and were less likely to understand the explanation of what was wrong with them; and
- Older people (76+) were less likely to have the potential side effects of treatment explained to them or to be given written information about these side effects; were less likely to be given a named Clinical Nurse Specialist in charge of their care; were less likely to be given information on a self-help or patient support group; and were less likely to be given information on benefits for which they may be eligible.

On all of these issues a statistically significant difference in responses was found.

3. Project methodology

3.1 As set out in Chapter 2, the evidence on the extent to which age impacts on treatment decisions is still emerging. The purpose of the study outlined in this report was to build on previous, smaller scale studies, and to further explore the extent – and reasons why – age is a factor in influencing clinical decisions in cancer treatment, beyond the extent to which it is correlated with other factors, such as comorbidities.

3.2 This chapter sets out the methodology used in approaching the project, including:

- The project objectives;
- Why a partnership approach was adopted;
- How different forms of cancer were selected;
- How different countries were selected;
- The research approach used;
- The implications of the sample size used for the project;
- The approach used in analysing differences in treatment intensity; and
- The limitations which are apparent in this methodology.

Project objectives

3.3 As set out in Chapter 1, the project had a number of objectives, including to:

- Explore the extent to which a patient's age is a factor in clinical decision-making;
- Examine the interplay between age and other influences on clinical decision-making;
- Assess whether similar patterns are observed across different forms of cancer, different stages of cancer and different countries; and
- Investigate whether clinical approaches to the treatment of older people vary in different countries.

Partnership approach

3.4 It was recognised that the NCEI and the POI have a shared interest in understanding that factors that influence clinical decision-making in the treatment of older people. The partnership approach to the delivery of the project, enabled access to greater resources than the public sector would have been able to provide, expertise in different approaches to treatment in different countries, as well as the use of qualitative and quantitative research with clinicians as a technique for exploring clinical attitudes.

3.5 The partnership has built on similar approaches used in other projects, including between:

- The National Cancer Action Team (NCAT) and the POI, in developing commissioning and capacity planning tools to support effective planning in cancer services in England;
- The Department of Health, IMS Health, and the pharmaceutical industry in exploring the extent and causes of international variations in drug usage[25]; and
- The Department of Health, international clinicians and academics, in undertaking the International Cancer Benchmarking Project (ICBP)[26].

Selection of different forms of cancer

3.6 In total, five different cancer types were selected for research so as to ensure that any findings would be applicable for the whole of cancer rather than just one particular tumour type.

3.7 Selection criteria included:

- The cancers selected should include both common and rarer forms of cancer;
- The cancers selected should include both solid tumours and haematological malignancies;
- There should be a consistent approach to treatment in different countries, so enabling comparison;
- Treatment options of different intensity should be available; and
- Incidence of the cancers selected must increase with age

3.8 The following cancers were selected:

- Breast cancer (non-HER2-positive);
- Chronic myeloid leukaemia (CML);
- Colorectal (bowel) cancer;
- Non-Hodgkin's lymphoma (NHL); and
- Renal cell carcinoma (RCC) (kidney cancer).

Selection of different countries

3.9 A range of countries were also selected for research. The selection built on knowledge gained from other exercises to compare different aspects of health service delivery, including the ICBP and the *Extent and causes of international variation in drug usage*. Selection criteria included:

- Countries with both good and poor cancer outcomes;
- Countries with both high and low levels of cancer drug usage; and
- Countries where it is relatively easy to interview a representative sample of oncologists and haematologists.

3.10 The following countries were selected for inclusion:

- England;
- Canada;
- Sweden;
- Germany;
- Denmark;
- Spain.

Research approach

3.11 Following a competitive tender process, Kantar Health was selected as the research partner for the project. Kantar Health is a global healthcare research company with a specialism in engaging with clinicians to seek insights into how they approach clinical decisions.

3.12 In order to inform the research, a series of ten in-depth telephone interviews were conducted with oncologists and haematologists in England and Canada to test the research approach, validate language and ensure that the assessment criteria used in the scenarios were robust across different countries. These interviews were undertaken in February 2011.

3.13 Evidence from other, smaller scale, research projects had suggested that clinicians' perceptions of what influences their decision-making might differ from the factors that influence their approach to treating a particular patient. In order to explore this, two different approaches were used during a 30 minute online questionnaire:

- Patient scenarios – clinicians were shown a series of scenarios (often known as vignettes in market research) with alternating variables, as set out in Box 3, and were then asked to select of treatment options. This approach was chosen because it is the best option for understanding clinician behaviour and attitude implicitly (i.e. respondents are not aware they are being tested for any bias against age). Respondents were each asked to complete 16 scenarios to test their behaviour with regard to choice of therapy. In order to produce an accurate predictor of behaviour/therapy choice across all possible permutations/combinations of patient features, a predictive model was designed to calculate what an individual's choices might be for any given scenario; and

- Clinical attitudes – clinicians were asked a series of direct questions about what they thought would influence their treatment decisions, as well as which factors they associated with the age of their patient. The Bradley-Terry statistical technique was used to convert rank variables into probabilities, allowing more precise conclusions to be made. The analysis is aggregate in nature, and so is based on the frequency with which one factor "beats" — that is, is ranked more important or higher than — another factor in the ranking task across a set of respondents. The resulting scores are such that it is possible to conclude that a factor with a score of 20 is twice as important as one with a score of 10 (ratio scale).

3.14 Interviews were conducted between 11th August 2011 and 27th September 2011.

Box 3
Variables in patient scenarios

- Patient age (50-59, 60-69, 70-79, 80-89);
- Cancer type and stage (breast, bowel, CML, NHL and renal) (early and advanced);
- Comorbidities (none, mild, moderate, severe); and
- Social support available to the patient (with a healthy spouse/partner and has support from local family members; with a healthy spouse/partner but has no support from local family members; alone but has support from local family members; and alone and has no support from local family members).

Clinicians were then presented with a range of different treatment options which varied according to intensity and were asked to recommend how they would approach treatment.

Each clinician was presented with 16 randomly generated and different clinical scenarios relevant to their cancer specialism. In total, there were 96 possible scenarios for each cancer type.

3.15 A summary of the theoretical basis for the model used, as well as the methodology applied in developing it, is included in Annex 1.

3.16 The scenarios were developed in cooperation with a series of clinical experts to ensure that the options presented were sufficiently realistic for the purpose. A list of the clinical experts is contained in Annex 2. For each cancer, a range of scenarios were generated within two basic scenarios:

- The patient had early stage cancer, where treatment would be given with curative intent; or
- The patient had advanced cancer, where treatment would normally be given with the intention of extending and / or enhancing the quality of life.

3.17 Treatment options made available for market research respondents were based on potential therapies which could be used within the framework of high, medium and low intensity treatments across tumour types and stages, on the feedback from the clinical expert panel. They do not represent recommendations for treatment by the ABPI, NCEI or the clinical experts. For information on the recommended use of medicines, please refer to the relevant Summary of Product Characteristics.

3.18 An example of a scenario is show in Box 4.

Box 4
Example of a patient scenario

A 75 year old patient presents following a lumpectomy to remove 1.5cm mass in their left breast. The patient also had axillary lymph node clearance. Investigation has revealed that it was a grade 3 cancer that is oestrogen receptor positive (ER +), progesterone receptor negative (PR -) and HER2 negative. The cancer was fully excised with clear surgical margins. One in eight of the axillary nodes were found to be involved. Further investigations have found no malignancies.

The patient is noted to have a non-productive cough that makes them short of breath walking 1km, which has been attributed to moderate COPD. The patient is living with a healthy spouse/partner and has support from local family members. The patient has a body mass index within normal range. Full Blood Count and the Liver Function Test were found to be normal and investigations into the patient's cardiac function have revealed no abnormalities or disease.

The patient is receiving best supportive care, is willing to receive further treatment and would like your guidance on how to proceed. Which of the following would you suggest to this patient as their best therapeutic option?

- Adjuvant chemotherapy followed by breast radiotherapy and then adjuvant endocrine therapy
- Adjuvant breast radiotherapy followed by adjuvant endocrine therapy
- Adjuvant endocrine therapy
- Observation

Sample size

3.19 Participants were recruited from Kantar Health's online panel of clinicians[27]. In total, 301 oncologists and haematologists were surveyed as part of the project. The distribution of participants according to country and cancer type is set out in Box 5.

Box 5
Distribution of respondents

	England	International total	Canada	Denmark	Germany	Spain	Sweden
Breast cancer	32	30	6	6	6	6	6
CML	30	27	6	3	6	6	6
Colorectal cancer	32	30	6	6	6	6	6
NHL	30	31	6	6	6	7	6
RCC	30	29	6	4	6	7	6
Total	154	147	30	25	30	32	30

3.20 The statistical model used and the relative number of respondents recruited from each country provides a sound basis for interpretation of the results in two ways:

- Analysis of behaviours in specific therapy areas – it is possible to compare clinical practice for a particular cancer in England with that in the other countries; and
- Analysis of behaviours in particular countries – it is possible to compare clinical practice for all cancers in one country against clinical practice for all cancers in other.

3.21 It is not possible to compare differences in the results between two non-English countries or indeed between cancer types within a non-English country, due to the relatively small sample size.

Analysing intensity of treatment

3.22 In order to compare different types of cancer, it was necessary to offer the range of specific treatment options which doctors might choose from, based on advice from clinical experts and also to categorise them, for purposes of later analysis, according to intensity. The following categories were used:

- High intensity – the patient is offered a treatment with the highest likelihood of efficacy but also the highest likelihood of side effects, alongside best supportive care;
- Medium intensity – the patient is offered an intermediate option, alongside best supportive care;
- Low intensity – the patient is offered a treatment with some efficacy but also a gentler side effect profile, alongside best supportive care; and
- No active treatment – the patient is offered best supportive care only.

3.23 It was then possible to assess the proportion of patients who would be given a particular intensity of treatment by country or cancer type. A summary of the different treatments offered for each cancer, banded according to intensity, is included in Annex 3.

3.24 Following feedback from the clinical experts, it was noted that for some cancers there was clearer distinction between different bands of intensity than there was for others. In order to adjust for this, the findings were therefore also analysed according to two categories:

- More intense treatment; and
- Less intense treatment.

3.25 A summary of the different treatments offered for each cancer, re-banded according to these categories of intensity, is included in Annex 4.

3.26 In both cases, findings have been analysed for statistical significance at the 95% confidence interval.

3.27 The full questionnaire used in the research is included as Annex 5.

Limitations

3.28 A study of this nature and complexity, covering a range of cancers, stages, treatments and countries, has not been attempted before and it is important to note that there are inevitable limitations to the findings and analysis. These include;

- The sample size was restricted by the budget available, making it more challenging to secure statistically significant findings. However, it was of the size necessary to explore the particular issues highlighted in the report;
- The range of comorbidities described in the scenarios was by necessity limited to the chronic obstructive pulmonary disease (COPD). This was considered by clinical experts to be relevant to treatment decisions for all forms of cancer considered, but may not be the most relevant comorbidity for particular cancers;
- Comorbidities may impact upon different treatment regimens in different ways. It is therefore possible that the comorbidities used in the scenarios – which had to be fixed in scope to enable comparability – may have a disproportionate impact on different treatment regimens;
- The statistical model used can only predict behaviour at a certain level – in this case bands of intensity;
- Not all cancers are the same and treatments for different cancers will have different efficacy and side effect profiles, making comparability between intensity inexact;
- The study sought information on treatment intention, rather than clinical practice. It is possible that clinicians may intend to treat in a different manner from their actual practice; and
- Due to the complexity of the study, it was not possible to seek information on intended duration or dose reduction.

3.29 Nonetheless, the study provides a new perspective the role of age as a factor in clinical decision-making, across a range of different cancer types and countries.

4. Clinical attitudes towards treatment decisions

4.1 Cancer treatment involves assessing a range of complex patient characteristics in order to recommend a series of interventions which both maximise potential efficacy and minimise potential side effects. It should be noted that as well as offering potential efficacy, modern cancer treatments can also improve a patient's quality of life. Nonetheless, treatments can be associated with significant toxicity.

4.2 For different patients, the trade-off between improved survival prospects and minimising side effects will vary and it will be important that clinicians present all appropriate options, alongside information about their implications, to patients so that they may make an informed decision about what is best for them. Patients will also often want advice from a clinician about which option is most appropriate. The role of clinical judgement is therefore of critical importance in cancer treatment.

4.3 This chapter explores clinical attitudes towards treatment decisions, including the factors that they feel are most important in determining the most appropriate options for patients.

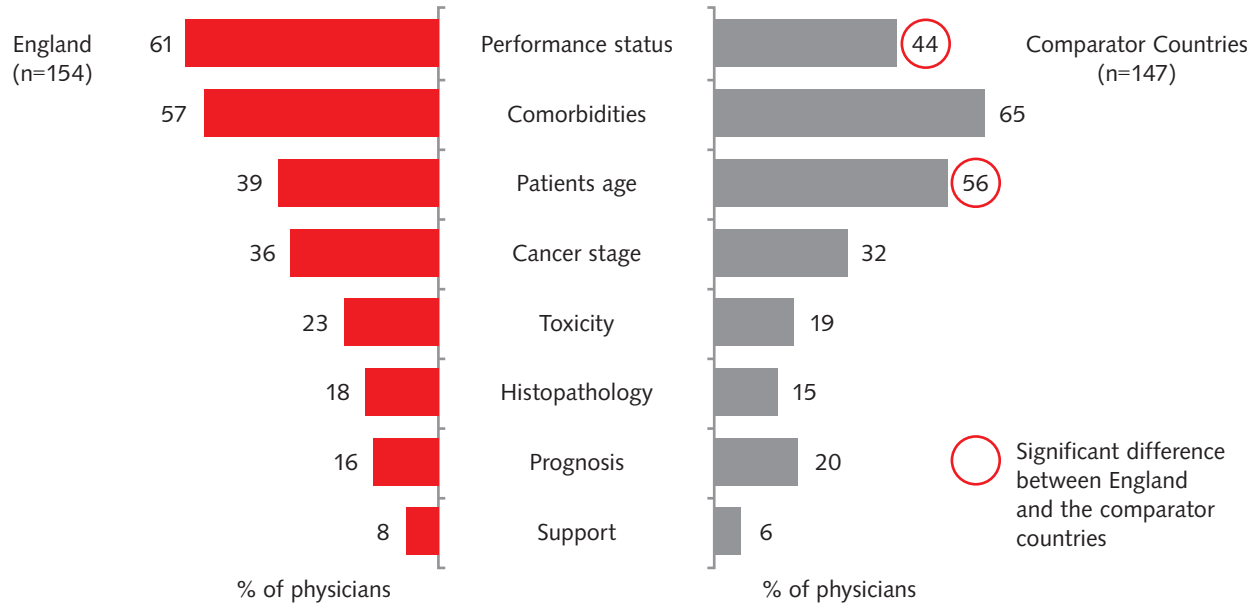
Key factors in clinical decision-making

4.4 When asked to list spontaneously factors which would be important in influencing decisions about the intensity of treatment, the five factors most commonly reported were:

- Performance status;
- Comorbidities;
- Patient's age;
- Stage of cancer; and
- Potential toxicity of treatment.

4.5 The full findings are set out in Figure 3. There is a high degree of consistency between the choices of clinicians in England and those from other countries. The only statistically significant differences are for performance status (a bigger factor in England) and patient age (a bigger factor in other countries).

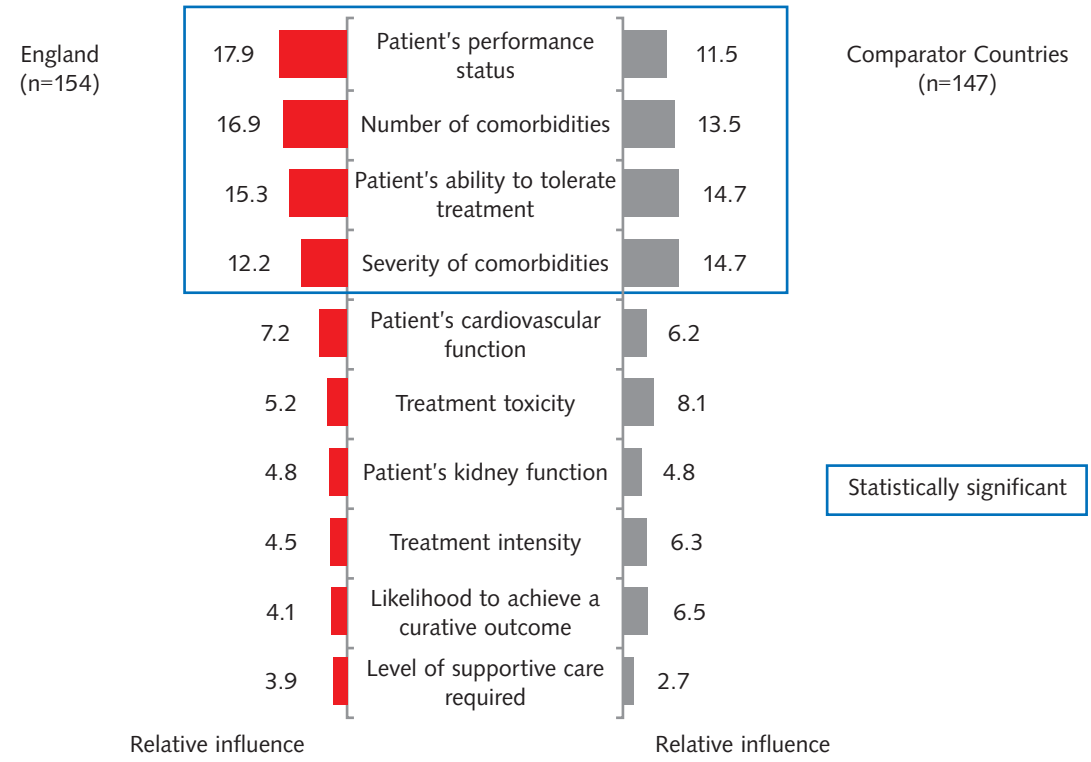
Figure 3: Factors that determine treatment intensity when curative outcome is the intention



Q12: What factors dictate how intensively you can treat a patient with [SPECIFIC CANCER] when your goal is to cure them?
Base: 301. All countries, all cancers

4.6 In both England and the comparator countries, the perception of 'old' is 78 years (range 65-100, Q18). Most clinicians asked directly did not consider that age affected the intensity of the treatment they could administer to a patient. Asked why, 40% cited the importance of biological age, comorbidities and performance status. (Q15). All respondents were then asked about the influence of chronological age on patients (Q17). Figure 4 sets out those answers where there was a statistically significant difference. Given this, and the close association between age and other factors which might influence treatment – such as comorbidities or performance status – it is not surprising to see that age is a characteristic which clinicians envisage taking into account.

Figure 4: Perceived impact of age on other patient characteristics

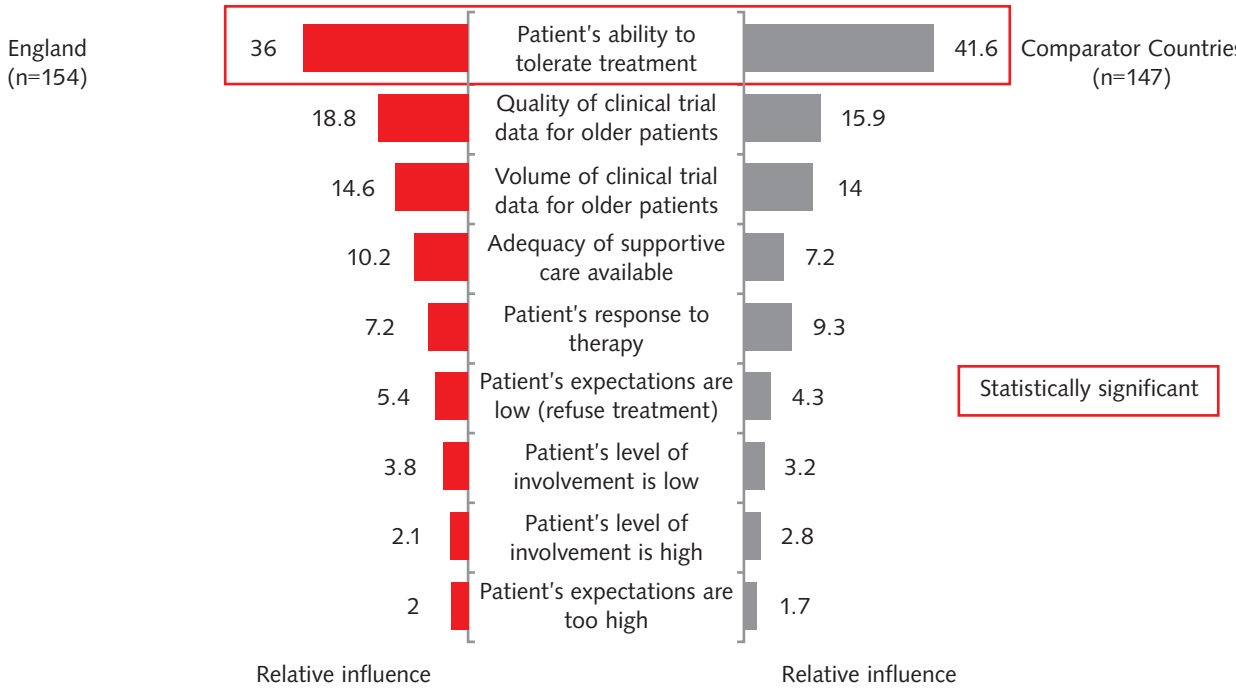


Q17: Please rank the following factors in terms of the influence chronological age has on patients with [SPECIFIC CANCER] cancer. Please rank the top 5 factors from 1 to 5 where 1 = most important and 5 = fifth most important
Base: 301. All countries, all cancers

Relative importance of age in clinical decision-making

4.7 In relation to treating older patients, clinicians perceive that the major challenge is patients' ability to tolerate treatment, as set out in Figure 5. Other notable challenges identified relate to the absence of clinical trial data on the efficacy of treatments in older patients. Again, there is a high level of consistency between responses from clinicians in England and those from other countries.

Figure 5: Perceived challenges in treating older patients

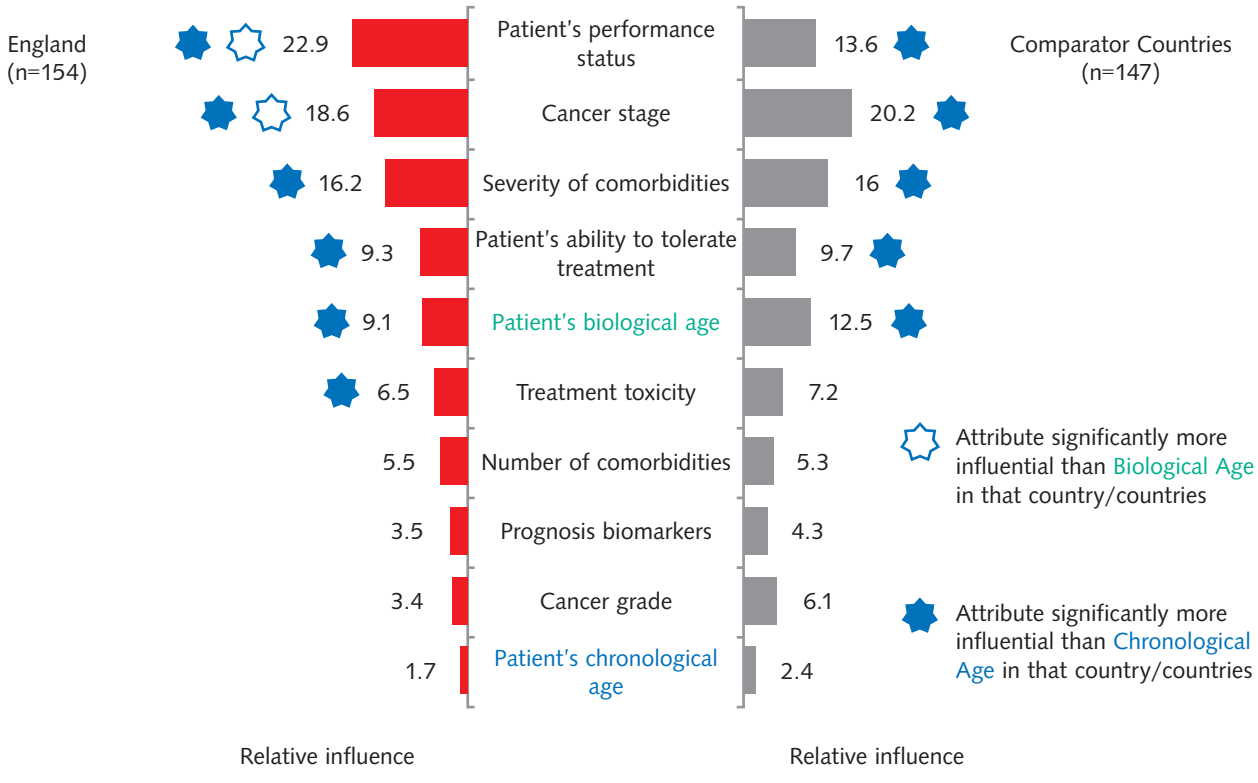


Q20: Please rank the following factors in terms of how challenging they are when treating older patients with [SPECIFIC CANCER] cancer
Base: 301. All countries, all cancers

4.8 In is notable that a number of the perceived challenges in treating older patients relate to the potential side effects that intense treatment may cause. This makes the findings from the National Cancer Patient Experience Survey summarised in Box 2, whereby older people were less likely to be given information about side effects or access to a named Clinical Nurse Specialist (who can play an important role in managing side effects), particularly concerning. This may be an issue on which cancer services and clinicians would wish to work to improve the support available to patients. Respondents (39% of English clinicians, 31% of the comparator countries), when asked in question 22 what treating older patients 'is all about' and invited to complete a sentence, said that it is all about patient-centredness rather than toxicity (3% of both groups.)

4.9 When asked to rank the importance of age in determining how intensively a patient can be treated, its influence was significantly less than other factors, as set out in Figure 6. In this exercise, clinicians were asked to consider both chronological and biological age. The difference in significance between biological and chronological age suggests that – at a theoretical level – clinicians recognise there are differences between the two concepts.

Figure 6: Relative influence of different factors in determining intensity of treatment



Q13: Please rank the following factors in terms of their importance when deciding how intensively you can treat [SPECIFIC CANCER] patients when your goal is to cure them.
Please rank the top 5 factors from 1 to 5 where 1 = most important and 5 = fifth most important
Base: 301. All countries, all cancers

4.10 Amongst English clinicians, performance status, cancer stage, comorbidities, ability to tolerate treatment, biological age and toxicity of treatment were all significantly more influential than chronological age. In addition, performance status and cancer stage were significantly more influential than biological age. Again, there was a high degree of consistency between the responses of clinicians in England and those in other countries.

4.11 In terms of the way in which clinicians report the factors that will influence their decision-making, this suggests that factors which may be associated with age (such as comorbidities, performance status and ability to tolerate treatment) – but not chronological age itself – are important determinants of decisions on intensity of treatment.

5. Impact of age as a factor in treatment decisions

5.1 The use of patient scenarios enables an analysis of the way in which clinical attitudes translate into clinical decision-making. This chapter sets out the key findings from this part of the project, including:

- The impact of different factors on clinical decision-making for both early stage and advanced cancers; and
- Patterns across countries.

5.2 A conjoint analysis model was used to both design and analyse the patient scenarios, specifically a Logit Hierarchical Bayesian Individual modelling approach was deemed the most appropriate for this study. In conjoint models, clinicians evaluate patient profiles that combine two or more characteristics / attributes. Clinicians are presented with a range of scenarios where the attributes (e.g. age) vary according to pre-determined levels (e.g. 75+ year old patients). For each scenario the clinician must decide which treatment they feel is most appropriate. Statistical analysis is then used to both assess the influence that each attribute has on clinician behaviour and how the preference for prescribing a particular therapy varies by levels within an attribute.

5.3 The conjoint analysis used in the study enables the identification of the influence that age, comorbidity and social support have on clinical decision-making. It is important to stress that there is no optimum level of intensity of treatment according to age, comorbidity or social support. Therefore the findings presented in this chapter should be used to consider the relative impact of these factors, as well as their influence on intensity of treatment, rather than to assess whether the proportion of patients offered a particular intensity of treatment is appropriate.

5.4 Findings are presented at an 'all cancer' level, with the intention of publishing cancer-specific data at a later date. As mentioned in Chapter 3, findings are analysed according to four categories of severity ('high,' 'medium,' 'low' and 'no treatment') and then according to two categories ('more' and 'less' intense). For the four-category analysis, results are presented in terms of the proportion of patients who were recommended high intensity treatment. For the two-category analysis, results are presented in terms of the proportion of patients receiving more intense treatment.

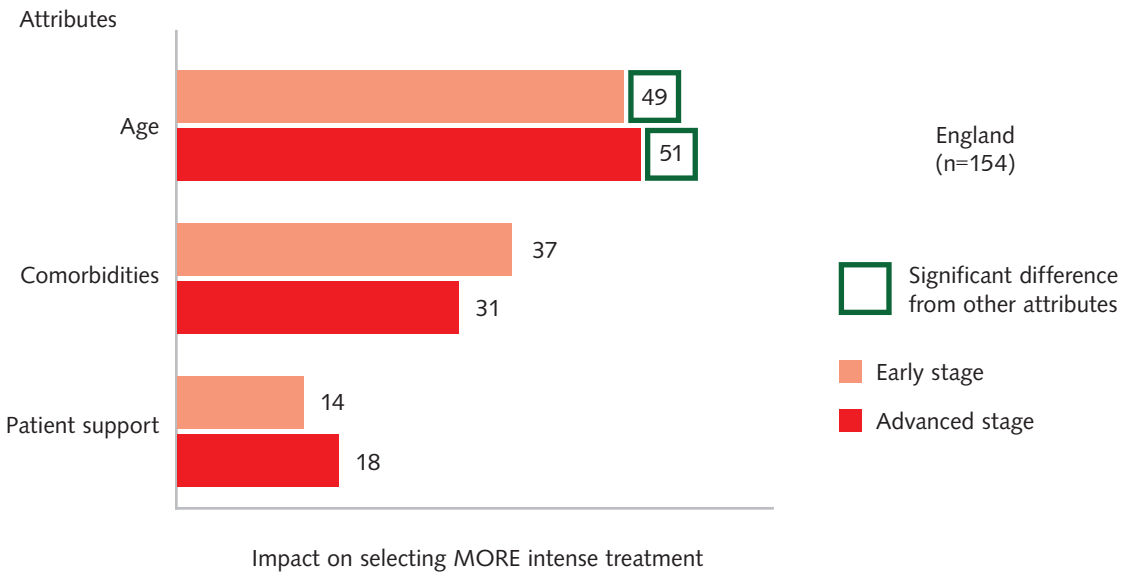
Role of age in clinical decision-making in England

5.5 Given that the focus of the National Cancer Equality Initiative is England, the attitudes and behaviours of clinicians in England have been assessed in detail.

5.6 Chapter 4 shows that English clinicians do perceive age to be an important factor in clinical decision-making. They also recognise that a number of factors which may influence the intensity of treatment they recommend to patients are linked to age, such as performance status and the existence of comorbidities. However, clinicians do not consider age itself to be a particularly important factor in determining the intensity of treatment they would recommend.

5.7 Despite this belief, the findings from the patient scenarios show that age alone is a significantly bigger factor than either comorbidities or social support in determining the intensity of the treatment they would recommend, as set out in Figure 7.

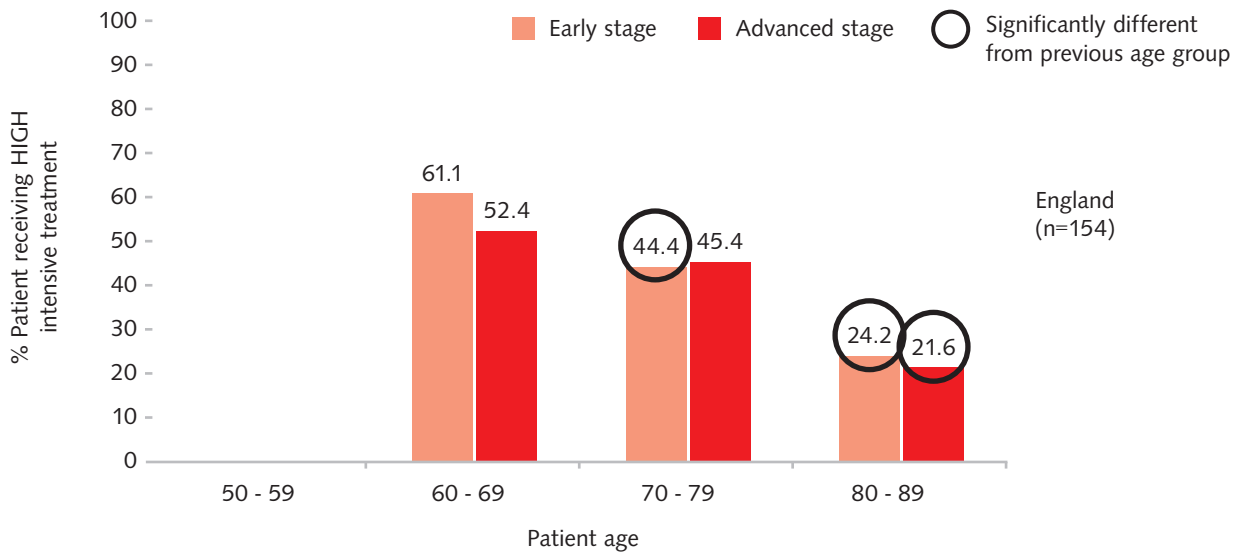
Figure 7: Influence of different factors in determining the intensity of cancer treatment recommended to patients in England



Base 301. All countries, all cancers

5.8 The impact of this finding on the level of intensity of treatment that clinicians would recommend for different age groups is notable. Figure 8 shows that for both patients in their 70s and 80s with early stage cancer, there were statistically significant reductions in the proportion who would be recommended to have more intensive treatment. For advanced cancers, there was a statistically significant reduction for patients in their 80s and a downward – although not statistically significant trend – for patients in their 70s.

Figure 8: Proportion of patients who would be offered high intensity treatment, by age group (England only)

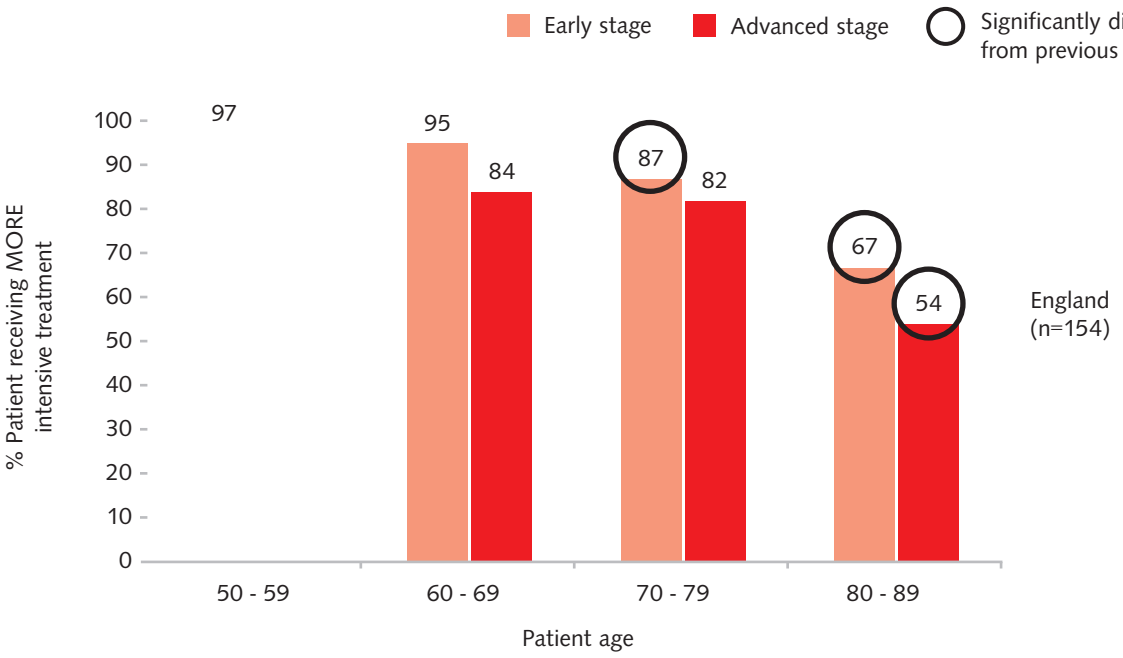


Base 301. All countries, all cancers
NOTE: Analysis conducting assuming patient has no comorbidities and good social support

Analysis model based on patients having no comorbidities and having full patient support

5.9 When the results were reanalysed according to whether the recommended treatment is more or less intense (grouping treatments deemed as being of high and medium intensity together), a similar pattern is observed. For patients in their 70s and 80s with early stage cancer, there were statistically significant reductions in the proportion who would be recommended to have more intensive treatment. For advanced cancers, there was a statistically significant reduction for patients in their 80s and a downward – although not statistically significant trend – for patients in their 70s. These findings are set out in Figure 9.

Figure 9: Proportion of patients for whom clinicians would offer more intensive treatment, by age group (England only)



Base 301. All countries, all cancers
NOTE: Analysis conducting assuming patient has no comorbidities and good social support

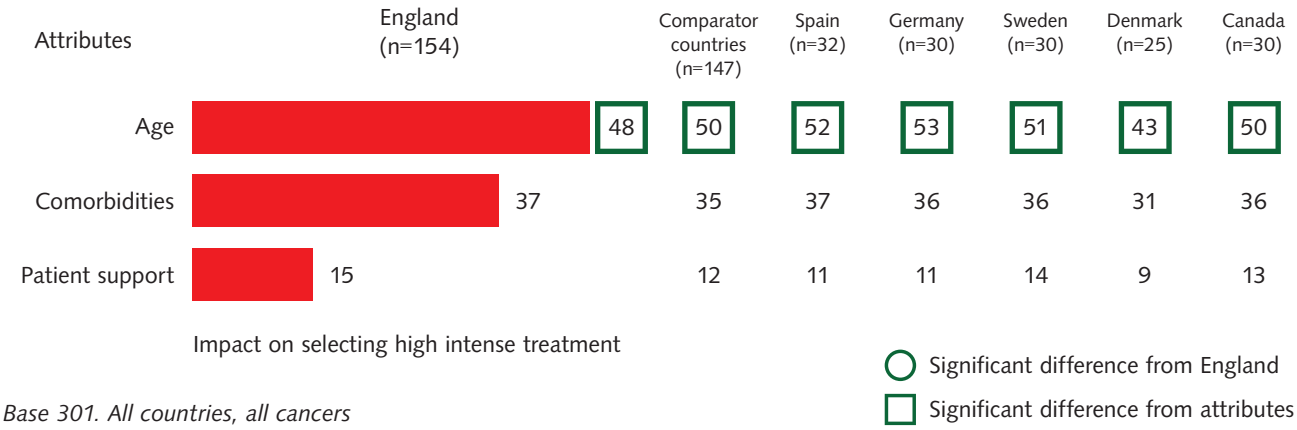
Analysis model based on patients having no comorbidities and having full patient support

Role of age in clinical decision-making in all countries

5.10 As with the clinical attitudes report in Chapter 4, there were remarkable similarities in the way in which clinicians from different countries responded to the patient scenarios. Figure 10 shows that, across all countries and for both early and advanced stage cancer, age is the most significant influence on the intensity of treatment that clinicians would recommend, followed by comorbidities and then social support. Although the impact of age is lower in Canada and Denmark, the difference with other countries is not statistically significant.

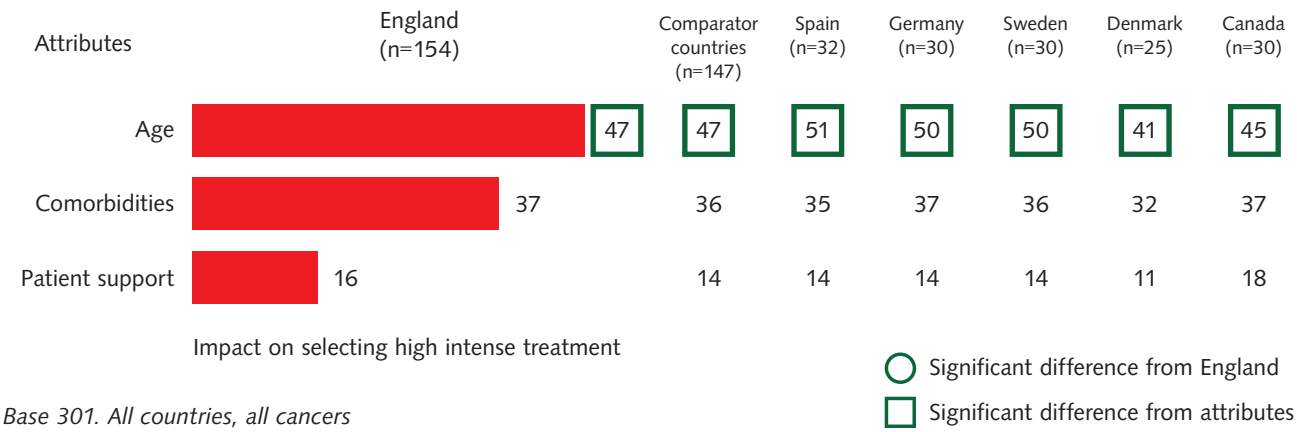
Figure 10: Influence of different factors in determining the intensity of cancer treatment recommended to patients, across countries (a. Early Stage Cancer; b. Advanced Stage Cancer)

a. Early Stage Cancer



Base 301. All countries, all cancers

b. Advanced Stage Cancer



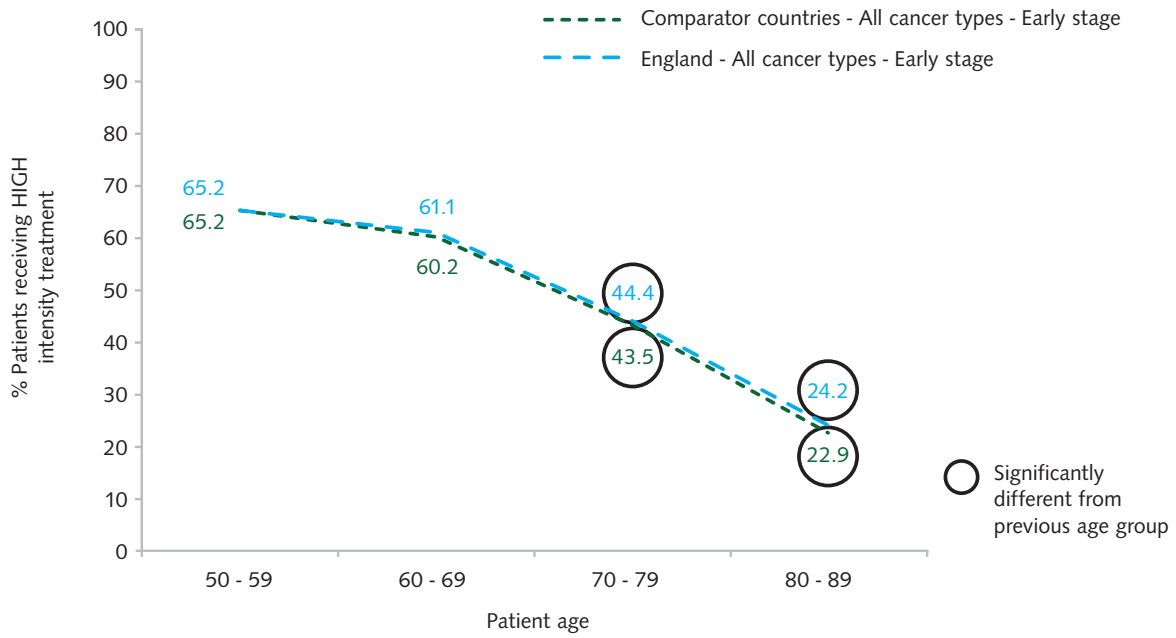
Base 301. All countries, all cancers

5.11 There is a similar impact on the intensity of treatment that clinicians in all countries would recommend for different age groups. Figure 11 shows that statistically significant reductions were observed in the proportion of patients in their 70s and 80s with early stage cancer who would be offered high intensity treatment, when compared with the earlier age group. For advanced cancers, there was a statistically significant reduction for patients in their 80s and a downward – although not statistically significant trend – for patients in their 70s.

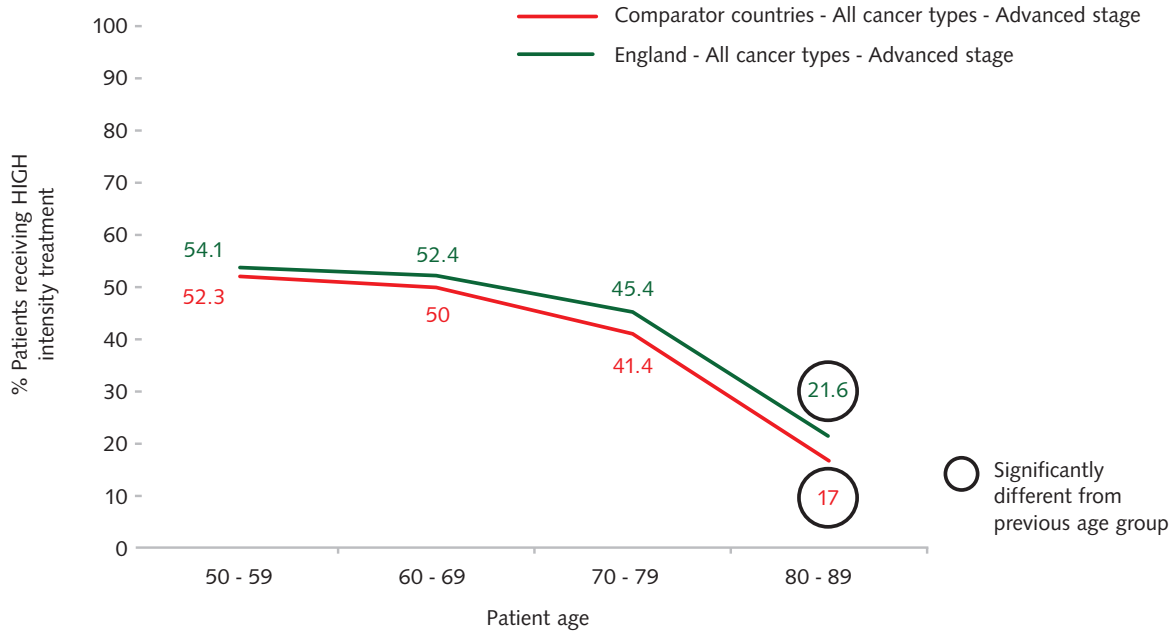
Please see overleaf

Figure 11: Proportion of patients who would be offered high intensity treatment, by age group across all countries (a. Early Stage Cancer; b. Advanced Cancer)

a. Early Stage Cancer



b. Advanced Stage Cancer

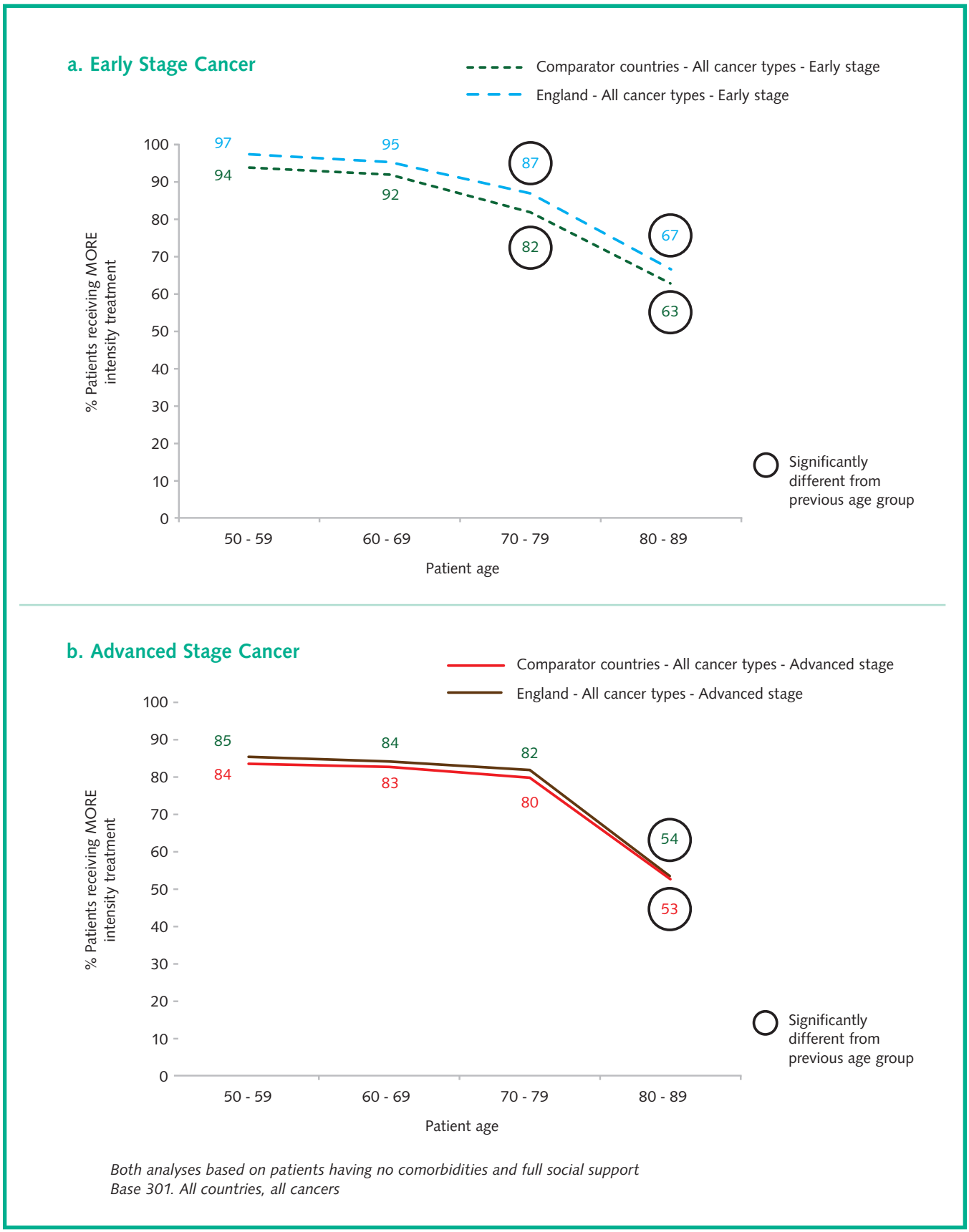


Both analyses based on patients having no comorbidities and full social support
Base 301. All countries, all cancers

5.12 Again, when the results were reanalysed according to whether the recommended treatment is more or less intense (grouping treatments deemed as being of high and medium intensity together), a similar pattern is observed. For both patients in their 70s and 80s with early stage cancer, there were statistically significant reductions in the proportion who would be recommended to have more intensive treatment. For advanced cancers, there was a statistically significant reduction for patients in their 80s and a downward – although not statistically significant trend – for patients in their 70s. These findings are set out in Figure 12.

Please see overleaf

Figure 12: Proportion of patients who would be offered more intensive treatment, by age group across all countries (a. Early Stage Cancer; b. Advanced Cancer)



Both analyses based on patients having no comorbidities and full social support
Base 301. All countries, all cancers

Impact on treatment approaches for older people

5.13 The findings from the patient scenarios suggest that, contrary to the approach towards clinical decision-making that clinicians report, chronological age is itself a significant factor in determining the intensity of treatment that would be recommended to patients.

5.14 If the approach observed in response to the patient scenarios was replicated in clinical practice, then age would indeed play a significant role in determining the nature of treatment offered to cancer patients. For example, analysis of the results from the patient scenarios suggest that, for a patient in their 70s, a decade of healthy ageing would have the same impact on the likelihood of their clinician to prescribe more intensive cancer therapy as if they were to develop a severe comorbidity that affected their everyday life, as set out in Box 6.

Box 6

Impact of healthy ageing on treatment intensity

Analysis of the findings from the patient scenarios suggests that the likelihood of a patient with advanced cancer receiving more intense cancer treatment reduces by a similar amount in the following scenarios:

- The patient changes from someone in their 70s with good social support and no comorbidities to a patient in their 80s with the same characteristics (reduction of 28%);
- The patient changes from someone in their 70s with good social support and no comorbidities to a patient of the same age and social support but with severe comorbidity which affects their everyday life (reduction of 13%).

6. Conclusion and next steps

6.1 There are often very good reasons why older people are offered less intensive cancer treatment. Age is associated with the development of comorbidities and older people may well be less able to withstand the toxicities which can be associated with cancer treatment. Age is often, therefore, a proxy for other factors.

6.2 Although clinicians cite age as a factor in determining the intensity of cancer treatment to recommend, they say that it is significantly less influential than other factors which might be associated with age, such as comorbidities, performance status or ability to tolerate treatment.

6.3 Nonetheless, this study suggests that chronological age alone is a significant factor in influencing clinical decision-making in cancer, in ways that clinicians would not consciously recognise. Indeed, age is a significantly more influential factor than comorbidities or social support.

6.4 This pattern is observed for a range of both early stage and advanced forms of cancer. Nor is it a phenomenon which is limited to certain countries, with a high degree of consistency being observed across six different countries.

6.5 The findings suggest that there is an issue which is worthy of attention, particularly given the current and growing impact of cancer on health outcomes for older people. Indeed the research documented in this report presents a challenge to the cancer community to consider how best it can support older people affected by cancer, including ensuring that they are offered the most appropriate treatment for them and are supported in making informed decisions.

6.6 The findings from this research will be relevant to a range of stakeholders committed to improving cancer outcomes, both in England and elsewhere. These include – but are not limited to – the clinical community, commissioners and providers of cancer services, the pharmaceutical industry, cancer charities and organisations of and for older people. There are a range of actions which these groups might wish to consider, including:

- Professional bodies should consider developing guidelines to support clinicians in offering appropriate treatment to older patients, based on a thorough assessment of their clinical characteristics;

- Geriatricians should consider the ways in which they could support cancer clinicians in delivering the most appropriate treatment to older people;

- Data on clinical practice – including national clinical audits and datasets on surgery, radiotherapy and chemotherapy – should wherever possible be published in such a way to enable analysis by age, building on the work undertaken to date by the NCIN;

- Those hospitals that already have high quality information on chemotherapy usage, as a result of adopting e-prescribing systems, may wish to work together to examine the age profile of their chemotherapy patients. The findings could be published in an anonymised format so as to provide a more detailed picture of the impact of age on the provision of chemotherapy;

- Guidance on the quality of cancer services should reflect the needs of older people and the fact that active treatment rates for older patients can be a marker of wider quality. In particular, NICE should consider the case for building on the example of the Breast Cancer Quality Standard, which includes active treatment rates for older people, when developing further cancer quality standards;

- Information should be provided to commissioners of cancer services in assessing the extent to which older cancer patients are being offered appropriate treatment, including publishing data on treatment rate and modality by age;

- Providers of cancer services should consider taking steps to ensure they are offering appropriate treatment to their patients and supporting informed decision making, including the application of multi-disciplinary team (MDT) equity audits, as described in Box 7;

- The work being led by the Department of Health, National Cancer Action Team and Macmillan Cancer Support to support clinicians in offering the most appropriate treatment to older people – including through testing new approaches to clinical assessment - should reflect and address the findings of this study;

- Commissioners and providers of cancer services should consider working together to improve the quality and consistency of the information on side effects of treatment which is provided to older patients as part of their efforts to improve outcomes in Domain 5 of the NHS Outcomes Framework ('Treating and caring for people in a safe environment and protecting them from avoidable harm');

- A systematic review of the evidence on the efficacy and tolerability of cancer treatment in the over 70s should be conducted. The pharmaceutical industry and other medical researchers should also consider what more can be done to publish evidence on treatment efficacy and side effects in older people. This evidence may be generated through pre-marketing authorisation trials or post-licensing audits or surveillance. An example of such a study is included in Box 8;

- Given that lack of clinical trial data supporting treatment choices for older people was cited by 80% of respondents as the second highest ranking challenge of treating older people, the National Cancer Research Network (NCRN) should consider working with the principal investigators of large scale clinical trials to assess whether or not the demographics of trial participation is representative of the demographics of the wider population of people affected by cancer. An example of how steps can be taken to include frail or older patients in clinical trials, led by Professor Mathew Seymour et al is included in Box 9; and

- Cancer charities should consider the case for developing tailored information aimed at supporting older people who are either considering or undergoing treatment.

Box 7
MDT equity audits

The equity audit, first announced in Improving Outcomes: a Strategy for Cancer, enables multidisciplinary teams or Site Specific Tumour Groups to consider demographic characteristics of their patients and reflect on their care and treatment. In this way, MDTs who record consistent variables, for example performance status and stage at presentation, and comorbidities will be able to reflect annually on treatment recommendations for older people. It is intended that the equity audit will be included in future peer review measures, ensuring its widespread use.

Box 8

Generating data on the efficacy of treatments in older people[28]

Older patients are often excluded from clinical trials due to concerns over comorbidity and this in turn can impact upon treatment rates in standard clinical practice. Yet it is possible to examine the impact of treatment in older people. For example, data from a large randomised study which was presented at the American Society of Clinical Oncology in 2010 found that more intensive combination therapy for lung cancer was effective and safe in patients between the ages of 70 and 89, with one-year survival improving from 26.9% on the single agent to 45.1% percent with the combination. Progression-free survival nearly doubled to 6.1 months for those patients receiving combination therapy.

Box 9

Including frail or older patients in clinical trials[29]

Standard treatment for advanced colorectal cancer includes palliative chemotherapy, with an expanding range of treatment options. However, the evidence supporting these treatments is from clinical trials that underrepresented older or frail and especially older frail patients. Even when there is no formal upper age limit in trials, there are impediments to recruiting older patients, including a lack of flexibility in dosing arrangements, which means that trials are often not representative of routine clinical practice.

The FOCUS2 trial, conducted on patients with advanced colorectal cancer who were not deemed to be suitable for other clinical trials, shows that with an appropriate design – including reduced starting doses of chemotherapy – frail or older patients can participate in a randomised controlled trial.

Annex 1 – background to the statistical model

Discussion of Methodology

Conjoint analysis is a statistical technique used in market research to determine how people value different features and which of these features or factors drive decision making. It is considered more powerful than direct questioning, as it examines behaviour rather than attitudes and perceptions.

The technique helps identify preferences by offering respondents a series of choices, rather than simply asking them to say what is important. The principle behind conjoint analysis is to break a situation down into its constituent parts, then to test combinations of these parts (in this case patient features) to examine the priority of these different features in therapy choice.

The objective of conjoint analysis is then to determine what combination of a limited number of patient features is most influential on respondent choice or decision making.

A controlled set of potential parameters (in this instance different permutations and combinations of patient features in the form of vignettes) is shown to respondents. The implicit value of each of the individual patient features can be understood by analysing how respondents make choices in treatment intensity between the vignettes. These implicit valuations can be used to create simulation models that help predict the impact of different patient features on the behaviour of clinicians making choices in treatment.

This allows the exploration of different levels of an attribute or feature – for example we don't ask just whether or not comorbidities are important – we can examine the actual impact that no / mild / moderate/ and severe comorbidities have on decision-making.

In terms of age, we can isolate the impact of changing the age in the profile in the different vignettes, by keeping everything else constant. We can then see how moving from ages 50 / 60 / 70 through to 80 impacts on therapy choice. By designing the study appropriately, it is then possible to use statistical analysis to work out the value of each patient feature and its level, in driving clinical decision-making.

In order to examine the impact of each patient feature and level within a series of 96 scenarios, the patient vignettes were constructed from different permutations and combinations of the patient features and their levels. Each respondent was asked to comment on their treatment choice in 16 different scenarios, with the full 96 scenarios being rotated through the sample using a statistical design.

Annex 2 – clinical advisers to the project

The following clinicians provided expert advice on the development of the patient scenarios, as well as the interpretation of the findings:

- Professor Jane Apperley, Chair of Haematology, Imperial College, London;
- Tim Eisen, Professor of Medical Oncology, University of Cambridge;
- Dr Rob Glynne-Jones, Mount Vernon Centre for Cancer Treatment, Northwood;
- Dr Alison Jones, UCLH and Royal Free Hospitals, London; and
- David Linch, Professor of Haematology and Head of the Department of Haematology at University College London (UCL)

Annex 3 – summary of treatment options, banded according to intensity

Treatment options made available for market research respondents were based on potential therapies which could be used within the framework of high, medium and low intensity treatments across tumour types and stages on the feedback from the clinical expert panel. They do not represent recommendations for treatment by the ABPI, NCEI or the clinical expert panel. For information on the recommended use of medicines, please refer to the relevant Summary of Product Characteristics.

		Cancer Type				
		Renal	Breast	Colorectal	NHL	CML
Early Stage	High intensity	• Nephrectomy followed by sunitinib – 50mg od	• Adjuvant chemotherapy followed by breast radiotherapy and then adjuvant endocrine therapy	• Surgery and adjuvant FOLFOX • Surgery and adjuvant XELOX	• Combination chemotherapy	• Imatinib
	Low intensity	• Nephrectomy • Sunitinib alone – 50mg od • Sunitinib alone – 37.5mg od • Sorafenib - 400mg bd • Observation	• Adjuvant breast radiotherapy followed by adjuvant endocrine therapy • Adjuvant endocrine therapy only • Observation	• Surgery and adjuvant Capecitabine • Surgery and adjuvant 5-FU (Fluorouracil) • Surgery alone	• Combined modality treatment • Radiation alone • Observation	• 2nd generation Tyrosine Kinase Inhibitor (dasatanib/ nilotinib) • 2nd generation Tyrosine Kinase Inhibitor (dasatanib/ nilotinib) via a national trial • Hydroxycarbamide • Observation
Advanced Stage	High intensity	• Nephrectomy followed by sunitinib – 50mg od	• Taxane or Anthracycline based chemotherapy regime with biphosphonates	• FOLFOX and Bevacizumab • FOLFOX and Cetuximab • FOLFIRI and Bevacizumab • FOLFIRI and Cetuximab	• Combination therapy including anthracycline i.e. CHOP regimen	• Imatinib
	Low intensity	• Nephrectomy • Sunitinib alone – 50mg od • Sunitinib alone – 37.5mg od • Sorafenib - 400mg bd • Observation	• Capecitabine with biphosphonates • Endocrine therapy with biphosphonates • Observation	• FOLFOX) • FOLFIRI • 5-FU (Fluorouracil) • Capecitabine • Observation	• Chemotherapy excluding anthracycline i.e. CVP regimen • Steroids/single agent palliative chemotherapy • Observation	• 2nd generation Tyrosine Kinase Inhibitor (dasatanib/ nilotinib) • 2nd generation Tyrosine Kinase Inhibitor (dasatanib/ nilotinib) via a national trial • Hydroxycarbamide • Observation

Annex 4 – summary of treatment options, in 'more intense' and 'less intense' categories

Treatment options made available for market research respondents were based on potential therapies which could be used within the framework of high, medium and low intensity treatments across tumour types and stages on the feedback from the clinical expert panel. They do not represent recommendations for treatment by the ABPI, NCEI or the clinical expert panel. For information on the recommended use of medicines, please refer to the relevant Summary of Product Characteristics.

		Cancer Type				
		Renal	Breast	Colorectal	NHL	CML
Early Stage	More intense	• Nephrectomy followed by sunitinib – 50mg od • Nephrectomy • Sunitinib alone – 50mg od	• Adjuvant chemotherapy followed by breast radiotherapy and then adjuvant endocrine therapy	• Surgery and adjuvant FOLFOX • Surgery and adjuvant 5-FU • Surgery and adjuvant Capecitabine • Surgery and adjuvant 5-FU (Fluorouracil)	• Combination chemotherapy • Combined modality treatment	• Imatinib • 2nd generation Tyrosine Kinase Inhibitor (dasatanib/nilotinib) [via a national trial]
	Less intense	• Sunitinib alone – 37.5mg od • Sorafenib – 400mg od	• Adjuvant breast radiotherapy followed by adjuvant endocrine therapy • Adjuvant endocrine therapy only	• Surgery alone	• Radiation alone	Hydroxycarbamide
Advanced Stage	More intense	• Nephrectomy followed by sunitinib – 50mg od • Nephrectomy • Sunitinib alone – 50mg od	• Taxane or Anthracycline based chemotherapy regime with biphosphonates	• FOLFOX and Bevacizumab • FOLFOX and Cetuximab • FOLFIRI and Bevacizumab • FOLIRI and Cetuximab • FOLFOX • FOLFIRI	• Combination therapy including anthracycline i.e. CHOP regimen • Chemotherapy excluding anthracycline i.e. CVP regimen	• Imatinib • 2nd generation Tyrosine Kinase Inhibitor (dasatanib/ nilotinib) [via a national trial]
	Less intense	• Sunitinib alone – 37.5mg od • Sorafenib – 400mg od	• Capecitabine with biphosphonates • Endocrine therapy with biphosphonates	• 5-FU (Fluorouracil) • Capecitabine	• Steroids/single agent palliative chemotherapy	• Hydroxycarbamide

Annex 5 – full questionnaire

Before you start with the main survey, we would like to confirm some eligibility questions with you.

S.1 What is your specialty?
Please select the answer that best describes your role

1. Haematologist
2. Medical Oncologist
3. Radiologist **(CLOSE)**
4. Gastrointestinal Surgeon **(CLOSE)**
5. General Medicine **(CLOSE)**
6. Nephrologist **(CLOSE)**
7. Breast Surgeon **(CLOSE)**

S.2 What is your grade?
Please select the answer that best describes your role

Professor (or equivalent)
Consultant (or equivalent)
Specialist Registrar/Senior Registrar (or equivalent)
Registrar/Junior Registrar (or equivalent) **(CLOSE)**
Not applicable – office based (or equivalent) **(CLOSE)**
Other **(CLOSE)**

S.3 For how many years have you been in practice for your speciality?

[**Digit box. 0-50**] years

S.4 What proportion of your time is spent in direct patient care?

[**Digit box**] %

S.5 How many cancer patients do you see overall in an average month?
[**Digit box**]

ASK HAEMATOLOGIST
S.6 Which of the following types of cancer do you treat?

1. Acute Lymphoblastic Leukaemia
2. Acute Myeloid Leukaemia

3. Myelodysplastic syndromes
4. Chronic Myeloid Leukaemia
5. Chronic Lymphocytic Leukaemia
6. Hodgkin's Lymphoma
7. Non- Hodgkin's Lymphoma
8. Polycthemia Rubra Vera
9. Myeloma
None of the above **[s/c]**

ASK ONCOLOGIST
S.7 Which of the following types of cancer do you treat?

1. Small Cell Lung Cancer
2. Non Small Cell Lung Cancer
3. Breast Cancer
4. Prostate Cancer
5. Renal Cell Carcinoma
6. Transitional Cell Carcinoma
7. Colorectal Cancer
8. Carcinoma of the Pancreas
9. Liver Cancer
None of the above **[s/c]**

S.8 What best describes the way in which you are paid for your role (excluding bonuses etc.). Are you paid…?

1. A salary (fixed per annum)
2. A service based reward (paid per treatment/procedure)
3. Part salary/part service based reward
4. Other PLEASE SPECIFY

I prefer not to answer this question **[s/c]**

Congratulations, you have qualified to participate in this survey. The following questions will focus on the treatment and management of **[INSERT CANCER]** patients

Survey Questions – Part 1

Q.1 On average how many patients do you see with [INSERT CANCER] a month?
[**Digit box**]

Q.2 Please rank the following factors in terms of the importance they have when you are assessing the severity of [INSERT CANCER]?

Please rank each factor from 1 to 5 where 1 = most important and 5 = fifth most important

RANDOMISE ORDER
The stage of the cancer
The grade/histology of the cancer
Diagnostic biomarkers
Prognostic biomarkers
The patient performance status

Q.3 Please rank the following factors in terms of the importance they have when you are deciding which treatment modality to use for a curative approach in [INSERT CANCER]?

Please rank the top 5 factors from 1 to 5 where 1 = most important and 5 = fifth most important

RANDOMISE ORDER
Cancer stage
Cancer grade
Prognostic biomarkers
Patient's performance status (measure of general wellbeing)
Treatment side effects
Patient's co morbidities
Patient's biological age
Patient's chronological age
Patient's sex
Intensity of treatment
Patient's expectations
Treatment toxicity
Level of professional supportive care available
Level of supportive care provided by the patient's family

Q.4 Which treatment approaches do you use when your goal is to cure [INSERT CANCER]?

Chemotherapy
Surgery
Radiotherapy
Endocrine Therapy **[Breast ONLY]**
Stem Cell Transplant **[CML ONLY]**
Immunotherapy **[RCC ONLY]**
Other (please specific)

Q.5 Which is your preferred treatment modality when your goal is to cure [INSERT CANCER]?

[ONLY SHOW OPTIONS AT SELECTED AT Q4]
Chemotherapy
Surgery
Radiotherapy
Endocrine Therapy **[Breast ONLY]**
Stem Cell Transplant **[CML ONLY]**
Immunotherapy **[RCC ONLY]**
Other (please specify)

Q.6 Please rank the following advisory factors in terms of their influence over which treatment you administer [INSERT CANCER] patients

Please rank the top 5 factors from 1 to 5 where 1 = most influential and 5 = fifth most influential

RANDOMISE ORDER
International Guidelines
European Guidelines
North American Guidelines
National Guidelines
Regional Guidelines
Hospital Guidelines
Personal clinical experience
Advice and guidance from colleagues
Key Opinion Leaders

Q.7 To what extent do you feel satisfied with the available treatments for [INSERT CANCER]

Please rate your satisfaction with a score of 1-5 where 1 = extremely satisfied and 5 = not satisfied at all

ORDER Q8 AND 9 AS FOLLOWS:
If respondent scores 1-2 at Q7 then the order goes Q9 then Q8
If respondent scores 3 please randomise the order of Q9 and Q8
If they score 4-5 then the order goes Q8 then Q9

Q.8 Please rank the following factors in terms of their impact on your dissatisfaction with current treatments for [INSERT CANCER]

Please rank the top 4 factors from 1 to 4 where 1 = most impactful and 4 = fourth most impactful

RANDOMISE ORDER
Cost of treatments
Local access to treatments
Tolerability of treatments
Predictability of the response to treatments
Consistency in the response to treatments
Effectiveness of therapies in achieving a cure
Effectiveness of therapies in providing palliative treatment

Quality of evidence supporting treatment options
Volume of evidence supporting treatment options
The number of patients that can be treated with existing treatments
Toxicity of treatments

Q.9 Please rank the following factors in terms of their impact on your satisfaction with current treatments for [INSERT CANCER]

Please rank the top 4 factors from 1 to 4 where 1 = most impactful and 4 = fourth most impactful

RANDOMISE ORDER
Cost of treatments
Local access to treatments
Tolerability of treatments
Predictability of the response to treatments
Consistency in the response to treatments
Effectiveness of therapies in achieving a cure
Effectiveness of therapies in providing palliative treatment
Quality of evidence supporting treatment options
Volume of evidence supporting treatment options
The number of patients that can be treated with existing treatments
Toxicity of treatments

Q.10 Please rank the following factors in terms of how significantly they might improve your perception of treatments for [INSERT CANCER]

Please rank the top 5 factors from 1 to 5 where 1 = most significant and 5 = fifth most significant

RANDOMISE ORDER
Reduced cost of treatments
Increased investment in research and development
More targeted/cancer specific therapies
Treatments with fewer side effects
Treatments that are more effective at prolonging life
Treatments that are more effective in reducing patient symptoms
Treatments that can be tolerated by more patients
Reduced toxicity of treatments

Conjoint Analysis

We are now going to show you a series of patient scenarios, please read each description carefully and decide how intensively you would treat each patient. Please consider each profile to represent a typical patient you would see in your own hospital/clinic and base your answer on the decision you would make in real life circumstances.

The treatment options presented to you for each scenario may not be a fully comprehensive list. Therefore, please select the most appropriate treatment option(s) from the list provided.

Q.11

Description of patient cancer type and any specific markers/description/text (need to ensure respondents are clear that the treatment aim is curative)

Patient Characteristics:

Stage:

Age:

Social status

Co morbidities:

Survey Questions – Part 2

Q.12 What factors dictate how intensively you can treat a patient with [INSERT CANCER] when your goal is to cure them?

Please write in as much detail as possible

Q.13 Please rank the following factors in terms of their importance when deciding how intensively you can treat [INSERT CANCER] patients when your goal is to cure them?

Please rank the top 5 factors from 1 to 5 where 1 = most important and 5 = fifth most important

RANDOMISE ORDER

Patient's biological age
Patient's chronological age
Patient's performance status
Patient's ability to tolerate treatment
Patient's sex
Cancer stage
Cancer grade
Number of co morbidities
Severity of co morbidities
Specific prognostic bio-markers
Level of professional supportive care available
Level of supportive care provided by the patient's family
Use of growth factors to allow patients to tolerate more intensive therapy
Treatment toxicity

Q.14 Please rank your level of agreement with the following statements regarding how doctors might measure the intensity of treatment to prescribe for a [INSERT CANCER] patient?

Please rank the top 5 factors from 1 to 5 where 1 = most strongly agree and 5 = fifth most strongly agree

RANDOMISE ORDER

1. Intensity is related to the duration of a cycle of chemotherapy
2. Intensity is related to the overall duration of therapy
3. Intensity is related to the dose of therapy
4. Intensity is related to the number of side-effects the treatment causes
5. Intensity is related to the severity of side-effects the treatment causes
6. The threshold for the intensity of treatment is higher in curative therapy than palliative care
7. Intensity is dependent on the patient's co morbidities
8. Intensity is dependent on the patient's assessed performance status
9. Intensity is dependent on the patient's biological age
10. Intensity is dependent on the patient's chronological age
11. Intensity is measured on an individual patient basis
12. Intensity is dependent on what the patient is prepared to tolerate
13. Intensity is related to the level of toxicity of therapy

ASK THOSE WHO DO NOT RANK AGE AFFECTING TREATMENT INTENSITY IN THE TOP 5

Q.15 Why do you think chronological age does not affect the intensity of treatment you can administer to a [INSERT CANCER] patient?

Please provide as much detail as possible

ASK THOSE WHO DO RANK AGE AFFECTING TREATMENT INTENSITY IN THE TOP 5

Q.16 Why do you think chronological age affects the intensity of treatment you can administer to a [INSERT CANCER] patient?

Please provide as much detail as possible

Q.17 Please rank the following factors in terms of the influence chronological age has on patients with [INSERT CANCER] cancer?

Please rank the top 5 factors from 1 to 5 where 1 = most influential and 5 = fifth most influential

RANDOMISE ORDER

A patient's performance status
A patient's ability to tolerate a treatment
The intensity of treatment a patient can be prescribed
The stage of cancer a patient is likely to have
The number of comorbidities a patient is likely to have
The severity of comorbidities a patient is likely to have
The patient's kidney function
The patient's liver function
The patient's lung function
The patient's cardiovascular function
The level of supportive care likely to be required by the patient
The likelihood of a patient to achieve a curative outcome
The patient's likelihood to respond to therapy
The toxicity of treatment a patient can be prescribed

Q.18 At what chronological age do you consider a patient with [INSERT CANCER] to be 'old'?

[Digit box] years
I do not believe a patient can be classified by age

Q.19 Up to what chronological age do you consider a patient with [INSERT CANCER] to be 'young'?

[Digit box] years
I do not believe a patient can be classified by age

Q.20 Please rank the following factors in terms of how challenging they are when treating older patients with [INSERT CANCER] cancer?

Please rank the top 5 factors from 1 to 5 where 1 = most challenging and 5 = fifth most challenging

RANDOMISE ORDER
The patient's expectations are too high
The patient's expectations are low (i.e. refuse treatment)
The quality of clinical trial data supporting the treatment choices for older patients
The volume of clinical trial data supporting the treatment choices for older patients
The patient's ability to tolerate treatment
The patient's response to therapy
The adequacy of supportive care available to the patient
The patient's level of involvement in their treatment is low
The patient's level of involvement in their treatment is high

Q.21 Please rank the following factors in terms of how challenging they are when treating younger patients with [INSERT CANCER]?

Please rank the top 5 factors from 1 to 5 where 1 = most challenging and 5 = fifth most challenging

RANDOMISE ORDER
The patient's expectations are too high
The patient's expectations are low (i.e. refuse treatment)
The quality of clinical trial data supporting the treatment choices for young patients
The volume of clinical trial data supporting the treatment choices for young patients
The patient's ability to tolerate treatment
The patient's response to the therapy
The adequacy of supportive care available to the patient
The patient's level of involvement in their treatment is low
The patient's level of involvement in their treatment is high

Q.22 Finally, please complete the following sentence:

Treating older patients with **[INSERT CANCER]** *is all about...*

Please write in as much detail as possible

[Open]

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27. Respondents were recruited using Kantar Health's partner agencies in each country, these agencies were All Global, MPI and QQFS. Respondents were recruited from the agencies online panels or call lists. These panels/call list consist of a large number of healthcare professionals per country, with a good geographic spread, who have been specifically recruited to ensure that members are unbiased, have actively opted into market research, and have had their details validated. The panels/call lists are regularly monitored for quality of responses and updated to cover change of details, new recruits and those dropping out. The respondents were selected because of their experience in managing at least one of the five conditions included in this study. The respondents were recruited on a first come first serve basis and received a reimbursement for their time in line with the market research guidelines applicable to the country in which they work.

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