IN-HOME Study:

Home Monitoring of Creatinine in Cancer Patients: Assessing Acceptability and Clinical Benefit

SHORT STUDY TITLE / ACRONYM	IN-HOME Study
PROTOCOL VERSION NUMBER AND DATE	Protocol version 3.0 Date 01/04/2019
SPONSOR	The University of Manchester
IRAS Number:	255751
SPONSORS Number:	R119106

This protocol has regard for the HRA guidance.

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the trial in compliance with the approved protocol and will adhere to the principles outlined in the Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031), amended regulations (SI 2006/1928) and any subsequent amendments of the clinical trial regulations, GCP guidelines, the Sponsor's (and any other relevant) SOPs, and other regulatory requirements as amended.

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 clinical investigation without the prior written consent of the Sponsor

I also confirm that I will make the findings of the trial publicly available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the trial will be given; and that any discrepancies and serious breaches of GCP from the trial as planned in this protocol will be explained.

For and on behalf of the Trial Sponsor:

Signature: Date:

...../...../.....

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Name (please print):

.....

Position:

.....

Chief Investigator:

Signature: Date:

..../...../.....

Name: (please print):

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KEY TRIAL CONTACTS

Table 1: Key Trial Contacts

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Committees	N/A

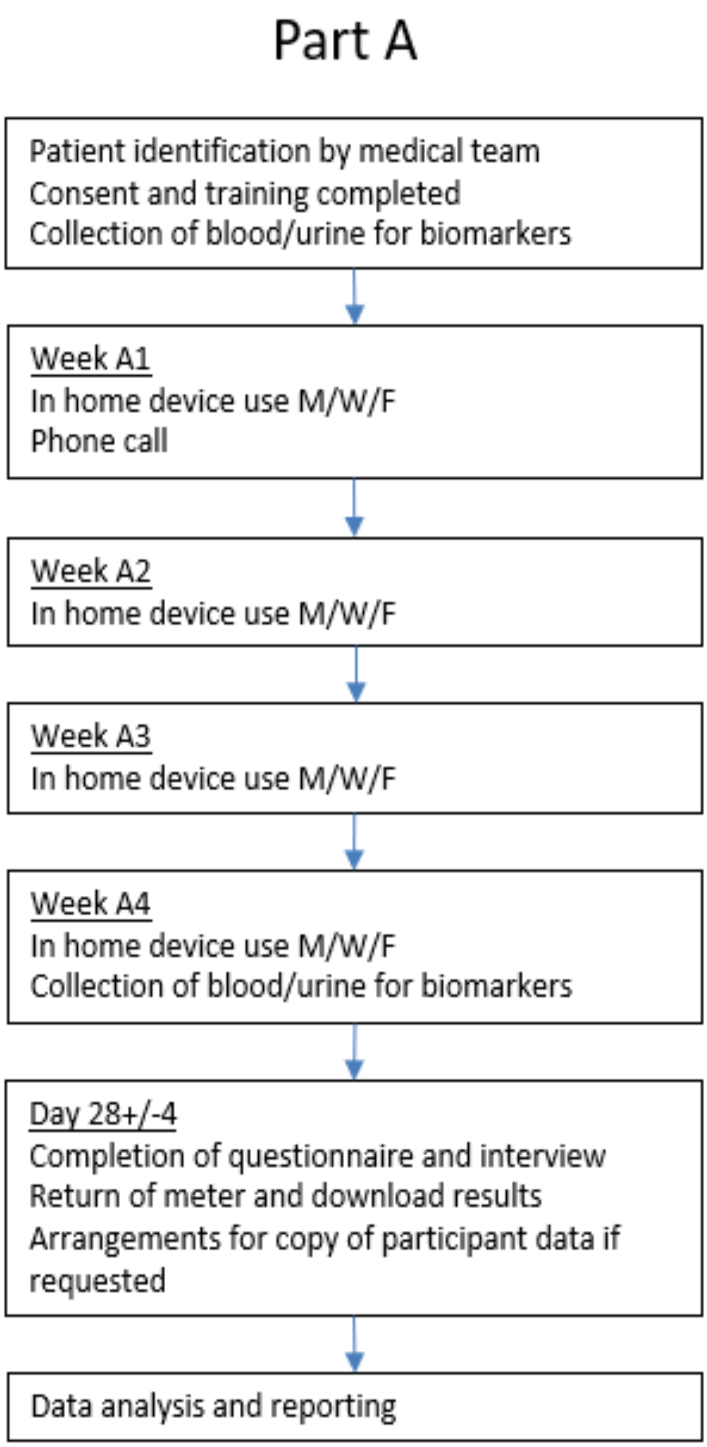
1. CONTENTS

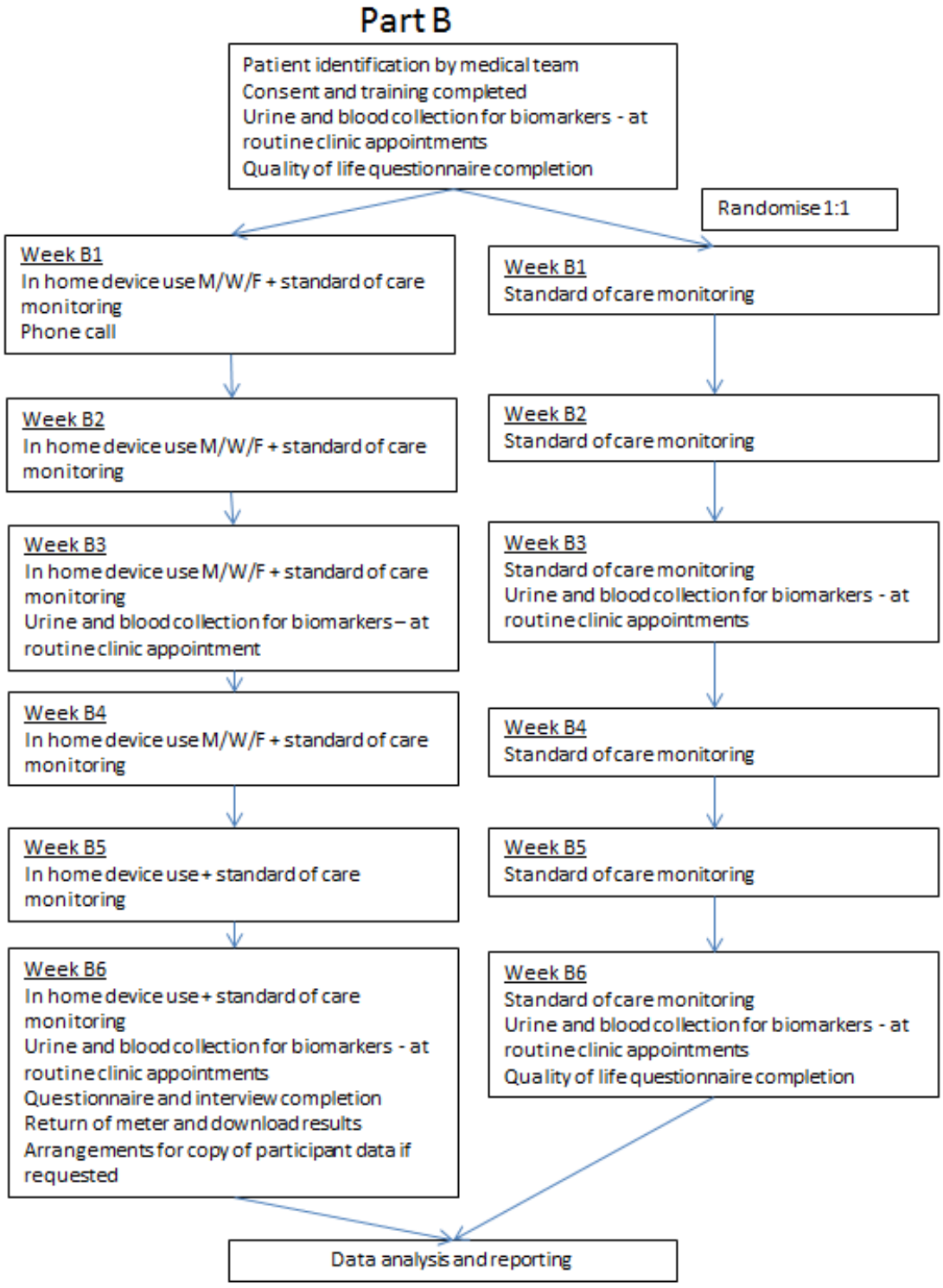
1.7 List of tables

1.8 List of abbreviations

AE	Adverse Event
AR	Adverse Reaction
CA	Competent Authority
CI	Chief Investigator
CRF	Case Report Form
CRO	Contract Research Organisation
CTA	Clinical Trial Authorisation
DMC	Data Monitoring Committee
GCP	Good Clinical Practice
NHS R&D	National Health Service Research & Development
PI	Principal Investigator
PIS	Participant Information Sheet
REC	Research Ethics Committee
SAE	Serious Adverse Event
SAR	Serious Adverse Reaction
SDV	Source Data Verification
SOP	Standard Operating Procedure
SUSAR	Suspected Unexpected Serious Adverse Reaction
TMF	Trial Master File
TSC	Trial Steering Committee

2. TRIAL FLOW CHART




Part B
Patient identification by medical team
Consent and training completed
Urine and blood collection for biomarkers - at routine clinic appointments
Quality of life questionnaire completion
Randomise 1:1
Week B1
In home device use M/W/F + standard of care monitoring
Phone call
Week B2
In home device use M/W/F + standard of care monitoring
Week B3
In home device use M/W/F + standard of care monitoring
Urine and blood collection for biomarkers – at routine clinic appointment
Week B4
In home device use M/W/F + standard of care monitoring
Week B5
In home device use + standard of care monitoring
Week B6
In home device use + standard of care monitoring
Urine and blood collection for biomarkers - at routine clinic appointments
Questionnaire and interview completion
Return of meter and download results
Arrangements for copy of participant data if requested
Week B1
Standard of care monitoring
Week B2
Standard of care monitoring
Week B3
Standard of care monitoring
Urine and blood collection for biomarkers - at routine clinic appointments
Week B4
Standard of care monitoring
Week B5
Standard of care monitoring
Week B6
Standard of care monitoring
Urine and blood collection for biomarkers - at routine clinic appointments
Quality of life questionnaire completion
Data analysis and reporting

3. BACKGROUND AND RATIONALE

3.1 Nephro-oncology: Treating people with kidney disease and cancer

Kidney disease is a major global health problem with over 850,000 deaths each year[1]. In the United States alone, the prevalence of the condition ranges between 14 and 17% of the population (dependent on ethnicity group), with a significant morbidity and mortality burden. Advances in cancer therapeutics have resulted in increased life-expectancy for many cancer patients. Nephro-oncology is an emerging sub-speciality tasked with managing the complex group of patients affected by both kidney disease and cancer. Izzedine and Perazella (2015) described a 'bidirectional relationship' between cancer and chronic kidney disease (CKD)[2]. They state 'cancer is an important complication noted in kidney disease as well as a major cause of morbidity and mortality in this group. On the other hand, improved cancer treatment has prolonged survival, but also increased the development of acute and chronic kidney disease.' Patients with cancer who are receiving anti-cancer treatment are at risk of acute kidney injury (AKI) for many reasons including direct nephrotoxicity, severe dehydration, intrinsic paraneoplastic renal diseases and increased susceptibility to infection and sepsis owing to their immunosuppressed state. Abudayyeh et al (2014) described 'onconephrology' and found that this group of patients are 'increasingly complex to manage because of the wider use of conditioning regimens and SCT (stem cell transplantation) and the introduction of newer and potentially nephrotoxic cancer therapies'[3].

3.2 Access to clinical trials and current barriers

Murthy et al (2004) found that recruitment in cancer clinical trials was low for all patient groups[4]. Specifically, they found that racial minorities, women and the elderly were less likely to be recruited in to cancer clinical trials than white people, men and younger patients. They also found that the proportion of black people who have been recruited to trials had reduced in 'recent years'. Ford et al (2007) carried out a systematic review of possible barriers to recruitment in to clinical trials and found they were numerous. Reasons included awareness and education with regards to clinical trials and opportunity to enrol (including co-morbidity exclusion)[5].

Current evidence suggests that people with reduced kidney function may have an increased risk of getting cancer[6] and that when cancer does occur their outcomes may be worse[7]. These patients may not be eligible for standard treatment options due to their reduced kidney function. However, at the current time, they are also not eligible for most oncology trials. This is because trial entry for majority of clinical trials is restricted to people with an eGFR (glomerular filtration rate) of above a certain standard level (for example ≥50ml/min). This is a largely arbitrary threshold and many drugs trialled are only partially renally excreted, if at all, therefore the clinical reasoning behind the cut off is

fundamentally flawed. Furthermore, yes/no to trial access is decided on a single time-point test at selection. This means that someone with a variable/uncontrolled renal function who happened to be eGFR 51ml/min on that day could access a trial, but someone with a more stable, managed renal function of eGFR 49ml/min would not. When in fact, the person with managed function may well cope better with the experimental drug.

Due to perceived risks of renal toxicity and causing harm to patients with CKD, patients with reduced kidney function are often excluded from cancer clinical trials[8]. Increasingly, the participation and barriers to recruiting in to cancer clinical trials is concerning, as is their lack of a true reflection of the 'real world' cancer population.

Jin et al (2017) performed a comprehensive review of the eligibility criteria for cancer clinical trials and stated, 'our findings suggest that eligibility criteria for current clinical trials tend to narrowly define the study population and limit the study to lower-risk patients, which may not be reflective of the greater patient population outside of the study'[9]. This has also been described in other studies which argue the tight inclusion/exclusion criterion of clinical trials lead to lower patient recruitment, increased timescales and cost and reduced relatability of trials to the general population[10]. Lichtman et al (2017) published recommendations to work towards modernising clinical trial eligibility criteria[11]. They found that 'exclusion of patients with a CrCl < 60ml/min would preclude between 20.3% and 45.9% of patients from participating in clinical trials' and suggested that this was likely a conservative estimate. They recommended that the inclusion criteria for cancer clinical trials, with regards to renal impairment, should be relaxed in certain situations including where the available clinical and non-clinical data indicates that it is safe for use in people with renal impairment; also, if renal clearance and nephrotoxicity is not of concern then a cut off of CrCl > 30mls/min (rather than commonly used >60mls/min) should be utilised.

3.3 Renal monitoring in oncology trials

Patients receiving anti-cancer therapies are at risk of renal insults for a multitude of reasons, including the treatments themselves, the underlying disease process and their possible higher risk of infections/sepsis and dehydration[12]. Increasing the monitoring of these patients could possibly lead to earlier identification of renal problems, allowing for greater medical support and potentially continuation on anti-cancer treatments that might have otherwise been stopped. Currently, when a patient is receiving chemotherapy, their kidney function is monitored at scheduled hospital appointments which may miss changes in creatinine indicating possible kidney damage, compounded by the fact that acute kidney injury is commonly associated with non-specific symptoms which could be attributed to chemotherapy side effects or the effects of cancer itself. Repeated episodes of AKI may lead to an increased risk of chronic kidney disease[13]. If these episodes of kidney injury can be picked up earlier, it may lead to reduced progression to more significant kidney dysfunction.

3.4 Prompt detection and diagnosis of AKI may improve the outcomes of AKI

AKI is described by the 'Think Kidneys Awareness Campaign' as a 'sudden and recent' decline in kidney function[14]. Prompt intervention focusing on the basic elements of care can improve the outcomes of AKI[15]. However, AKI is often poorly recognised by patients and clinicians[16]. To ensure that AKI cases are detected and diagnosed in a timely, consistent manner, the NHS recommends use of a standardised algorithm based on changes in serum creatinine levels[17]. The algorithm is intended for use as part of a Laboratory Information Management System (LIMS), to identify and classify potential cases of AKI from laboratory data in real time. Application of the algorithm is currently limited to hospital settings, but it is anticipated that the algorithm will also be used in primary care, subject to appropriate preparation[16].

Several papers have been published studying the effect of e-alerts on the mortality and AKI progression in patients with AKI, albeit all in the hospital setting. Colpaert et al (2012) enrolled 951 patients into a prospective interventional study evaluating whether an electronic alert system would influence therapeutic interventions in AKI cases and progression of AKI. They found that a higher percentage of patients within the alert group had therapeutic intervention commenced within 60 minutes of the alert. They also found a 'borderline significant' improvement in outcomes of AKI, in the short term, in the alert group[18]. However, Wilson et al (2015) found that an e-alert system did not improve clinical outcomes in patients with AKI[19]. In this randomised controlled trial, 2393 participants were enrolled and randomised to the standard care group and e-alert group. Maximum change in creatinine, dialysis and death at 7 days did not differ between the 2 groups. Clearly this area of AKI management needs further investigation, especially in the oncology setting.

Patients receiving anti-cancer treatments are at higher risk of AKI. Salahudeen et al (2013) found that rates of AKI in patients admitted to a cancer centre were higher than that in a non-cancer centre[20]. Lam et al (2012) discuss the different cause of AKI in the cancer patient[12]. These causes include pre-renal causes – nausea, vomiting and diarrhoea, concomitant medications such as NSAIDS, ACE inhibitors and diuretics, hypercalcaemia; intrinsic causes – lymphomatous infiltration of the kidney, cast nephropathy, tumour lysis syndrome; and post renal causes – obstruction of the urinary tract.

3.5 Self-monitoring of kidney function could help manage risks associated with cancer treatments

Usually, renal function is monitored at set times during a clinical trial, unless an unexpected event warrants it being checked. If monitoring of renal function can be improved upon, this could potentially lead to earlier detection of adverse renal events and a subsequent improvement in patient outcomes.

Self-monitoring has been shown to be an effective and acceptable form of monitoring in other chronic health conditions such as diabetes and anti-coagulation monitoring. Gardiner et al (2004) explored self-testing of INR in the home compared to in hospital laboratory testing in 84 patients. They found that 87% of patients found self-testing straight forward and were confident in the result and that 77% preferred self-testing[21]. Karter et al (2001) found that 'more frequent self-monitoring of blood glucose levels was associated with clinically and statistically better glycaemic control regardless of diabetes type or therapy'[22]. Self-monitoring of kidney function has been described in the literature previously. Van der Boog et al (2015) explored self-monitoring of renal function in the kidney transplant population[23]. They found that this population of patients were highly motivated to self-monitor and reported high levels of satisfaction with self-monitoring. If self-monitoring of renal function in cancer clinical trials can be shown to be acceptable and effective it could ultimately lead to the inclusion of patients with reduced kidney function being recruited to cancer clinical trials in a safe and accepted manner.

3.6 Renal Biomarkers

Renal biomarkers are an increasingly researched area. Limitations of the traditional marker of kidney function – creatinine – are well established[24]. Research in to renal biomarkers in the cancer population is a less studied area. It is hoped that this study will add to the body of knowledge by collecting samples of urine and whole blood to analyse for cystatin C and other renal biomarkers. Assessing renal biomarkers and their role in the cancer population could also add to the monitoring of kidney function and potentially pick up signals of deterioration earlier and allow patients with reduced kidney function to be enrolled in to clinical trials.

3.7 How this study addresses the research question

Part A of this study aims to explore whether patients who are currently receiving anti-cancer treatments are willing and able to perform intensive home monitoring of creatinine and send their results in to a cloud environment via an app to be run through an amended version of the NICE AKI algorithm to assess for evidence of AKI[17]. The algorithm has been amended for practicality and feasibility reasons. It is hoped that this will show the process to be convenient and acceptable to patients and clinicians and that the results are reliable. Furthermore, Part B of the study aims to show that home monitoring of creatinine will detect adverse kidney events and AKI earlier as compared to standard of care monitoring along with less overall change in kidney function in the intensively monitored group as compared with the standard of care group.

It is increasingly apparent that treatment options for this complex group of patients affected by both cancer and CKD are needed. Expanding the population of people with reduced kidney function recruited into clinical trials will be one way of meeting this clinical need.

3.8 Impact of this study on existing research

It is hoped that this research will show that home monitoring of renal function in a cancer population is not only acceptable to patients and clinicians but also leads to clinical benefit in terms of time to diagnosis of adverse renal events and acute kidney injury. This in turn may pave the way for patients with reduced renal function to be recruited in to cancer clinical trials in the future. This will ensure that future research has broader applicability as well as providing much needed information on how best to approach the treatment of a challenging group of patients who have both kidney disease and cancer.

3.9 Patient and public involvement

There were 17 individual interactions with people currently involved in early oncology trials within The Christie NHS Foundation Trust. These included patients, carers, and staff, and focussed mainly on gaining insight into the applicability of the research question, usability and practicality of the device, performing readings, and the information provided. Feedback gathered during these discussions has directly informed the protocol and processes described within.

Two focus groups have also been conducted. The first with 3 participants who have previously had cancer. The second, with 4 renal patients at various stages of their treatment journey, 2 of whom had also received a treatment for cancer that affected their kidney function. The project was unanimously felt to be worthwhile and many were surprised by the current limitations that reduced kidney function can have on peoples' cancer-treatment options. Both groups liked the idea of having some control over their results and having more responsibility over their own health. Participants from the renal focus group specifically embraced taking their own readings and thought that it would be motivating for taking ownership of their health overall. Both groups of participants questioned whether a study involving this sort of technology and smart phones/apps would exclude a section of the population who are not 'tech-literate' or able to perform the reading for various reasons such as dexterity problems. They queried whether a reading could be carried out by carers as, at certain timepoints, patients undergoing cancer treatments may be intensely fatigued or unable to carry out readings for other reasons. If a patient would like to participate in the study and has a carer they would like to perform the testing, they will be trained to take the readings as such. In addition to providing feedback on the practicality of the approach and information provided, they have since reviewed and approved the final information leaflets and videos accompanying this trial.

4. STUDY AIMS AND OBJECTIVES

This study will be delivered in two sections: Part A and Part B. The aim of Part A is to assess whether intensive home monitoring of creatinine is an acceptable and feasible form of monitoring for patients. Part B of the study will aim to show earlier detection of deteriorating kidney function and AKI as compared to standard of care renal monitoring.

Table 2: Study objectives, outcomes and measures

Objectives	**Outcome Measures**	**Timepoint(s) of evaluation of this outcome measure (if applicable)**
Primary Objectives		
Part A: To evaluate patient acceptance of intensive home-monitoring of whole-blood creatinine.	Questionnaire and interview Absolute number of creatinine readings received-expected vs actual Time sample taken vs. time expected to take Value sent/received vs. value on device (when downloaded at the end of the study period)	Week 4
Part B: To evaluate the potential for earlier diagnosis of AKI/change in renal function with intensive home-monitoring of whole-blood creatinine.	Time from beginning of current cycle treatment to detection of AKI by amended algorithm or clinician/laboratory reading Severity of AKI at detection (as per Kidney Disease Improving Global Outcomes AKI Work Group staging) Overall change in renal function from beginning to end of study period	Throughout study period

Secondary Objectives		
Part B: To assess whether intensive monitoring influences the change in kidney function over the study period compared to standard of care	Comparing kidney function at the beginning and end of the study	Weeks 1 and 6
Part B: To assess whether home monitoring of kidney function has a positive impact on a patient's quality of life.	Medical outcomes study short form 36 (SF-36) questionnaire	Week 6
Part B: To evaluate the adherence of patients to intensive home monitoring regimen	Absolute number of creatinine readings received Time sample taken vs. time expected to take Value sent/received vs. value on device (when downloaded at the end of the study period)	Week 6
Exploratory Objectives		
Part A: Using data gathered to improve and test amended AKI algorithm	Amended algorithm outcome vs clinician assessment Feedback and analysis from interviews and questionnaires	On completion of Part A
Part B: To explore the value of novel renal biomarkers in the cancer population for early detection and monitoring of AKI.	Urine and serum analysis	Throughout study period

Part B: Document any other issues that patients may have experienced during the study period.	Patient interview	Week 6
Part B: Clinician opinions towards home monitoring and the impact it could have on their treatment schedules for patients.	Clinician interview	Week 6
Part B: Are there ethical/justice considerations in carrying out studies which require access to smart phones/socioeconomic factors	Analysis of demographic information of patients enrolled, and those who declined, in study and those who decline to take part Patient interview	Week 6

5. STUDY DESIGN

5.7 Part A

Twelve patients being treated for cancer with potentially nephrotoxic anti-cancer therapies (according to the judgement of the CI) will be enrolled during Part A. Following consent, each will be trained on the use of the at-home creatinine detector and provided with the device to check their creatinine at home three times per week for 4 weeks. This will be in addition to the standard care they are receiving as part of their treatment. Participants will be advised to contact their parent medical team if they have any concerns regarding their health during the study period. The participants will upload their readings to the secure cloud environment 3 times a week (Monday/Wednesday/Friday) for 4 weeks. They will be required to use their own compatible smart phone or device to access the app, and to upload the data over their own internet connection.

Part A is an evaluation of a process that has not been tested in full before, along with a device that has not been used in this setting previously. The data gathered will be run through the amended AKI algorithm to look for evidence of AKI, participants will receive confirmation that the measurement has been successfully sent. Once a week, alerts from the algorithm and creatinine readings will be reviewed by the Chief Investigator and flagged to the parent medical team if there are concerns over a reading or alert.

At the end of week A1, participants will receive a phone call to ensure they are managing with the general process of sampling and sending results through the app, and to deal with any troubleshooting issues that may have arisen. At week A1 and A4 blood and urine will be collected for

exploratory biomarker analysis, along with renal function and cystatin C. When a participant attends a clinic appointment, a creatinine reading will be taken (either by the study participant or a member of the study team) using the device, for comparison with the laboratory creatinine reading taken that day.

At the end of Part A (in line with planned appointments), the participants will complete a questionnaire assessing the acceptability of the monitoring and take part in a short interview to establish any other issues that may have arisen during the study period. At the end of Part A, all readings and other data stored on the device will be downloaded directly from the device in order to confirm the accuracy and frequency of the readings uploaded via the app. If participants would like a copy of their data at the end of Part A, this will be arranged.

Each scheduled visit allows for a +- 1-week window to allow for possible variation amongst treatment regimens.

5.2 Part B

If, following Part A, the process is found to be an acceptable form of monitoring to patients, the study will continue to Part B. This will evaluate the potential for earlier diagnosis of AKI with intensive home monitoring of kidney function (plus standard of care monitoring) compared with standard of care only. The decision of whether to proceed to this stage of the study is described in further detail below. Participants who have been recruited to Part A of the study can continue to Part B if they so wish (and will be randomised).

Part B will enrol 60 patients being treated for cancer with potentially nephrotoxic anti-cancer therapies, randomised to either the intensive monitoring (device) group or the standard of care monitoring group, in a 1:1 ratio. Participants in both groups will be asked to complete a quality of life questionnaire at baseline. Both groups will receive standard of care monitoring of kidney function. In addition, participants in the intensive monitoring group will upload their creatinine reading three times per week (Mon/Wed/Fri) for 6 weeks. As in Part A, participants in the intensive monitoring group will be required to access the app on their own compatible device and upload their readings over their own internet connection. In both study arms, in line with scheduled clinic appointments (weeks B1, B3 and B6), blood and urine will be collected for exploratory biomarker analysis, along with renal function and cystatin C. When a participant attends a clinic appointment, a creatinine reading will be taken (either by the study participant or by a member of the study team) using the device, for comparison with the laboratory reading of creatinine taken that day.

During Part B of the study, when a participant has submitted their creatinine reading they will receive a successful submission message on the app and may receive feedback based on their reading (this depends on feedback from Part A of the study, performance of the amended algorithm from Part A and development of the smart phone application). As with Part A, participants will be directed to their

parent medical team if there is concern over their reading. Creatinine readings and AKI alerts from the algorithm will also be reviewed by the Chief Investigator once a week and highlighted to the parent medical team if there are concerns.

At the end of Part B, all participants in both groups will be asked to complete a quality of life questionnaire, and those in the intensive monitoring arm will also be asked to take part in a short interview and complete a questionnaire reviewing the process of home monitoring and sending in creatinine results, (as in Part A). As in Part A, all readings and other data stored on the device will be downloaded directly from the device at the end of Part B to confirm the accuracy and frequency of the readings uploaded via the app.

At the end of Part B, a short interview will be carried out with clinicians to explore their opinions towards home monitoring and the impact it could have on their treatment schedules for patients.

Each scheduled visit allows for a +- 1-week window to allow for possible variation amongst treatment regimens.

5.3 Progression of Study: Part A to Part B Go/No Go decision

A steering committee review of initial data from Part A along with the above information will occur with a view to deciding whether to proceed to Part B of the study. Factors that will be reviewed to help make this decision will be:

1. Recruitment rate – the recruitment rate in Part A will be reviewed by members of the steering committee and may lead to amendments to Part B study duration
2. Adherence to required readings ≤ 75%

The steering committee has the following core members: the Chief Investigator, the protocol project manager and a representative from the Experimental Cancer Medicine's Team. Ad hoc members can contribute on an agenda-driven basis and voluntary contribution from patients is welcomed. There will be a clinical representative from both Nephrology and Oncology.

A red/amber/green traffic light (stop/amend/continue) approach, as described in the literature[25], will be applied to the criteria used to determine whether to progress with Part B. Hence, if a progression criterion is not met and cannot be mitigated, data gathered during the study will be used to revise the study protocol. If this is required regulatory processes will be followed as per Section 10 - Study Governance.

5.4 Randomisation

Participants will be randomised using a simple randomisation technique using an internet-based randomisation service[26]. A permuted block technique will be used to ensure equal numbers in both groups.

6. SELECTION OF STUDY POPULATION AND WITHDRAWAL CRITERIA

Participants for both Part A and Part B will be identified from the general oncology outpatient population, with an initial focus on the Head and Neck Outpatient clinics. Anecdotally, this group of patients are high risk for AKI due to the nature of the treatment (platinum-based therapies) and increased risk of severe dehydration due to treatments that affect swallowing. Patients who have taken part in Part A of the study can continue to Part B if they wish and will be randomised prior to their participation in Part B.

Inclusion criteria

- Provision of signed and dated, written informed consent prior to participation in the study.
- Aged at least 18 years
- Receiving treatment for cancer with potentially nephrotoxic anti-cancer therapies (according to the judgement of the CI)
- Individuals whose medical team consider to be medically stable and able enough to take part or designated carer who would be able to perform the tasks required.
- Willingness and ability to self-monitor creatinine using device at home or have a designated carer who would be able to perform the tasks required. Part A device will be the NovaBiomedical StatSensor®.
- Access to smart phone and willingness to use, without reimbursement of any potential additional costs incurred, their iOS/Android device for the collection and transmission of information.

Exclusion criteria

- Being an employee, or closely linked with an employee, of the device company
- Judgment by the Investigator that the individual should not participate if they are unlikely to comply with study procedures and requirements.

- WHO performance status > 2
- Pregnancy

If withdrawal from the study occurs, permission will be sought to use their existing study data as well as data which forms part of their routine clinical care for the remainder of the study period. This will not require any further participation from the subject for the purposes of the study.

Possible reasons for withdrawal:

1. Withdrawal of consent
2. Pregnancy
3. Loss of capacity/ability to carry out study requirements as deemed by participants primary medical team

During pregnancy, physiological changes affect creatinine readings and therefore they would not be a true reflection of renal function. For this reason, negative pregnancy status will be confirmed for all women of child bearing age who are taking part in the study if this has not already been done by the parent medical team prior to commencement of anti-cancer treatment.

7. STUDY PROCEDURES

Once a patient has agreed to take part in the study and informed consent is gathered the following will be gathered from medical records and the patient:

1. Baseline kidney function – urea, creatinine and eGFR at point of diagnosis and 3 months previous
2. Significant past medical and surgical history
3. Previous cancer treatments relating to incident cancer diagnosis
4. Risk factors for AKI
5. Blood pressure at previous clinic attendances relating to incident cancer diagnosis
6. Urine collection and dipstick results at previous clinic attendances relating to incident cancer diagnosis
7. Concomitant medication and recent acute prescriptions

Table 3: Trial Procedures Part A

Procedures – Part A	**Visits**			
	Screening	Baseline Week 1 (+- 1 week)	Week 2 (+- 1 week)	Week 4 (+- 1 week)
Informed consent	x			
Demographics (from medical notes)		x		
Medical history (from medical notes)		x		
Phone call		x		
Blood Pressure		x		x
Urine Collection		x		x
Blood Collection		x		x
Usability Questionnaire				x
Workbook completion		x		x
Semi-structured interview				x

Table 4: Trial Procedures Part B

* - intensive monitoring group only

Procedures – Part B	**Visits**			
	Screening	Baseline Week 1 (+-1 Week)	Week 4 (+- 1 week)	Week 8 (+- 1 week)
Informed consent	x			
Demographics (from medical notes)		x		

Medical history (from medical notes)		x		
Phone call*		x		
Blood Pressure		x	x	x
Urine Collection		x	x	x
Blood Collection		x	x	x
Usability Questionnaire*				x
QoL Assessment		x		x
Workbook completion		x	x	x
Semi-structured interview – participant*				x
Clinician interview				x

7.1 Qualitative assessments

In both Part A and Part B of the study**,** a questionnaire based on a previously validated tool[27] will be used to assess participants view of the monitoring device along with the process of sending in data to the secure cloud environment. This will occur as outlined above.

At the beginning and end of Part B of the study, a previously validated quality of life questionnaire will be completed[28].

Semi-structured, individual interviews will be performed at the end of the study period for both Part A and Part B of the study. Participants will be asked a series of open-ended questions relating to their experience of the process and all aspects of the study. An interview guide is included in the appendix. The questions will broadly assess the following parameters:

- Overall impressions of the study
- Acceptability of StatSensor® (Part A) including calibration and operation
- Feedback on app
- Adherence with measurements including calibration and appropriateness of frequency
- For Part A – opinion on frequency of readings – too many or too few
- Opinions on value of readings/trust of readings
- Any other participant-initiated reflections or observations

All interviews should last no more than 1 hour and will take place in a private room in the hospital. Interviews will be recorded using a digital recorder and will be transcribed verbatim by the lead researcher. Recordings and transcripts will be stored in a secure environment at The Christie Hospital. The recording will be used for thematic analysis during data analysis.

At the end of Part B of the study, a clinician interview will take place, exploring:

- Overall impressions of the study
- Trust of results and future applications

7.2 The System

The system described the whole process of a participant sampling their creatinine with the device and sending the result in with the smart phone application.

A smart phone application has been developed which has the capabilities to transfer the creatinine reading from the study participant to the secure cloud environment. It does not store any personal data or readings or perform any calculations. This app will be used in Part A of the study.

Using feedback from Part A of the study, the app will be developed to improve its functionality and performance.

For Part A of the study, the Nova biomedical StatSensor Xpress creatinine monitoring system has been chosen. This is a CE-Marked device for point of care testing. However, although use by patients has previously been assessed[23 29], its current intended use is by health care professionals in the hospital setting[30].

Part B of the study may require a device change depending upon available options at this time. If a device change is made, regulatory processes will be followed as per Section 10 - Study Governance.

7.3 Baseline data

Weight and blood pressure will be taken. If these are checked routinely in the clinic appointment, then the clinic readings will be used.

A mid-stream urine sample in universal container will be collected and standard urine dipstick will be performed. This urine will be kept for assessment of novel renal biomarkers.

A blood sample will be taken in addition to any standard of care samples for exploratory biomarkers and cystatin C.

7.4 Blood collection

- **Volume of blood**

The number of samples taken, as well as the volume required for each analysis, may be changed during the study as emerging data become available. However, the estimated total volume of blood that will be drawn from each patient in this study during screening and the first cycle of treatment will not exceed approximately 50 mL, in addition to standard of care (over a 1-month period).

- **Storage and analysis of clinical samples**

A sample of whole blood and urine will be collected in addition to routine blood tests to assess cystatin C and stored for further analysis of novel biomarkers. Samples will be collected, labelled, stored and shipped as detailed in the Laboratory Manual. Samples will be taken as outlined in the study plan.

Samples will be taken at the Christie Hospital and transported for storage at the Manchester Institute of Nephrology and Transplantation biobank. Further biomarker analysis. will be carried out at Manchester Metropolitan University Laboratories and Medicines Discovery Catapult Laboratories.

8. CONSENT

For both Part A and B of the study, after identification the potential participant will be approached by a member of the research team who will:

- Ask whether they're interested in hearing about the study and potentially take part.
- Describe the aims of this study
- Walk them through the consent form and ensure that they have a copy to keep.
- Potential participants will be given the option to watch the training video, patient information leaflet and/or device if they wish
- Give them chance to ask questions and leave the support email address in case they think of questions after they leave the hospital. Allow them as much time to consider the information as they themselves feel they need.

Following consent, the study participant (or nominated carer) will be trained in use of the device and submission of reading with smart phone app. This includes a training video and leaflet which both detail the process of taking a sample and submitting the result using the app. Participants will be given the opportunity to run through the sampling process with a member of the research team.

9. STATISTICAL CONSIDERATIONS AND DATA ANALYSIS

For Part A of the study, a powered sample size calculation has not taken place. In line with published recommendations[31] 12 patients will be recruited to receive the StatSensor® to assess the general process of taking creatinine readings and sending in results via the app. Descriptive statistics will be used to summarise demographic data and clinical variables. Categorical data will be reported using frequencies and percentages. Quantitative variables will be reported using either the mean and standard deviation or the median and interquartile range depending on the distribution of the data. The standard error of the mean will also be calculated.

For Part B current powered sample size calculations estimate 30 study participants to be satisfactory. This number will be sufficient as overall creatinine levels will be used as an end point for higher statistical power as well as AKI rate. A Student's t-test and one-way ANOVA test will be used to analyse data for statistical significance.

The significance has been calculated using the assumption during standard treatment for head and neck cancer, the mean creatinine readings are 1.2 +/- 0.2 mg/dl, with closer monitoring having the potential to bring it down to 0.9+/-0.2 mg/dl based on the results of docetaxel, cisplatin, and 5-fluorouracil therapy[32].

Themes from the interviews will be developed and analysed in more detail in line with published guidance on qualitative study analysis[33].

Analysis of data from this study will be in conjunction with the statistics department of the sponsor and in-house statistician support and other statistical analyses will be used as appropriate.

10. STUDY GOVERNANCE

10.1 Regulatory and Ethical Considerations

Prior to study initiation, a favourable ethical opinion will be obtained from the NHS Health Research Authority. All research activity will be conducted in accordance with the International Standard of Good Clinical Practice. The study sponsor will be the University of Manchester and all research activity will be conducted in accordance with trust policies. This feasibility study will be registered with the International Standard Randomised Controlled Trial Number Registry.

Study participants need access to a smart phone device to be able to take part in the study. This could possibly exclude a population of patients who may want to take part in the study but do not have a smart phone, for whatever reason. If this is found to be an issue, an amendment to the inclusion criteria to provide smart devices to these participants will be considered, or other options for these people to submit their results, such as computers.

Some study participants may not be able to physically take readings and send in the results. For these participants a carer will be designated to take the reading and send in the result.

Study amendments will be submitted as directed by regulatory requirements.

10.2 Data Management

Study participant data will be recorded in a workbook which will be collated in to a Microsoft Excel spreadsheet-based database. This will be password protected and stored on The Christie server. This will be discussed in further detail in the data management form found in the appendix.

Workbooks will be stored in a secure environment within The Christie Hospital.

Confidentiality of personal data will be maintained throughout the study. There will be pseudoanonymisation of data only whilst necessary, after which there will be complete anonymisation of data.

Management of clinical data will be performed in accordance with the NHS Code of Confidentiality and the local Information Governance Policy

10.3 GDPR and Data Protection

Sensitive participant data will be collected, stored and used in accordance with GDPR regulations.

10.4 Access to Data

Direct access will be granted to authorised representatives from the Sponsor. Participants of the study who wish to gain access to their own data will be provided with information on how to access this at the end of the trial period.

10.5 Archiving

Archiving will be authorised by the Sponsor following submission of the end of trial report. The site will be responsible for archiving all trial documents. The trial database and essential documents will be retained in a secure environment at The Christie NHS Hospital for a minimum of 5 years following completion of the trial.

Destruction of essential documents will require authorisation from the Sponsor.

10.6 Reporting Requirements

A progress report will be submitted to the REC which gave the favourable opinion 12 months after the date on which the favourable opinion was given.
An HRA annual progress report form will completed in typescript and signed by the Chief Investigator.
An electronic copy will be emailed to the REC within 30 days of the end of the reporting period.

10.7 Amendments

Any proposed protocol amendment will be flagged to the Chief Investigator, who will work with the steering committee to ascertain whether it should be actioned and whether it constitutes a substantial amendment. Please refer to section 5.3 for details on the steering committee members.
If the committee wishes to make a substantial amendment to the REC application or the supporting documents, the sponsor must submit a valid notice of amendment to the REC for consideration. The

REC will provide a response regarding the amendment within 35 days of receipt of the notice. It is the sponsor's responsibility to decide whether an amendment is substantial or non-substantial for the purposes of submission to the REC.

If applicable, other specialist review bodies need to be notified about substantial amendments in case the amendment affects their opinion of the study.

Amendments also need to be notified to NHS R&D departments of participating sites to assess whether the amendment affects the NHS permission for that site. Note that some amendments that may be non-substantial for the purposes of REC and/or MHRA may still need to be notified to NHS R&D (e.g. a change to the funding arrangements). For studies with English sites processed in NIHR CSP the amendment should be submitted in IRAS to the lead CRN, which will determine whether the amendment requires notification to English sites or may be implemented immediately (subject to REC approval were necessary)

Details of all protocol amendments will be documented in the Appendix whenever a new version of the protocol is produced.

11. MONITORING, AUDIT & INSPECTION

A Trial Monitoring Plan will be developed and agreed by the Trial Management Group (TMG), TSC and CI based on the trial risk assessment which may include on site monitoring.

12. SAFETY REPORTING AND RISK ASSESSMENT

12.1 Definitions

Table 5: Safety Reporting Definitions

Term	Definition
Adverse Event (AE)	Any untoward medical occurrence, unintended disease or injury or any untoward clinical signs (including an abnormal laboratory finding) in subjects, users or other persons whether or not it is related to the medical device.
Serious Adverse Event (SAE)	An AE (as defined above) that: • results in death, injury or permanent impairment to a body structure or a body

	function
	• Led to a serious deterioration in health of the subject, that either resulted in:
	  ○ A life-threatening illness or injury
	  ○ A permanent impairment of a body structure or function
	  ○ In-patient hospitalisation or prolongation of existing hospitalisation
	  ○ Medical or surgical intervention to prevent life threatening illness
	• Led to foetal distress, foetal death or a congenital abnormality or birth defect

Adverse Device Effect (ADE)	An AE related to the use of an investigational medical device. This includes any AE resulting from insufficiencies or inadequacies in the instructions for use, the deployment, implantation, the installation, the operation, or any malfunction of the medical device. This also includes any AE that is a result of an error in use or intentional misuse of the medical device.
Serious Adverse Device Effect (SADE)	An Adverse Device Effect (ADE) that results in any of the consequences characteristic of an SAE.
Unanticipated Serious Adverse Device Effect (USADE)	A SADE which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report.
Device Deficiency	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance. Device Deficiencies include malfunctions, user error, or inadequacy in the information supplied by the manufacturer.

- Related – that is, it resulted from administration of any of the research procedures, insufficiencies or inadequacies in the instructions for use, the operation of the medical device or any malfunctions of technical equipment and is
- Unexpected – that is, the type of event is not listed in the protocol as an expected occurrence.

12.2 Reporting Procedures

Reportable events will be communicated from research staff to the sponsor immediately, but not later than 3 calendar days following the awareness of the event at site.
Having received notification of an SAE from research staff, the CI will notify the Research Ethics committee immediately, but not later than 2 calendar days for all reportable events which indicate an imminent risk of death, serious injury or serious illness that requires prompt remedial action. For all SAEs which are related to the device and are unexpected the CI will notify the Research Ethics Committee immediately, but not later than 15 days from awareness.
For all reportable events which indicate an imminent risk of death, serious injury, or serious illness and that requires prompt remedial actions, the sponsor will inform the MHRA immediately, but no later than 2 calendar days after awareness by the sponsor of a new reportable event or of new information in relation with an already reported event. Any other reportable event or new finding will be reported by the sponsor immediately, but no later than 7 calendar days following the date of awareness by the sponsor.
For each SAE, considered related and unexpected, information with be gathered as per the HRA reporting form (see Appendix 14.8).

12.3 Notification of deaths

All deaths whilst in study will be reported to the sponsor within 7 days irrespective of suspected causality. This is to ensure monitoring and annual reporting requirements can be met, and user accounts can be managed.

12.4 Expected Adverse Events

There are few expected adverse events in this study, related to both the process and the device.
They have been summarised as follows along with the avoidance/mitigation steps taken:

- Localised tenderness around the site of sampling – a standard lance is being used which draws a small amount of blood. Study participants will be trained to use this appropriately and prepared that they may be some short-lived tenderness in this area. Participants will also be encouraged to rotate which finger they use for sampling.

12.5 Responsibilities

Table 6: Responsibilities

Person/Group	Responsibility
Principal Investigator (PI)	Checking for adverse events, when participants attend for visits and following up for information as needed. Assigning seriousness, causality and whether it was expected. Ensuring that information is captured and reported to sponsor in line with the requirements of the protocol
Chief Investigator (CI) / delegate or independent reviewer	Oversight of the safety of patients participating in the trial, including an ongoing review of the risk / benefit. Assigning seriousness, causality and whether it was expected where it has not been possible to obtain local assessment. Immediate review of all SUSARs, USADEs, and device deficiencies and assigning Medical Dictionary for Regulatory Activities (MedDRA) or Body System coding to all SAEs. Contributing to annual update report and review of information. Undertaking delegated sponsor responsibilities.
Trial Steering Committee (TSC)	In accordance with the Trial Terms of Reference for the TSC, periodically reviewing safety data.

12.6 Risk Assessment

Table 7: Risks and Mitigations

Potential Risk	Mitigations for each potential risk
Sharp in the home	Standard safety lance will be used, sharps bin provided as well as training and instructions for use.
Risk of infection from a sample of bodily fluid (blood)	Sample size is microlitres and to be disposed of in the sharps bin provided. Strips and lances are for once only use. Training and instructions for use will be given. Any meters which are to be re-used will undergo a decontamination protocol before being reassigned to a new person.

False sense of security from home readings, i.e. a lack of action due to these readings when in standard of care there would have been action	Addition to standard of care so baseline pathway and support for patients is preserved as a minimum throughout. Clear guidance is provided on how the patient should act based on their results.
Patients worry	Clear and up-front training given. What to do, how to action high readings and ask for help, as well as up-front description of how to handle predictable situations (e.g. missing a reading). Discussions about how the patient has been will occur during each visit. If worried, reassurance and any extra training will be given.
Occurrence of a personal data leak or privacy breach	End-to-end security. If device lost no identifiable link back to study participant, only creatinine readings.
Potential risk for trial	People not using the devices or sending results. Training will be given, and support provided throughout. Feasibility run-in to protocol to be able to improve risk mitigation.

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14. APPENDICIES

14.1 System Usability Questionnaire

Part A/Part B (delete as appropriate)

Participant Identification Number:

Please complete this questionnaire by indicating how much you agree with the following statements – from 1 (strongly disagree) to 5 (strongly agree). The process refers to everything from taking your sample of blood, using the device and sending the result in using the app. If you want to comment on any part of the process specifically please use the free comment section at the bottom.

1. I think that I would like to use this process frequently.

Strongly disagree Strongly agree

1	2	3	4	5

2. I found the process unnecessarily complex.

1	2	3	4	5

3. I thought the process was easy to use.

1	2	3	4	5

4. I think that I would need the support of a technical person to be able to use this process.

1 2 3 4 5

5. I found the various functions in this process were well integrated.

1 2 3 4 5

6. I thought there was too much inconsistency in this process.

1 2 3 4 5

7. I would imagine that most people would learn to use this process very quickly.

1 2 3 4 5

8. I found the process very cumbersome to use.

1 2 3 4 5

9. I felt very confident using the process.

1 2 3 4 5

10. I needed to learn a lot of things before I could get going with this process.

1	2	3	4	5

11. I would recommend this process to friends and family

1	2	3	4	5

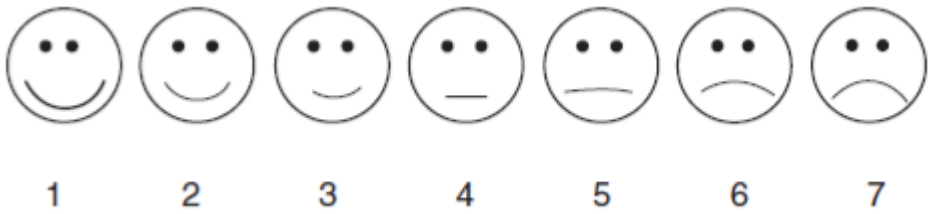
12. Any other comments?

Many thanks for taking the time to complete this questionnaire

This questionnaire is based on the System Usability Scale (SUS), which was developed by John Brooke while working at Digital Equipment Corporation. © Digital Equipment Corporation, 1986.

14.2 Quality of Life Questionnaire

Participant ID:



Which face comes closest to expressing how you feel about:

1. Your health? _____
2. Your relations with your wife or husband (girlfriend or boyfriend)? _____
3. Your relations with other relatives? _____
4. Your relations with friends? _____
5. Your body? _____
6. Your ability to go about your daily activities? _____
7. Your job/school/household work? _____
8. The way you spend your leisure time? _____
9. Your appearance? _____
10. How much physical strength you have? _____
11. How comfortable overall you feel? _____
12. Your medical treatment? _____
13. Your ability to attain sexual satisfaction? _____
14. Your ability to eat? _____
15. Your ability to control your personal circumstances? _____
16. The quality of your life? _____

17. Your future? _____

18. How satisfied you feel with your life as a whole? _____

Thank you for taking the time to complete this questionnaire.

This Questionnaire has been adapted from The Satisfaction with Life Domains Scale.

14.3 Participant Information Sheet and Consent Form (Part A)

You are being invited to take part in a research study which is investigating if we can improve monitoring of people's kidney function during cancer treatment. This work will be part of a project for a post-graduate degree. Before you decide whether to take part, it is important for you to understand why the research is being conducted and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Please ask if there is anything that is not clear or if you would like more information. Take time to decide whether you wish to take part. Thank you for taking the time to read this.

Who will conduct the research?
The research team for this study are from the Digital Experimental Cancer Research Team (Digital ECMT), who work within the University of Manchester and Cancer Research UK (Manchester Institute). The study will be led by Dr Leanne Ogden and she will work with a team of people to help organise and run the study. The work is being conducted under the supervision of Professor Sandip Mitra and will be supported by a team of experts to ensure all aspects of the trial are run to correct standards. Different members of the team have different roles and it is likely that you will only meet a couple of these people whilst you are on the study.
Within the University of Manchester there are several divisions and responsibility for this study lies within the Faculty of Biology, Medicine and Health (Division of Cardiovascular Studies):
Core Technology Facility
46 Grafton Street
Manchester
M13 9NT

What is the purpose of the research?
People with partly-working kidneys often don't get the choice of taking part in cancer trials because of worries over damaging their kidneys further. This means that there are fewer treatment options for people who have both cancer and kidney disease.

We want to understand whether people monitoring their kidneys at home using a blood test that works on a single drop of blood could help with this. If so, then this may eventually allow patients with partly-working kidneys to take part in cancer trials to improve treatment options in the future.

Why have I been chosen?
Because you are going to be having cancer treatments that could potentially affect their kidneys.

What would I be asked to do if I took part?
There are 2 parts to this study (Part A and Part B). This information sheet refers to Part A of the study.
A member of the research team will arrange to come to your routine appointments to see you. The first meeting we will train you in how to use the device/creatinine meter and take a blood sample. This is likely to take between 30 minutes and an hour, but it doesn't matter if it's shorter or longer – whatever you need to feel comfortable with the approach. We will also take your blood pressure and collect a urine and blood sample from you during the same appointment.
Then on Mondays, Wednesdays and Friday mornings for 4 weeks we would like you to check how your kidneys are working with the meter provided in the comfort of your own home. This involves you taking a drop of blood using a standard finger-pricker (a sharp) and then using the meter to check for creatinine (a marker of how well your kidneys are working) as shown. This means that you will prick your finger a total of 12 times over the 4-week period. The result on the meter needs to be sent using the app provided on your smart phone. You will have been trained on how to do this at the start. This app has been designed for securely sending information. This blood is not stored or used in any other way and you will throw it away in special bins we will provide to you.

After about a week, a member of the research team will give you a quick phone call to see how things are going and give you a chance to ask any additional questions you may have.
We will see you in person for a second time 4 weeks later. You will have your blood pressure checked and a blood and urine sample taken again. At this point please return all equipment that you have been loaned and we will help you to delete the app off your phone. A member of the research team will have an informal chat with you so we can learn from you how you think everything has gone (15-20 minutes), ask you to complete a short questionnaire (10 minutes). The readings will also be downloaded from the meter and if you'd like a copy of these please ask – we can provide you with these in a secure way. To help with our note-taking (so we don't miss valuable feedback) we would like to make an audio-recording of our informal chat. Afterwards this will be transcribed – any information that is personal to you will not be included in this transcription, the only identifier remaining will be the code used for you during the trial. The audio-recording itself will be permanently deleted after the transcription has been made. This recording will be deleted within 4 weeks of the study ending.
Both times we see you it will be planned so that this happens while you are already in hospital for your usual visits.
After taking part in this trial you will continue with the standard monitoring of kidney function and cancer treatment as you will have discussed with your medical team.

What are the extra samples for?
We would like to collect an extra blood (10mls) and urine sample (50mls) when you come to the hospital for your planned appointments this is to look for new markers of kidney damage. For Part A of the study we will collect the urine and blood samples during your visit to hospital in Weeks 1 and 4 of the trial. Samples will be collected by a member of the research team and will be labelled with a code unique to you. The sample will be transported to a laboratory to be analysed and will be stored in a special storage facility at Manchester Royal Infirmary. There will be no DNA analysis in this study. As these samples are being analysed to try and find new markers that could potentially

improve the detection of kidney damage in the future, their usefulness now will not have been proven. The aim is to find them so that they can be researched. As such, your GP or team at the hospital will not receive any results of these tests as not enough will be known about them to be help your personal care at the moment.
We would like to keep the samples for a maximum of 2 years from the end of the study. We may use the samples for solely for the purpose of further health care research related to this research project. They will not identify you and will not be combined with other information in a way that could identify you. In addition, no information gleaned from future research with these samples will be used to contact you, affect your care, or affect future services available to you. Once the 2-year period has been reached, the samples will be destroyed in accordance with the laboratory's usual procedures.

What are the potential benefits of taking part?

- **Yourself:** None.

- **Other patients:** We hope this research is the beginning of improving people's treatment options for people who have both cancer and kidney disease.

What are the potential risks of taking part?

Risks around security of personal information have been minimised by building the system with data security and privacy at its core (this is also discussed later).

To send your creatinine reading to us, what it will cost you depends on your service-provider. If you have an unlimited data plan on your phone, or are connected to a Wi-Fi network, there should be no cost for sending a message. However, they may charge you for using 3G or 4G if you don't have such a data plan, and especially if you're travelling abroad. Costs can be minimised by sending your measurements when on Wi-Fi and checking your data allowances before you travel abroad.

We will give you a sharps bin to dispose of your sharp to reduce the risk of you or anyone else hurting themselves on the sharp and we will teach you how to use it. The sharp that pricks the skin is protected inside a plastic case to help prevent accidental damage. You will be trained how to use this.

Using the finger-pricker (sharp) will possibly cause some discomfort or pain around the immediate area. It may leave you with a small bruise.

What will happen to my personal information?

In order to undertake the research project, we will need to collect the following personal information/data about you:

- Name
- Date of birth
- Past medical history and previous operations
- Information regarding your cancer diagnosis and treatment plan
- Medication history
- Hospital admission details when you are on the study
- Kidney function before entry to and during the study
- Your blood pressure, urine and blood samples collected whilst in hospital (as described previously)

- Your responses to questionnaires, as well as audio recording of our informal chat (also described previously).

We are collecting and storing this personal information in accordance with the General Data Protection Regulation (GDPR) and Data Protection Act 2018 which legislate to protect your personal information. The legal basis upon which we are using your personal information is "public interest task" and "for research purposes" if sensitive information is collected. For more information about the way we process your personal information and comply with data protection law please see our Privacy Notice for Research Participants (http://documents.manchester.ac.uk/display.aspx?DocID=37095)

The University of Manchester, as Data Controller for this project, takes responsibility for the protection of the personal information that this study is collecting about you. In order to comply with the legal obligations to protect your personal data the University has safeguards in place such as policies and procedures. All researchers are appropriately trained, and your data will be looked after in the following way:

- Data will be stored securely using your unique code. This is described further in the section 'How secure is it?' on the next page.
- Physical workbooks will be stored in a secure office in The Christie Hospital and will not be removed from the hospital site.

If you agree to take part in the study, you will be given a unique code that is used to represent you instead of your name or hospital number. Once this is done, any information that you send in or give to us will be linked to this code rather than any information that could identify you.

The research team at the University of Manchester will have access to your personal identifiable information, that is data which could identify you, but your unique code will be used as soon as possible. However, your consent form, contact details and work book will be retained for 5 years at The Christie Hospital in a secure location within the research department.

The app used to send your creatinine reading to us from home does not store data, it simply sends us the reading.

How secure is it?

As with all systems, there are two aspects to consider for security: The technical system itself and the conduct of those that are using it.

- **The secure cloud environment**
    - The whole system has been created with highest levels of security (equivalent to banking). The system has undergone extensive security testing, including having people try to hack into it. This testing will continue and if anything is identified it will be remedied. In the unlikely event that there is a data breach, we will let you know and close the system temporarily rather than risk your information.
- **The people using it:**

- The analysts and researchers are bound by an ethical code of conduct to behave responsibly, treat your data with respect, and protect any information that you may share.

- When you send in a reading it will be stored in a secure environment. The device you use to check your kidney function will 'remember' a certain number of readings therefore if someone was able to use the device, they could potentially see your readings, but the device has no information that would link the readings back to you. We would recommend you keep your device somewhere safe at home when you are not using it. When you come in to hospital for your last visit with us we will download all of the readings and delete them from the device.

You have several rights under data protection law regarding your personal information. For example, you can request a copy of the information we hold about you, including audio recordings. This is known as a Subject Access Request. If you would like to know more about your different rights, please consult our privacy notice for research (http://documents.manchester.ac.uk/display.aspx?DocID=37095) and if you wish to contact us about your data protection rights, please email dataprotection@manchester.ac.uk or write to The Information Governance Office, Christie Building, University of Manchester, Oxford Road, M13 9PL. at the University and we will guide you through the process of exercising your rights.

You also have a right to complain to the Information Commissioner's Office (https://ico.org.uk/make-a-complaint/), Tel 0303 123 1113

Who will see my information?

Your participation in the study will be kept confidential to the study team and those with access to your personal information as listed in this section.

The team looking after you at the hospital will know you are taking part in the study and members of the team will have access to your personal information and results.

Individuals from the University, the site where the research is taking place and regulatory and NHS authorities (Health Research Authority - HRA) may need to review the study information for auditing and monitoring purposes or in the event of an incident.

In some extreme circumstances, we may need to inform other organisations of your enrolment in the study. The following are examples of such circumstances:

- If there are concerns about your safety or the safety of others, we may need to contact your GP or a family member

- Reporting of current/future illegal activities to the authorities

- In the event of incidental or unexpected findings that could have implications for your health or may need further investigation we may need to inform your GP and care team

What happens if I do not want to take part or if I change my mind?

It is up to you to decide whether to take part. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. You will still be free to withdraw at any time without giving a reason and without detriment to yourself. However, it will not be possible to remove your data from the project once it has been anonymised and forms part of the dataset as we

will not be able to identify which specific bit came from you. This does not affect your data protection rights.
If you do not wish to be recorded during our informal chat at the end of the study, we can carry out the discussion without the audio recorder – please just tell the member of the research team on the day. Recording can also be stopped at any time if you do not feel comfortable.

Will my data be used for future research?

When you agree to take part in a research study, the information about you may be provided to researchers running other research studies in this organisation. The future research would be related to kidney disease or cancer. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research (https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/).
This information will not identify you and will not be combined with other information in a way that could identify you. The information will only be used for the purpose of health and care research and cannot be used to contact you regarding any other matter or to affect your care. It will not be used to make decisions about future services available to you.

Will I be paid for participating in the research?

You will not be paid for taking part in this research. You will be provided with the equipment needed to take part in the study, but you will need to use your own smart phone and Wi-Fi/3G/4G data.

What is the duration of the research?

Part A of the study takes place over 4 weeks. Part B of the study takes place over 6 weeks. If you wish to take part in Part B following Part A, we will discuss this with you and provide you with further study information related to Part B of the study.

Where will the research be conducted?

The Christie Hospital, we will come to your treatment area.

Will the outcomes of the research be published?

The results of analyses will be published in scientific literature and journals so that others can also learn and help to improve research in this area. At no time will anything be published that can identify you personally.

Who has reviewed the research project?

This research has been reviewed and approved by a research ethics committee within the UK Health Departments' Research Ethics Service, and the Health Research Authority.

What if I want to make a complaint?

Minor complaints

If you have a minor complaint, then you need to contact the research team in the first instance. If you would like to complain about any aspect of the study please contact the research team at leanne.ogden@digitalecmt.org and the lead investigator will contact you to discuss the issues further.

Alternatively, you can contact Professor Sandip Mitra, Consultant Nephrologist (Manchester Royal Infirmary) or the University of Manchester. He can be contacted through the MRI switchboard 0161 276 1234.

Formal Complaints

If you wish to make a formal complaint or if you are not satisfied with the response you have gained from the researchers in the first instance, then please contact:

The Research Governance and Integrity Manager, Research Office, Christie Building, University of Manchester, Oxford Road, Manchester, M13 9PL, by emailing: research.complaints@manchester.ac.uk or by telephoning 0161 275 2674.

Indemnity Arrangements

The University of Manchester has arranged insurance for research involving human subjects that provided cover for legal liabilities arising from it actions or those of its staff or supervised students, subject to policy terms and conditions. This covers both the design and management of the study.

What Do I Do Now?

If you have any queries about the study or if you are interested in taking part, then please contact the research team**:**

Support@digitalecmt.org
Leanne.ogden@digitalecmt.org
0161 918 2374
This research has been reviewed and approved by a research ethics committee within the UK Health Departments' Research Ethics Service, and the Health Research Authority.

Name:

Name of Researcher:

If you are happy to participate please complete and sign the consent form below

	Activities	Initials
1	I confirm that I have read the attached information sheet (version 4.0, 01/04/2019) for the above study and have had the opportunity to consider the information and ask questions and had these answered satisfactorily.	
2	I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving a reason and without detriment to myself. I understand that it will not be possible to remove my data from the project once it has been anonymised and forms part of the data set. I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals delivering this study, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	
3	I agree to have blood and urine sample taken for the research purpose as explained to me. I agree that these samples will be stored for a maximum of two years after the study finishes for use in further research and this will be done in an anonymised way.	

4	I understand that the information collected about me will be used to support other research in the future and may be shared anonymously with other researchers.	
5	I agree that any data collected may be published in anonymous form in academic books, reports or journals.	
6	I agree that the researchers/researchers at other institutions may contact me in future about other research projects. This is optional.	
7	I agree that the researchers may retain my contact details in order to provide me with a summary of the findings for this study.	
8	I agree to the audio recording of the end of study interview. The recording will be used to transcribe the discussion and will then be deleted.	
9	I agree to take part in this study	

Data Protection

The personal information we collect and use to conduct this research will be processed in accordance with data protection law as explained in the Participant Information Sheet and the Privacy Notice for Research Participants (http://documents.manchester.ac.uk/display.aspx?DocID=37095**.**

_____	_____	_____
Name of Participant	Signature	Date
_____	_____	_____
Name of the person taking consent	Signature	Date

1 copy for the participant
1 copy for the research team (original)
1 copy for the medical notes

14.4 Participant Information Sheet and Consent Form (Part B)

You are being invited to take part in a research study which is investigating if we can improve monitoring of people's kidney function during cancer treatment. This work will be part of a project for a post-graduate degree. Before you decide whether to take part, it is important for you to understand why the research is being conducted and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Please ask if there is anything that is not clear or if you would like more information. Take time to decide whether you wish to take part. Thank you for taking the time to read this.

Who will conduct the research?
The research team for this study are from the Digital Experimental Cancer Research Team (Digital ECMT), who work within the University of Manchester and Cancer Research UK (Manchester Institute). The study will be led by Dr Leanne Ogden and she will work with a team of people to help organise and run the study. The work is being conducted under the supervision of Professor Sandip Mitra and will be supported by a team of experts to ensure all aspects of the trial are run to correct standards. Different members of the team have different roles and it is likely that you will only meet a couple of these people whilst you are on the study.
Within the University of Manchester there are several divisions and responsibility for this study lies within the Faculty of Biology, Medicine and Health (Division of Cardiovascular Studies):
Core Technology Facility
46 Grafton Street
Manchester
M13 9NT

What is the purpose of the research?
People with partly-working kidneys often don't get the choice of taking part in cancer trials because of worries over damaging their kidneys further. This means that there are fewer treatment options for people who have both cancer and kidney disease.

We want to understand whether people monitoring their kidneys at home using a blood test that works on a single drop of blood could help with this. If so, then this may eventually allow patients with partly-working kidneys to take part in cancer trials to improve treatment options in the future.
Why have I been chosen?
We are looking for people to take part who are going to be having cancer treatments that could potentially affect their kidneys. You have been provided with this information sheet to give you more information.
What would I be asked to do if I took part?
There are 2 parts to this study (Part A and Part B). This information sheet refers to Part B of the study.
A member of the research team will arrange to come to your routine appointments to see you. The first meeting we will train you in how to use the device/creatinine meter and take a blood sample. This is likely to take between 30 minutes and an hour, but it doesn't matter if it's shorter or longer – whatever you need to feel comfortable with the approach. We will also take your blood pressure and collect a urine and blood sample from you during the same appointment. We would also like you to complete a short (5-10 minute) quality of life questionnaire.
Then on Mondays, Wednesdays and Friday mornings for 6 weeks we would like you to check how your kidneys are working with the meter provided in the comfort of your own home. This involves you taking a drop of blood using a standard finger-pricker (a sharp) and then using the meter to check for creatinine (a marker of how well your kidneys are working) as shown. This means that you will prick your finger a total of 18 times over the 6-week period. The result on the meter needs to be sent using the app provided on your smart phone. You will have been trained on how to do this at the start. This app has been designed for securely sending information. This blood is not stored or used in any other way and you will throw it away in special bins we will provide to you.

After about a week, a member of the research team will give you a quick phone call to see how things are going and give you a chance to ask any additional questions you may have.

We will see you in person for a second time 3 weeks later. You will have your blood pressure checked and a blood and urine sample taken again.
We will see you for a third and final time in person at the end of the 6-week study. We will take your blood pressure, blood and urine samples once again. At this point please return all equipment that you have been loaned and we will help you to delete the app off your phone. A member of the research team will have an informal chat with you so we can learn from you how you think everything has gone (15-20 minutes), ask you to complete a short questionnaire (10 minutes) and repeat the quality of life questionnaire. The readings will also be downloaded from the meter and if you'd like a copy of these please ask – we can provide you with these in a secure way. To help with our note-taking (so we don't miss valuable feedback) we would like to make an audio-recording of our informal chat. Afterwards this will be transcribed – any information that is personal to you will not be included in this transcription, the only identifier remaining will be the code used for you during the trial. The audio-recording itself will be permanently deleted after the transcription has been made. This recording will be deleted within 4 weeks of the study ending.
Both times we see you it will be planned so that this happens while you are already in hospital for your usual visits.
After taking part in this trial you will continue with the standard monitoring of kidney function and cancer treatment as you will have discussed with your medical team.

What are the extra samples for?

We would like to collect an extra blood (10mls) and urine sample (50mls) when you come to the hospital for your planned appointments this is to look for new markers of kidney damage. For Part B of the study we will collect the urine and blood samples during your visit to hospital in Weeks 1, 3 and 6 of the trial. Samples will be collected by a member of the research team and will be labelled with a code unique to you. The sample will be transported to a laboratory to be analysed and will be stored in a special storage facility at Manchester Royal Infirmary. There will be no DNA analysis in this study. As these samples are being analysed to try and find new markers that could potentially improve the detection of kidney damage in the future, their usefulness now will not have been proven. The aim is to find them so that they can be researched. As such, your GP or team at the hospital will not receive any results of these tests as not enough will be known about them to be help your personal care at the moment.
We would like to keep the samples for a maximum of 2 years from the end of the study. We may use the samples for solely for the purpose of further health care research. If the samples are used for further research, they will not identify you, and will not be combined with other information in a way that could identify you. In addition, no information gleaned from future research with these samples will be used to contact you, affect your care, or affect future services available to you. Once the 2-year period has been reached, the samples will be destroyed in accordance with the laboratory's usual procedures.

What are the potential benefits of taking part?

- **Yourself:** None.

- **Other patients:** We hope this research is the beginning of improving people's treatment options for people who have both cancer and kidney disease.

What are the potential risks of taking part?

Risks around security of personal information have been minimised by building the system with data security and privacy at its core (this is also discussed later).

To send your creatinine reading to us, what it will cost you depends on your service-provider. If you have an unlimited data plan on your phone, or are connected to a Wi-Fi network, there should be no cost for sending a message. However, they may charge you for using 3G or 4G if you don't have such a data plan, and especially if you're travelling abroad. Costs can be minimised by sending your measurements when on Wi-Fi and checking your data allowances before you travel abroad.

We will give you a sharps bin to dispose of your sharp to reduce the risk of you or anyone else hurting themselves on the sharp and we will teach you how to use it. The sharp that pricks the skin is protected inside a plastic case to help prevent accidental damage. You will be trained how to use this.

Using the finger-pricker (sharp) will possibly cause some discomfort or pain around the immediate area. It may leave you with a small bruise.

What will happen to my personal information?

In order to undertake the research project, we will need to collect the following personal information/data about you:

- Name
- Date of birth
- Past medical history and previous operations
- Information regarding your cancer diagnosis and treatment plan
- Medication history
- Hospital admission details when you are on the study
- Kidney function before entry to and during the study
- Your blood pressure, urine and blood samples collected whilst in hospital (as described previously)
- Your responses to questionnaires, as well as audio recording of our informal chat (also described previously).

We are collecting and storing this personal information in accordance with the General Data Protection Regulation (GDPR) and Data Protection Act 2018 which legislate to protect your personal information. The legal basis upon which we are using your personal information is "public interest task" and "for research purposes" if sensitive information is collected. For more information about the way we process your personal information and comply with data protection law please see our Privacy Notice for Research Participants (http://documents.manchester.ac.uk/display.aspx?DocID=37095)

The University of Manchester, as Data Controller for this project, takes responsibility for the protection of the personal information that this study is collecting about you. In order to comply with the legal obligations to protect your personal data the University has safeguards in place such as policies and procedures. All researchers are appropriately trained, and your data will be looked after in the following way:

- Data will be stored securely using your unique code. This is described further in the section 'How secure is it?' on the next page.
- Physical workbooks will be stored in a secure office in The Christie Hospital and will not be removed from the hospital site.

If you agree to take part in the study, you will be given a unique code that is used to represent you instead of your name or hospital number. Once this is done, any information that you send in or give to us will be linked to this code rather than any information that could identify you.

The research team at the University of Manchester will have access to your personal identifiable information, that is data which could identify you, but your unique code will be used as soon as possible. However, your consent form, contact details and work book will be retained for 5 years at The Christie Hospital in a secure location within the research department.

The app used to send your creatinine reading to us from home does not store data, it simply sends us the reading.

How secure is it?

As with all systems, there are two aspects to consider for security: The technical system itself and the conduct of those that are using it.

- **The secure cloud environment**
    - The whole system has been created with highest levels of security (equivalent to banking). The system has undergone extensive security testing, including having people try to hack into it. This testing will continue and if anything is identified it will be remedied. In the unlikely event that there is a data breach, we will let you know and close the system temporarily rather than risk your information.
- **The people using it:**
    - The analysts and researchers are bound by an ethical code of conduct to behave responsibly, treat your data with respect, and protect any information that you may share.
    - When you send in a reading it will be stored in a secure environment. The device you use to check your kidney function will 'remember' a certain number of readings therefore if someone was able to use the device, they could potentially see your readings, but the device has no information that would link the readings back to you. We would recommend you keep your device somewhere safe at home when you are not using it. When you come in to hospital for your last visit with us we will download all the readings and delete them from the device.

You have several rights under data protection law regarding your personal information. For example, you can request a copy of the information we hold about you, including audio recordings. This is known as a Subject Access Request. If you would like to know more about your different rights, please consult our privacy notice for research

(http://documents.manchester.ac.uk/display.aspx?DocID=37095) and if you wish to contact us about your data protection rights, please email dataprotection@manchester.ac.uk or write to The Information Governance Office, Christie Building, University of Manchester, Oxford Road, M13 9PL. at the University and we will guide you through the process of exercising your rights.

You also have a right to complain to the Information Commissioner's Office (https://ico.org.uk/make-a-complaint/), Tel 0303 123 1113

Who will see my information?

Your participation in the study will be kept confidential to the study team and those with access to your personal information as listed in this section.

The team looking after you at the hospital will know you are taking part in the study and members of the team will have access to your personal information and results.

Individuals from the University, the site where the research is taking place and regulatory and NHS authorities (Health Research Authority - HRA) may need to review the study information for auditing and monitoring purposes or in the event of an incident.

In some extreme circumstances, we may need to inform other organisations of your enrolment in the study. The following are examples of such circumstances:

- If there are concerns about your safety or the safety of others, we may need to contact your GP or a family member
- Reporting of current/future illegal activities to the authorities
- In the event of incidental or unexpected findings that could have implications for your health or may need further investigation we may need to inform your GP and care team

What happens if I do not want to take part or if I change my mind?

It is up to you to decide whether to take part. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. You will still be free to withdraw at any time without giving a reason and without detriment to yourself. However, it will not be possible to remove your data from the project once it has been anonymised and forms part of the dataset as we will not be able to identify which specific bit came from you. This does not affect your data protection rights.

If you do not wish to be recorded during our informal chat at the end of the study, we can carry out the discussion without the audio recorder – please just tell the member of the research team on the day. Recording can also be stopped at any time if you do not feel comfortable.

Will my data be used for future research?

When you agree to take part in a research study, the information about you may be provided to researchers running other research studies in this organisation. The future research would be related to kidney disease or cancer. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research (https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/).

This information will not identify you and will not be combined with other information in a way that could identify you. The information will only be used for the purpose of health and care research and

cannot be used to contact you regarding any other matter or to affect your care. It will not be used to make decisions about future services available to you.

Will I be paid for participating in the research?

You will not be paid for taking part in this research. You will be provided with the equipment needed to take part in the study, but you will need to use your own smart phone and Wi-Fi/3G/4G data.

What is the duration of the research?

Part A of the study takes place over 4 weeks. Part B of the study takes place over 6 weeks.

Where will the research be conducted?

The Christie Hospital, we will come to your treatment area.

Will the outcomes of the research be published?

The results of analyses will be published in scientific literature and journals so that others can also learn and help to improve research in this area. At no time will anything be published that can identify you personally.

Who has reviewed the research project?

This research has been reviewed and approved by a research ethics committee within the UK Health Departments' Research Ethics Service, and the Health Research Authority.

What if I want to make a complaint?

Minor complaints

If you have a minor complaint, then you need to contact the research team in the first instance. If you would like to complain about any aspect of the study please contact the research team at leanne.ogden@digitalecmt.org and the lead investigator will contact you to discuss the issues further.

Alternatively, you can contact Professor Sandip Mitra, Consultant Nephrologist (Manchester Royal Infirmary) or the University of Manchester. He can be contacted through the MRI switchboard 0161 276 1234.

Formal Complaints

If you wish to make a formal complaint or if you are not satisfied with the response you have gained from the researchers in the first instance, then please contact:

The Research Governance and Integrity Manager, Research Office, Christie Building, University of Manchester, Oxford Road, Manchester, M13 9PL, by emailing: research.complaints@manchester.ac.uk or by telephoning 0161 275 2674.

Indemnity Arrangements

The University of Manchester has arranged insurance for research involving human subjects that provided cover for legal liabilities arising from it actions or those of its staff or supervised students, subject to policy terms and conditions. This covers both the design and management of the study.

What Do I Do Now?

If you have any queries about the study or if you are interested in taking part, then please contact the research team**:**

Support@digitalecmt.org
Leanne.ogden@digitalecmt.org

0161 918 2374
This research has been reviewed and approved by a research ethics committee within the UK Health Departments' Research Ethics Service, and the Health Research Authority.

Consent Form – Part B

Name:

Name of Researcher:

If you are happy to participate please complete and sign the consent form below

	Activities	Initials
1	I confirm that I have read the attached information sheet (version 4.0, 01/04/2019) for the above study and have had the opportunity to consider the information and ask questions and had these answered satisfactorily.	
2	I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving a reason and without detriment to myself. I understand that it will not be possible to remove my data from the project once it has been anonymised and forms part of the data set. I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals delivering this study, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	
3	I agree to have blood and urine sample taken for the research purpose as explained to me. I agree that these samples will be stored for a maximum of two years after the study finishes for use in further research and this will be done in an anonymised way.	
4	I understand that the information collected about me will be used to support other research in the future and may be shared anonymously with other researchers.	
5	I agree that any data collected may be published in anonymous form in academic books, reports or journals.	
6	I agree that the researchers/researchers at other institutions may contact me in future about other research projects. This is optional.	
7	I agree that the researchers may retain my contact details in order to provide me with a summary of the findings for this study.	
8	I agree to the audio recording of the end of study interview. The recording will be used to transcribe the discussion and will then be deleted.	

9	I agree to take part in this study	

Data Protection

The personal information we collect and use to conduct this research will be processed in accordance with data protection law as explained in the Participant Information Sheet and the Privacy Notice for Research Participants (http://documents.manchester.ac.uk/display.aspx?DocID=37095**.**

_____	_____	_____
Name of Participant	Signature	Date
_____	_____	_____
Name of the person taking consent	Signature	Date

1 copy for the participant
1 copy for the research team (original)
1 copy for the medical notes

14.5 Data Management Plan

Home Monitoring of Creatinine in Cancer Patients: Assessing Acceptability and Clinical Benefit

0. Proposal name
Home Monitoring of Creatinine in Cancer Patients: Assessing Acceptability and Clinical Benefit
1. Description of the data
1.1 Type of study Single centre, randomised clinical trial to assess the acceptability and clinical benefit of home monitoring of creatinine by cancer patients **1.2 Types of data** Quantitative data - creatinine results from home-based device and laboratory results; urine dipstick and protein creatinine ratio; blood pressure; weight; medications. Qualitative data – Participant and clinician questionnaire and interview **1.3 Format and scale of the data** Approximately 20 creatinine readings per study participant captured in encrypted electronic form. Baseline data capture in paper workbook and consolidated into excel workbook Participant feedback from paper-based questionnaires. Approximately 72 participants to be recruited (30 will be randomised in to the non-device group therefore will not be sending in creatinine readings)

2. Data collection / generation

2.1 Methodologies for data collection / generation

atinine measurements will be collected by study participants using a point of care creatinine device in r home. These measurements will be transferred to a secure Microsoft Azure environment.
er data capture in paper workbook and consolidated into excel workbook

2.2 Data quality and standards

icipant measured creatinine readings will be compared with the data downloaded directly from the t of care analyser to assess the accuracy of reporting. each device will be calibrated by the study icipant prior to use and has been calibrated with the hospital laboratory.

3. Data management, documentation and curation

3.1 Managing, storing and curating data.

obile application will be used to capture creatinine readings from a point of care device to storage in rosoft Azure environment. These data files are backed up and data is retained or the duration of the ly.

3.2 Metadata standards and data documentation

aim of the study is to publish the results of the study, this would include summary data

3.3 Data preservation strategy and standards

nymised data will be archived with associated meta data

4. Data security and confidentiality of potentially disclosive information

4.1 Formal information/data security standards

Digital Experimental Cancer Medicines Team have an information security policy that will be wed.

4.2 Main risks to data security

Data Collection:

Participant identification from collected data - the unique participant ID used in the study is pseudonymised and no identifiable data is collected. Likelihood of risk occurring is low
Participant identification by the creatinine images sent in if they contain personal identifiable information in error - all images will be reviewed by the study team and any image that is at risk of identify the patient will be deleted. Patients will receive training on how to use the app and specifically how to take an image of the creatine device. Likelihood of risk occurring is low

Data Access:

Data is transmitted and stored in encrypted form. Access to the data is controlled and can only be authorised by the study data manager.

5. Data sharing and access

5.1 Suitability for sharing

The purpose of this research and the consent obtained extends only to establishing that the device can be used effectively for home-based creatine readings. Data will be pseudonymised during the study. At the end of the study the data will be anonymised to enable data sharing and protection of patient privacy.

5.2 Discovery by potential users of the research data

The results of the work will be published in Open Access journals

5.3 Governance of access

The Sponsor is the Data Controller and makes all decisions on data sharing

5.4 The study team's exclusive use of the data

There is no exclusivity by the study team over this data. Requests for sharing within the participant consent agreement will be considered by the Sponsor

5.5 Restrictions or delays to sharing, with planned actions to limit such restrictions

Requests for sharing within the patient consent agreement will be considered by the Sponsor

5.6 Regulation of responsibilities of users

Access will be considered for external users to anonymized data under a data agreement that ensures compliance with the original patient consent agreements

6. Responsibilities
The Sponsor is accountable for the information in this study. The Sponsor may delegate information control responsibility to the Chief Investigator
7. Relevant institutional, departmental or study policies on data sharing and data security
PolicyURL or Reference
Data Protection PolicyThe University of Manchester Data Protection Policy
8. Author of this Data Management Plan (Name) and, if different to that of the Principal Investigator, their **telephone & email contact details**
Paul Fitzpatrick Paul.fitzpatrick@digitalecmt.org

14.6 Participant Booklet

Getting help

If you have problems with the test kit, app, or answering the questions please get in touch so that we can help. To do this either:

- Pop in to see us next time you're in hospital. We're in the new bit of the clinical trials unit. Go up ramp next to reception, turn right, we're next to the mosaic.
- Contact support: support@digitalECMT.org. This email is checked 9-5 throughout the working week.

The Christie Hotline

It is essential that you continue to contact your medical team as normal if you have any concerns about your health.

If you feel unwell, do not delay, call the Christie Hotline Immediately

0161 446 3658

Thank you

Kidney monitoring research

How to take a reading at home

What we're doing

People with partly-working kidneys often don't get the choice of taking part in cancer trials because of worries over damaging their kidneys further. This means that there are fewer treatment options for people who have both cancer and kidney disease.

We want to understand whether people monitoring their kidneys at home via a simple blood test could help with this. Can it improve the understanding of what's happening with their kidneys and support they're given? If so, then this may eventually allow patients with partly-working kidneys to take part in cancer trials to improve treatment options of the future?

What you'll be asked to do

On Mondays, Wednesdays and Friday mornings for the next 8 weeks we would like you to check your kidneys by taking a 'creatinine reading' with the meter provided. Then send us the result using an app on your smart phone (designed for securely sending information). We'd also like to hear your feedback on the whole process at set points throughout the 8 weeks and through an informal interview at the end of the study.

This booklet aims to walk you through the use of the kidney monitoring kit and how to send your information in.

First: Testing the device itself

Digital Experimental Cancer Medicine Team

Take the test strips and bottles out of the fridge so that they are at room temperature before starting. Then wash your hands.

Step A: Put a new test strip in your meter. Press the left and right buttons until the screen says C1 as shown.

Step B: Shake the C1 (green) bottle. Discard the first drop into a tissue then put the next drop onto the top of the lid or a clean surface. Touch the strip onto the drop and wait for the beep. The meter will count 30 seconds then display a reading. You don't need to send this in, just bring the meter with you at your next hospital visit and they'll download it there.

Step C: Eject the used strip using the button on the side put it in the yellow bin provided.

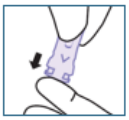
Step D: Repeat Steps A-C with the C3 (Red) bottle, and pressing the buttons until the screen says C3 this time.

Second: Taking your reading

Digital Experimental Cancer Medicine Team

After testing the device, you need to then take your own reading.

Step 1: Insert a new test strip in to device. A blood drop symbol will appear on the screen.



Step 2: Rub your hands together to help blood flow. Then put the finger-pricker onto your finger and press down the end. A blood drop will form.

Step 3: Touch the end of the strip to the top of the blood drop. The blood will be 'sucked up' and the device will beep when it's got enough. Again, the meter counts 30 seconds and your result is shown.

Step 4: Open the app on your phone and add a picture of the result, enter the date and also type in your result value. Press 'Submit' to send the results in; you will receive confirmation when it has been successfully sent.

Step 5: Eject the test strip and put it in the yellow bin, along with the used finger-pricker. Clean up and put unused test strips, along with the bottles, back in the fridge.

14.7 Frequently Asked Questions – for study participants

FAQs

Why am I checking my creatinine?

Everybody has creatinine in their blood and it's usually at a fairly constant level. It's formed through the normal process of your body looking after itself. Without you ever knowing it's happening, every day your body keeps your muscles working properly by quietly replacing older muscle cells with new ones. Creatinine is formed as these older cells are cleaned up. Your kidneys sieve this out (getting rid of it in your urine when you go to the toilet) and maintain a level in your blood that's pretty level for you. If your kidneys are not working normally, then they can't sieve as well as they should and the amount of creatinine in your blood goes up. It is the main way that doctors currently monitor how well your kidneys are working. Having a higher than expected level can suggest that there has been some damage to your kidneys but doesn't cause you any harm.

This monitoring is especially important when taking certain medicines. Some anti-cancer drugs can affect the way the kidneys work and therefore, logically, improving the way that creatinine is checked, should help doctors improve the way that they can support you. However, no one has tested yet whether people checking their creatinine more frequently in the comfort of their own home and sending the results in makes a difference. As part of this study we want to see if checking kidney

function at home is possible, learn the best way to do this, and understand whether it is a useful way of monitoring kidney function during cancer treatments.

What is a normal level?

Not everyone's creatinine reading is the same. It can be affected by many things such as age, gender, race and muscle mass. The best way to find out what your normal level is, is to talk to your doctor and find out what your results are saying.

How long do the test strips and bottles need to be out of the fridge for before they are used?

The test strips and bottles need to be at room temperature, so about half an hour should be fine. Remember to put them back in the fridge once you have done your test for the day.

What happens if I break a test strip?

The strips are quite difficult to break so it's unlikely that you will. Keep them stored in the pot they came in with the lid closed when you're not using them. As long as individual test strips are not left in a puddle of water, they should be fine. If you think you have broken one, then discard that one and pick a fresh one from the pot.

Why do I have to test the liquids in the bottles each time?

The liquids in the bottles provided are used to check that your machine is working properly. The liquids in them have known amounts of creatinine in and so should give roughly 'standard' results. You don't need to do anything with these results, but make sure you measure them before you test your own blood each time, and they'll be stored in the machine's memory. When you bring your machine into hospital for the scheduled visit, the study team will download them and store them alongside the rest of the information. This tells us two main things:

- Whether the machine is working properly when used at home. This is a key thing for us to learn early in the trial, while we're assessing whether reliable home monitoring is possible.
- Giving context to your own results. For example, if your result goes down – it may be that the level of creatinine in your blood has gone down, or, it may be that the machine is 'measuring lighter' – checking whether the readings from the bottles have also changed will help us to figure this out.

Why don't I have to send in results from the bottles?
As the results from the bottles are only checking that your machine is working properly and giving context, sending these in each time is not needed. It's going to be quicker and easier to just hand over the machine when you're in hospital and someone can download all of them in one go.

What if the blood result or either of the calibration results are different to expected?
If your blood result is not what you expect, for example its very different to the reading you got the last time you checked, then the first thing to do is to repeat your sample with a new strip and a new sample of blood. If this remains different please contact your hospital team as you normally do if you feel unwell.

What number is expected?
Everyone's creatinine result will be slightly different depending on your age, sex, race, muscle mass and even what you have eaten. When you start the study, we will give you an idea of what your baseline kidney function is. This will vary day to day, and it is completely normal for some variation in the results. Most people will have results between 60 and 120.

What do I do if the device screen goes blank?

The device times out after a minute, putting in a test strip or pressing a button on the device will wake it up again.

There is an error code on the device – what do I do?
If this happens please have a look in the device info leaflet. If this doesn't give you the answer, please let us know on the contact details provided. You do not need to change the battery of your device. If you have concerns with how your device is working, please contact us on **support@digitalecmt.org.**

Why are the readings being checked Monday/Wednesday/Friday?
Ideally the home tests would be done every 2 days, however, people are only in the hospital to review them Monday to Friday. Therefore, for purely practical reasons, we chose to do the readings Monday, Wednesday, and Friday each week rather than asking people to do more.

What do I do if I lose or break my phone? What if the battery dies when I have taken a reading?
If you lose or break your phone, then let us know when you are able to. If you have taken a reading and your battery dies, please send us the reading as soon as you can when your phone is up and running again (even if it's just the number value and you didn't manage to get a photo of the reading at the same time).

I've missed a reading – what do I do?
If you miss a reading or can't do one on a particular day for whatever reason (e.g. travelling) please take a reading as soon as you can and send it in the normal way then go back to the usual schedule afterwards (Monday/Wednesday/Friday). The reading will still be very useful for us. If you don't have very good network and can't send a reading in, then just try again later or the next day. You will receive confirmation when you're reading has been successfully sent, if you have not received this, please try again.

How often would they be reviewed by staff?
A member of the study team will check the results once a week. We will not contact you about the readings during the study. If you feel unwell or are concerned in any way you should contact your team at the Christie/GP in the normal way.

What do I do if I can't get a sample of blood with the lancet?
It is a good idea to make sure your hands are warm (e.g. by running under warm water or rubbing your hands together) before you try and get a blood sample. Once you have used the lancet, try not to squeeze your finger too much. You might need to try another finger if you're struggling.

My device is different to that in the video, how do I get access to the app?
A member of the team will show you this when you learn to use the device. If you need any help after this, please don't hesitate to contact us.

Help/support number
Problems with the app or device – support@digitalecmt.org
Concerns with health/treatment/reading – 0161 446 3658

14.8 Interview Guide

Interview Guide

1. What are your overall impressions of the study?
2. What did you think of the device? Calibration?
3. How could the device be improved?
4. What did you think of the app?
5. How could the app be improved?
6. Did you feel that the testing was too frequent?
7. Did the testing become part of your routine or was it a chore?
8. What did you think of the readings? Did you trust the results? Worry about the results?
9. Any other feedback you would like to give?

14.9 SAE Reporting Form

REPORT OF SERIOUS ADVERSE EVENT (SAE)

(For all studies except clinical trials of investigational medicinal products)

The Chief Investigator should report any SAE that is both related to the research procedures and is unexpected. Send the report to the Research Ethics Committee that gave a favourable opinion of the research within 15 days of the CI becoming aware of the event.

1. Details of Chief Investigator

Name:	
Address:	
Telephone:	
Email:	
Fax:	

2. Details of study

Full title of study:	
Name of main REC:	
Main REC reference number:	
Research sponsor:	
Sponsor's reference for this report: (if applicable)	

3. Type of event
Please categorise this event, ticking all appropriate options:

Death ☐	Life threatening ☐	Hospitalisation or prolongation of existing hospitalization ☐
Persistent or significant disability or incapacity ☐	Congenital anomaly or birth defect ☐	Other ☐

4. Circumstances of event

Date of SAE:	
Location:	
Describe the circumstances of the event: *(Attach copy of detailed report if necessary)*	
What is your assessment of the implications, if any, for the safety of study participants and how will these be addressed?	

5. Declaration

Signature of Chief Investigator:	
Print name:	
Date of submission:	

6. Acknowledgement of receipt by main REC (please insert name):

The [ ] Research Ethics Committee acknowledges receipt of the above.

Signed:	
Name:	
Position on REC:	
Date:	

Signed original to be sent back to Chief Investigator (or other person submitting report)

Copy to be kept for information by main REC.