Royal Surrey County Hospital
NHS Foundation Trust

The role of Electronic Frailty Index in improving outcomes for newly diagnosed cancer patients undergoing systemic chemotherapy treatment

Short title: EFI in Cancer

Sponsor	Royal Surrey County Hospital NHS Foundation Trust
Funder	NIHR RfPB
Protocol Version and Date	Version 4.0 23.11.2020
Chief Investigator	Dr Agnieszka Michael
Trial Management Group	Surrey CTU, Dr Jo Armes, Professor Simon De Lusignan, Dr Janine Mansi
Statistician	Professor Simon Skene

Signature Page

The undersigned confirm that the following protocol has been agreed and accepted and that the Principal Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, the International Conference on Harmonisation Topic E6: Guideline for Good Clinical Practice (ICH GCP), any relevant SOPs, and other regulatory requirements.
I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor.
I also confirm that I will make the findings of the study publicly available through publication or other dissemination tools without any unnecessary delay and that an honest, accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

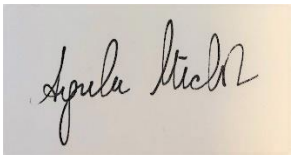
For and on behalf of the Study Sponsor: Kate Penhaligon

Signature:  Date: 02.07.2020

Name (please print): Kate Penhaligon

Position: R&D Manager.....

Chief Investigator: Agnieszka Michael

Signature: .....  ..... Date: 02.07.2020

Name: (please print): Agnieszka Michael .....

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1. Glossary

AE	Adverse Event
CRF	Case Report Form
EFI	Electronic Frailty Index
GCP	Good Clinical Practice
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
ISF	Investigator Site File
PI	Principal Investigator
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
SUSAR	Suspected Unexpected Serious Adverse Reaction
TMF	Trial Master File

2. Contacts

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Key Protocol Contributors	Prof Simon Skene, Dr Jo Armes, Dr Janine Mansi
Statistician	Prof Simon Skene
Committees	Scientific Committee chaired by Prof Peter Selby

3. Protocol Summary

Title	The role of Electronic Frailty Index (eFI) in improving outcomes for newly diagnosed cancer patients undergoing systemic chemotherapy treatment
Short title	EFI in Cancer
Sponsor	Royal Surrey County Hospital
Funder reference	NIHR200517
Clinical trials / ISRCTN	TBC
Design	This study explores the potential utility of eFI in predicting adverse treatment outcomes for people with cancer. It is a research project in two parts; this protocol outlines the first part, the development phase, which has two parallel work-packages. Work-package 1 includes an analysis of a national systemic chemotherapy dataset (SACT) records 2013-2016 of patients with breast, lung and colorectal cancer linked with the data from GP electronic health records and Hospital Episode Statics (HES) to include eFI: HES-eFI and GP-eFI as well as 30-day chemotherapy mortality and hospital admissions during chemotherapy. The outcome measure is 30-day chemotherapy mortality and hospital admissions during chemotherapy for the above described cohort of patients Work-package 2 includes a qualitative study that will examine patients, carers and clinicians' attitudes to using an automated frailty score that can influence the decision-making process.
Primary objectives	The primary objective of this research project is to investigate whether eFI is predictive of adverse outcomes of chemotherapy in frail patients with cancer
Secondary objectives	1. The acceptability of eFI as a tool in assessing frailty in cancer patients and in influencing clinical decision making over treatment with chemotherapy. 2. The suitability of the endpoints for a future definitive study that will test a clinical decision tool based on eFI prospectively in a randomised trial. 3. The overlap and accuracy between hospital derived eFI (HES-eFI) and GP medical records derived eFI (GP-eFI). The GP-eFI and HES-eFI will be compared for the ability to predict the adverse chemotherapy outcomes such as hospital admissions and 30-day mortality. 4. The ease of access to GP-eFI and HES-eFI. This step will help to determine the best tool to use in the prospective study (this will include mapping coverage of GP surgeries referring to individual cancer centres and the cost comparison between the HES-eFI and GP-eFI)

<table>
<tr><td></td><td>5. Comparison of EFI with ECOG performance status as predictors of adverse outcomes of chemotherapy</td></tr>
<tr><td>Target accrual</td><td>Recruitment will only take place for the work-package 2-the qualitative study; we will aim to recruit and interview:
Stakeholders 10: 5 medical and clinical oncologists, general practitioner, geriatrician, 5 chemotherapy and clinical nurse specialists
Patients – 10 purposely selected for age- 60-70, >70 and gender
Carers – 5 purposely selected for gender and whether partner or children</td></tr>
<tr><td>Inclusion criteria</td><td>Stakeholders (10)-5 medical and clinical oncologists, general practitioner, geriatrician, 5 chemotherapy and nurse specialists
Patients (10):
<table><tr><td>Newly diagnosed stage II or III breast cancer</td><td>2 aged 60-70y.o.</td><td>2-aged >70y.o.</td></tr><tr><td>Stage III colon cancer</td><td>1 aged 60-70y.o.</td><td>2-aged > 70y.o</td></tr><tr><td>Stage IIIB-IV NSCLC</td><td>1 aged 60-70y.o.</td><td>2-aged > 70y.o</td></tr></table>
Carers: 5 purposely selected for gender (3 men,2 women) and whether partner (3) or children (2)</td></tr>
<tr><td>Exclusion criteria</td><td>Patients and stakeholders who do not fall under the categories described above
Patients /carers who are unable to give an interview or do not speak English</td></tr>
<tr><td>Number of sites</td><td>Single site; RSCH</td></tr>
<tr><td>Duration of recruitment</td><td>12 months</td></tr>
<tr><td>Duration of patient follow-up</td><td>No follow up</td></tr>
<tr><td>Definition of end of trial</td><td>Completed interviews with stakeholders, patients and carers</td></tr>
</table>

4. Study Schedule

Investigations	Baseline and screening	Visit 1- interview
Informed consent	**X**	
Participant Demographics[a]	**X**	
Medical History[b]	**X**	
Questionnaire		**X**

a Participant Demographics – for stakeholders only job title will be collected,
b for patients –year of birth, cancer type, chemotherapy type, for carers-type of cancer and age .

5. Background

5.1. Rationale for study

Older and frail patients with cancer are a group for whom it is acknowledged that potentially curative treatment rates often fall significantly below that seen in other patient groups. There is evidence that older patients who are often fit receive less aggressive treatment and as a result have worse survival [1, 2]. We also know that many older and frail patients often do not tolerate systemic chemotherapy well and are frequently harmed as a result of treatment [2]. Current methods of assessment of fitness (performance status) for intensive cancer treatment such as chemotherapy are inadequate [3]. Despite a growing field of geriatric oncology and a number of comprehensive assessments recommended for use in clinical practice the outcomes for older patients have not improved. The complexity of geriatric assessments, lack of training and time pressures in busy NHS clinics, as well as difficulties that clinicians face when deciding on the correct treatment for frail patients mean that better solutions are needed [4]. The developments in the digital field and electronic sources of information give new opportunities and offer solutions that can be accessed at the point of referral from GPs and have a potential to change daily clinical practice.

Frailty is a condition of increased vulnerability to major changes in health as a result of seemingly small problems, such as infection or new medication. It is common in older age, affecting around 10% of people aged over 65 and increases with age. It develops because as we get older our bodies change and can lose their inbuilt reserves, for example we lose muscle strength. People with frailty are at increased risk of falls, disability, loneliness, hospitalisation and care home admission. These problems can reduce quality of life and are costly for the NHS and social care.

Cancer is also more common as we get older. Treatment of cancer in frail people remains one of the biggest challenges that face health care professionals. The balance of side effects and harms that can be caused by the treatment needs to be offset against the chance of cure or longer survival. In 2017 nearly 12 million people were over 65, with the low population growth rate, the number of older and frail people in UK is on the rise [5]. Good health and adequate treatment provision for older population is on the forefront of healthcare priorities. The Expert Reference Group for the Older Person with Cancer (ERG) convened by Macmillan in 2014 helped to inform the aims of the 2015 National Cancer Strategy for England, aiming specifically at older people to improve the treatment outcomes, with a reduction in survival deficit in older people [6, 7]. Using a comprehensive assessment of frailty in each discipline will lead to improvement in clinical outcomes.

Current clinical practice

In practice, in oncology clinics, an adequate assessment of older or frail patient is frequently absent. The decision about cancer treatment and systemic chemotherapy is based on protocols, patients' choice, clinician's experience and pre-existing comorbidities rather that a comprehensive assessment which is complex and time-consuming. Many oncologists struggle with the decision-making process and fear over-treating patients and inducing

severe toxicity and complications as a result of treatment rather than an underlying malignancy. The only universally accepted method of assessment that most clinicians use in current oncological practice is performance status, using either the Eastern Cooperative Oncology Group (ECOG) (adopted by WHO) or Karnofsky scale.

ECOG (Eastern Cooperative Oncology Group) performance status (PS) is a scale developed in 1982 with a view to assessing how a patient's disease is progressing, how the disease affects the daily living abilities of the patient and determine appropriate treatment and prognosis [8]. This scale allows researchers who design and analyse clinical trials to standardise patients' assessment. In practice there is evidence that the ECOG scale may not be the best way to assess patients for chemotherapy. A review of recent advances in the treatment of elderly patients with non-small cell lung cancer (NSCLC) concluded that patients commonly excluded from trials with a PS 2 can still tolerate some treatments and therefore the ECOG PS alone should not be used to decide whether the treatment can be offered [9]. In addition, there is a lack of inter-rater reliability with ECOG PS and the assessment can be inaccurate [10].

Another method of PS assessment is the Karnofsky scale which was first described in 1949 [11]. Using this scale each patient is allocated a score on a linear scale between 0 (dead) and 100 (normally active, without evidence of disease), summarizing their ability to perform daily activities and the level of assistance they require in order to do so [12]. This scale is more complex and often interchanged with ECOG PS. Both of these standard measurement instruments of PS are simple and useful, they are however subject to bias and limitations [13] and do not take into account functional assessment.

The International Society of Geriatric Oncology (SIOG) recommends practitioners perform a comprehensive geriatric assessment (CGA) to profile patient frailty levels both to optimise therapeutic decisions and to help estimate life expectancy [14]. CGA is defined as 'a multidimensional, interdisciplinary diagnostic process focusing on determining an older person's medical, psychosocial, and functional capabilities to develop a coordinated and integrated plan for treatment and long-term follow-up' [15] . The domains assessed in a CGA are social status, comorbidity, functional status, cognition, depression, nutrition, fatigue, polypharmacy and geriatric syndromes (e.g. dementia, delirium, falls, constipation and sarcopenia). Each of the domains in CGA has various tools to assess the status such as Activities of Daily Living (ADL), Timed-up-and-Go, Grip strength and other. Full CGA requires expertise and time and such assessments are not available in the majority of the centres in UK. Various "screening" tools have been published to help oncologists to identify patients who need a full geriatric assessment and a referral to a geriatrician [14]. In addition, multiple attempts to simplify an older patient assessment have been undertaken and several other forms of geriatric assessment have been developed. SIOG has recently performed a systematic review of 17 different screening tests to determine which test was more prognostic of impaired function in older patients with cancer. They found that the G8 and the Vulnerable Elders Survey (VES-13) were among the most commonly used screening tools in older patients with cancer [14]. Unfortunately, in the UK CGA and recommended screening tools are not performed by oncologists due to the lack of training, time pressures and inadequate geriatric oncology provision [4]. This situation is unlikely to change in view of the pressures facing the NHS.

The concept of frailty assessment and electronic frailty index (eFI)

Increasingly the broader concept of frailty is being proposed as the basis of assessment of fitness for major oncological interventions rather than age. An adequate frailty assessment can help to determine the levels of fitness in older people and often shows that biological age is misleading as many older people can be fitter and healthier than some younger people with cancer.

There are a number of frailty assessments that are applied in healthcare such as the Multidimensional Prognostic Index [16], score based on Mini Nutritional Assessment [17] , Clinical Frailty Score or Hospital Frailty risk Score [18, 19]. These are useful in acute medicine setting and hospital care and can help to identify patients who are likely to have a prolonged admission and those who are at greater risk of adverse outcomes [18, 19]. None of those risks scores have been tested or validated in the setting of systemic chemotherapy treatment.

A UK initiative - the electronic frailty index - has been derived from a cumulative deficit frailty model and provides a measure of frailty alongside pre-existing conditions; frailty and multimorbidity are related in older adults [20] . Clegg et al analysed data from 931,541 patients [21]. The researchers used 36 deficits (table 1) that are common in general population such as arthritis, cardiac abnormalities, history of falls, cognitive problems, polypharmacy and a number of other comorbidities. Based on the 36 clinical deficits they developed and validated an electronic frailty index (eFI) that is automatically populated from routinely collected data contained within the primary health care records. Patients were classified int the following groups: no frailty, mild, moderate or severe frailty. One-year adjusted hazard ratios (HRs) for mortality were 1.92 (95% CI 1.81–2.04) for mild frailty, 3.10 (95% CI 2.91–3.31) for moderate frailty and 4.52 (95% CI 4.16–4.91) for severe frailty. The three groups were also associated with the risk of hospital admission as well as the likelihood of admission to the nursing home within one year.

Table 1: List of 36 deficits contained in the eFI

List of 36 deficits contained in the eFI	
Activity limitation	Skin ulcer
Memory and cognitive problems	Foot problems
Anaemia and haematinic deficiency	Sleep disturbance
Mobility and transfer problems	Fragility fracture
Arthritis	Social vulnerability
Osteoporosis	Hearing impairment
Atrial fibrillation	Thyroid disease
Parkinsonism and tremor	Heart failure
Cerebrovascular disease	Urinary incontinence
Peptic ulcer	Heart valve disease
Chronic kidney disease	Urinary system disease
Peripheral vascular disease	Housebound
Diabetes	Visual impairment
Polypharmacy	Hypertension
Dizziness	Weight loss and anorexia
Requirement for care	Hypotension/syncope
Dyspnoea	Ischaemic heart disease
Respiratory disease	
Falls	

How can eFI help in cancer treatment decision-making?

A national breast cancer audit has successfully used eFI extracted from hospital episode statistics records (HES-eFI) as opposed to GP electronic medical records (GP-eFI) [1]. HES-eFI, however, does not contain information on polypharmacy and therefore may lack vital information. On the other hand, HES-eFI would be easier to compile as it uses one database and once linked to chemotherapy data it could be successfully used in the future prospective trial. GP records derived eFI may however more accurate as it contains cumulative data gathered over several years and it may be a better reflect frailty status. Gathering GP-eFI will be more complex due to a number of different GP electronic medical records databases (listed in the plan of research section) and the cost of extracting the data is considerably higher. However, once implemented GP-eFI can be easily obtained at no extra cost and included on two-week rule referrals for cancer investigations. This research project will compare the accuracy of HES-eFI as well as GP-eFI (as described below) and recommend which score to use in the future prospective study.

Above mentioned national audit of breast cancer outcomes in older patients showed that women over 70 years old were frequently offered less surgery and had poorer overall survival [1]. The study analysed 126,111 women with regards to their cancer pathway, disease presentation, and patterns of referrals, treatment modalities and survival. The final recommendation to improve patients' outcomes was "to collaborate and define the need for a reliable, consistent and recordable description of patient fitness". Similar findings in people with lung, colorectal and breast cancer were presented at the NCRI conference this year [22]. This large cancer registry study looked at 107,303 patients treated in the years 2013-2015 and concluded that among breast, lung and colorectal cancer patients, older people were significantly less likely to receive systemic anti-cancer chemotherapy (SACT),

but in those who did the outcome at 2 years was similar to patients under 70 years. It recommended that treatment decision making should be based on clinical and pathological factors, patient fitness or frailty and preferences, rather than being unduly influenced by chronological age alone. Conversely, we have evidence that complications and mortality related to systemic chemotherapy increases with age [2, 23]. Wallington et al published a population based observational study of 23,228 patients who were treated with systemic chemotherapy for breast and lung cancer which showed that 30- day mortality from chemotherapy increased with age [23]. The 2008 National Confidential Enquiry into Patient Outcome and Death (NCEPOD) report found that in 27% of patients reviewed, SACT had caused death or hastened death [2]. Although the NCEPOD recommended changes led to improvement in the rates of 30-day mortality, these figures for frail and elderly patients continue to be higher than in the younger and fitter patients [23].

The increasing incidence of comorbidities, polypharmacy and social isolation with age and the associated interactions amongst these factors make determination of the true, independent impact of age on the observed differences in management, very complex. It is vital to ensure that the methodologies used acknowledge this complexity, in order to understand whether "ageism" alone accounts for the reductions in treatments observed. This problem is frequently encountered when attempting to determine any causal relationship between age and cancer management. In order to accurately assess this, rich real-world data is required, particularly with regard to fitness and suitability for treatment. The relative simplicity of the eFI makes it an attractive prognostically important index that should be appropriately tested and could be used in routine clinical practice. In hospital care it could be used in conjunction with Clinical Frailty Score as well as Hospital Frailty risk Score The electronic evaluation of patient frailty (eFI) can be built into cancer patient evaluation and consultations and has the potential to lead to improved awareness of the key issues to be considered when taking shared decisions about major cancer interventions, for both patients and professionals. Obtaining eFI does not require additional clinic time as it is already routinely available from electronic health records. The aim of this approach is to improve outcomes in frail cancer patients such that they are comparable to those of younger people with cancer through improved survival, less toxicity, fewer hospital admissions and reduced 30-day mortality from chemotherapy.

Current study

The current proposal seeks to evaluate an electronic frailty index (eFI) in patients who are referred for systemic chemotherapy for newly diagnosed cancer. EFI can be automatically calculated from GP electronic records and also from Hospital Episode statistics (HES). It is easily accessible but not possible to interpret at the moment in the context of cancer and cancer treatment. The studies investigating eFI have not assessed its' validity in patients with cancer or undergoing cancer treatment. We propose to conduct this research in two phases:

- the development phase (current study) and
- the validation phase (a randomised, point of care clinical trial) that will follow in the future.

The development phase will consist of historical data analysis of SACT (systemic anticancer chemotherapy) dataset, GP electronic medical records and HES data (hospital episode

statistics) alongside a qualitative study to examine the views of patients, their carers and clinicians to the use of an electronic score in daily clinical practice.

6. Aims and objectives of the study

Hypothesis
We believe that eFI can be successfully used as a tool to improve clinical decision making in frail cancer patients who undertake major anti-cancer treatment such as chemotherapy. It has the potential to accurately predict adverse outcomes from chemotherapy such as 30-day chemotherapy mortality and hospital admissions and, at the same time, it can help clinicians to decide about the intensity of treatment for older but fit people with cancer who can derive benefit or cure from chemotherapy.

6.1. Primary objectives

The primary objective of this research project is to investigate whether eFI is predictive of adverse outcomes of chemotherapy in frail patients with cancer. The adverse effects of chemotherapy will be defined as 30-day mortality from chemotherapy and hospital admissions during chemotherapy. The 30-day period is defined as 30 days from day 1 of the chemotherapy cycle immediately prior to death or if chemotherapy was continuous as 30 days from the date of the last prescription [24]. The long-term plan is to validate the eFI as a tool that can be used in daily clinical practice to accurately predict adverse outcomes of chemotherapy. Part 2 of the study (not covered in the current proposal) will test the use of eFI in a clinical trial.

6.2. Secondary objectives

The secondary objectives are listed below:

1. The acceptability of eFI as a tool in assessing frailty in cancer patients and in influencing clinical decision making over treatment with chemotherapy.
   This part of the project comprises a qualitative study exploring the attitude of clinicians, patients and their carers to the use of eFI in clinical practice in oncology.
2. The suitability of candidate endpoints for a future definitive study that will test a clinical decision tool based on eFI prospectively in a randomised trial.
3. The overlap and accuracy between hospital derived eFI (HES-eFI) and GP database derived eFI (GP-eFI). The GP-eFI and HES-eFI will be compared for the ability to predict adverse chemotherapy outcomes such as hospital admissions and 30-day mortality.
4. Evaluation of ease of access to GP-eFI and HES-eFI. This step will help to determine the best tool to use in the prospective study (this will include mapping of coverage of GP surgeries referring to individual cancer centres and cost comparison between the HES-eFI and GP-eFI)
5. Comparison of eFI with ECOG performance status as predictors of adverse outcomes of chemotherapy

6.3. Outcome measures/endpoints

To explore the potential utility of eFI in predicting adverse treatment outcomes for people with cancer we will undertake a research project in two parts. This protocol concerns the first part, the development stage, which has two parallel work-packages.

Work-package 1 includes an analysis of historical systemic chemotherapy dataset (SACT) records. We have previously analysed 2013-2015 SACT data of patients with breast, lung and colorectal cancer and the results of this work have been presented at the NCRI conference [24]. We plan to extend this analysis to include eFI: HES-eFI and GP-eFI as well as 30-day chemotherapy mortality and hospital admissions during chemotherapy (see research plan).

> **Primary endpoint/ outcome:** 30-day chemotherapy mortality and hospital admissions during chemotherapy for the above described cohort of patients

Work-package 2 comprises a qualitative study that will examine patients, carers and clinicians' attitudes to using an automated frailty score that can influence the decision-making process.

> **Secondary endpoints/ outcomes**: Secondary endpoints for the future study will be explored as part of Work-package 2.

7. Trial design/methodology

Work-package 1

7.1. Data Analysis Project

1. The data on cancer patients treated with chemotherapy will be obtained from PHE following Research Ethics Committee (REC) approval. The request will be made to Public Health England's Office for Data Release (ODR). The PHE dataset will include systemic anti-cancer therapy (SACT) data for patients with stage II or III breast cancer, stage III colon cancer or stage IIIB–IV non-small-cell lung cancer (NSCLC) in England between January 1st 2013 and December 31st 2015. Patients with early breast cancer, stage III colon cancer as well as patients with NSCLC are considered for SACT and have improved survival as a result of SACT. We focus on this dataset as we have previously analysed these data and presented this at the NCRI conference [23]. These data sets are already linked with some of the hospital records and survival data.
2. Data from SACT will be linked to Hospital Admissions statistics (HES data obtained from NHS-Digital) to calculate 30-day chemotherapy mortality for this cohort, hospital admissions during this time (starting day 1 cycle 1 to six months after day 1 cycle 1) as well as HES-eFI. HES-eFI will be calculated from the 35 fields described in table 1, with the exception of polypharmacy. The NHS-digital data for linkage will be requested through Data Access Request Service online following ethics approval.
3. The data on eFI for the patients identified in the SACT dataset above will be obtained from the following databases:

- The Clinical Practice Research Datalink (CPRD) is one of the world's largest databases of primary care electronic health records, including ≈7% of UK general practices, with

anonymized data collected from 1990 to present. The registered active population of ≈5 million is generally representative of the UK population in terms of age and sex [25]. Data collected in CPRD comprise clinical diagnoses and other clinical measurements, prescriptions, results of investigations and referrals to specialist services. Data are made available to the CPRD by the Public Health England (PHE) in separate files. These files can then be linked to the corresponding CPRD primary care data using the pseudonymised CPRD patient identifier. The electronic frailty index can be built into the analysis and similar analyses in patients with hypertension have already been published [26]

- Royal College of General Practitioners (RCGP) Research and Surveillance Centre - this is a research database that collects data from 420 practices on close to 4 million patients. The data can be linked with SACT data as described above

Work-package 2

7.2. Qualitative study

Alongside the data analysis we will conduct a qualitative study that will examine patients, carers and clinicians' attitudes to using an automated frailty score that can inform the decision-making process. We will conduct semi-structured interviews either face to face, over the telephone, or virtually via video conferencing, using applications such as Microsoft Teams, Skype or Zoom, with patients, carers and clinical teams. Following written consent, the interviews will be semi-structured and audio-recorded and will include:

- Clinicians: n=10: 5 medical and clinical oncologists, general practitioners, geriatricians, 5 chemotherapy and specialist nurses. The interviews will last approximately 30 min and will be conducted either face to face, over the telephone or via video conferencing, according to the interviewee's preference.
- Patients: n=10,
- Carers: n=5, purposively selected according to gender and whether partner or child. Individual interviews will be undertaken either face to face, over the telephone or via video conferencing, depending on the interviewee's preference and will last approximately 45 mins.

Interviews will explore:

- Acceptability of using an electronic score to inform decision making about whether to have chemotherapy and if so which treatment is best for the person

Stakeholders will also be asked for their views regarding the design of the future prospective study in terms of:

- Appropriateness and acceptability of secondary outcome measures for the future prospective study
- Acceptability of randomisation process and recruitment process to the future prospective study

8. Eligibility criteria

Work-package 1

Retrospective data analysis on patients with stage II or III breast cancer, stage III colon cancer or stage IIIB–IV non-small-cell lung cancer (NSCLC) in England between January 1 2013 and December 31 2015

Work-package 2

8.1. Inclusion criteria

Secondary care clinicians (n=8) will be eligible to participate if they are employed by the Royal Surrey NHS Foundation Trust as:

- medical oncologist
- clinical oncologist
- geriatrician
- chemotherapy nurse
- clinical nurse specialist

Clinicians with <2 years' experience of working in the oncology setting will not be eligible to participate as they may have insufficient experience of caring for older people diagnosed with cancer. General practitioners (n=2) who have worked in the South East region for >2 years will be eligible to participate

Patients (n=10) will be eligible to participate if they were diagnosed and/or treated for breast, colorectal and lung (NSCL) cancer at the Royal Surrey NHS Foundation Trust, are ≥60 years of age, and the clinician responsible for their cancer treatment judges they are well enough to participate. Table X below outlines the purposive sampling frame for the according to stage at diagnosis, age and gender.

Table X: Patient sampling frame according to age and gender

Cancer diagnosis	**Stage**	**Gender**		**Age (years)**	
		Male	**Female**	**60-70**	**>70**
Breast	II-III	0	4	2	2
Colon	III	2	1	0 1	1 1
NSCLC	IIIB-IV	2	1	1 0	1 1
Total		**4**	**6**	**4**	**6**

Carers (n=5) will be eligible to participate if: they are the main carer (partner or child) for someone diagnosed with breast, colon or lung cancer who is ≥60 years of age and was diagnosed/treated at The Royal Surrey NHS Foundation Trust. Potential carer participants will be nominated by the patient. It is not a requirement that the patient participates in the

study as well. Carers will be purposely selected for gender (men = 2, women = 3) and relationship to the patient (partner=3 or child=2).

All participants are required to speak/understand English and be willing to participate in an interview that will last between 30 and 45min. Patients must have received at least one cycle of chemotherapy.

8.2. Exclusion criteria

Patients and stakeholders who do not fulfil the criteria described above or are unable to participate in an interview or do not speak/understand English are not eligible for inclusion.

9. Trial procedures

Trial procedures will only involve an interview with an experienced researcher. The interview will last between 30 and 45min and will be audio-recorded. Data will be anonymised and transcribed verbatim by a professional transcribing service and analysed using Framework Analysis method [27]. The interviews will take place either face to face in St Luke's Cancer Centre, over the telephone or via a video conferencing platform (Zoom, Skype or Microsoft Teams).

9.1. Recruitment

- Participants for the qualitative study (work-package 2) will be approached at St Luke's Cancer Centre based at the Royal Surrey NHS Foundation Trust. It is a large regional cancer centre that covers a population of 1.2 million.
- Cancer patients and their carers will be identified by oncologists who review patients with lung, breast and colorectal cancer and prescribe their next cycle of chemotherapy. They will obtain consent for the Research Associate to contact the person to provide information about the study. To enable consent for patients who would prefer not to come to the hospital, we will post the consent and a stamped addressed return envelope. Patients will have a detailed conversation with the researcher before they are asked to consent. The Research Associate will either telephone the patients or see them in the Chemotherapy Day Unit when they attend for their next cycle of chemotherapy
- Carers will be approached with the patients' consent (see Appendix 1). It is not a requirement, however, that both the patient and the carer consent to participate. It is possible that the patient may not be willing to participate but they consent to their carer being approached. For carers who do not routinely attend the Cancer Centre there will be an opportunity to conduct the interview over the phone or via video conferencing. Similarly, to enable consent for carers who would prefer not to come to the hospital we will post the consent and a stamped addressed return envelope.
- Medical and clinical oncologists from St Luke's Cancer Centre will be approached by CI whilst attending diagnosis-specific multi-disciplinary team (MDT) meetings. Clinicians will be provided information about the study and then invited to participate. If the clinicians prefer the option of a telephone or a video conference interview, such arrangements will be made.

- General practitioners- We will approach the local referring surgeries and invite participation in a brief video conferencing or telephone interview. This will be facilitated by Prof de Lusignan who is a practising GP locally.
- Geriatricians - we will approach geriatricians from Royal Surrey NHS Foundation Trust .
- Chemotherapy nurses and clinical nurse specialists – we will attend Chemotherapy Day Unit team meetings in St Luke's Cancer Centre at which we will provide information about the study and invite the nurses to participate. Clinical Nurse Specialists attend the MDT meetings and so we will recruit them in the same way as medical/clinical oncologists outlined above. An option of a telephone or a video conference interview will be offered to all potential participants.

9.2. Consent

Patients, carers and stakeholders will be asked to provide written informed consent (see Appendix 2) prior to participating in the interview.

9.3. Baseline data

We will collect baseline data on the participants that will include the following information:

- Stakeholders: job title, length of time working in oncology and description of the role in the context of chemotherapy provision
- Patients: type of cancer, stage of cancer, age, gender, medical history, cancer treatment, social circumstances.
- Carers: relationship with the cared for person, age, gender, social circumstances.

9.4. Trial assessments

There will be no trial assessments or follow up as part of this study

9.5. Withdrawal criteria

Patients, carers or stakeholders who will be approached for an interview will be able to withdraw at any time prior to or during the interview. Once the interview is recorded and anonymised it will be analysed together with other qualitative data, and so participants will only be able to withdraw their data prior to this process.

10. Adverse events

We do not expect any adverse events to take place during the interview and no such data will be collected. If patients feel distressed during the interview the interview will be abandoned. As we do not expect adverse events in this qualitative study we will only report the final analysis.

11. Statistics and data analysis

The dataset comprises records of >100,000 patients, 40% of whom are >70 years of age. Linkage to HES, see below, will allow estimation of 30-day mortality and rates of hospitalisation in elderly patients with cancer (both receiving and not receiving SACT) within a standard error of 0.25%. The data will allow sufficient events to support the predictive modelling described later. For example, in the SACT dataset 18% (2453/13,813) of breast cancer patients >70 years received SACT compared with 70% (10,180/17,214) <70. With an

estimated 30-day mortality of 2% in such cases, we would expect >550 deaths following SACT in this cohort (with around 50 of them from the elderly patients). The mortality rate in non-small-cell lung cancer can be as high as 8% suggesting >920 deaths in this cohort (120 comprising elderly patients) [23]. Adopting a composite endpoint of 30-day chemotherapy mortality or hospital admission (which could be as high as 11% for cancer patients undergoing SACT) [24] will give a higher event rate and allow a comprehensive analysis of outcomes by cancer type in each age group for both those who received and did not receive SACT.

11.1. Statistical analysis plan

Descriptive analysis will be undertaken to describe the prevalence of frailty and above-mentioned outcomes (30- day chemotherapy mortality, hospital admissions during chemotherapy) in this cohort. Multivariate logistic regression will be undertaken in order to assess the utility of frailty as a predictor of adverse clinical outcomes in the selected cohort. Models will assess the sensitivity of frailty at different thresholds, adjusting for other prognostic factors such as cancer type and stage. Other analyses will include survival analysis (time to event) and multilevel modelling accounting for differences in local clinical pathways. A comparison will be undertaken to determine whether GP-eFI or HES-eFI is a more accurate predictor of poor outcomes amongst an older cancer population. In addition, we will, where possible, compare two different chemotherapy regimens as patients in each of the tumour groups will receive different chemotherapy.

11.2. Qualitative analysis plan

All interview data will be analysed using Framework Analysis (ref). This is a widely used analytical approach which involves summarising and classifying data within a framework of themes, therefore more systematic [28, 29] . Using this method, the data is sifted, charted and sorted in accordance with key issues and themes. This involves a five step process [29]:

1. Familiarization
2. Identifying a thematic framework
3. Indexing
4. Charting in a matrix
5. Mapping and interpretation

Framework Analysis facilitates constant comparison through the review of data across the data matrices thereby enabling systematic examination of how perspectives differ between the three groups of people interviewed [27].

12. Data handling

Work-package 1

SACT, PHE, CPRD and RCGP data sets are pseudonymised. All GP practices in the UK use a computerised medical system to maintain patient medical records. The overwhelming majority of the large volume of research derived from UK primary care is based on coded data. Data are entered into a patient's computerised medical record as coded data or free text. Primary care data is pseudonymised at source and can be extracted by specialised software for example Apollo, part of Wellbeing Software.

12.1. Access to data

The RCGP RSC and CPRD extract coded data, i.e. where the GP or other health professional codes a disease or symptom into the Electronic Health Record (EHR) system. Data are held on dedicated secure servers, for example the RCGP RSC dedicated secure servers are at the RCGP data and analytics hub in the Clinical Informatics and Health Outcomes Research Group, University of Surrey. Patients who have withheld consent for data sharing are excluded from the extraction processes.

Similarly, CPRD collects fully-coded patient electronic health records from GP Practices using the Vision® or EMIS® software systems. Access to data from CPRD is subject to a full licence agreement containing detailed terms and conditions of use. Patient level datasets can be extracted for researchers against specific study specifications, following protocol approval from the Independent Scientific Advisory Committee (ISAC).
Data from PHE is released upon approval of the request from The Office for Data Release (ODR) which is mandatory for all requests (separate protocol)

Work-package 2

Data from the interviews will be audio recorded using an encrypted recording device. Data will be transcribed verbatim by professional transcribing service. Transcribers are bound by a confidentiality agreement. During this process identifying personal information (eg names etc) will be removed and replaced with a pseudonym. Interviews will be stored securely on a password protected computer at the University of Surrey. Each individual file will also be password protected and only the research team will be able to access it. Interview recordings will be destroyed once data analysis is completed.

12.2. Archiving

The data will be pseudo-anonymised, and the audio recordings of interviews will not be archived. The anonymised interview data will be stored securely for 10 years. A report will be constructed and published in a peer reviewed journal.

13. Monitoring, audit & inspection

The project will be managed by Surrey CTU on behalf of the sponsor with the CI overseeing all aspects of the study. Surrey CTU will oversee data governance.
The project will also have input and oversight from the Scientific Committee whose members will meet twice a year. The Committee will advise on the data analysis progress and the progress of the qualitative study. Once the results are available the committee will advise whether there is justification to proceed with the prospective randomised study and will support the development of the next phase of this proposal.

14. Ethical and regulatory considerations

14.1. Research Ethics Committee (REC) review & reports

Before the start of this study approval will be sought from a REC for the trial protocol. The participants in the qualitative study will receive an information sheet about the study and will be asked to sign the consent form.
Data analysis in the work-package 1 will be on pseudonymised data and no identifiable data will be handled by the study team. Surrey CTU will oversee the data governance.
An annual progress report (APR) will be submitted to the REC within 30 days of the anniversary date on which the favourable opinion was given and annually until the project is declared ended. It is the Chief Investigator's (CI) responsibility to produce the annual reports as required. The CI will notify the REC at the end of the project.

14.2. Peer review

This project has undergone a stringent peer review within the RfPB NIHR grant application process. It was reviewed and amended in the round 1 of the application process by the RfPB grant panel and in the round 2 by external reviewers. Additional changes recommended following the round 2 were incorporated into this protocol.

14.3. Public and Patient Involvement

The outline and the concept of this study was discussed with several patients from St Luke's Cancer Centre at the Royal Surrey County Hospital as well as with members of the clinical team. The patients were surprised that there is such a difference in outcomes for older people living with frailty and felt strongly that this problem needs to be addressed. Patients and chemotherapy nurses read through the lay summary and commented that it was "easy to follow" and "that it makes sense". Patients welcomed the planned qualitative study. In addition, a member of the public who is also a cancer sufferer living with frailty has agreed to join the Scientific Committee. The Committee will meet twice a year to oversee the progress of the project and to ensure its delivery. In addition, the committee will discuss and advise whether to proceed to the next phase of this project. This decision will be based on the results of the study proposed in this application.

14.4. Regulatory Compliance, data protection and patient confidentiality

The proposed project will comply with Good Clinical Practice (GCP) Guidelines as well as GDPR and patient confidentiality. All investigators will comply with GDPR and the Data Protection Act 1998 with regards to the collection storage, processing and disclosure of personal information and will uphold the Act's core principles. Surrey CTU will manage the data governance

14.5. Indemnity

It is not anticipated that the participants in the study will come to any harm as the only intervention will be an interview.

14.6. Dissemination policy

We will ensure our study is publicised through the Trust R&D website and in the outpatients' department. Participants for the qualitative part of the study will be recruited through the Trust research network system with the support of the research coordinators and nurses. Patients and relatives will be approached in the outpatients department as well as in the

chemotherapy unit. Specialist and chemotherapy nurses and clinicians, including general practitioners, will be recruited in the cancer centre, referring GP surgeries and in cancer units that refer patients to St Luke's Cancer Centre.

The final results will be disseminated at the national conferences including National Cancer Research Institute annual meeting (NCRI), local Kent Surrey and Sussex Clinical Research Network annual meeting, and in peer reviewed journals. The results of the analysis will form the basis of a prospective randomised point of care study looking at the use of eFI compared with the standard of care. Should the study produce results that confirm the link between eFI and chemotherapy outcomes and this is confirmed in a prospective randomised trial the impact of this research will directly lead to changes in patients' care.

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APPENDIX 1

INFORMATION SHEET FOR PARTICIPANTS

The Electronic Frailty Index in newly diagnosed cancer patients undergoing chemotherapy treatment

Name of PI: Dr Agnieszka Michael

YOU WILL BE GIVEN A COPY OF THIS INFORMATION SHEET

Invitation Paragraph

You are invited to take part in a study looking at a role of electronic frailty index in patients who are treated with chemotherapy. As part of this study we would like to ask what you think about a new way of assessing frailty and whether this could be useful for patients suffering from cancer. This information sheet provides the rationale for the study.

Before you decide whether you want to take part, it is important for you to understand why the research is being done and what your participation will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask me if there is anything that is not clear or if you would like more information.

What is the purpose of the study?

Diagnosis of cancer is a fearful event for most people. It is a common occurrence and adequate information and provision of the best treatment can not be underestimated. The treatment of many cancers involves major interventions such as surgery, chemotherapy and radiotherapy. All of these can cause severe side effects and can be life changing.

Treatment of people who are frail is even more challenging. Our health can be affected by cancer itself and a range of other conditions and it is really important that we balance the side effects of cancer treatment against the harms it can cause. We know from several studies that clinicians struggle with adequate assessment of older people living with frailty and with cancer and sometimes offer less aggressive treatment even if they are not frail which can result in poorer outcomes. We also know that many frail and older patients suffer multiple side effects of treatment and sometimes die as a result of the treatment itself. This approach leads to older patients with cancer living shorter lives.

We need an improved way of assessing frail patients with cancer. We believe it is possible to use a score that can be calculated from medical records that will help us to better estimate the risks of chemotherapy. This score is known as electronic frailty index and has been useful in general practice for a number of years for deciding on the appropriate treatment for other conditions and improving outcomes. Electronic

frailty index is now automatically calculated by GPs from electronic medical records. To validate this type of score in cancer we need to undertake the research project in 2 parts. The first part will look at the information we can obtain form historical chemotherapy records as well as GP databases.

In addition, in this study we would like to interview several cancer patients, carers and clinical teams to make sure such an approach is acceptable to them and that they would be prepared to use it in clinical practice.

In part 2 of the project that will follow in the future, we plan to run a large clinical trial and test the electronic frailty index in patients who are referred for chemotherapy treatment. We believe that it will give both patients and clinicians more information and help them make the right decision regarding cancer treatment. In the long term this project has the potential to improve lives of frail patients with cancer

Why have I been invited to take part?

I am inviting you to take part in the study and participate in the interview about this type of project in which we would use an electronic frailty scale to help in assessing individual risks from chemotherapy. We believe that your views will shape the design of a future much larger project and take into account your feelings and opinions.

Do I have to take part?

Participation is voluntary. You do not have to take part. You should read this information sheet and if you have any questions you should ask the research team.

What will happen to me if I take part?

If you decide to take part, you will be given this information sheet to keep and will be asked to sign a consent form. We will then conduct an interview with you and ask you a series of questions in relation to the design of this project. The interview will be taped but the information you provide will be anonymised. The interview will last between 30 and 45 min. We will only do it once and there will be no additional commitments as part of this study.

We will ask you questions related to the diagnosis of cancer, your feelings at the time of diagnosis and decisions regarding treatment. We will also ask what you think about an electronic tool that may be used to help guide patients and clinicians to choose the best cancer treatment and what you think is important when such issues are discussed.

We can conduct the interview face to face, over the telephone or via video conferencing using the internet. Whichever way you feel most comfortable with. If you do not want to come in to the hospital, we can post you the consent form to sign, along with a stamped addressed envelope for you to return it to us.

The interview will be transcribed be a professional transcription company and the information you provide may be used in future projects.
There will be no payment for participation in the study.

What are the possible benefits of taking part?

The information we will get from the study will help to design a larger project in the future that may lead to an improvement in chemotherapy experience for many patients with cancer. There will be no personal benefit for you.

What are the possible disadvantages and risks of taking part?

Apart from the time you spend giving an interview (30-45min) there are no disadvantages or risks associated with this study.

How is the project being funded?

The project is being funded by Research for Patients' Benefit grant scheme from National Institute of Health Research. This study has been given a favourable ethical opinion by the Ethics Committee.

What if something goes wrong?

If you wish to make a complaint about the conduct of the study, or have any concern about any aspect of the way you have been treated during the course of this study, please contact:

The Patient Advice and Liaison Service (PALS).

Who should I contact for further information?

If you have any questions or require more information about this study, please contact me using the following contact details:

Dr Agnieszka Michael a.michael@surrey.ac.uk.
01483 688546

How is my data handled?

Royal Surrey County Hospital NHS Foundation Trust (RSCH), as the sponsor, will be the Data Controller responsible for this study. This means that RSCH has a legal obligation to comply will all appropriate Data Protection Legislation and GDPR in respect with how your personal data is processed for the purpose that you consent and intend it to be used. Some of the data will be governed by Surrey Clinical Trials Unit.

Personal data means any information relating to you that has the means to identify you directly or indirectly, for example, name, contact details, hospital/NHS Number. Together with Special Categories Personal Data for the purpose of this research study this would be data concerning your physical health condition.

We have to ensure that your personal data is processed fairly and lawfully and will only be used for the purpose in which it is intended to conduct and analyse for the research study.

All data related to this research study including administration data (e.g. the consent form) will be held in accordance with current legislation under the Records Management Code of Practice for Health and Social Care 2016.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you decide to withdraw your data from the study, we may not be able to do so. We will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information
https://www.royalsurrey.nhs.uk/about/privacy-notice/

If you would like to know more about how we use your information or if, for any reason, you do not wish to have your information used in any of the ways described in this leaflet, then please speak to your health care professional.

You can also contact:

Head of Information Governance
Royal Surrey County Hospital NHS Foundation Trust
Egerton Road
Guildford
GU2 7XX

Tel: 01483 571 122

Email: rsc-tr.InformationGovernance@nhs.net

What will happen to the results of the study?

We will produce a final report summarising the main findings, which will be sent to you. I also plan to disseminate the research findings through publication and conferences.
Pseudonymised data will be deposited or submitted to an open source online research data repository at the end of the study. This data may be used for future research.

Will my data be used for future research?

When you agree to take part in a research study, the information we collect may be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in research in this country or abroad. Your information will only

be used by organisations and researchers to conduct research and processed on the basis of public interest.

What if I want to complain about the way data is handled?

If you wish to raise a complaint on how we have handled your personal data, you can contact RSCH Data Protection Officer [*Ruth Drewett*] who will investigate the matter. If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Patient Advice and Liaison Service (PALS).

We welcome and value your feedback on our services as we recognise that this helps us to identify those aspects of our service where we can improve.

For full details on our complaints procedure please see link below.

Alternatively, you can contact our complaints team by emailing your complaint to rsc-tr.Complaints@nhs.net or writing to the Chief Executive, Royal Surrey County Hospital, Egerton Road, Guildford, Surrey, GU2 7XX.
https://www.royalsurrey.nhs.uk/patients/compliments-complaints/

Limits to confidentiality

Confidentiality will be respected unless there are compelling and legitimate reasons for this to be overridden e.g. in the public interest. If this was the case we would normally inform you first of any decisions that might limit confidentiality.

Thank you for reading this information sheet and for considering taking part in this research.

INFORMATION SHEET FOR CARERS

The Electronic Frailty Index in newly diagnosed cancer patients undergoing chemotherapy treatment

Name of PI: Dr Agnieszka Michael

YOU WILL BE GIVEN A COPY OF THIS INFORMATION SHEET

Invitation Paragraph

You are invited to take part in a study looking at a role of electronic frailty index in patients who are treated with chemotherapy. As part of this study we would like to ask what you think about a new way of assessing frailty and whether this could be useful for patients suffering from cancer. This information sheet provides the rationale for the study. We are asking you to participate in this study as you are caring for someone with a diagnosis of cancer and your views are really important to us.

Before you decide whether you want to take part, it is important for you to understand why the research is being done and what your participation will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask me if there is anything that is not clear or if you would like more information.

What is the purpose of the study?

Diagnosis of cancer is a fearful event for most people. It is a common occurrence and adequate information and provision of the best treatment can not be underestimated. The treatment of many cancers involves major interventions such as surgery, chemotherapy and radiotherapy. All of these can cause severe side effects and can be life changing.

Treatment of people who are frail is even more challenging. Our health can be affected by cancer itself and a range of other conditions and it is really important that we balance the side effects of cancer treatment against the harms it can cause. We know from several studies that clinicians struggle with adequate assessment of older people living with frailty and with cancer and sometimes offer less aggressive treatment even if they are not frail which can result in poorer outcomes. We also know that many frail and older patients suffer multiple side effects of treatment and sometimes die as a result of the treatment itself. This approach leads to older patients with cancer living shorter lives.

We need an improved way of assessing frail patients with cancer. We believe it is possible to use a score that can be calculated from medical records that will help us to better estimate the risks of chemotherapy. This score is known as electronic frailty index and has been useful in general practice for a number of years for deciding on the appropriate treatment for other conditions and improving outcomes. Electronic frailty index is now automatically calculated by GPs from electronic medical records.

To validate this type of score in cancer we need to undertake the research project in 2 parts. The first part will look at the information we can obtain form historical chemotherapy records as well as GP databases.

In addition, in this study we would like to interview several cancer patients, carers and clinical teams to make sure such an approach is acceptable to them and that they would be prepared to use it in clinical practice.

In part 2 of the project that will follow in the future, we plan to run a large clinical trial and test the electronic frailty index in patients who are referred for chemotherapy treatment. We believe that it will give both patients and clinicians more information and help them make the right decision regarding cancer treatment. In the long term this project has the potential to improve lives of frail patients with cancer

Why have I been invited to take part?

I am inviting you to take part in the study and participate in the interview about this type of project in which we would use an electronic frailty scale to help in assessing individual risks from chemotherapy. As a carer your views are really important to us and will help to shape the design of a future much larger project taking into account your feelings and opinions.

Do I have to take part?

Participation is voluntary. You do not have to take part. You should read this information sheet and if you have any questions you should ask the research team.

What will happen to me if I take part?

If you decide to take part, you will be given this information sheet to keep and will be asked to sign a consent form. We will then conduct and interview with you and ask you a series of questions in relation to the design of this project. The interview will be taped but the information you provide will be anonymised. The interview will last between 30 and 45 min. We will only do it once and there will be no additional commitments as part of this study.

We will ask you questions related to the diagnosis of cancer in your relative, how it happened and how was the treatment discussed. We will also ask your thoughts about using an electronic tool to help with treatment related decisions and what factors are important when choosing the best treatment.

We can conduct the interview face to face, over the telephone or if you prefer, via video conference using the internet. Whichever way you feel most comfortable with. If you do not want to come in to the hospital, we can post you the consent form to sign, along with a stamped address envelope for you to return it to us.

The interview will be transcribed by a professional transcription company and the information you provide may be used in the future projects. There will be no payment for participation in the study.

What are the possible benefits of taking part?

The information we will get from the study will help to design a larger project in the future that may lead to an improvement in chemotherapy experience for many patients with cancer. There will be no personal benefit for you.

What are the possible disadvantages and risks of taking part?

Apart from the time you spend giving an interview (30-45min) there are no disadvantages or risks associated with this study.

How is the project being funded?

The project is being funded by Research for Patients' Benefit grant scheme from National Institute of Health Research. This study has been given a favourable ethical opinion by the Ethics Committee.

What if something goes wrong?

If you wish to make a complaint about the conduct of the study, or have any concern about any aspect of the way you have been treated during the course of this study, please contact:

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01483 688546

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Personal data means any information relating to you that has the means to identify you directly or indirectly, for example, name, contact details. Together with Special Categories Personal Data for the purpose of this research study this would be data concerning your family member.

We have to ensure that your personal data is processed fairly and lawfully and will only be used for the purpose in which it is intended to conduct and analyse for the research study.

All data related to this research study including administration data (e.g., the consent form) will be held in accordance with current legislation under the Records Management Code of Practice for Health and Social Care 2016.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you decide to withdraw your data from the study, we may not be able to do so. We will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

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Royal Surrey County Hospital NHS Foundation Trust
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Guildford
GU2 7XX

Tel: 01483 571 122

Email: rsc-tr.InformationGovernance@nhs.net

What will happen to the results of the study?

We will produce a final report summarising the main findings, which will be sent to you. I also plan to disseminate the research findings through publication and conferences.
Pseudonymised data will be deposited or submitted to an open source online research data repository at the end of the study. This data may be used for future research.

Will my data be used for future research?

When you agree to take part in a research study, the information we collect may be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in research in this country or abroad. Your information will only

be used by organisations and researchers to conduct research and processed on the basis of public interest.

What if I want to complain about the way data is handled?

If you wish to raise a complaint on how we have handled your personal data, you can contact RSCH Data Protection Officer [*Ruth Drewett*] who will investigate the matter. If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Patient Advice and Liaison Service (PALS).

We welcome and value your feedback on our services as we recognise that this helps us to identify those aspects of our service where we can improve.

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Alternatively, you can contact our complaints team by emailing your complaint to rsc-tr.Complaints@nhs.net or writing to the Chief Executive, Royal Surrey County Hospital, Egerton Road, Guildford, Surrey, GU2 7XX.
https://www.royalsurrey.nhs.uk/patients/compliments-complaints/

Limits to confidentiality

Confidentiality will be respected unless there are compelling and legitimate reasons for this to be overridden e.g. in the public interest. If this was the case we would normally inform you first of any decisions that might limit confidentiality.

Thank you for reading this information sheet and for considering taking part in this research.

INFORMATION SHEET FOR STAKEHOLDERS
(The Clinical Team)

The Electronic Frailty Index in newly diagnosed cancer patients undergoing chemotherapy treatment

Name of PI: Dr Agnieszka Michael

YOU WILL BE GIVEN A COPY OF THIS INFORMATION SHEET

Invitation Paragraph

You are invited to take part in a study looking at a role of electronic frailty index in patients who are treated with chemotherapy. As part of this study we would like to ask what you think about a new way of assessing frailty and whether this could be useful for patients suffering from cancer. This information sheet provides the rationale for the study.

Before you decide whether you want to take part, it is important for you to understand why the research is being done and what your participation will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask me if there is anything that is not clear or if you would like more information. We are inviting you to participate in the study as a clinician looking after patients with a diagnosis of cancer.

What is the purpose of the study?

Diagnosis of cancer is a fearful event for most people. It is a common occurrence and adequate information and provision of the best treatment can not be underestimated. The treatment of many cancers involves major interventions such as surgery, chemotherapy and radiotherapy. All of these can cause severe side effects and can be life changing.

Treatment of people who are frail is even more challenging. Our health can be affected by cancer itself and a range of other conditions and it is really important that we balance the side effects of cancer treatment against the harms it can cause. We know from several studies that clinicians struggle with adequate assessment of older people living with frailty and with cancer and sometimes offer less aggressive treatment even if they are not frail. We also know that many frail and older patients suffer multiple side effects of treatment and sometimes die because of the treatment itself. This approach leads to older patients with cancer living shorter lives.

We need an improved way of assessing frail patients with cancer. We believe it is possible to use a score that can be calculated from medical records that will help us to better estimate the risks of chemotherapy. This score is known as electronic frailty index and has been useful in general practice. Electronic frailty index is now automatically calculated by GPs from electronic medical records. To validate this type of score in cancer we need to undertake the research project in 2 parts. The first part will look at the information we can obtain form historical chemotherapy records as well as GP databases.

In addition, in this study we would like to interview several cancer patients, carers and clinical teams to make sure such an approach is acceptable to them and that they would be prepared to use it in clinical practice.

In part 2 of the project that will follow in the future, we plan to run a large clinical trial and test the electronic frailty index in patients who are referred for chemotherapy treatment. We believe that it will give both patients and clinicians more information and help them make the right decision regarding cancer treatment. In the long term this project has the potential to improve lives of frail patients with cancer

Why have I been invited to take part?

I am inviting you to take part in the study and participate in the interview about this type of project in which we would use an electronic frailty scale to help in assessing individual risks from chemotherapy. We believe that your views as a stakeholder and clinician are really important and will shape the design of a future much larger project.

Do I have to take part?

Participation is voluntary. You do not have to take part. You should read this information sheet and if you have any questions you should ask the research team.

What will happen to me if I take part?

If you decide to take part, you will be given this information sheet to keep and will be asked to sign a consent form. We will then conduct and interview with you and ask you a series of questions in relation to the design of this project. The interview will be taped but the information you provide will be anonymised. The interview will last between 30 and 45 min. We will only do it once and there will be no additional commitments as part of this study.

We will ask your opinion about choosing cancer treatment and what factors are important when such decisions are made. We will ask your thoughts about an electronic tool to help in decision making processes and what you think about the current information provided when choosing cancer treatments.

We can conduct the interview face to face, over the telephone or via video conferencing using the internet. Whichever way you feel most comfortable with. If you do not want to come in to the hospital, we can post you the consent form to sign, along with a stamped addressed envelope for you to return it to us.

The interview will be transcribed by a professional transcription company and the information you provide may be used in the future projects.
There will be no payment for participation in the study.

What are the possible benefits of taking part?

The information we will get from the study will help to design a larger project in the future that may lead to an improvement in chemotherapy experience for many patients with cancer. There will be no personal benefit for you.

What are the possible disadvantages and risks of taking part?

Apart from the time you spend giving an interview (30-45min) there are no disadvantages or risks associated with this study.

How is the project being funded?

The project is being funded by Research for Patients' Benefit grant scheme from National Institute of Health Research. This study has been given a favourable ethical opinion by the Ethics Committee.

What if something goes wrong?

If you wish to make a complaint about the conduct of the study, or have any concern about any aspect of the way you have been treated during the course of this study, please contact:

The Patient Advice and Liaison Service (PALS).

Who should I contact for further information?

If you have any questions or require more information about this study, please contact me using the following contact details:

Dr Agnieszka Michael amichael@nhs.net
01483 688546

How is my data handled?

Royal Surrey County Hospital NHS Foundation Trust (RSCH), as the sponsor, will be the Data Controller responsible for this study. This means that RSCH has a legal obligation to comply will all appropriate Data Protection Legislation in respect with how your personal data is processed for the purpose that you consent and intend it to be used. Some of the data will be governed by Surrey Clinical Trials Unit.

Personal data means any information relating to you that has the means to identify you directly or indirectly, for example, name, contact details. Together with Special

Categories Personal Data for the purpose of this research study this would be data concerning your job role.

We have to ensure that your personal data is processed fairly and lawfully and will only be used for the purpose in which it is intended to conduct and analyse for the research study.

All data related to this research study including administration data (e.g., the consent form) will be held in accordance with current legislation under the Records Management Code of Practice for Health and Social Care 2016.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you decide to withdraw your data from the study, we may not be able to do so. We will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information
https://www.royalsurrey.nhs.uk/about/privacy-notice/

If you would like to know more about how we use your information or if, for any reason, you do not wish to have your information used in any of the ways described in this leaflet, then please speak to your health care professional.

You can also contact:

Head of Information Governance
Royal Surrey County Hospital NHS Foundation Trust
Egerton Road
Guildford
GU2 7XX

Tel: 01483 571 122

Email: rsc-tr.InformationGovernance@nhs.net

What will happen to the results of the study?

We will produce a final report summarising the main findings, which will be sent to you. I also plan to disseminate the research findings through publication and conferences.
Pseudonymised data will be deposited or submitted to an open source online research data repository at the end of the study. This data may be used for future research.

Will my data be used for future research?

When you agree to take part in a research study, the information we collect may be provided to researchers running other research studies in this organisation and in

other organisations. These organisations may be universities, NHS organisations or companies involved in research in this country or abroad. Your information will only be used by organisations and researchers to conduct research and processed on the basis of public interest.

What if I want to complain about the way data is handled?

If you wish to raise a complaint on how we have handled your personal data, you can contact RSCH Data Protection Officer [*Ruth Drewet*] who will investigate the matter. If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Patient Advice and Liaison Service (PALS).

We welcome and value your feedback on our services as we recognise that this helps us to identify those aspects of our service where we can improve.

For full details on our complaints procedure please see link below.

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APPENDIX 2

CONSENT FORM FOR PATIENTS

Full title: The Electronic Frailty Index in newly diagnosed cancer patients undergoing chemotherapy treatment

Name of the Chief Investigator: Dr Agnieszka Michael

		Please initial beside each statement
1	I confirm that I have read the information sheet dated…….. (version number……..) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
2	I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason and without my medical care or legal rights being affected.	
3	I understand that my data will be kept confidential in accordance with the Data Protection Act.	
4	I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from Royal Surrey County Hospital, Surrey Clinical Trials Unit, regulatory authorities, NHS Trust, or any other third parties where it is relevant to my taking part in this research. I give my permission for these individuals to have access to my records.	
5	I agree to my GP being informed of my participation in the study.	
6	I agree that any interviews I take part in can be audio recorded and transcribed by a professional transcription company.	
7	I understand that I will be asked questions about the diagnosis and treatment of my cancer.	
8	I understand that the information collected about me may be used to support other research in the future.	
9	I agree to take part in the above study.	

_____	_____	_____
Name of Participant	Date	Signature
_____	_____	_____
Name of Person Obtaining Consent	Date	Signature

CONSENT FORM FOR CARERS

Full title: The Electronic Frailty Index in newly diagnosed cancer patients undergoing chemotherapy treatment

Name of the Chief Investigator: Dr Agnieszka Michael

		Please initial beside each statement
1	I confirm that I have read the information sheet dated…….. (version number……..) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily	
2	I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason and without my legal rights being affected.	
3	I understand that my data will be kept confidential in accordance with the Data Protection Act.	
4	I understand that the data collected during the study may be looked at by individuals from Surrey Clinical Trials Unit, regulatory authorities, NHS Trust, or any other third parties where it is relevant to my taking part in this research.	
5	I agree that any interviews I take part in can be audio recorded and transcribed by a professional transcription company.	
6	I understand that I will be asked questions about the diagnosis and treatment of my relative's cancer.	
7	I understand that the information collected about me may be used to support other research in the future.	
8	I agree to take part in the above study	

_____	_____	_____
Name of Participant	Date	Signature
_____	_____	_____
Name of Person Obtaining Consent	Date	Signature

CONSENT FORM FOR STAKEHOLDERS
(The Clinical Team)

Full title: The Electronic Frailty Index in newly diagnosed cancer patients undergoing chemotherapy treatment

Name of the Chief Investigator: Dr Agnieszka Michael

		Please initial beside each statement
1	I confirm that I have read the information sheet dated…….. (version number……..) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily	
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4	I understand that the data collected during the study may be looked at by individuals from Surrey Clinical Trials Unit, regulatory authorities, NHS Trust, or any other third parties where it is relevant to my taking part in this research.	
5	I agree that any interviews I take part in can be audio recorded and transcribed by a professional transcription company.	
6	I understand that I will be asked questions about the diagnosis and treatment of cancer.	
7	I understand that the information collected about me may be used to support other research in the future.	
8	I agree to take part in the above study	

_____	_____	_____
Name of Participant	Date	Signature
_____	_____	_____
Name of Person Obtaining Consent	Date	Signature