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The Suspected CANcer (SCAN) pathway: protocol for evaluating a new standard of care for patients with non-specific symptoms of cancer.

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ABSTRACT

Introduction: Cancer survival in England lags behind most European countries, due partly to lower rates of early stage diagnosis. We report the protocol for the evaluation of a multidisciplinary diagnostic centre based pathway for the investigation of 'low risk but not no risk' cancer symptoms called the Suspected CANcer (SCAN) pathway. SCAN is a new standard of care being implemented in Oxfordshire; one of a number of pathways implemented during the second wave of the ACE programme, an initiative which aims to improve England's cancer survival rates through establishing effective routes to early diagnosis.

Methods and analysis: To evaluate SCAN, we are collating a prospective database of patients referred onto the pathway by their GP. Patients aged over 40 years, with non-specific symptoms such as weight loss or fatigue, who do not meet urgent cancer referral criteria or for whom symptom causation remains unclear after investigation via other existing pathways, can be referred to SCAN. SCAN provides rapid CT scanning, laboratory testing, and clinic review within 2 weeks. We will follow all patients in the primary and secondary care record for at least two years. The data will be used to understand the diagnostic yield of the SCAN pathway in the short term (28 days) and the long term (2 years). Routinely collected primary and secondary care data from patients not referred to SCAN but with similar symptoms, will also be used to evaluate SCAN. We will map the routes to diagnosis for patients referred to SCAN to assess cost-effectiveness. Patient acceptability will be evaluated using a patient survey.

Ethics and dissemination: The Oxford Joint Research Office Study Classification Group has judged this to be a service evaluation and so outside of research governance. The results of this project will be disseminated by peer reviewed publication and presentation at conferences.

Strengths and limitations of this study:

- SCAN will be evaluated in relation to diagnostic yield, time to diagnosis, cost effectiveness, patient satisfaction, and incidental diagnoses.
- Data from both the primary and secondary care record will be used to populate a bespoke database including all patients referred to SCAN.
- SCAN will be evaluated against the previous standard of care in the same region, operated by the same CCG.
- The outcomes of this evaluation will only indicate SCAN's effectiveness in Oxfordshire and should not be generalised to the rest of England.

BACKGROUND

England's rates of cancer survival lag behind many other European countries, and late stage at diagnosis is thought to play a large part in this.(1, 2) It is estimated that, if diagnosed at early stage, 5000 cancer deaths could be prevented every year for breast, colorectal, and lung cancers alone.(2, 3) Twenty-one percent of cancers are diagnosed as an emergency, which is associated with advanced tumour stage and increased short term mortality.(4, 5) The ACE (Accelerate, Coordinate & Evaluate) Programme is an early diagnosis initiative supported by NHS England, Cancer Research UK (CRUK), and Macmillan Cancer Support. It was formed to help improve England's cancer survival rates by generating evidence on how best to configure diagnostic pathways to drive a shift from late to early cancer at diagnosis, reduce the number of cancers diagnosed as an emergency, and improve patient experience. The first wave of ACE comprised around 60 projects aiming to evaluate local initiatives to develop a national body of evidence to inform cancer commissioning.

A weakness in the current system identified during Wave 1 was the lack of a clear urgent referral pathway for patients with non-specific but concerning symptoms of cancer, such as fatigue, abdominal pain, and weight loss, known to be associated with a range of cancer sites. Anecdotally, these patients are referred for multiple (sometimes inappropriate) tests and "fall through the gaps" between existing urgent referral pathways for site specific "red flag" symptoms, such as rectal bleeding or dysphagia, resulting in delays in diagnosis. The Independent Cancer Taskforce's strategy recommendations outlined the need to explore new models of care to speed up diagnosis making references to the multidisciplinary diagnostic centre (MDC) concept.(6) The MDC is a medical unit with access to a broad range of diagnostic investigations and specialist expertise in managing this patient group. ACE Wave 2 was set up to facilitate the development of a small number MDC based pathways in England to understand the effectiveness of the MDC concept in the NHS context. These pathways are implemented as standards of care in participating regions, in addition to the already existing urgent referral pathways.

Oxfordshire's Suspected CANcer (SCAN) pathway emulates the Danish MDC pathway, the Non-Specific Symptoms and Signs of Cancer Patient Pathway (NSSC-CPP).(7) Patients referred to the NSSC-CPP first receive a battery of diagnostic investigations including blood and urine tests and diagnostic imaging. If no diagnosis is made on the results of these tests but cancer or other serious disease is still suspected the patient is referred to an MDC.(7, 8) Of 1,278 patients referred to the NSSC-CPP pathway by their General Practitioners (GPs), 16% of patients were diagnosed with a cancer.(9) The most common symptoms recorded were weight loss (53%), fatigue (50%), and pain (37%). The most common clinical findings were "affected general condition" (36%), GP "gut feeling" (23%), and abnormal abdominal examination (13%). Forty-eight percent of patients were referred with abnormal blood test results. Cancer was diagnosed across a broad range of 18 subgroups, the most common of which were lung (18%), colorectal (13%), haematological (10%), pancreatic (9%), and upper-gastrointestinal (8.2%).(9)

We report here the protocol for the evaluation of the SCAN pathway.

Aim

To evaluate the SCAN pathway, a new standard of care for the rapid investigation of patients with non-specific cancer symptoms in Oxfordshire.

Objectives

In line with the CRUK ACE initiative, the objectives of the SCAN pathway are to:

- Reduce time from initial primary care presentation with symptoms to diagnosis.
- Achieve a higher proportion of early stage cancer at diagnosis.

- Improve patient experience of the diagnostic pathway.
- Establish whether the MDC model is cost-effective.

SETTING

Oxfordshire's cancer incidence (600 cases per 100,000) is lower than the UK average (615 cases per 100,000). Cancer mortality (261 per 100,000) is also lower than the national average.(10) Comprising a predominantly white (90.85%) population, Oxfordshire has smaller foci of Asian (4.84%), Black (1.75%), and mixed ethnic (2.02%) groups. Black and minority ethnic (BME) communities form 22.4% of Oxford City's population, with lower proportions in more rural districts: 7.8% in Cherwell, 3.2% in West Oxfordshire (Source: 2011 Census (11)). Rural districts (67%) rank in the 10% least deprived, and urban (33%) in the 20% most deprived in England. There are no ACE Wave 1 sites in Oxfordshire.

Oxfordshire Clinical Commissioning Group (CCG) serves a population of over 700,000 through 70 General Practices.(12) Oxford University Hospitals NHS Foundation Trust (OUHFT) is made up of four hospitals providing a range of specialist services (John Radcliffe, Churchill Hospital, Nuffield Orthopaedic Centre, and the Horton General Hospital). SCAN imaging takes place at the Churchill Hospital and the SCAN MDC is located at the John Radcliffe Hospital. SCAN links with the Oxford Allied Health Science Network (AHSN) Imaging Network, aiming to develop a model for expansion through the seven adjoining NHS network trusts.

THE SCAN PATHWAY

SCAN retains the GP's gate-keeping role, requiring patients to first attend their GP with symptoms to access the pathway through GP referral.(13) The SCAN referral algorithm was developed by consensus between a multidisciplinary team including GPs, Radiologists, physicians, and health service researchers (Appendix 1). It incorporates age-thresholds and "low-risk but not no-risk" symptoms that fall outside of existing urgent 2-week-wait (2ww) referral pathways based on the National Institute of Care Excellence (NICE) suspected cancer guidelines, but remain at risk of cancer. SCAN was adopted by OUHFT as a standard of care for eligible patients in Oxfordshire on 15th March 2017. To assess demand, SCAN will be opened up to GPs in each of the six regions of Oxfordshire CCG sequentially dependent on uptake.

Referral criteria

A structured standardised electronic referral form has been disseminated to all GPs in Oxfordshire (Appendix 2). If there is no other urgent referral pathway for the clinical scenario, patients aged ≥40 years of age are accepted if their GP is concerned about cancer or serious disease following face-to-face primary care assessment of individual or combined "low-risk but not no-risk" symptoms, such as: weight loss, appetite loss, nausea, fatigue, malaise, abdominal pain, anaemia and thrombocytopenia. In addition patients may be referred based on their GPs clinical suspicion of cancer or serious disease (their "gut feeling").(14, 15) GPs are also requested to indicate their suspicion of malignancy at this stage (Table 1).

Table 1. SCAN referral criteria.

Essential	**There is no other urgent referral pathway suitable for this clinical scenario**
Essential	**≥40 years of age**

Essential *Tick all that still apply* ***after primary care assessment***	**Unexplained Weight Loss**	Measured Patient Reported	☐ ☐	Kg loss	___ kg	Duration ____ weeks
	Severe unexplained fatigue	TSH (within 1m)	_____ miu/L			
	Persistent nausea or appetite loss					
	New atypical pain (eg. diffuse abdominal or bone pain).	Site?	_____			
	Unexplained laboratory test findings (eg. anaemia, thrombocytopaenia, hypercalcaemia)		Please specify			_____
	GP Clinical Suspicion of cancer or serious disease / GP "gut feeling"					

Stages of the pathway

As part of their initial work-up to exclude more common causes of non-specific symptoms in primary care, GPs will conduct investigations essential to allow access to the SCAN pathway: creatinine (necessary prior to IV contrast) and thyroid function tests (hypothyroidism as a cause of fatigue). Once referred, a member of the SCAN team (the SCAN pathway navigator) assumes clinical responsibility for the patient, confirms that the patient meets the inclusion criteria, and provides a point of contact for the patient. Demographic and clinical information are captured by the GP referral form.

Consent: At the point of referral, patients are given a participant information sheet detailing the SCAN pathway and consent form (Online Supplementary Material 1) to allow their anonymised medical records to be used for the purposes of evaluating the pathway. Patients are given time to take the information away and consider whether they wish to participate. If patients decide to participate, they are asked to take the consent form to the initial appointment, at which time they may ask any outstanding questions. Patients who do not wish to have their medical records used may still be referred onto the SCAN pathway.

Stage 1: GP direct access triage tests: At the first appointment, a battery of standard diagnostic investigations with rapid turnaround (request-test-report) of <7 days are performed. These tests include a panel of blood tests, faecal immunochemical testing, and appropriate low-dose CT imaging with separate reporting lines to ensure report turnaround times of 24 hours (Table 2). Separate reporting lines for radiology facilitate evaluation, and the Academic Health Science Network (AHSN) imaging consultants provide additional reporting capacity to ensure turnaround times.

Table 2. Tests performed at SCAN Stage 1

- Full Blood Count
- Erythrocyte Sedimentation Rate
- C-reactive protein
- Urea and electrolytes
- Creatinine
- Calcium
- Phosphate
- HBA1c

- Thyroid function
- CA125 (females)
- PSA (males)
- Faecal Immunochemical Testing
- Computed Tomography (Thorax, Abdomen, Pelvis)

Stage 2: The clinical information obtained in stage 1 directs the patient's subsequent progression through the pathway. Patients are either referred:

2-a. onto a Cancer Multi-Disciplinary Team (MDT) or Specialist clinic via an existing urgent pathway.
2-b. for additional direct access investigation within 1 week prior to clinician review.
2-c. to the Multi-disciplinary Diagnostic Centre (MDC) for medical review.

Stage 3: If symptom causation remains unclear after 2-a or 2-b, the patient is automatically referred to the MDC (2-c). At the point of referral to the MDC, the accepting hospital clinician becomes the responsible MDC clinician. At the MDC, the sequence of testing to further explain the patient's clinical problem is determined by the accepting clinician.

Stage 4: All patients referred to SCAN will be followed up for 2 years, including patients for whom cancer and serious disease is excluded. The GP will receive a structured follow-up plan allowing return to the MDC to avoid repeat CT scanning for patients with new, recurrent, or persistent symptoms meeting SCAN entry criteria. By passing through the MDC, the patient is granted access to allied health professional input (dietician, physiotherapy, psychology) where necessary.

METHODS FOR EVALUATION

Detailed analysis of the consecutive cohort of patients referred to the SCAN pathway, whose medical records are gathered retrospectively and followed up prospectively, will form the basis of the evaluation of the SCAN pathway.

SCAN Database

The OpenClinica computer package (https://www.openclinica.com/) is being used to store a database of demographic information, symptoms leading to referral, investigations performed, referrals made, appointments, diagnoses, and short term and long-term outcomes for all patients referred to SCAN. The time-point and outcome of each clinical encounter will be recorded for at least 2 years following referral to identify short-term and long-term diagnoses.

Patients will enter the database on the date the SCAN team confirms their eligibility. At this point data collected retrospectively from the primary care record using the auto-populating referral form (Appendix 2) will be entered into the SCAN database, and prospective data collection will begin using the OUHFT record.

The SCAN pathway will be evaluated based on its short term and long term diagnostic yield and its cost effectiveness in terms of the resources and time needed for a diagnosis to be reached. Patients' route to diagnosis and satisfaction with their experience of the SCAN pathway will also be evaluated as secondary outcomes. The primary and secondary points of evaluation are described in detail below.

Primary points of evaluation.

a. Short-term: diagnoses made within 28 days of referral
   - Cancer site and stage at diagnosis- histopathology or MDT determined.
   - Non-cancer diagnoses determined by MDC or another specialist clinic.
b. Long-term: diagnoses made within 2 years of referral
   - Confirmed by primary and secondary care database review at 2 years.

Secondary points of evaluation

a. To map the route to diagnosis for SCAN patients in terms of time intervals associated with diagnosis (i.e. each diagnostic interval in line with the Aarhus statement (16)) and the number and sequence of patient encounters (investigations and appointments leading to diagnosis).
b. To quantify incidental findings detected by the SCAN pathway.
c. To evaluate the cost effectiveness of the SCAN pathway.
d. To assess patient satisfaction with the SCAN pathway.

SCAN implementation.

The implementation of the SCAN pathway will be carried out in six stages corresponding to the six Oxfordshire CCG sub-regions. This pragmatic decision was made to allow the OUFHT and CCG to monitor GP uptake of the pathway in real-time to ensure that the capacity of the pathway is not exceeded and to allow early problems with service delivery to be overcome. This is an opportunity for a rigorous evaluation of the pathway in real-time, in the same county, and which will avoid the potential confounding that could arise from comparing SCAN patients to patients in different regions operated by different CCGs.

Pre-SCAN period: Before having access to SCAN, GPs in each region will be asked to prospectively identify patients meeting SCAN entry criteria and to complete a "dummy" data collection form to be submitted by email to a secure CCG email inbox (Appendix 3). Anonymised referral information is extracted electronically to maintain patient confidentiality. This group of "dummy" patients will provide data about patients receiving the standard of care prior to the introduction of SCAN (the new standard of care). In addition, an audit of local GP electronic records of patients with symptoms meeting SCAN referral criteria, but referred by other routes for investigation, will provide further contemporaneous data against which to evaluate SCAN.

SCAN period: Depending on uptake of the pathway, each CCG region will transition to the SCAN pathway over time.

Follow-up: All patients will be followed up in the primary and secondary care record for at least 2 years from entry by the pathway navigators.

STATISTICAL ANALYSIS

Primary point of evaluation - Diagnostic Yield

Our primary point of evaluation is yield from the new SCAN pathway with respect to the number and proportion of patients (1) with a new diagnosis within 28 days, (2) with disease excluded within 28 days, (3) who did not attend or were lost to follow-up. For newly diagnosed patients we will report the diagnostic interval (first presentation to primary care to date of diagnosis); the doctor interval (first presentation to primary care to the first primary care investigation); the primary care interval (first presentation to primary care to referral to secondary care); secondary care interval (referral to secondary care to start of treatment); and the treatment interval (diagnosis to the start of

treatment).(16) For people with indeterminate abdominal findings which require further investigation we will report the number of follow-up consultations or investigations up until discharge.

An additional analysis of long-term outcomes will be conducted after 2 years, where missed diagnoses (false negatives) will be defined as diagnoses not picked up in the short-term but picked up in the longer term and attributed to the initial symptomatic presentation allowing entry to the cohort. Within this analysis, the proportion of patients diagnosed with cancer and surviving 1 year will be ascertained.

Secondary points of evaluation - Route to diagnosis, cost effectiveness, and patient satisfaction

In relation to the secondary outcome related to routes to diagnosis, the number (and type) of healthcare contacts required to make a diagnosis will be counted for each participant starting from the initial primary care visit for the symptoms permitting referral to SCAN.

Medians and inter-quartile ranges (IQRs) will be calculated for each of the diagnostic intervals (days) stratified by symptom group, disease type, disease site and severity/stage where possible and presented graphically using boxplots.

Patients not referred to SCAN

The phased introduction of the SCAN pathway affords comparison with outcomes under the previous standard of care. Robust statistical comparisons between SCAN and the period prior to SCAN may be limited dependent on gathering data on sufficient numbers of patients with symptoms meeting SCAN referral criteria but not referred to SCAN. Therefore, the data collected on patients not referred to SCAN will be presented in tables with descriptive statistics and only compared to SCAN outcomes when appropriate.

Additional analyses

Incidental findings: To understand incidental findings in patients referred to SCAN, demographic, clinical, and radiological information will be extracted from SCAN. Imaging findings will be categorised per anatomical location. Each finding will be defined as of potential clinical importance (e.g. cancer, aneurysms, and cardiac findings), and probable or consistent with, or equivocal or unlikely to explain the symptoms at the time of referral. In the case of multiple lesions of the same type, the number will be recorded and reported. As the SCAN pathway uses ungated low dose CT imaging, an approach to avoid the over interpretation of cardiac findings was developed. The TeraRecon software package (https://www.terarecon.com/) will be used to look at any coronary artery calcification and an Agatson score will be calculated. This approach has been adopted due to the success that has been reported in a number of American studies assessing the prognostic accuracy of calcium scoring coronary arteries from an ungated low dose CT scan.(17-21) The data gathered from patients' medical records will be used to evaluate the ability of this protocol to show relevant coronary artery calcification. Incidental findings that have potential clinical importance will be followed up according to the standards issued by the American College of Radiologists, the British Thoracic Society, and the Royal College of Radiologists.(22-24) In addition, any further investigations (e.g. MRI) required to determine if CT findings are truly incidental will be recorded as part of mapping routes to diagnosis.

Patient survey: All patients referred to SCAN will be asked to complete a set of questionnaires about their experience of the pathway. The Consequence of Screening (COS) questionnaire (originally Psychological Consequences Questionnaire (PCQ)) (25) will be given to patients shortly after the referral to the MDC and then again 6-12 months after their referral. Individual items on the COS scales will be combined into themes of anxiety, behaviour, sense of dejection, and sleep, and item scores added together. COS domain scores will be compared across patients who had a confirmed diagnosis of cancer or other serious disease, false positive finding, and probably benign finding using non-parametric tests.

Patient satisfaction surveys will also be distributed to SCAN patients to gather their responses to questions about the speed and ease of diagnosis or all clear result, treatment, and/or follow-up.

Cost-effectiveness: The cost-effectiveness of the SCAN pathway will be assessed by recording each patient encounter from referral to SCAN up until a final diagnosis is made or excluded. The outcome will be incremental cost-effectiveness compared to the pre-SCAN pathway, with effectiveness measured in unit reduction in time to diagnosis, and in additional diagnosis within 28 days. The comparison group will be the pre-SCAN patient cohort, supplemented with data from a local audit. The resource use of patients in the SCAN pathway and its comparator will be estimated from the database and costed using national unit costing databases.(26) In addition patients will be asked to complete the UK Cancer Costs Questionnaire (27) to record on going financial and opportunity costs.

Data handling and data management

A data management plan (DMP) is in place outlining in detail the specific procedures to ensure that high quality data are produced for statistical analysis. The DMP was reviewed and signed off by all relevant parties prior to data management activities commencing.

Data will be collected electronically in OpenClinica (https://www.openclinica.com/) and data validation is achieved through electronic programmed checks or through manual review of listing outputs. All discrepancies generated by electronic validation checks or manual listings will be reviewed by the data manager.

ETHICS AND DISSEMINATION

Evaluation of a newly established service/adopted pathway does not require research governance as such activity falls outside of the definition of research as set out by the Health Research Authority (HRA) and would not be considered research in the NHS. As such, this study is not subject to the Department of Health's Research Governance Framework for Health and Social Care (2005). This opinion can be reviewed by reference to the HRA's algorithm, available at http://www.hra-decisiontools.org.uk/research/ and attendant leaflet, Defining Research, or by reference to The Health Care Quality Improvement Partnership (HQIP)'s Guide for Clinical Audit, Research and Service Review.(28) The results of this evaluation will be reported in peer-reviewed journals and on the websites of the various funding bodies describing the ACE Wave 2 project. Abstracts for oral or poster presentations will be submitted to national and international conferences. Data resulting from this study will be made available following a request to the authors.

CONCLUSION

Cancer prognosis improves with early diagnosis but the UK lags behind many European countries in terms of the proportion of patients diagnosed at an early stage. For this reason, the Independent Cancer Taskforce has highlighted the need for alternative routes to diagnosis to be explored and has made specific reference to MDC based pathways. The SCAN pathway is such an MDC based pathway which has been adopted in Oxfordshire with the aim of reducing the time from initial presentation of non-specific but concerning symptoms to diagnosis, and increasing the proportion of cancers diagnosed at an early stage. We will evaluate the ability of the SCAN pathway to meet these aims over two years, will assess the patient experience of the diagnostic pathway, and appraise the cost-effectiveness of the pathway.

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STATEMENT OF CONTRIBUTION

The clinical pathway was designed by FG, SH, SA, BN, and DL. BN, JO, and LA designed this pathway evaluation. The patient information leaflet was developed by BN and reviewed by JL, JAP, JO, SH and Shahista Hussain from OUHFT Research and Development. BN, JO and CFS wrote this protocol, all authors reviewed and gave comments. All authors will be involved in the running of this evaluation study and the analysis of the results. All authors have read and approve this protocol.

COMPETING INTERESTS

The authors declare no competing interests.

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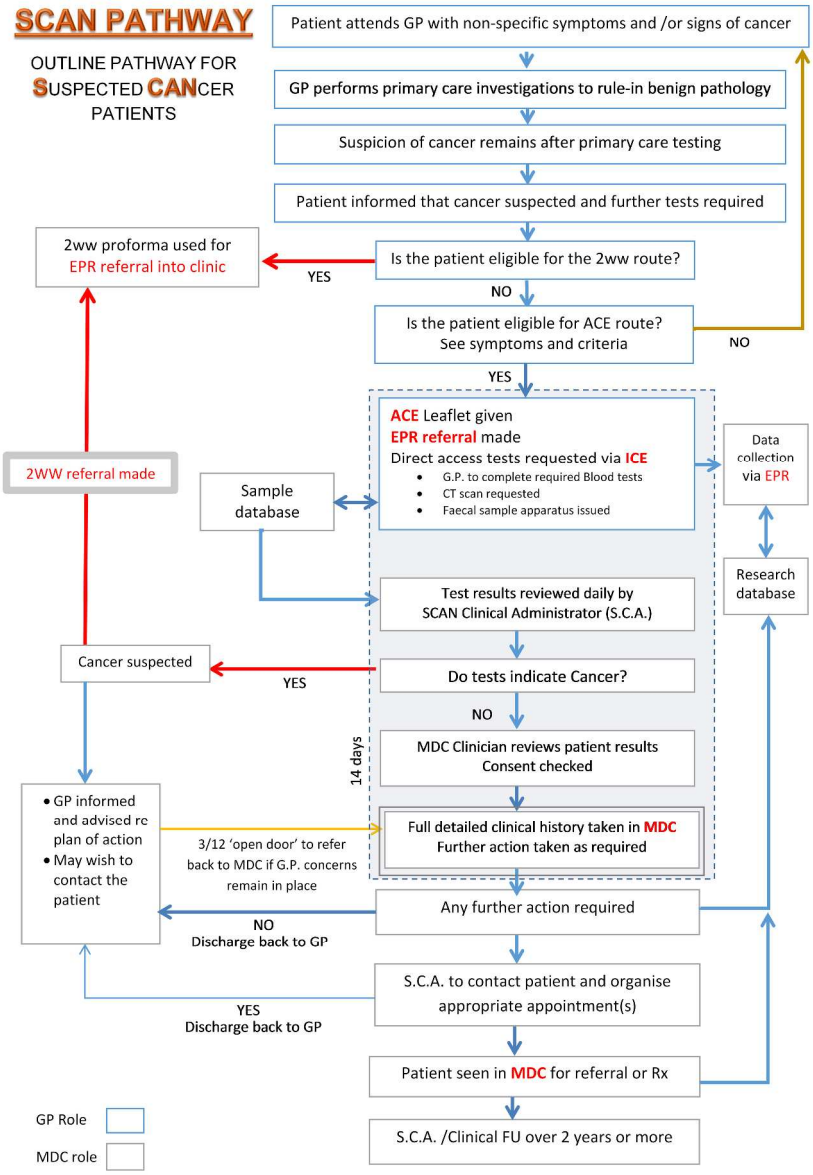

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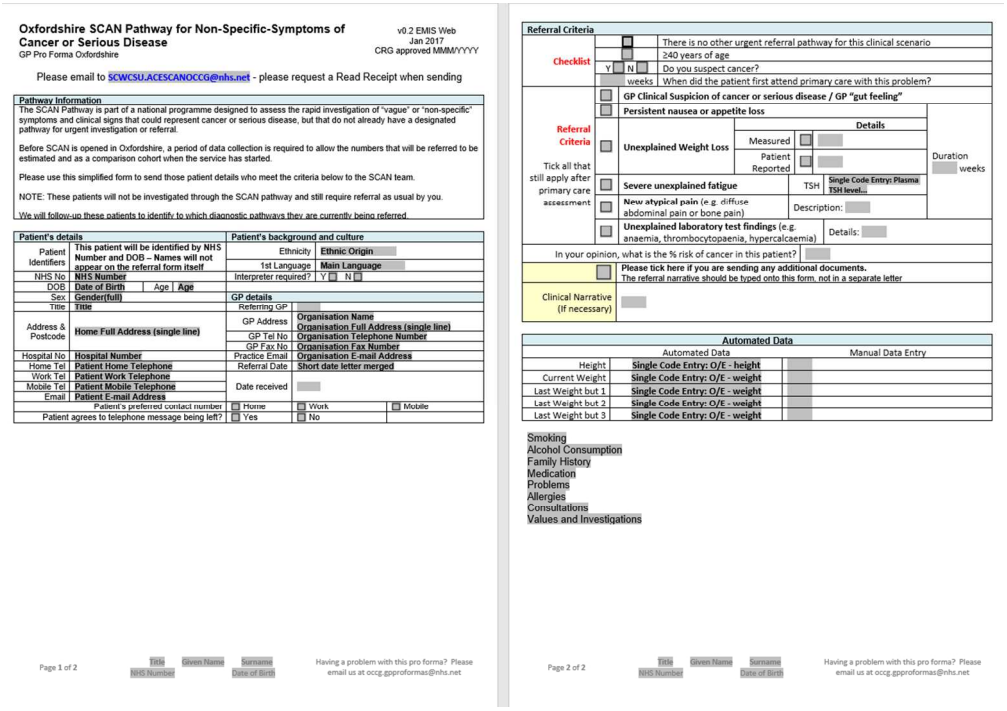

Oxfordshire SCAN Pathway for Non-Specific-Symptoms of Cancer or Serious Disease
GP Pro Forma Oxfordshire

v0.2 EMIS Web
Jan 2017
CRG approved MMM/YYYY

Please email to SCWCSU.ACESCANOCCG@nhs.net - please request a Read Receipt when sending

Pathway Information

The SCAN Pathway is part of a national programme designed to assess the rapid investigation of "vague" or "non-specific" symptoms and clinical signs that could represent cancer or serious disease, but that do not already have a designated pathway for urgent investigation or referral.

Before SCAN is opened in Oxfordshire, a period of data collection is required to allow the numbers that will be referred to be estimated and as a comparison cohort when the service has started.

Please use this simplified form to send those patient details who meet the criteria below to the SCAN team.

NOTE: These patients will not be investigated through the SCAN pathway and still require referral as usual by you.

We will follow-up these patients to identify to which diagnostic pathways they are currently being referred.

Patient's details		Patient's background and culture	
Patient Identifiers	This patient will be identified by NHS Number and DOB – Names will not appear on the referral form itself	Ethnicity	Ethnic Origin
		1st Language	Main Language
NHS No	NHS Number	Interpreter required?	Y N
DOB	Date of Birth / Age		
Sex	Gender(full)	GP details	
Title	Title	Referring GP	
Address & Postcode	Home Full Address (single line)	GP Address	Organisation Name Organisation Full Address (single line)
		GP Tel No	Organisation Telephone Number
		GP Fax No	Organisation Fax Number
Hospital No	Hospital Number	Practice Email	Organisation E-mail Address
Home Tel	Patient Home Telephone	Referral Date	Short date letter merged
Work Tel	Patient Work Telephone	Date received	
Mobile Tel	Patient Mobile Telephone		
Email	Patient E-mail Address		
Patient's preferred contact number		☐ Home	☐ Work ☐ Mobile
Patient agrees to telephone message being left?		☐ Yes	☐ No

Page 1 of 2 — Title Given Name Surname NHS Number Date of Birth — Having a problem with this pro forma? Please email us at occg.gpproformas@nhs.net

Referral Criteria

Checklist	☐	There is no other urgent referral pathway for this clinical scenario
	☐	≥40 years of age
	Y ☐ N ☐	Do you suspect cancer?
	weeks	When did the patient first attend primary care with this problem?

Referral Criteria — Tick all that still apply after primary care assessment

☐	GP Clinical Suspicion of cancer or serious disease / GP "gut feeling"			
☐	Persistent nausea or appetite loss			
☐	Unexplained Weight Loss	Details: Measured / Patient Reported		Duration weeks
☐	Severe unexplained fatigue	TSH	Single Code Entry: Plasma TSH level...	
☐	New atypical pain (e.g. diffuse abdominal pain or bone pain)	Description:		
☐	Unexplained laboratory test findings (e.g. anaemia, thrombocytopaenia, hypercalcaemia)	Details:		

In your opinion, what is the % risk of cancer in this patient?

☐ Please tick here if you are sending any additional documents. The referral narrative should be typed onto this form, not in a separate letter

Clinical Narrative (If necessary)

Automated Data

	Automated Data	Manual Data Entry
Height	Single Code Entry: O/E - height	
Current Weight	Single Code Entry: O/E - weight	
Last Weight but 1	Single Code Entry: O/E - weight	
Last Weight but 2	Single Code Entry: O/E - weight	
Last Weight but 3	Single Code Entry: O/E - weight	

Smoking
Alcohol Consumption
Family History
Medication
Problems
Allergies
Consultations
Values and Investigations

Page 2 of 2 — Title Given Name Surname NHS Number Date of Birth — Having a problem with this pro forma? Please email us at occg.gpproformas@nhs.net

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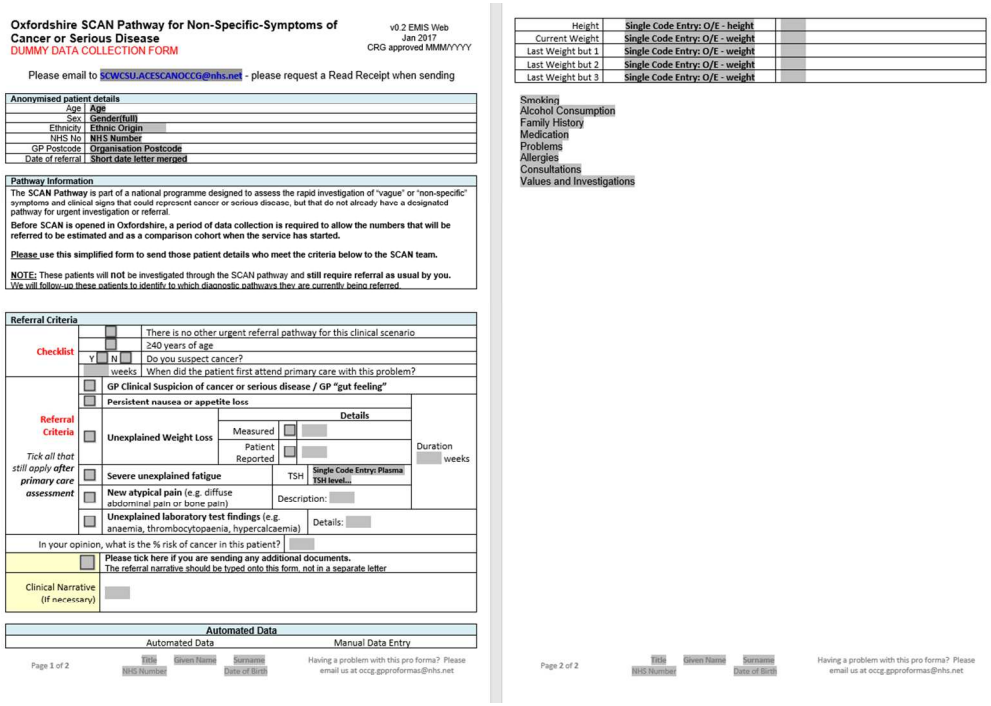

Oxfordshire SCAN Pathway for Non-Specific-Symptoms of Cancer or Serious Disease
DUMMY DATA COLLECTION FORM

v0.2 EMIS Web
Jan 2017
CRG approved MMM/YYYY

Please email to SCWCSU.ACESCANOCCG@nhs.net - please request a Read Receipt when sending

Anonymised patient details	
Age	Age
Sex	Gender(full)
Ethnicity	Ethnic Origin
NHS No	NHS Number
GP Postcode	Organisation Postcode
Date of referral	Short date letter merged

Pathway Information

The **SCAN Pathway** is part of a national programme designed to assess the rapid investigation of "vague" or "non-specific" symptoms and clinical signs that could represent cancer or serious disease, but that do not already have a designated pathway for urgent investigation or referral.

Before SCAN is opened in Oxfordshire, a period of data collection is required to allow the numbers that will be referred to be estimated and as a comparison cohort when the service has started.

Please use this simplified form to send those patient details who meet the criteria below to the SCAN team.

NOTE: These patients will **not** be investigated through the SCAN pathway and **still require referral as usual by you.** We will follow-up these patients to identify to which diagnostic pathways they are currently being referred.

Referral Criteria

Checklist

- ☐ There is no other urgent referral pathway for this clinical scenario
- ☐ ≥40 years of age
- Y ☐ N ☐ Do you suspect cancer?
- ____ weeks | When did the patient first attend primary care with this problem?

Referral Criteria
Tick all that still apply after primary care assessment

- ☐ **GP Clinical Suspicion of cancer or serious disease / GP "gut feeling"**
- ☐ **Persistent nausea or appetite loss**
- ☐ **Unexplained Weight Loss** — Details: Measured ☐ ____ / Patient Reported ☐ ____ — Duration ____ weeks
- ☐ **Severe unexplained fatigue** — TSH: Single Code Entry: Plasma TSH level...
- ☐ **New atypical pain** (e.g. diffuse abdominal pain or bone pain) — Description: ____
- ☐ **Unexplained laboratory test findings** (e.g. anaemia, thrombocytopaenia, hypercalcaemia) — Details: ____

In your opinion, what is the % risk of cancer in this patient? ____

☐ **Please tick here if you are sending any additional documents.**
The referral narrative should be typed onto this form, not in a separate letter

Clinical Narrative (If necessary) ____

Automated Data

Automated Data	Manual Data Entry

Page 1 of 2 — Title, Given Name, Surname, NHS Number, Date of Birth — Having a problem with this pro forma? Please email us at occg.gpproformas@nhs.net

Height	Single Code Entry: O/E - height
Current Weight	Single Code Entry: O/E - weight
Last Weight but 1	Single Code Entry: O/E - weight
Last Weight but 2	Single Code Entry: O/E - weight
Last Weight but 3	Single Code Entry: O/E - weight

Smoking
Alcohol Consumption
Family History
Medication
Problems
Allergies
Consultations
Values and Investigations

Page 2 of 2 — Title, Given Name, Surname, NHS Number, Date of Birth — Having a problem with this pro forma? Please email us at occg.gpproformas@nhs.net

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Oxford University Hospitals NHS
NHS Foundation Trust

Suspected CANcer (SCAN) Pathway

Information for patients

Your GP has advised you may benefit from investigation via the **SCAN** pathway.

The **SCAN** pathway is part of a national programme called ACE (Accelerate, Co-ordinate and Evaluate). It is coordinated by Cancer Research UK and supported by NHS England's National Clinical Director for Cancer.

ACE was established to pilot a new diagnostic pathway for people with 'non-specific but concerning symptoms'. This uses a Multidisciplinary Diagnostic Centre (MDC), which allows people to undergo several diagnostic tests in one location.

Further information about the ACE programme can be found online at:

www.cancerresearchuk.org/health-professional/early-diagnosis-activities/ace-programme

Thank you for reading this information sheet. Do take time to talk to your family and friends about it. If you decide to take part you will be asked to sign and date a consent form at your first appointment.

What is the purpose of the SCAN pathway?

Many people visit their GP with 'vague' symptoms, such as weight loss and tiredness. These symptoms are called 'non-specific', as they affect the whole person. Often the cause of these symptoms remains unclear after your GP has assessed you, and sometimes there is a minor cause for such symptoms. However, there is a small chance that they could be the signs of a serious illness, such as cancer. Therefore, these symptoms are often called 'low-risk but not no-risk symptoms'.

At present, GPs do not have a way to get rapid investigations for people with 'non-specific' symptoms. People may go back and forth between their GP and the hospital many times until a diagnosis is made, all of which takes time. As a result there could be delay in diagnosis and treatment, which may have a negative effect on the person's health and the overall outcome.

Although the risk of serious disease is low, the cause of these symptoms can be difficult to diagnose. As a result, there are some people for whom earlier scans and tests could diagnose the cause more quickly, allowing treatment to be started sooner. **SCAN** may enable doctors and the NHS to better understand which people would benefit from early scanning, highlighting the need for more efficient access to radiology services.

As part of the ACE programme the **SCAN** project will carry out a service evaluation of a diagnostic pathway for people in Oxfordshire with 'non-specific symptoms'. This involves:

- rapid diagnostic imaging (Computed Tomography or CT scan)
- laboratory tests (blood and stool (faeces) tests)
- further testing or an appointment with a specialist, depending on the results.

The aim is that people on the **SCAN** pathway will have a diagnosis and be able to begin treatment faster than the previous pathways allowed.

Why have I been referred to SCAN?

Your GP has assessed you as having one of the 'non-specific' symptoms for which **SCAN** has been developed.

Do I have to take part?

No. Taking part in **SCAN** is entirely voluntary. It is up to you to decide if you want to be investigated by the **SCAN** pathway.

If you choose not to take part in the **SCAN** pathway, you will continue to receive care following the standard local guidelines agreed by Oxford University Foundation Hospital NHS Trust (OUHFT), Oxfordshire Clinical Commissioning Group (OCCG), and National Institute for Health and Clinical Excellence (NICE) guidelines.

What will I have to do if I take part?

Your GP will send the ACE team detailed information about your clinical problem, your symptoms, examination findings, medical history and any recent test results.

If you have any questions at this point, please contact the **SCAN** team.

Email: **scanpathway@ouh.nhs.uk**

Tel: **01865 227 780**
(8.30am to 4.30pm, Monday to Friday)

You will be asked to come for an appointment at the Radiology department in the Churchill Hospital in Oxford, within one week of the referral for a CT scan. You will need to collect a stool sample in the blue-topped specimen pot provided in the **SCAN** information envelope, the day before your **SCAN** appointment.

Following your first appointment, the clinical information received from your GP and all of your test results will be reviewed

by the **SCAN** team (a group of specialist doctors skilled in managing 'non-specific' symptoms).

Depending on your results, within one week the **SCAN** team will do one of the following:

1. refer you to a specialist clinic in Oxford
2. refer you for further rapid testing (within two weeks) in Oxford
3. invite you for a clinic appointment with the SCAN team in Oxford
4. refer you back to your GP with advice.

Taking part in the SCAN pathway

Please take any time you need to discuss this with your family and friends.

Before you sign the consent form at your **SCAN** appointment, you will be given time to ask questions to help you decide whether or not to take part.

When we ask you to sign the consent form, a member of our team will sign it too.

The consent form will confirm that you have read and understood the information in this leaflet. It will confirm that you have had a chance to ask questions and that these questions have been answered.

There will be another consent form which will confirm whether you agree to your blood being stored for research purposes. This is optional and does not affect your eligibility to use the **SCAN** pathway.

You can still change your mind after you have signed the consent form. You are free to withdraw from the pathway at any time, without giving a reason. This will not affect the standard of care you receive.

The SCAN Pathway

Before the start of the pathway

Your GP will discuss the **SCAN** pathway with you and will give you this information sheet.

You will be contacted by telephone by a member of the **SCAN** team, who will offer you an appointment for a CT scan and blood and stool tests.

You will have time to discuss the **SCAN** pathway in more detail and to ask any questions either at the first appointment, by telephone (01865 227 780), or by email (scanpathway@ouh.nhs.uk). Research staff may ask you some further questions during this discussion.

At your first appointment

Please bring your stool sample in the blue topped pot. You will be asked to:

1. sign a consent form to say you agree to continue on the **SCAN** pathway (see enclosed form)
2. sign a consent form to say you agree to your blood and urine samples being stored for research (see enclosed form). This is optional.
3. possibly have further blood taken and sent to the laboratory
4. hand in your filled blue-topped stool specimen pot
5. have a CT scan of your chest, abdomen, and pelvis
6. fill out a questionnaire about your experience.

Preparing for the CT scan

Please do not have anything to eat two hours prior to your appointment, as this may affect the results of the scan. You may drink water or clear fluids (no milk) up to the time of your scan. You do not need to have a full bladder.

During your scan you will have an injection of a special dye, called contrast, to enhance the scan quality. The CT scan will take approximately 20 minutes. A further information leaflet is included to give you more details about the CT scan.

Follow-up

Your follow-up care will be based on your medical history and test results. The various options are shown in the flowchart on page 10. If the results from the CT scan and other tests do not show that further evaluation is needed, the **SCAN** team will write to your GP with information and treatment suggestions.

If you take part in the **SCAN** pathway, the information collected during your follow-up care will be included in the SCAN database and will be used to help develop more effective pathways to diagnose people with non-specific symptoms. All of the information we collect will be kept strictly confidential.

At the end of the SCAN pathway

You will not be required to have any more appointments, tests or scans. You may be asked to fill out a further questionnaire about your experiences of the **SCAN** pathway.

Data from your medical records will be collected on the outcome of your investigations and any further diagnoses or treatments that you have over the next two years. Your GP or specialist will discuss with you any further NHS treatments, care, monitoring or testing that may be necessary. If you move away or change Health Authority, data will be collected about your health status from the Health and Social Care information Centre and other NHS bodies.

What if there is a problem during the course of the pathway?

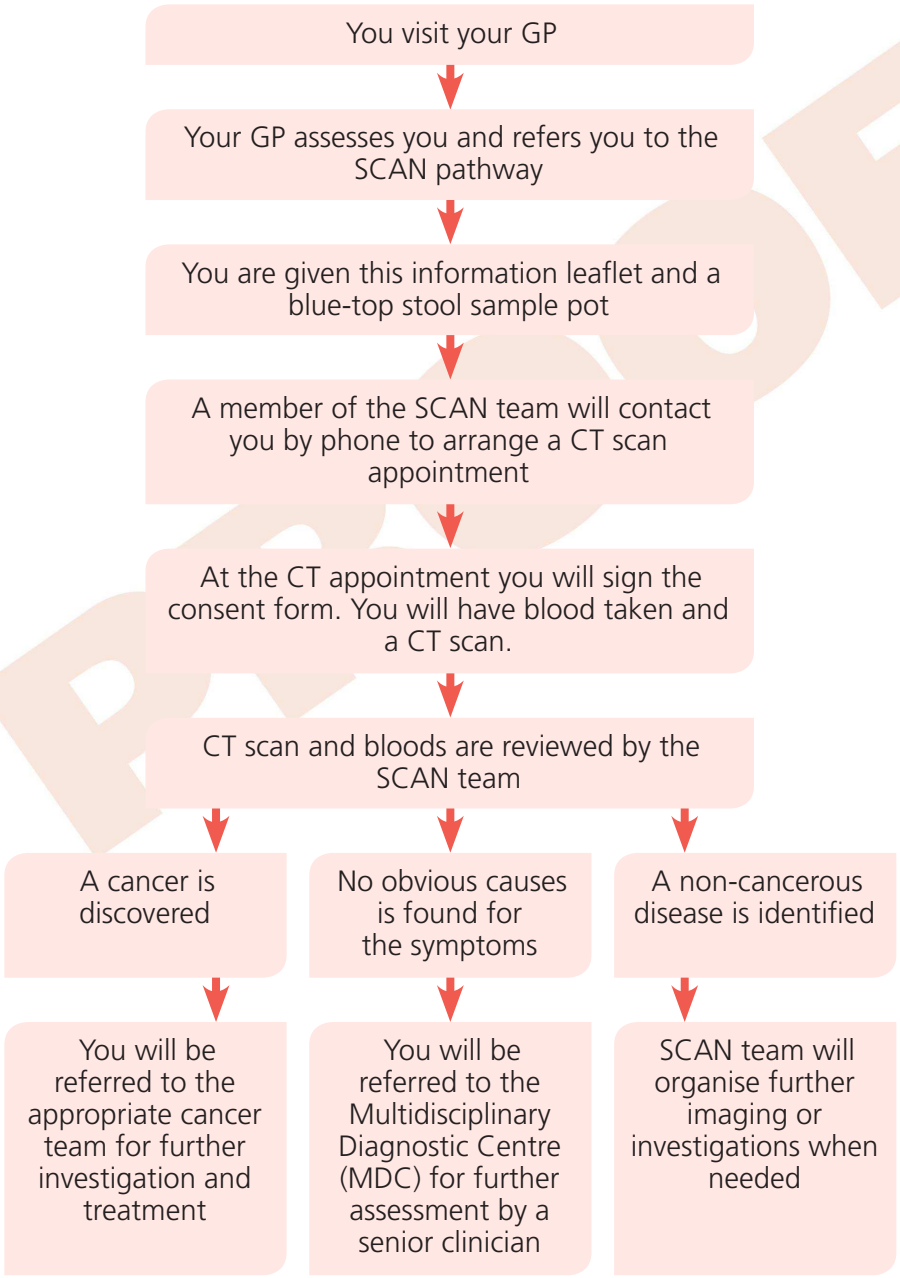
Every care will be taken during the course of the pathway. If you have a concern about any aspect of the pathway, you should ask to speak with the **SCAN** team, who will do their best to answer your questions.

Tel: **01865 227 780**

Email: **scanpathway@ouh.nhs.uk**

If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Additional information is available from your local Patient Advice and Liaison Service office.

Email: **www.pals.nhs.uk**



page 10

Will my taking part in this service evaluation be kept confidential?

If you join the **SCAN** pathway, all information which is collected about you during the course of the research will be kept strictly confidential. Documents relating to you will be kept by the OUHFT and at the University of Oxford, Nuffield Department of Primary Health Sciences, in secure areas and on a password protected computer and database.

You will be entered into the **SCAN** database. All data collected about you will be linked with your NHS number and year of birth. Your medical records and the data collected for the pathway will be looked at by authorised persons involved in your care or the service evaluation. Authorised people from OUHFT may also check them to make sure that the service evaluation is being carried out correctly.

Oxford Imaging Trials Unit (OITU) at the Churchill Hospital will also keep your current and previous names, date of birth and NHS number, to find out if you were diagnosed by **SCAN** or an alternative pathway as part of the service evaluation. Any test results received will have been anonymised at site; this involves blacking out/removing any personal information.

Responsibility for compliance with national and international data protection standards lies with the Oxford University Hospital NHS Foundation Trust.

What will happen to any samples I give?

The blood and stool samples that you give as part of this pathway will be analysed immediately in the laboratory of Oxford University Hospitals.

In addition, we would like to collect blood and urine samples for research purposes, to investigate tests for cancer or other diseases in people with non-specific symptoms. This may sometimes involve diagnostic companies or researchers, who have developed specialist tests for these symptoms. There would be no financial gain for the **SCAN** team in relation to these samples. The additional consent form asks you to consent to the use of your samples in this way.

What will happen to the results of the SCAN pathway service evaluation?

The combined anonymised results of the SCAN pathway will be analysed by the SCAN researchers, shared with other ACE pilot projects, the Department of Health, Macmillan Cancer Support, Cancer Research UK, and published in medical journals.

The service evaluation will take 2-4 years to complete and the results should be available and published after 2019. If you are interested in the results, please look up ACE Wave 2 on the Cancer Research UK website or contact the SCAN team at scanpathway@ouh.nhs.uk

If the results show conclusively that rapid investigation of non-specific symptoms leads to earlier diagnosis of cancer, they may be used to influence future NHS guidelines.

Who is sponsoring this pathway?

The SCAN pathway is funded by the Department of Health, Macmillan Cancer Support, and Cancer Research UK. The pathway is supported by Oxford University Hospitals NHS Foundation Trust, the Oxfordshire Clinical Commissioning Group (OCCG) and the University of Oxford. It is being carried out by the Oxford Imaging Trials Unit and the OCCG.

Contact details

If you have any further questions about the SCAN pathway, please contact:

Julie-Ann Phillips (SCAN Navigator)

Tel: **01865 227 780**
(8.30am to 4.30pm, Monday to Friday)

Email: **scanpathway@ouh.nhs.uk**

Thank you for reading this information booklet. If you decide to take part in this pathway you must personally sign and date the consent form.

We will give you a copy of this information sheet and your signed consent form.
We will keep a second copy of this document with the service evaluation records on and will place a third copy in your radiology records.

This pathway is being supported by:
- Oxfordshire Clinical Commissioning Group
- Cancer Research UK
- NHS England
- Macmillan Cancer Support
- Nuffield Department of Primary Care Health Sciences
- Oxford University Hospitals NHS Foundation Trust

If you have a specific requirement, need an interpreter, a document in Easy Read, another language, large print, Braille or audio version, please call **01865 221 473** or email **PALS@ouh.nhs.uk**

Author: Julie-Ann Phillips, SCAN Navigator
March 2017
Review: March 2020
Oxford University Hospitals NHS Foundation Trust
Oxford OX3 9DU
www.ouh.nhs.uk/information

OMI 14548P

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Page where met
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1,2
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	NA
	2b	All items from the World Health Organization Trial Registration Data Set	NA
Protocol version	3	Date and version identifier	NA
Funding	4	Sources and types of financial, material, and other support	3, 10
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	10
	5b	Name and contact information for the trial sponsor	NA
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	10
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	9, 10
Introduction			

Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3
	6b	Explanation for choice of comparators	7
Objectives	7	Specific objectives or hypotheses	3, 4
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	3 – 6
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	4
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	4
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	5, 6
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	NA
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	NA
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	NA

Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	7
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	7
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	NA
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	NA
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	NA
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	NA
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	6 (enrolment of participants, all else NA)

Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	NA
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	6
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	NA
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	9
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	7 – 9
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	8, 9
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	NA
Methods: Monitoring			

Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	9, 10
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	NA
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	8
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	NA
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	10
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	NA
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	5
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	5
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	7
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	10

Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	9, 10
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	9
	31b	Authorship eligibility guidelines and any intended use of professional writers	NA
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	NA
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Online material 1
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

BMJ Open

The Suspected CANcer (SCAN) pathway: protocol for evaluating a new standard of care for patients with non-specific symptoms of cancer.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-018168.R1
Article Type:	Protocol
Date Submitted by the Author:	14-Sep-2017
Complete List of Authors:	Nicholson, Brian; University of Oxford, Nuffield Department of Primary Care Health Sciences Oke, Jason; University of Oxford, Nuffield Department of Primary Care Health Sciences Friedemann Smith, Claire; University of Oxford, Nuffield Department of Primary Care Health Sciences Phillips, Julie-Ann; Oxford University Hospitals NHS Foundation Trust, Radiology Lee, Jennifer; Oxford University Hospitals NHS Foundation Trust Abel, Lucy; University of Oxford, Nuffield Department of Primary Care Health Sciences Kelly, Sadie; University of Oxford, Nuffield Department of Primary Care Health Sciences Gould, Isabella ; University of Oxford, Nuffield Department of Primary Care Health Sciences Mackay, Toni; Oxford University Hospitals NHS Foundation Trust Kaveney, Zoe; NHS Oxfordshire Clinical Commissioning Group Anthony, Suzie; Oxford University Hospitals NHS Foundation Trust Hayles, Shelley; NHS Oxfordshire Clinical Commissioning Group Lasserson, Daniel; Oxford University Hospitals NHS Foundation Trust, NIHR Oxford Biomedical Research Centre Gleeson, Fergus; Oxford University Hospitals NHS Foundation Trust, Radiology
Primary Subject Heading:	Health services research
Secondary Subject Heading:	Diagnostics, Evidence based practice, Oncology, Patient-centred medicine
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The Suspected CANcer (SCAN) pathway: protocol for evaluating a new standard of care for patients with non-specific symptoms of cancer.

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ABSTRACT

Introduction: Cancer survival in England lags behind most European countries, due partly to lower rates of early stage diagnosis. We report the protocol for the evaluation of a multidisciplinary diagnostic centre based pathway for the investigation of 'low risk but not no risk' cancer symptoms called the Suspected CANcer (SCAN) pathway. SCAN is a new standard of care being implemented in Oxfordshire; one of a number of pathways implemented during the second wave of the ACE programme, an initiative which aims to improve England's cancer survival rates through establishing effective routes to early diagnosis.

Methods and analysis: To evaluate SCAN, we are collating a prospective database of patients referred onto the pathway by their GP. Patients aged over 40 years, with non-specific symptoms such as weight loss or fatigue, who do not meet urgent cancer referral criteria or for whom symptom causation remains unclear after investigation via other existing pathways, can be referred to SCAN. SCAN provides rapid CT scanning, laboratory testing, and clinic review within 2 weeks. We will follow all patients in the primary and secondary care record for at least two years. The data will be used to understand the diagnostic yield of the SCAN pathway in the short term (28 days) and the long term (2 years). Routinely collected primary and secondary care data from patients not referred to SCAN but with similar symptoms, will also be used to evaluate SCAN. We will map the routes to diagnosis for patients referred to SCAN to assess cost-effectiveness. Acceptability will be evaluated using patient and GP surveys.

Ethics and dissemination: The Oxford Joint Research Office Study Classification Group has judged this to be a service evaluation and so outside of research governance. The results of this project will be disseminated by peer reviewed publication and presentation at conferences.

Strengths and limitations of this study:

- SCAN will be evaluated in relation to diagnostic yield, time to diagnosis, cost effectiveness, patient satisfaction, and incidental diagnoses.
- Data from both the primary and secondary care record will be used to populate a bespoke prospective database detailing the cohort of patients evaluated by the SCAN pathway.
- A randomised GP or patient level implementation of SCAN was not feasible within the constraints of the local health system, nor a randomised stepped-wedge roll-out to the six Oxfordshire CCG regions.
- Instead a pragmatic service evaluation is being conducted around a phased rollout of the pathway against the previous standard of care in the same region, operated by the same Clinical Commissioning Group (CCG).
- The findings of this evaluation will only indicate SCAN's effectiveness in Oxfordshire and should not be generalised to the rest of England.

BACKGROUND

England's rates of cancer survival lag behind many other European countries, and late stage at diagnosis is thought to play a large part in this.(1, 2) Twenty-one percent of cancers are diagnosed as an emergency, which is associated with advanced tumour stage and increased short-term mortality.(3, 4) It is estimated that, if diagnosed early, 5000 cancer deaths could be prevented every year for breast, colorectal, and lung cancers alone.(2, 5) The ACE (Accelerate, Coordinate & Evaluate) Programme is an early diagnosis initiative supported by NHS England, Cancer Research UK (CRUK), and Macmillan Cancer Support.(6) It was formed to help improve England's cancer survival rates by generating evidence on how best to configure diagnostic pathways to drive a shift from late to early cancer at diagnosis, reduce the number of cancers diagnosed as an emergency, and improve patient experience.

The first wave of ACE comprised around 60 projects aiming to evaluate local initiatives to develop a national body of evidence to inform cancer commissioning.(7) A weakness in the current system identified during Wave 1 was the lack of a clear urgent referral pathway for patients with non-specific but concerning symptoms known to be associated with a range of cancer sites, such as fatigue, abdominal pain and weight loss.(8) Consequently, before reaching a cancer diagnosis, these patients often have multiple tests and non-urgent referrals resulting in delays in diagnosis.(9) The Independent Cancer Taskforce outlined the need to explore new models of care to speed up diagnosis in patients with non-specific symptoms, making references to the multidisciplinary diagnostic centre (MDC) concept.(10) ACE Wave 2 was set up to facilitate the development and evaluation of a small number of MDC based pathways in the English National Health Service (NHS).(6) These pathways are implemented as standards of care in participating regions, in addition to site-specific urgent cancer referral pathways.

Oxfordshire's Suspected CANcer (SCAN) pathway emulates a Danish MDC pathway, the Non-Specific Symptoms and Signs of Cancer Patient Pathway (NSSC-CPP).(11) Patients first undergo a panel of diagnostic investigations including blood and urine tests and diagnostic imaging. If no diagnosis is made, but cancer or another serious disease is suspected, the patient is referred to the MDC.(11, 12) The MDC is a diagnostic unit with access to a broad range of investigations and specialist expertise in managing patients with non-specific symptoms. Of 1,278 patients referred to the NSSC-CPP pathway by their General Practitioners (GPs), a cross-sectional study reported that 16% of patients were diagnosed with a cancer.(13) The most common symptoms recorded were weight loss (53%), fatigue (50%), and pain (37%). The most common clinical findings were "affected general condition" (36%), GP "gut feeling" (23%), and abnormal abdominal examination (13%). Forty-eight percent of patients were referred with abnormal blood test results. Cancer was diagnosed across a broad range of 18 subgroups, the most common of which were lung (18%), colorectal (13%), haematological (10%), pancreatic (9%), and upper-gastrointestinal (8.2%).(13) A later cohort study including 938 patients referred to the NSSC-CPP reported that 35% were diagnosed with serious disease within 3 months, of which one third had cancer.(14)

As is the case in the UK, health care in Denmark is mostly free to access for residents, and Danish GPs act as 'gatekeepers' to specialist services.(15) Five-year survival rates for several cancer types are also among the lowest in Organisation for Economic Co-operation and Development (OECD) countries.(15) Both countries have introduced a one month standard for the time between referral and diagnosis to increase the proportion of cancers diagnosed at an early stage.(15, 16) Furthermore, following the introduction of cancer pathways in Denmark which incorporate patient

review by multidisciplinary teams, waiting times have significantly reduced across almost all cancer types.(17) The similarities between the Danish and UK health systems, the challenges faced by both, and the improvements brought about by MDC based pathways, suggest that these pathways for non-specific symptoms warrant evaluation in the UK. At the time of writing, we retrieved no peer-reviewed articles detailing MDC pathways for cancer diagnosis in the UK and only one conference abstract describing 91 patients assessed via an alternative MDC pathway developed during ACE Wave 1 in London.(18) Robust evaluation of the SCAN pathway has the potential to contribute to the evidence base for the MDC concept in cancer diagnosis. We report here the protocol for the SCAN pathway evaluation.

Aim

The aim of this study is to evaluate the SCAN pathway, a new standard of care for the rapid investigation of patients with non-specific cancer symptoms in Oxfordshire. SCAN will be evaluated in terms of how well it meets its objectives, which are detailed below.

Objectives

In line with the CRUK ACE initiative which aims to reduce late and increase early cancer diagnosis, decrease cancer diagnoses made through emergency presentations, and improve patient experience (6), the objectives of the SCAN pathway are to:

- Reduce time from initial primary care presentation with symptoms to diagnosis.
- Achieve a higher proportion of early stage cancer at diagnosis.
- Improve patient experience of the diagnostic pathway.
- Establish whether the MDC model is cost-effective.

SETTING

Oxfordshire's cancer incidence (600 cases per 100,000) is lower than the UK average (615 cases per 100,000). Cancer mortality (261 per 100,000) is also lower than the national average, with fewer cancers diagnosed through emergency presentation (17.1% vs. 20.1%) and more patients diagnosed at an early stage (56.8% vs. 54.3%) than the national average.(19) Comprising a predominantly white (90.85%) population, Oxfordshire has smaller foci of Asian (4.84%), Black (1.75%), and mixed ethnic (2.02%) groups. Black and minority ethnic (BME) communities form 22.4% of Oxford City's population, with lower proportions in more rural districts: 7.8% in Cherwell, 3.2% in West Oxfordshire (Source: 2011 Census (20)). Rural districts (67%) rank in the 10% least deprived, and urban (33%) in the 20% most deprived in England. There are no ACE Wave 1 sites in Oxfordshire.

The Oxfordshire Clinical Commissioning Group (CCG) serves a population of over 700,000 through 70 General Practices.(21) Oxford University Hospitals NHS Foundation Trust (OUHFT) is made up of four hospitals providing a range of specialist services (John Radcliffe, Churchill Hospital, Nuffield Orthopaedic Centre, and the Horton General Hospital). SCAN imaging takes place at the Churchill Hospital and the SCAN MDC is located at the John Radcliffe Hospital. SCAN links with the Oxford Allied Health Science Network (AHSN) Imaging Network, aiming to develop a model for expansion through the seven adjoining NHS network trusts.

THE SCAN PATHWAY

SCAN retains the GP's gate-keeping role, requiring patients to first attend their GP with symptoms to access the pathway through GP referral.(22) The SCAN referral algorithm was developed by consensus between a multidisciplinary team including GPs, Radiologists, physicians, and health service researchers (Appendix 1). It incorporates age-thresholds and "low-risk but not no-risk" symptoms that fall outside of existing urgent 2-week-wait (2ww) referral pathways based on the National Institute of Care Excellence (NICE) NG12 suspected cancer guidelines (23), but remain predictive of cancer in primary care.

SCAN will be opened up sequentially to GPs in each of the six sub-regions of Oxfordshire CCG, to ensure that the team has enough capacity to meet demand. The first region opened 15th March 2017, the second on the 5th June 2017. In response to demand, regions three and four were opened on 6th September 2017, and the final two regions are expected to open on the 30th October 2017.

Estimated referral rate

We used the following data to estimate expected referral rates: (i) Oxfordshire population statistics (20); (ii) the number of GPs in Oxfordshire (21); (iii) the referral rate reported for the Danish NSSC-CPP pathway (12); (iv) the estimated prevalence of non-specific symptoms meeting SCAN referral criteria in primary care populations, derived from the control groups of primary care based case-control studies.(24) Using these sources, an estimate of 20-40 referrals per week was anticipated, taking into account that not all patients presenting to primary care with qualifying symptoms will be referred by their GP: symptoms may not occur in isolation or a pre-existing condition will provide explanation; GPs may identify an alternative explanation for new symptoms negating the need for referral; patients may be referred by other routes; or patients may decline referral.

Referral criteria

A structured standardised electronic referral form has been disseminated to all GPs in Oxfordshire (Appendix 2). If there is no other urgent referral pathway for the clinical scenario, patients aged ≥40 years of age are accepted if their GP is concerned about cancer or serious disease following face-to-face primary care assessment of individual or combined "low-risk but not no-risk" symptoms, such as: weight loss, appetite loss, nausea, fatigue, malaise, abdominal pain, anaemia and thrombocytopenia. In addition, patients may be referred based on their GPs clinical suspicion of cancer or serious disease (their "gut feeling").(25, 26) GPs are also requested to indicate their suspicion of malignancy at this stage (Table 1).

Table 1. SCAN referral criteria.

Essential	**There is no other urgent referral pathway suitable for this clinical scenario**					
Essential	**≥40 years of age**					
Essential *Tick all that still apply* ***after primary care***	**Unexplained Weight Loss**	Measured	☐	Kg loss	___ kg	Duration ____ weeks
		Patient Reported	☐			
	Severe unexplained fatigue	TSH (within 1m)	_____ miu/L			
	Persistent nausea or appetite loss					

assessment	**New atypical pain** (eg. diffuse abdominal or bone pain).	Site?	_____	
	Unexplained laboratory test findings (eg. anaemia, thrombocytopaenia, hypercalcaemia)		Please specify	_____
	GP Clinical Suspicion of cancer or serious disease / GP "gut feeling"			

STAGES OF THE PATHWAY

As part of their initial work-up to exclude more common causes of non-specific symptoms in primary care, GPs will conduct investigations essential to allow access to the SCAN pathway: creatinine (necessary prior to IV contrast) and thyroid function tests (hypothyroidism as a cause of fatigue). The referral form completed by the GP constitutes a referral for all aspects of the SCAN pathway including the CT scan and blood tests. Once referred, a member of the SCAN team (the SCAN pathway navigator) assumes clinical responsibility for the patient, confirms that the patient meets the inclusion criteria, orders and coordinates the CT and blood tests, and provides a point of contact for the patient. Demographic and clinical information are captured by the GP referral form.

Consent: At the point of referral, patients are given a participant information sheet detailing the SCAN pathway and consent form (Online Supplementary Material 1) to allow their anonymised medical records to be used for the purposes of evaluating the pathway. Patients are given time to take the information away and consider whether they wish to participate. If patients decide to participate, they are asked to take the consent form to the initial appointment, at which time they may ask any outstanding questions. Patients who do not wish to have their medical records used may still be referred onto the SCAN pathway but will not be followed-up for the purposes of the evaluation. At the time of writing none of the patients accepted onto SCAN had refused consent.

Stage 1: GP direct access triage tests: At the first hospital appointment, a panel of standard diagnostic investigations with rapid turnaround (request-test-report) of <7 days are performed. These tests include a panel of blood tests, faecal immunochemical testing, and appropriate low-dose CT imaging with separate reporting lines to ensure report turnaround times of 24 hours (Table 2). Separate reporting lines for radiology facilitate evaluation, and the Academic Health Science Network (AHSN) imaging consultants provide additional reporting capacity to ensure turnaround times.

Table 2. Tests performed at SCAN Stage 1

- Full Blood Count
- Erythrocyte Sedimentation Rate
- C-reactive protein
- Urea and electrolytes
- Creatinine
- Calcium
- Phosphate
- HBA1c
- Thyroid function

- CA125 (females)
- PSA (males)
- Faecal Immunochemical Testing
- Computed Tomography (Thorax, Abdomen, Pelvis)

Stage 2: The clinical information obtained in stage 1 directs the patient's subsequent progression through the pathway. Patients are either referred:

2-a. onto a Cancer Multi-Disciplinary Team (MDT) or specialist clinic via an existing urgent pathway.
2-b. for additional direct access investigation within 1 week prior to clinician review.
2-c. to the Multi-disciplinary Diagnostic Centre (MDC) for medical review.

The referring GP receives a copy of the CT report and a letter from the SCAN team explaining which arm of the pathway their patient has been referred to. Any urgent findings are communicated to the GP via telephone. Any telephone conversations are followed by a letter detailing the conversation and the actions the GP and SCAN team have agreed to.

Stage 3: If symptom causation remains unclear after 2-a or 2-b, the patient is automatically referred to the MDC (2-c). At the point of referral to the MDC, the accepting hospital clinician becomes the responsible MDC clinician. At the MDC, the sequence of testing to further explain the patient's clinical problem is determined by the accepting clinician.

Stage 4: All patients who consent to participate in the SCAN pathway will be followed up for 2 years, including patients for whom cancer and serious disease is excluded. The GP will receive a structured follow-up plan allowing return to the MDC to avoid repeat CT scanning for patients with new, recurrent, or persistent symptoms meeting SCAN entry criteria. By passing through the MDC, the patient is granted access to allied health professional input (dietician, physiotherapy, psychology) where necessary. The patient journey along the SCAN pathway is summarised in Appendix 3.

METHODS FOR EVALUATION

The sequential implementation of the SCAN pathway in Oxfordshire has allowed a short informal 'pilot' period during which we have been able to assess the functioning of the pathway to address any issues that may arise before it is opened to all GPs. A detailed analysis of the consecutive cohort of patients referred to the SCAN pathway, whose medical records are gathered retrospectively and followed up prospectively, will form the basis of the pathway's evaluation. We will also evaluate the pathway in terms of its cost effectiveness as well as a number of other indicators detailed below, thereby following the framework for evaluating complex interventions as laid out by the Medical Research Council.(27)

SCAN Database

The OpenClinica computer package (https://www.openclinica.com/) is being used to store a database of demographic information, symptoms leading to referral, investigations performed, referrals made, appointments, diagnoses, and short term and long-term outcomes for all patients referred to SCAN. The time-point and outcome of each clinical encounter will be recorded for at least 2 years following referral to identify short-term and long-term diagnoses.

Patients will enter the database on the date the SCAN team confirms their eligibility. At this point data collected retrospectively from the primary care record using the auto-populating referral form (Appendix 2) will be manually entered into the SCAN database, and prospective data collection will begin using the OUHFT record.

The SCAN pathway will be evaluated based on its short term and long term diagnostic yield and its cost effectiveness in terms of the resources and time needed for a diagnosis to be reached. Patients' route to diagnosis and satisfaction with their experience of the SCAN pathway will also be evaluated as secondary outcomes. The primary and secondary points of evaluation are described in detail below.

Primary points of evaluation.

Diagnostic Yield

a. Short-term: diagnoses made within 28 days of referral
   - Cancer site and stage at diagnosis- histopathology or MDT determined.
   - Non-cancer diagnoses determined by MDC or another specialist clinic.
b. Long-term: diagnoses made within 2 years of referral
   - Confirmed by primary and secondary care database review at 2 years.

Secondary points of evaluation

a. To map the route to diagnosis for SCAN patients in terms of time intervals associated with diagnosis (i.e. each diagnostic interval in line with the Aarhus statement (28)) and the number and sequence of patient encounters (investigations and appointments leading to diagnosis), including the number of diagnoses made following an emergency presentation.
b. To quantify incidental findings detected by the SCAN pathway.
c. To evaluate the cost effectiveness of the SCAN pathway.
d. To assess patient and GP satisfaction with the SCAN pathway.

SCAN implementation.

The implementation of the SCAN pathway will be carried out in six stages corresponding to the six Oxfordshire CCG sub-regions. This pragmatic decision was made to allow the OUHFT and CCG to monitor GP uptake of the pathway in real-time to ensure that the capacity of the pathway is not exceeded and to allow early problems with service delivery to be overcome. This is an opportunity for a rigorous evaluation of the pathway in real-time, in the same county, and which will avoid the potential confounding that could arise from comparing SCAN patients to patients in different regions operated by different CCGs.

Pre-SCAN period: Before having access to SCAN, GPs in each region will be asked to prospectively identify patients meeting SCAN entry criteria and to complete a "dummy" comparator data collection form to be submitted by email to a secure CCG email inbox (Appendix 4). Anonymised referral information is extracted electronically to maintain patient confidentiality. This group of comparator patients will provide data about patients receiving the standard of care prior to the introduction of SCAN (the new standard of care). In addition, an audit of local GP electronic records

of patients with symptoms meeting SCAN referral criteria, but referred by other routes for investigation, will provide further contemporaneous data against which to evaluate SCAN.

SCAN period: Depending on uptake of the pathway, each CCG region will transition to the SCAN pathway over time. The set up and evaluation of the SCAN pathway is currently funded for a period of at least 2 years of patient intake and 2 years of follow-up. ACE Wave 2 projects are expected to report results in late 2018 (6). Following this, it is anticipated that Oxfordshire CCG will adopt SCAN indefinitely and will take on its funding as the MDC model is of interest to NHS England.

Follow-up: All patients will be followed up in the primary and secondary care record for at least 2 years from entry by the pathway navigators.

STATISTICAL ANALYSIS

Primary point of evaluation - Diagnostic Yield

Our primary point of evaluation is yield from the new SCAN pathway with respect to the number and proportion of patients (a) with a new diagnosis or with disease excluded within 28 days, and (b) with a diagnosis made within 2 years of referral. For newly diagnosed patients we will report the diagnostic interval (first presentation to primary care to date of diagnosis); the doctor interval (first presentation to primary care to the first primary care investigation); the primary care interval (first presentation to primary care to referral to secondary care); secondary care interval (referral to secondary care to start of treatment); and the treatment interval (diagnosis to the start of treatment).(28) For patients with indeterminate abdominal findings which require further investigation, we will report the number of follow-up consultations or investigations up until discharge.

The analysis of long-term outcomes will be conducted after 2 years, where missed diagnoses (false negatives) will be defined as diagnoses not picked up in the short-term but in the longer term and attributed to the initial symptomatic presentation allowing entry to the cohort. Within this analysis, the proportion of patients diagnosed with cancer and surviving 1-year will be ascertained.

Secondary points of evaluation - Route to diagnosis, cost effectiveness, GP and patient satisfaction

For the secondary outcome assessing routes to diagnosis, the number (and type) of healthcare contacts required to make a diagnosis will be counted for each participant starting from the initial primary care visit for the symptoms permitting referral to SCAN. The number of patients diagnosed following an emergency presentation will also be counted. Medians and inter-quartile ranges (IQRs) will be calculated for each of the diagnostic intervals (days) stratified by symptom group, disease type, disease site and severity/stage where possible and presented graphically using boxplots.

Incidental findings: Incidental findings are radiological abnormalities not caused by the symptoms being investigated that may drive further imaging and concern.(29) To understand incidental findings in patients referred to SCAN, demographic, clinical, and radiological information will be extracted from the SCAN database. Imaging findings will be categorised per anatomical location. Each finding will be defined as of potential clinical importance (e.g. cancer, aneurysms, and cardiac findings), and probable or consistent with, or equivocal or unlikely to explain the symptoms at the time of referral. In the case of multiple lesions of the same type, the number will be recorded and

reported. As the SCAN pathway uses ungated low dose CT imaging, an approach to avoid the over interpretation of cardiac findings was developed. The TeraRecon software package (https://www.terarecon.com/) will be used to look at any coronary artery calcification and an Agatson score will be calculated. This approach has been adopted due to the success that has been reported in a number of American studies assessing the prognostic accuracy of calcium scoring coronary arteries from an ungated low dose CT scan.(30-34) The data gathered from patients' medical records will be used to evaluate the ability of this protocol to show relevant coronary artery calcification. Incidental findings that have potential clinical importance will be followed up according to the standards issued by the American College of Radiologists, the British Thoracic Society, and the Royal College of Radiologists.(35-37) In addition, any further investigations (e.g. MRI) required to determine if CT findings are truly incidental will be recorded as part of mapping routes to diagnosis.

Patient survey: All patients who consent to participate in the evaluation of the SCAN pathway will be asked to complete a set of questionnaires about their experience of the pathway. The Consequence of Screening (COS) questionnaire (originally Psychological Consequences Questionnaire (PCQ)) (38) will be given to patients shortly after the referral to the MDC and then again 6-12 months after their referral. Individual items on the COS scales will be combined into themes of anxiety, behaviour, sense of dejection, and sleep, and item scores added together. COS domain scores will be compared across patients who had a confirmed diagnosis of cancer or other serious disease, false positive finding, and probably benign finding using non-parametric tests.

Patient satisfaction surveys will also be distributed to all patients (regardless of participation in the pathway evaluation) at the end of their CT scan. This questionnaire has been designed to evaluate the patient's experience of the staff and the service provided by the radiology department.

GP satisfaction survey: A brief satisfaction survey will be distributed to all participating GPs. This survey will assess satisfaction with the ease of use of the SCAN pathway, speed with which referred patients are seen by the SCAN team, and the quality of the information provided to GPs by the SCAN team both in terms of the functioning and purpose of the pathway, and the results of the diagnostic tests undergone by their patient(s). The survey will be distributed and completed online using the Bristol Online Surveys tool (https://www.onlinesurveys.ac.uk/).

Cost-effectiveness: The cost-effectiveness of the SCAN pathway will be assessed from the perspective of the NHS in England, using a within trial analysis. Each patient encounter from referral to SCAN up until a final diagnosis is made or excluded will be recorded. The outcome will be incremental cost-effectiveness compared to the pre-SCAN pathway, with effectiveness measured in unit reduction in time to diagnosis, and in additional diagnosis within 28 days. The comparison group will be the pre-SCAN patient cohort. Although the numbers of comparator patients should closely resemble those of patients referred to the pathway as the inclusion criteria are identical, we expect comparator patient numbers to be lower as GPs are requested to take time to complete the referral forms with no tangible benefit to their patients. Due to the expected lower response rate we will supplement comparator data from GPs with an audit of Oxfordshire surgeries with the appropriate data sharing agreement, approximately 60 practices, up to March 2017. The resource use of patients in the SCAN pathway and its comparator will be estimated from the database and costed using national unit costing databases.(39) In addition, patients will be asked to complete the UK Cancer Costs Questionnaire (40) to record on going financial and opportunity costs. Sensitivity analyses will

be carried out on the key assumptions of the evaluation, including resource use assumptions, the impact of adjusting for baseline characteristics, and extending the analysis to cost utility.

Eligible patients not referred to SCAN

The phased introduction of the SCAN pathway affords comparison with outcomes under the previous standard of care for patients meeting SCAN referral criteria. This will include patients with SCAN eligible symptoms identified by their GPs and diagnosed via alternative routes, for example by 2ww pathways, non-urgent specialist referral, or by emergency presentation. Robust statistical comparisons between SCAN and the period prior to SCAN may be limited dependent on gathering data on a sufficient number of patients with symptoms meeting SCAN referral criteria who are not referred to SCAN, which is in turn dependent on GPs completing the comparator referral forms. Therefore, the data collected on patients not referred to SCAN provided by GPs will be supplemented with an audit of the primary care record and will be presented in tables with descriptive statistics, only comparing SCAN and pre-SCAN outcomes when appropriate.

Sample Size

In order to have power >80% (alpha = 5%) and if the SCAN pathway halves the average length of the diagnostic interval compared to usual care (Hazard ratio = 2), we would need at least 43 patients diagnosed with cancer during the pre-SCAN period and at least 173 patients diagnosed with cancer following the introduction of the pathway. (41) If 15% of patients presenting to their GP with non-specific symptoms have cancer (12) we need to recruit at least 1460 patients.

Data handling and data management

A data management plan (DMP) is in place outlining in detail the specific procedures to ensure that high quality data are produced for statistical analysis. The DMP was reviewed and signed off by all relevant parties prior to data management activities commencing.

Data will be collected electronically in OpenClinica (https://www.openclinica.com/) and data validation is achieved through electronic programmed checks or through manual review of listing outputs. All discrepancies generated by electronic validation checks or manual listings will be reviewed by the data manager.

ETHICS AND DISSEMINATION

Evaluation of a newly established service/adopted pathway does not require research governance as such activity falls outside of the definition of research as set out by the Health Research Authority (HRA) and would not be considered research in the NHS. As such, this study is not subject to the Department of Health's Research Governance Framework for Health and Social Care (2005). This opinion can be reviewed by reference to the HRA's algorithm, available at http://www.hra-decisiontools.org.uk/research/ and attendant leaflet, Defining Research, or by reference to The Health Care Quality Improvement Partnership (HQIP)'s Guide for Clinical Audit, Research and Service Review.(42) In addition, a Privacy Impact Assessment concluded that individual patient consent was not necessary to collect data on the comparator patients. The primary reason for this was that

obtaining consent was likely to cause unnecessary distress to patients who were not yet able to make use of the new pathway. Instead, a data sharing agreement was signed by all participating GP surgeries and all comparator data will be sent electronically to the CCG Commissioning Support Unit (CSU) and pseudonomised before being shared with the SCAN team.

The results of this evaluation will be reported in peer-reviewed journals and on the websites of the various ACE Wave 2 funding bodies. Abstracts for oral or poster presentations will be submitted to national and international conferences. Data resulting from this study will be made available following a request to the authors.

STRENGTHS AND LIMITATIONS

This is the first published protocol for the evaluation of a MDC pathway based in the UK. The evaluation outlined will provide detailed information on the diagnostic yield and time to diagnosis for comparison of the MDC model with existing routes to diagnosis in the NHS. Our focus on incidental findings and cost-effectiveness will add valuable evidence about the value of early CT scanning of patients with non-specific symptoms, especially in response to concerns about overdiagnosis.

Our evaluation, however, has some limitations. First, due to the pragmatic nature of SCAN's implementation the evaluation has had to take into account resource constraints and logistical realities of Oxfordshire's health system. Consequently, we have been unable to randomise individual patients or GPs to the SCAN pathway, nor could we randomise the sequence of a stepped-wedge rollout of SCAN across CCG regions. Secondly, collection of comparator data is reliant upon local GPs opting to do so as an additional task in an already busy health service without additional financial incentive. We are supplementing this approach with a retrospective review of primary care records to identify eligible pre-SCAN patients. The method of symptom capture using this approach is in development but may be limited to retrospective electronic coded entries. Due to these factors the generalisability of our findings outside of Oxfordshire will be limited.

CONCLUSION

Cancer prognosis improves with early diagnosis but the UK lags behind many European countries in terms of the proportion of patients diagnosed at an early stage. For this reason, the Independent Cancer Taskforce has highlighted the need for alternative routes to diagnosis to be explored and has made specific reference to MDC based pathways. The SCAN pathway is such an MDC based pathway which has been adopted in Oxfordshire with the aim of reducing the time from initial presentation of non-specific but concerning symptoms to diagnosis, and increasing the proportion of cancers diagnosed at an early stage. We will evaluate the ability of the SCAN pathway to meet these aims over two years, will assess the patient experience of the diagnostic pathway, and appraise the cost-effectiveness of the pathway.

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publication. Going forward, the funders will have no role in data collection, management, or interpretation.

STATEMENT OF CONTRIBUTION

The clinical pathway was designed by FG, SH, SA, BDN, and DL. BDN, JO, and LA designed this pathway evaluation. The patient information leaflet was developed by BDN and reviewed by JL, JAP, JO, SH and Shahista Hussain from OUHFT Research and Development. BDN, JO and CFS wrote this protocol, all authors reviewed and gave comments. All authors will be involved in the running of this evaluation study and the analysis of the results. All authors have read and approve this protocol.

COMPETING INTERESTS

The authors declare no competing interests.

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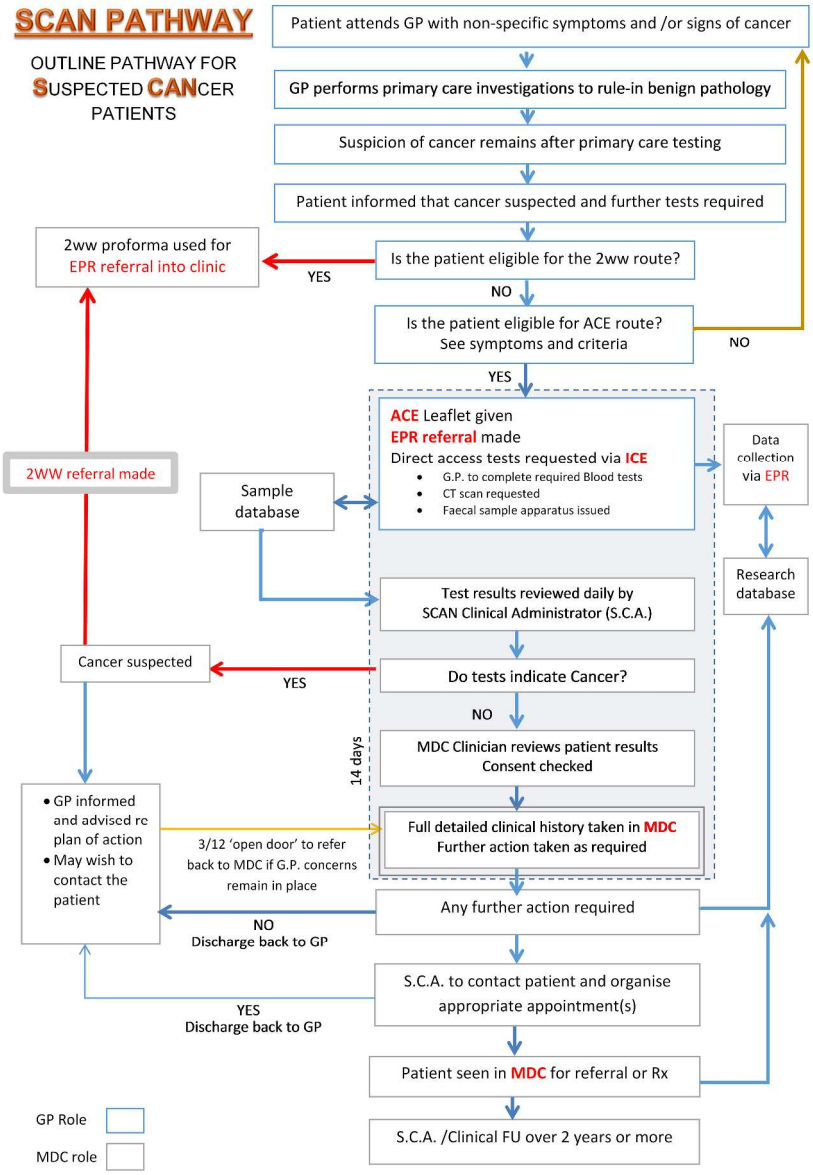

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Oxfordshire SCAN Pathway for Non-Specific-Symptoms of Cancer or Serious Disease

GP Pro Forma Oxfordshire

v3.1 EMIS Web
August 2017

Please email to **orh-tr.ace2scan@nhs.net** - please request a Read Receipt when sending

Pathway Information

The **SCAN Pathway** is part of a national programme designed to assess the rapid investigation of "vague" or "non-specific" symptoms and clinical signs that could represent cancer or serious disease, but that do not already have a designated pathway for urgent investigation or referral

Within 7 days of referral, a CT Neck, Thorax, Abdomen, and Pelvis and a broad panel of laboratory investigations will be completed and the results reviewed by a virtual Multidisciplinary Clinic (MDC) for non-specific symptoms.

If there is high suspicion of a specific diagnosis (cancer or non-cancer) from the CT the MDC will automatically refer your patient to an urgent referral pathway, a specialist clinic, or for further specialist testing (e.g. colonoscopy). If doubt remains following initial testing, the patient will be reviewed in person at the MDC for non-specific symptoms. Your patient will be referred back to you with a diagnosis or management plan once all investigations are completed. You will automatically receive the results of all blood tests and CT performed.

If you have already referred a patient to a pre-existing cancer pathway, and these tests are negative, and you wish the patient to be referred to the ACE Pathway, then if you have checked the box below, this will happen automatically – and you will be informed.

Patient's details				**Patient's background and culture**		
Forenames	**Given Name**			Ethnicity	**Ethnic Origin**	
Surname	**Surname**			1st Language	**Main Language**	
Known As	**Calling Name**					
NHS No	**NHS Number**			Interpreter required?	Y ☐ N ☐	
DOB	**Date of Birth**	Age	**Age**			
Sex	**Gender(full)**			**GP details**		
Title	**Title**			Referring GP		
Address & Postcode	**Home Full Address (single line)**			GP Address	**Organisation Name** **Organisation Full Address (single line)**	
				GP Tel No	**Organisation Telephone Number**	
				GP Fax No	**Organisation Fax Number**	
Hospital No	**Hospital Number**			Practice Email	**Organisation E-mail Address**	
Home Tel	**Patient Home Telephone**			Referral Date	**Short date letter merged**	
Work Tel	**Patient Work Telephone**			Date received		
Mobile Tel	**Patient Mobile Telephone**					
Email	**Patient E-mail Address**					
Patient's preferred contact number				☐ Home	☐ Work	☐ Mobile
Patient agrees to telephone message being left?				☐ Yes	☐ No	

Referral Criteria						
Checklist	☐	There is no other urgent referral pathway for this clinical scenario				
	☐	≥40 years of age				
	Y ☐ N ☐	Do you suspect cancer?				
	weeks	When did the patient first attend primary care with this problem?				
Referral Criteria *Tick all that still apply* ***after primary care assessment***	☐	**GP Clinical Suspicion of cancer or serious disease / GP "gut feeling"**				
	☐	**Persistent nausea or appetite loss**				Duration weeks
	☐	**Unexplained Weight Loss**	**Details**			
			Measured	☐		
			Patient Reported	☐		
	☐	**Severe unexplained fatigue**	TSH	**Single Code Entry: Plasma TSH level...**		
	☐	**New atypical pain** (e.g. diffuse abdominal pain or bone pain)	Description:			
	☐	**Unexplained laboratory test findings** (e.g. anaemia, thrombocytopenia, hypercalcaemia)	Details:			
In your opinion, what is the % risk of cancer in this patient?						
☐	**Please tick here if you are sending any additional documents.** The referral narrative should be typed onto this form, not in a separate letter					
Clinical Narrative (If necessary)						

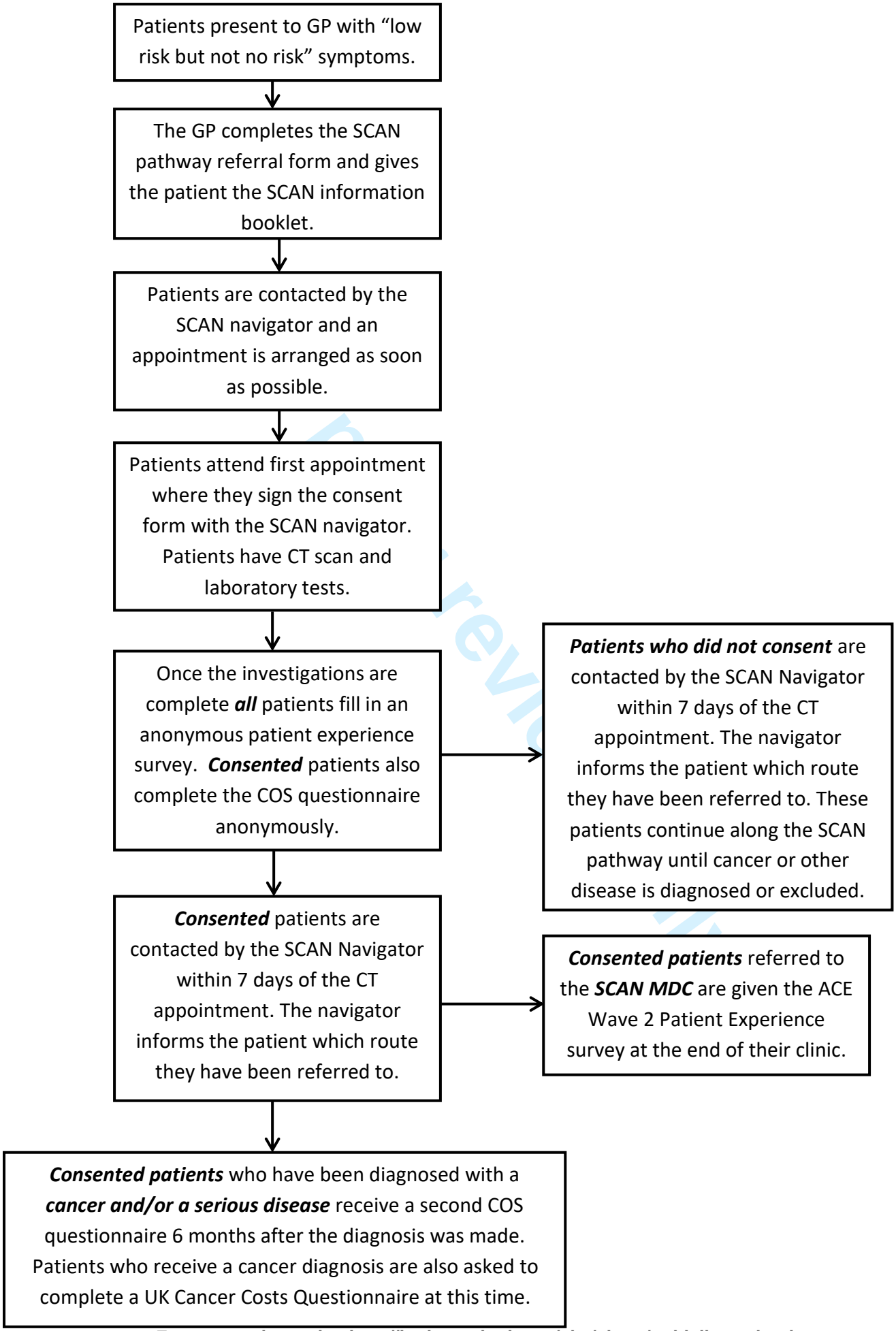
Automated Data		
	Automated Data	Manual Data Entry
Height	**Single Code Entry: O/E - height**	
Current Weight	**Single Code Entry: O/E - weight**	
Last Weight but 1	**Single Code Entry: O/E - weight**	
Last Weight but 2	**Single Code Entry: O/E - weight**	
Last Weight but 3	**Single Code Entry: O/E - weight**	

Smoking
Alcohol Consumption
Family History
Medication
Problems
Allergies
Consultations
Values and Investigations

Title Given Name Surname
NHS Number Date of Birth

Having a problem with this pro forma? Please email us at OCCG.GPproformas@nhs.net

Appendix 3. Patient journey in SCAN Pathway



Oxfordshire SCAN Pathway for Non-Specific-Symptoms of Cancer or Serious Disease

v0.3.2 EMIS Web
September 2017

DUMMY DATA COLLECTION FORM

Please email to **SCWCSU.ACESCANOCCG@nhs.net** - please request a Read Receipt when sending

Anonymised patient details	
Age	**Age**
Sex	**Gender(full)**
Ethnicity	**Ethnic Origin**
NHS No	**NHS Number**
GP Postcode	**Organisation Postcode**
Date of referral	**Short date letter merged**

Pathway Information

The **SCAN Pathway** is part of a national programme designed to assess the rapid investigation of "vague" or "non-specific" symptoms and clinical signs that could represent cancer or serious disease, but that do not already have a designated pathway for urgent investigation or referral.

Before SCAN is opened in Oxfordshire, a period of data collection is required to allow the numbers that will be referred to be estimated and as a comparison cohort when the service has started.

Please use this simplified form to send those patient details who meet the criteria below to the SCAN team.

NOTE: These patients will **not** be investigated through the SCAN pathway and **still require referral as usual by you.** We will follow-up these patients to identify to which diagnostic pathways they are currently being referred.

Referral Criteria

Checklist	☐	There is no other urgent referral pathway for this clinical scenario
	☐	≥40 years of age
	Y ☐ N ☐	Do you suspect cancer?
	weeks	When did the patient first attend primary care with this problem?

Referral Criteria *Tick all that still apply* ***after primary care assessment***						
	☐	**GP Clinical Suspicion of cancer or serious disease / GP "gut feeling"**				
	☐	**Persistent nausea or appetite loss**				Duration weeks
	☐	**Unexplained Weight Loss**	**Details**			
			Measured	☐		
			Patient Reported	☐		
	☐	**Severe unexplained fatigue**	TSH	**Single Code Entry: Plasma TSH level...**		
	☐	**New atypical pain** (e.g. diffuse abdominal pain or bone pain)	Description:			
	☐	**Unexplained laboratory test findings** (e.g. anaemia, thrombocytopenia, hypercalcaemia)	Details:			

In your opinion, what is the % risk of cancer in this patient?	
☐	**Please tick here if you are sending any additional documents.** The referral narrative should be typed onto this form, not in a separate letter
Clinical Narrative (If necessary)	

Automated Data	
Automated Data	Manual Data Entry

Having a problem with this pro forma? Please email us at OCCG.GPproformas@nhs.net

Height	**Single Code Entry: O/E - height**	
Current Weight	**Single Code Entry: O/E - weight**	
Last Weight but 1	**Single Code Entry: O/E - weight**	
Last Weight but 2	**Single Code Entry: O/E - weight**	
Last Weight but 3	**Single Code Entry: O/E - weight**	

Smoking
Alcohol Consumption
Family History
Medication
Problems
Allergies
Consultations
Values and Investigations

Having a problem with this pro forma? Please email us at OCCG.GPproformas@nhs.net

Oxford University Hospitals NHS
NHS Foundation Trust

Suspected CANcer (SCAN) Pathway

Information for patients

Your GP has advised you may benefit from investigation via the **SCAN** pathway.

The **SCAN** pathway is part of a national programme called ACE (Accelerate, Co-ordinate and Evaluate). It is coordinated by Cancer Research UK and supported by NHS England's National Clinical Director for Cancer.

ACE was established to pilot a new diagnostic pathway for people with 'non-specific but concerning symptoms'. This uses a Multidisciplinary Diagnostic Centre (MDC), which allows people to undergo several diagnostic tests in one location.

Further information about the ACE programme can be found online at:

www.cancerresearchuk.org/health-professional/early-diagnosis-activities/ace-programme

Thank you for reading this information sheet. Do take time to talk to your family and friends about it. If you decide to take part you will be asked to sign and date a consent form at your first appointment.

What is the purpose of the SCAN pathway?

Many people visit their GP with 'vague' symptoms, such as weight loss and tiredness. These symptoms are called 'non-specific', as they affect the whole person. Often the cause of these symptoms remains unclear after your GP has assessed you, and sometimes there is a minor cause for such symptoms. However, there is a small chance that they could be the signs of a serious illness, such as cancer. Therefore, these symptoms are often called 'low-risk but not no-risk symptoms'.

At present, GPs do not have a way to get rapid investigations for people with 'non-specific' symptoms. People may go back and forth between their GP and the hospital many times until a diagnosis is made, all of which takes time. As a result there could be delay in diagnosis and treatment, which may have a negative effect on the person's health and the overall outcome.

Although the risk of serious disease is low, the cause of these symptoms can be difficult to diagnose. As a result, there are some people for whom earlier scans and tests could diagnose the cause more quickly, allowing treatment to be started sooner. **SCAN** may enable doctors and the NHS to better understand which people would benefit from early scanning, highlighting the need for more efficient access to radiology services.

As part of the ACE programme the **SCAN** project will carry out a service evaluation of a diagnostic pathway for people in Oxfordshire with 'non-specific symptoms'. This involves:

- rapid diagnostic imaging (Computed Tomography or CT scan)
- laboratory tests (blood and stool (faeces) tests)
- further testing or an appointment with a specialist, depending on the results.

The aim is that people on the **SCAN** pathway will have a diagnosis and be able to begin treatment faster than the previous pathways allowed.

Why have I been referred to SCAN?

Your GP has assessed you as having one of the 'non-specific' symptoms for which **SCAN** has been developed.

Do I have to take part?

No. Taking part in **SCAN** is entirely voluntary. It is up to you to decide if you want to be investigated by the **SCAN** pathway.

If you choose not to take part in the **SCAN** pathway, you will continue to receive care following the standard local guidelines agreed by Oxford University Foundation Hospital NHS Trust (OUHFT), Oxfordshire Clinical Commissioning Group (OCCG), and National Institute for Health and Clinical Excellence (NICE) guidelines.

What will I have to do if I take part?

Your GP will send the ACE team detailed information about your clinical problem, your symptoms, examination findings, medical history and any recent test results.

If you have any questions at this point, please contact the **SCAN** team.

Email: **scanpathway@ouh.nhs.uk**

Tel: **01865 227 780**
(8.30am to 4.30pm, Monday to Friday)

You will be asked to come for an appointment at the Radiology department in the Churchill Hospital in Oxford, within one week of the referral for a CT scan. You will need to collect a stool sample in the blue-topped specimen pot provided in the **SCAN** information envelope, the day before your **SCAN** appointment.

Following your first appointment, the clinical information received from your GP and all of your test results will be reviewed

by the **SCAN** team (a group of specialist doctors skilled in managing 'non-specific' symptoms).

Depending on your results, within one week the **SCAN** team will do one of the following:

1. refer you to a specialist clinic in Oxford
2. refer you for further rapid testing (within two weeks) in Oxford
3. invite you for a clinic appointment with the SCAN team in Oxford
4. refer you back to your GP with advice.

Taking part in the SCAN pathway

Please take any time you need to discuss this with your family and friends.

Before you sign the consent form at your **SCAN** appointment, you will be given time to ask questions to help you decide whether or not to take part.

When we ask you to sign the consent form, a member of our team will sign it too.

The consent form will confirm that you have read and understood the information in this leaflet. It will confirm that you have had a chance to ask questions and that these questions have been answered.

There will be another consent form which will confirm whether you agree to your blood being stored for research purposes. This is optional and does not affect your eligibility to use the **SCAN** pathway.

You can still change your mind after you have signed the consent form. You are free to withdraw from the pathway at any time, without giving a reason. This will not affect the standard of care you receive.

The SCAN Pathway

Before the start of the pathway

Your GP will discuss the **SCAN** pathway with you and will give you this information sheet.

You will be contacted by telephone by a member of the **SCAN** team, who will offer you an appointment for a CT scan and blood and stool tests.

You will have time to discuss the **SCAN** pathway in more detail and to ask any questions either at the first appointment, by telephone (01865 227 780), or by email (scanpathway@ouh.nhs.uk). Research staff may ask you some further questions during this discussion.

At your first appointment

Please bring your stool sample in the blue topped pot. You will be asked to:

1. sign a consent form to say you agree to continue on the **SCAN** pathway (see enclosed form)
2. sign a consent form to say you agree to your blood and urine samples being stored for research (see enclosed form). This is optional.
3. possibly have further blood taken and sent to the laboratory
4. hand in your filled blue-topped stool specimen pot
5. have a CT scan of your chest, abdomen, and pelvis
6. fill out a questionnaire about your experience.

Preparing for the CT scan

Please do not have anything to eat two hours prior to your appointment, as this may affect the results of the scan. You may drink water or clear fluids (no milk) up to the time of your scan. You do not need to have a full bladder.

During your scan you will have an injection of a special dye, called contrast, to enhance the scan quality. The CT scan will take approximately 20 minutes. A further information leaflet is included to give you more details about the CT scan.

Follow-up

Your follow-up care will be based on your medical history and test results. The various options are shown in the flowchart on page 10. If the results from the CT scan and other tests do not show that further evaluation is needed, the **SCAN** team will write to your GP with information and treatment suggestions.

If you take part in the **SCAN** pathway, the information collected during your follow-up care will be included in the SCAN database and will be used to help develop more effective pathways to diagnose people with non-specific symptoms. All of the information we collect will be kept strictly confidential.

At the end of the SCAN pathway

You will not be required to have any more appointments, tests or scans. You may be asked to fill out a further questionnaire about your experiences of the **SCAN** pathway.

Data from your medical records will be collected on the outcome of your investigations and any further diagnoses or treatments that you have over the next two years. Your GP or specialist will discuss with you any further NHS treatments, care, monitoring or testing that may be necessary. If you move away or change Health Authority, data will be collected about your health status from the Health and Social Care information Centre and other NHS bodies.

What if there is a problem during the course of the pathway?

Every care will be taken during the course of the pathway. If you have a concern about any aspect of the pathway, you should ask to speak with the **SCAN** team, who will do their best to answer your questions.

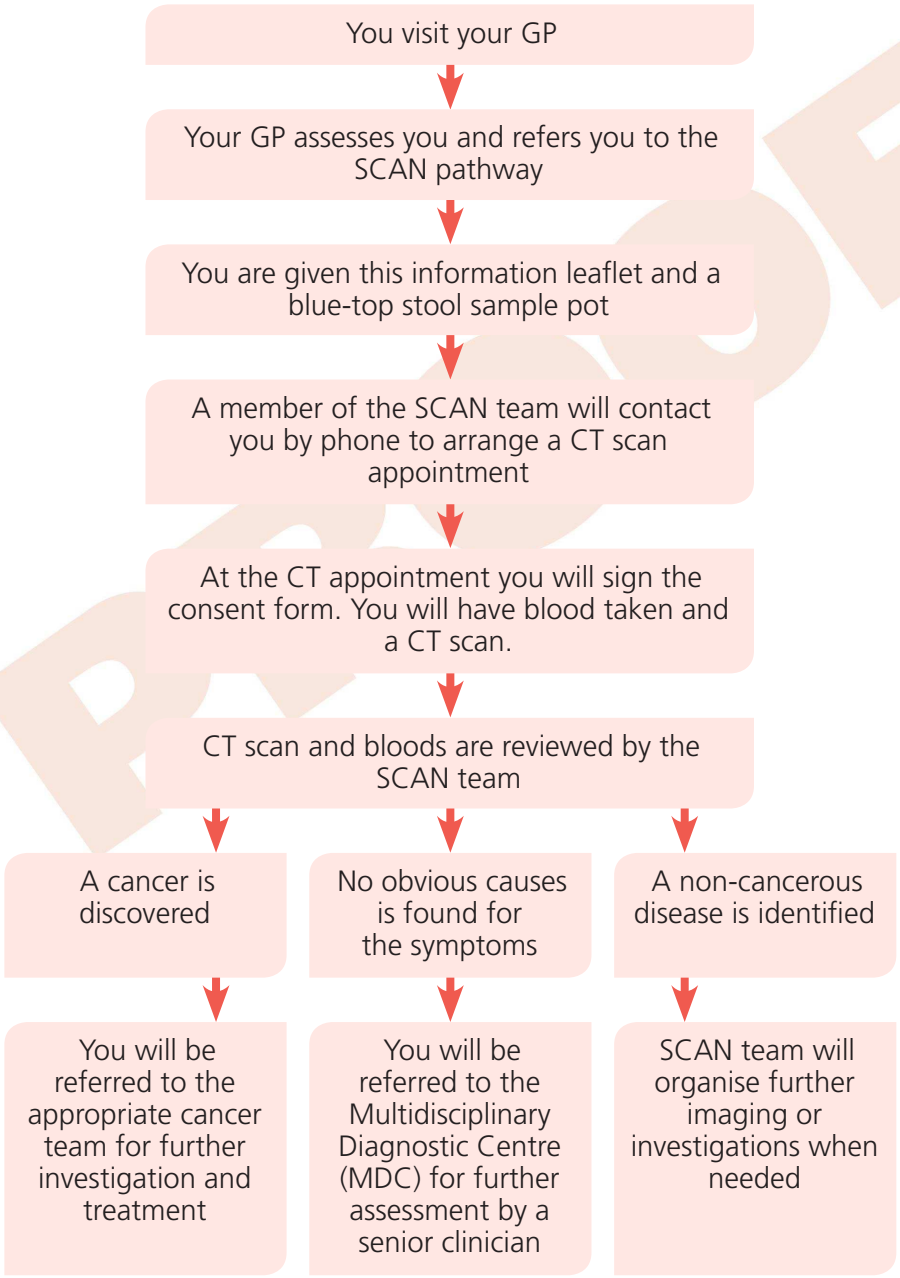
Tel: **01865 227 780**

Email: **scanpathway@ouh.nhs.uk**

If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Additional information is available from your local Patient Advice and Liaison Service office.

Email: **www.pals.nhs.uk**

Summary of SCAN pathway



page 10

Will my taking part in this service evaluation be kept confidential?

If you join the **SCAN** pathway, all information which is collected about you during the course of the research will be kept strictly confidential. Documents relating to you will be kept by the OUHFT and at the University of Oxford, Nuffield Department of Primary Health Sciences, in secure areas and on a password protected computer and database.

You will be entered into the **SCAN** database. All data collected about you will be linked with your NHS number and year of birth. Your medical records and the data collected for the pathway will be looked at by authorised persons involved in your care or the service evaluation. Authorised people from OUHFT may also check them to make sure that the service evaluation is being carried out correctly.

Oxford Imaging Trials Unit (OITU) at the Churchill Hospital will also keep your current and previous names, date of birth and NHS number, to find out if you were diagnosed by **SCAN** or an alternative pathway as part of the service evaluation. Any test results received will have been anonymised at site; this involves blacking out/removing any personal information.

Responsibility for compliance with national and international data protection standards lies with the Oxford University Hospital NHS Foundation Trust.

What will happen to any samples I give?

The blood and stool samples that you give as part of this pathway will be analysed immediately in the laboratory of Oxford University Hospitals.

In addition, we would like to collect blood and urine samples for research purposes, to investigate tests for cancer or other diseases in people with non-specific symptoms. This may sometimes involve diagnostic companies or researchers, who have developed specialist tests for these symptoms. There would be no financial gain for the **SCAN** team in relation to these samples. The additional consent form asks you to consent to the use of your samples in this way.

What will happen to the results of the SCAN pathway service evaluation?

The combined anonymised results of the SCAN pathway will be analysed by the SCAN researchers, shared with other ACE pilot projects, the Department of Health, Macmillan Cancer Support, Cancer Research UK, and published in medical journals.

The service evaluation will take 2-4 years to complete and the results should be available and published after 2019. If you are interested in the results, please look up ACE Wave 2 on the Cancer Research UK website or contact the SCAN team at scanpathway@ouh.nhs.uk

If the results show conclusively that rapid investigation of non-specific symptoms leads to earlier diagnosis of cancer, they may be used to influence future NHS guidelines.

Who is sponsoring this pathway?

The SCAN pathway is funded by the Department of Health, Macmillan Cancer Support, and Cancer Research UK. The pathway is supported by Oxford University Hospitals NHS Foundation Trust, the Oxfordshire Clinical Commissioning Group (OCCG) and the University of Oxford. It is being carried out by the Oxford Imaging Trials Unit and the OCCG.

Contact details

If you have any further questions about the SCAN pathway, please contact:

Julie-Ann Phillips (SCAN Navigator)

Tel: **01865 227 780**
(8.30am to 4.30pm, Monday to Friday)

Email: **scanpathway@ouh.nhs.uk**

Thank you for reading this information booklet. If you decide to take part in this pathway you must personally sign and date the consent form.

We will give you a copy of this information sheet and your signed consent form.
We will keep a second copy of this document with the service evaluation records on and will place a third copy in your radiology records.

This pathway is being supported by:

- Oxfordshire Clinical Commissioning Group
- Cancer Research UK
- NHS England
- Macmillan Cancer Support
- Nuffield Department of Primary Care Health Sciences
- Oxford University Hospitals NHS Foundation Trust

If you have a specific requirement, need an interpreter, a document in Easy Read, another language, large print, Braille or audio version, please call **01865 221 473** or email **PALS@ouh.nhs.uk**

Author: Julie-Ann Phillips, SCAN Navigator
March 2017
Review: March 2020
Oxford University Hospitals NHS Foundation Trust
Oxford OX3 9DU
www.ouh.nhs.uk/information

OMI 14548P

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Page where met
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1,2
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	NA
	2b	All items from the World Health Organization Trial Registration Data Set	NA
Protocol version	3	Date and version identifier	NA
Funding	4	Sources and types of financial, material, and other support	3, 10
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	10
	5b	Name and contact information for the trial sponsor	NA
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	10
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	9, 10
Introduction			

Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3
	6b	Explanation for choice of comparators	7
Objectives	7	Specific objectives or hypotheses	3, 4
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	3 – 6
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	4
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	4
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	5, 6
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	NA
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	NA
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	NA

Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	7
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	7
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	NA
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	NA
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	NA
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	NA
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	6 (enrolment of participants, all else NA)

Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	NA
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	6
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	NA
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	9
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	7 – 9
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	8, 9
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	NA
Methods: Monitoring			

Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	9, 10
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	NA
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	8
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	NA
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	10
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	NA
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	5
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	5
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	7
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	10

Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	9, 10
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	9
	31b	Authorship eligibility guidelines and any intended use of professional writers	NA
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	NA
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Online material 1
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

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The Suspected CANcer (SCAN) pathway: protocol for evaluating a new standard of care for patients with non-specific symptoms of cancer.

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The Suspected CANcer (SCAN) pathway: protocol for evaluating a new standard of care for patients with non-specific symptoms of cancer.

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The Suspected CANcer (SCAN) pathway: protocol for evaluating a new standard of care for patients with non-specific symptoms of cancer.

ABSTRACT

Introduction: Cancer survival in England lags behind most European countries, due partly to lower rates of early stage diagnosis. We report the protocol for the evaluation of a multidisciplinary diagnostic centre based pathway for the investigation of 'low risk but not no risk' cancer symptoms called the Suspected CANcer (SCAN) pathway. SCAN is a new standard of care being implemented in Oxfordshire; one of a number of pathways implemented during the second wave of the ACE programme, an initiative which aims to improve England's cancer survival rates through establishing effective routes to early diagnosis.

Methods and analysis: To evaluate SCAN, we are collating a prospective database of patients referred onto the pathway by their GP. Patients aged over 40 years, with non-specific symptoms such as weight loss or fatigue, who do not meet urgent cancer referral criteria or for whom symptom causation remains unclear after investigation via other existing pathways, can be referred to SCAN. SCAN provides rapid CT scanning, laboratory testing, and clinic review within 2 weeks. We will follow all patients in the primary and secondary care record for at least two years. The data will be used to understand the diagnostic yield of the SCAN pathway in the short term (28 days) and the long term (2 years). Routinely collected primary and secondary care data from patients not referred to SCAN but with similar symptoms, will also be used to evaluate SCAN. We will map the routes to diagnosis for patients referred to SCAN to assess cost-effectiveness. Acceptability will be evaluated using patient and GP surveys.

Ethics and dissemination: The Oxford Joint Research Office Study Classification Group has judged this to be a service evaluation and so outside of research governance. The results of this project will be disseminated by peer reviewed publication and presentation at conferences.

Strengths and limitations of this study:

- SCAN will be evaluated in relation to diagnostic yield, time to diagnosis, cost effectiveness, patient satisfaction, and incidental diagnoses.
- Data from both the primary and secondary care record will be used to populate a bespoke prospective database detailing the cohort of patients evaluated by the SCAN pathway.
- A randomised GP or patient level implementation of SCAN was not feasible within the constraints of the local health system, nor a randomised stepped-wedge roll-out to the six Oxfordshire CCG regions.
- Instead a pragmatic service evaluation is being conducted around a phased rollout of the pathway against the previous standard of care in the same region, operated by the same Clinical Commissioning Group (CCG).
- The findings of this evaluation will only indicate SCAN's effectiveness in Oxfordshire and should not be generalised to the rest of England.

BACKGROUND

England's rates of cancer survival lag behind many other European countries, and late stage at diagnosis is thought to play a large part in this.(1, 2) Twenty-one percent of cancers are diagnosed as an emergency, which is associated with advanced tumour stage and increased short-term mortality.(3, 4) It is estimated that, if diagnosed early, 5000 cancer deaths could be prevented every year for breast, colorectal, and lung cancers alone.(2, 5) The ACE (Accelerate, Coordinate & Evaluate) Programme is an early diagnosis initiative supported by NHS England, Cancer Research UK (CRUK), and Macmillan Cancer Support.(6) It was formed to help improve England's cancer survival rates by generating evidence on how best to configure diagnostic pathways to drive a shift from late to early cancer at diagnosis, reduce the number of cancers diagnosed as an emergency, and improve patient experience.

The first wave of ACE comprised around 60 projects aiming to evaluate local initiatives to develop a national body of evidence to inform cancer commissioning.(7) A weakness in the current system identified during Wave 1 was the lack of a clear urgent referral pathway for patients with non-specific but concerning symptoms known to be associated with a range of cancer sites, such as fatigue, abdominal pain and weight loss.(8) Consequently, before reaching a cancer diagnosis, these patients often have multiple tests and non-urgent referrals resulting in delays in diagnosis.(9) The Independent Cancer Taskforce outlined the need to explore new models of care to speed up diagnosis in patients with non-specific symptoms, making references to the multidisciplinary diagnostic centre (MDC) concept.(10) ACE Wave 2 was set up to facilitate the development and evaluation of a small number of MDC based pathways in the English National Health Service (NHS).(6) These pathways are implemented as standards of care in participating regions, in addition to site-specific urgent cancer referral pathways.

Oxfordshire's Suspected CANcer (SCAN) pathway emulates a Danish MDC pathway, the Non-Specific Symptoms and Signs of Cancer Patient Pathway (NSSC-CPP).(11) Patients first undergo a panel of diagnostic investigations including blood and urine tests and diagnostic imaging. If no diagnosis is made, but cancer or another serious disease is suspected, the patient is referred to the MDC.(11, 12) The MDC is a diagnostic unit with access to a broad range of investigations and specialist expertise in managing patients with non-specific symptoms. Of 1,278 patients referred to the NSSC-CPP pathway by their General Practitioners (GPs), a cross-sectional study reported that 16% of patients were diagnosed with a cancer.(13) The most common symptoms recorded were weight loss (53%), fatigue (50%), and pain (37%). The most common clinical findings were "affected general condition" (36%), GP "gut feeling" (23%), and abnormal abdominal examination (13%). Forty-eight percent of patients were referred with abnormal blood test results. Cancer was diagnosed across a broad range of 18 subgroups, the most common of which were lung (18%), colorectal (13%), haematological (10%), pancreatic (9%), and upper-gastrointestinal (8.2%).(13) A later cohort study including 938 patients referred to the NSSC-CPP reported that 35% were diagnosed with serious disease within 3 months, of which one third had cancer.(14)

As is the case in the UK, health care in Denmark is mostly free to access for residents, and Danish GPs act as 'gatekeepers' to specialist services.(15) Five-year survival rates for several cancer types are also among the lowest in Organisation for Economic Co-operation and Development (OECD) countries.(15) Both countries have introduced a one month standard for the time between referral and diagnosis to increase the proportion of cancers diagnosed at an early stage.(15, 16) Furthermore, following the introduction of cancer pathways in Denmark which incorporate patient

review by multidisciplinary teams, waiting times have significantly reduced across almost all cancer types.(17) The similarities between the Danish and UK health systems, the challenges faced by both, and the improvements brought about by MDC based pathways, suggest that these pathways for non-specific symptoms warrant evaluation in the UK. At the time of writing, we retrieved no peer-reviewed articles detailing MDC pathways for cancer diagnosis in the UK and only one conference abstract describing 91 patients assessed via an alternative MDC pathway developed during ACE Wave 1 in London.(18) Robust evaluation of the SCAN pathway has the potential to contribute to the evidence base for the MDC concept in cancer diagnosis. We report here the protocol for the SCAN pathway evaluation.

Aim

The aim of this study is to evaluate the SCAN pathway, a new standard of care for the rapid investigation of patients with non-specific cancer symptoms in Oxfordshire. SCAN will be evaluated in terms of how well it meets its objectives, which are detailed below.

Objectives

In line with the CRUK ACE initiative which aims to reduce late and increase early cancer diagnosis, decrease cancer diagnoses made through emergency presentations, and improve patient experience (6), the objectives of the SCAN pathway are to:

- Reduce time from initial primary care presentation with symptoms to diagnosis.
- Achieve a higher proportion of early stage cancer at diagnosis.
- Improve patient experience of the diagnostic pathway.
- Establish whether the MDC model is cost-effective.

SETTING

Oxfordshire's cancer incidence (600 cases per 100,000) is lower than the UK average (615 cases per 100,000). Cancer mortality (261 per 100,000) is also lower than the national average, with fewer cancers diagnosed through emergency presentation (17.1% vs. 20.1%) and more patients diagnosed at an early stage (56.8% vs. 54.3%) than the national average.(19) Comprising a predominantly white (90.85%) population, Oxfordshire has smaller foci of Asian (4.84%), Black (1.75%), and mixed ethnic (2.02%) groups. Black and minority ethnic (BME) communities form 22.4% of Oxford City's population, with lower proportions in more rural districts: 7.8% in Cherwell, 3.2% in West Oxfordshire (Source: 2011 Census (20)). Rural districts (67%) rank in the 10% least deprived, and urban (33%) in the 20% most deprived in England. There are no ACE Wave 1 sites in Oxfordshire.

The Oxfordshire Clinical Commissioning Group (CCG) serves a population of over 700,000 through 70 General Practices.(21) Oxford University Hospitals NHS Foundation Trust (OUHFT) is made up of four hospitals providing a range of specialist services (John Radcliffe, Churchill Hospital, Nuffield Orthopaedic Centre, and the Horton General Hospital). SCAN imaging takes place at the Churchill Hospital and the SCAN MDC is located at the John Radcliffe Hospital. SCAN links with the Oxford Allied Health Science Network (AHSN) Imaging Network, aiming to develop a model for expansion through the seven adjoining NHS network trusts.

THE SCAN PATHWAY

SCAN retains the GP's gate-keeping role, requiring patients to first attend their GP with symptoms to access the pathway through GP referral.(22) The SCAN referral algorithm was developed by consensus between a multidisciplinary team including GPs, Radiologists, physicians, and health service researchers (Appendix 1). It incorporates age-thresholds and "low-risk but not no-risk" symptoms that fall outside of existing urgent 2-week-wait (2ww) referral pathways based on the National Institute of Care Excellence (NICE) NG12 suspected cancer guidelines (23), but remain predictive of cancer in primary care.

SCAN will be opened up sequentially to GPs in each of the six sub-regions of Oxfordshire CCG, to ensure that the team has enough capacity to meet demand. The first region opened 15th March 2017, the second on the 5th June 2017. In response to demand, regions three and four were opened on 6th September 2017, and the final two regions are expected to open on the 30th October 2017.

Estimated referral rate

We used the following data to estimate expected referral rates: (i) Oxfordshire population statistics (20); (ii) the number of GPs in Oxfordshire (21); (iii) the referral rate reported for the Danish NSSC-CPP pathway (12); (iv) the estimated prevalence of non-specific symptoms meeting SCAN referral criteria in primary care populations, derived from the control groups of primary care based case-control studies.(24) Using these sources, an estimate of 20-40 referrals per week was anticipated, taking into account that not all patients presenting to primary care with qualifying symptoms will be referred by their GP: symptoms may not occur in isolation or a pre-existing condition will provide explanation; GPs may identify an alternative explanation for new symptoms negating the need for referral; patients may be referred by other routes; or patients may decline referral.

Referral criteria

A structured standardised electronic referral form has been disseminated to all GPs in Oxfordshire (Appendix 2). If there is no other urgent referral pathway for the clinical scenario, patients aged ≥40 years of age are accepted if their GP is concerned about cancer or serious disease following face-to-face primary care assessment of individual or combined "low-risk but not no-risk" symptoms, such as: weight loss, appetite loss, nausea, fatigue, malaise, abdominal pain, anaemia and thrombocytopenia. In addition, patients may be referred based on their GPs clinical suspicion of cancer or serious disease (their "gut feeling").(25, 26) GPs are also requested to indicate their suspicion of malignancy at this stage (Table 1).

Table 1. SCAN referral criteria.

Essential	**There is no other urgent referral pathway suitable for this clinical scenario**					
Essential	**≥40 years of age**					
Essential *Tick all that still apply* ***after primary care***	**Unexplained Weight Loss**	Measured	☐	Kg loss	___ kg	Duration ____ weeks
		Patient Reported	☐			
	Severe unexplained fatigue	TSH (within 1m)	_____ miu/L			
	Persistent nausea or appetite loss					

assessment	**New atypical pain** (eg. diffuse abdominal or bone pain).	Site?	_____	
	Unexplained laboratory test findings (eg. anaemia, thrombocytopaenia, hypercalcaemia)		Please specify	_____
	GP Clinical Suspicion of cancer or serious disease / GP "gut feeling"			

STAGES OF THE PATHWAY

As part of their initial work-up to exclude more common causes of non-specific symptoms in primary care, GPs will conduct investigations essential to allow access to the SCAN pathway: creatinine (necessary prior to IV contrast) and thyroid function tests (hypothyroidism as a cause of fatigue). The referral form completed by the GP constitutes a referral for all aspects of the SCAN pathway including the CT scan and blood tests. Once referred, a member of the SCAN team (the SCAN pathway navigator) assumes clinical responsibility for the patient, confirms that the patient meets the inclusion criteria, orders and coordinates the CT and blood tests, and provides a point of contact for the patient. Demographic and clinical information are captured by the GP referral form.

Consent: At the point of referral, patients are given a participant information sheet detailing the SCAN pathway and consent form (Online Supplementary Material 1) to allow their anonymised medical records to be used for the purposes of evaluating the pathway. Patients are given time to take the information away and consider whether they wish to participate. If patients decide to participate, they are asked to take the consent form to the initial appointment, at which time they may ask any outstanding questions. Patients who do not wish to have their medical records used may still be referred onto the SCAN pathway but will not be followed-up for the purposes of the evaluation. At the time of writing none of the patients accepted onto SCAN had refused consent.

Stage 1: GP direct access triage tests: At the first hospital appointment, a panel of standard diagnostic investigations with rapid turnaround (request-test-report) of <7 days are performed. These tests include a panel of blood tests, faecal immunochemical testing, and appropriate low-dose CT imaging with separate reporting lines to ensure report turnaround times of 24 hours (Table 2). Separate reporting lines for radiology facilitate evaluation, and the Academic Health Science Network (AHSN) imaging consultants provide additional reporting capacity to ensure turnaround times.

Table 2. Tests performed at SCAN Stage 1

- Full Blood Count
- Erythrocyte Sedimentation Rate
- C-reactive protein
- Urea and electrolytes
- Creatinine
- Calcium
- Phosphate
- HBA1c
- Thyroid function

- CA125 (females)
- PSA (males)
- Faecal Immunochemical Testing
- Computed Tomography (Thorax, Abdomen, Pelvis)

Stage 2: The clinical information obtained in stage 1 directs the patient's subsequent progression through the pathway. Patients are either referred:

2-a. onto a Cancer Multi-Disciplinary Team (MDT) or specialist clinic via an existing urgent pathway.
2-b. for additional direct access investigation within 1 week prior to clinician review.
2-c. to the Multi-disciplinary Diagnostic Centre (MDC) for medical review.

The referring GP receives a copy of the CT report and a letter from the SCAN team explaining which arm of the pathway their patient has been referred to. Any urgent findings are communicated to the GP via telephone. Any telephone conversations are followed by a letter detailing the conversation and the actions the GP and SCAN team have agreed to.

Stage 3: If symptom causation remains unclear after 2-a or 2-b, the patient is automatically referred to the MDC (2-c). At the point of referral to the MDC, the accepting hospital clinician becomes the responsible MDC clinician. At the MDC, the sequence of testing to further explain the patient's clinical problem is determined by the accepting clinician.

Stage 4: All patients who consent to participate in the SCAN pathway will be followed up for 2 years, including patients for whom cancer and serious disease is excluded. The GP will receive a structured follow-up plan allowing return to the MDC to avoid repeat CT scanning for patients with new, recurrent, or persistent symptoms meeting SCAN entry criteria. By passing through the MDC, the patient is granted access to allied health professional input (dietician, physiotherapy, psychology) where necessary. The patient journey along the SCAN pathway is summarised in Appendix 3.

METHODS FOR EVALUATION

The sequential implementation of the SCAN pathway in Oxfordshire has allowed a short informal 'pilot' period during which we have been able to assess the functioning of the pathway to address any issues that may arise before it is opened to all GPs. A detailed analysis of the consecutive cohort of patients referred to the SCAN pathway, whose medical records are gathered retrospectively and followed up prospectively, will form the basis of the pathway's evaluation. We will also evaluate the pathway in terms of its cost effectiveness as well as a number of other indicators detailed below, thereby following the framework for evaluating complex interventions as laid out by the Medical Research Council.(27)

SCAN Database

The OpenClinica computer package (https://www.openclinica.com/) is being used to store a database of demographic information, symptoms leading to referral, investigations performed, referrals made, appointments, diagnoses, and short term and long-term outcomes for all patients referred to SCAN. The time-point and outcome of each clinical encounter will be recorded for at least 2 years following referral to identify short-term and long-term diagnoses.

Patients will enter the database on the date the SCAN team confirms their eligibility. At this point data collected retrospectively from the primary care record using the auto-populating referral form (Appendix 2) will be manually entered into the SCAN database, and prospective data collection will begin using the OUHFT record.

The SCAN pathway will be evaluated based on its short term and long term diagnostic yield and its cost effectiveness in terms of the resources and time needed for a diagnosis to be reached. Patients' route to diagnosis and satisfaction with their experience of the SCAN pathway will also be evaluated as secondary outcomes. The primary and secondary points of evaluation are described in detail below.

Primary points of evaluation.

Diagnostic Yield

a. Short-term: diagnoses made within 28 days of referral
   - Cancer site and stage at diagnosis- histopathology or MDT determined.
   - Non-cancer diagnoses determined by MDC or another specialist clinic.
b. Long-term: diagnoses made within 2 years of referral
   - Confirmed by primary and secondary care database review at 2 years.

Secondary points of evaluation

a. To map the route to diagnosis for SCAN patients in terms of time intervals associated with diagnosis (i.e. each diagnostic interval in line with the Aarhus statement (28)) and the number and sequence of patient encounters (investigations and appointments leading to diagnosis), including the number of diagnoses made following an emergency presentation.
b. To quantify incidental findings detected by the SCAN pathway.
c. To evaluate the cost effectiveness of the SCAN pathway.
d. To assess patient and GP satisfaction with the SCAN pathway.

SCAN implementation.

The implementation of the SCAN pathway will be carried out in six stages corresponding to the six Oxfordshire CCG sub-regions. This pragmatic decision was made to allow the OUHFT and CCG to monitor GP uptake of the pathway in real-time to ensure that the capacity of the pathway is not exceeded and to allow early problems with service delivery to be overcome. This is an opportunity for a rigorous evaluation of the pathway in real-time, in the same county, and which will avoid the potential confounding that could arise from comparing SCAN patients to patients in different regions operated by different CCGs.

Pre-SCAN period: Before having access to SCAN, GPs in each region will be asked to prospectively identify patients meeting SCAN entry criteria and to complete a "dummy" comparator cohort data collection form to be submitted by email to a secure CCG email inbox (Appendix 4). Anonymised referral information is extracted electronically to maintain patient confidentiality. This group of comparator patients will provide data about patients receiving the standard of care prior to the introduction of SCAN (the new standard of care) who are diagnosed via alternative routes, such as 2ww pathways, non-urgent specialist referral, or by emergency presentation. In addition, an audit of

local GP electronic records of patients with symptoms meeting SCAN referral criteria, but referred by other routes for investigation, will provide further contemporaneous data against which to evaluate SCAN.

SCAN period: Depending on uptake of the pathway, each CCG region will transition to the SCAN pathway over time. The set up and evaluation of the SCAN pathway is currently funded for a period of at least 2 years of patient intake and 2 years of follow-up. ACE Wave 2 projects are expected to report results in late 2018 (6). Following this, it is anticipated that Oxfordshire CCG will adopt SCAN indefinitely and will take on its funding as the MDC model is of interest to NHS England.

Follow-up: All patients will be followed up in the primary and secondary care record for at least 2 years from entry by the pathway navigators.

STATISTICAL ANALYSIS

Primary point of evaluation - Diagnostic Yield

Our primary point of evaluation is yield from the new SCAN pathway with respect to the number and proportion of patients (a) with a new diagnosis or with disease excluded within 28 days, and (b) with a diagnosis made within 2 years of referral. For newly diagnosed patients we will report the diagnostic interval (first presentation to primary care to date of diagnosis); the doctor interval (first presentation to primary care to the first primary care investigation); the primary care interval (first presentation to primary care to referral to secondary care); secondary care interval (referral to secondary care to start of treatment); and the treatment interval (diagnosis to the start of treatment).(28) For patients with indeterminate abdominal findings which require further investigation, we will report the number of follow-up consultations or investigations up until discharge.

The analysis of long-term outcomes will be conducted after 2 years, where missed diagnoses (false negatives) will be defined as diagnoses not picked up in the short-term but in the longer term and attributed to the initial symptomatic presentation allowing entry to the cohort. Within this analysis, the proportion of patients diagnosed with cancer and surviving 1-year will be ascertained.

Secondary points of evaluation - Route to diagnosis, cost effectiveness, GP and patient satisfaction

For the secondary outcome assessing routes to diagnosis, the number (and type) of healthcare contacts required to make a diagnosis will be counted for each participant starting from the initial primary care visit for the symptoms permitting referral to SCAN. The number of patients diagnosed following an emergency presentation will also be counted. Medians and inter-quartile ranges (IQRs) will be calculated for each of the diagnostic intervals (days) stratified by symptom group, disease type, disease site and severity/stage where possible and presented graphically using boxplots.

Incidental findings: Incidental findings are radiological abnormalities not caused by the symptoms being investigated that may drive further imaging and concern.(29) To understand incidental findings in patients referred to SCAN, demographic, clinical, and radiological information will be extracted from the SCAN database. Imaging findings will be categorised per anatomical location. Each finding will be defined as of potential clinical importance (e.g. cancer, aneurysms, and cardiac findings), and probable or consistent with, or equivocal or unlikely to explain the symptoms at the

time of referral. In the case of multiple lesions of the same type, the number will be recorded and reported. As the SCAN pathway uses ungated low dose CT imaging, an approach to avoid the over interpretation of cardiac findings was developed. The TeraRecon software package (https://www.terarecon.com/) will be used to look at any coronary artery calcification and an Agatson score will be calculated. This approach has been adopted due to the success that has been reported in a number of American studies assessing the prognostic accuracy of calcium scoring coronary arteries from an ungated low dose CT scan.(30-34) The data gathered from patients' medical records will be used to evaluate the ability of this protocol to show relevant coronary artery calcification. Incidental findings that have potential clinical importance will be followed up according to the standards issued by the American College of Radiologists, the British Thoracic Society, and the Royal College of Radiologists.(35-37) In addition, any further investigations (e.g. MRI) required to determine if CT findings are truly incidental will be recorded as part of mapping routes to diagnosis.

Patient survey: All patients who consent to participate in the evaluation of the SCAN pathway will be asked to complete a set of questionnaires about their experience of the pathway. The Consequence of Screening (COS) questionnaire (originally Psychological Consequences Questionnaire (PCQ)) (38) will be given to patients shortly after the referral to the MDC and then again 6-12 months after their referral. Individual items on the COS scales will be combined into themes of anxiety, behaviour, sense of dejection, and sleep, and item scores added together. COS domain scores will be compared across patients who had a confirmed diagnosis of cancer or other serious disease, false positive finding, and probably benign finding using non-parametric tests.

Patient satisfaction surveys will also be distributed to all patients (regardless of participation in the pathway evaluation) at the end of their CT scan. This questionnaire has been designed to evaluate the patient's experience of the staff and the service provided by the radiology department.

GP satisfaction survey: A brief satisfaction survey will be distributed to all participating GPs. This survey will assess satisfaction with the ease of use of the SCAN pathway, speed with which referred patients are seen by the SCAN team, and the quality of the information provided to GPs by the SCAN team both in terms of the functioning and purpose of the pathway, and the results of the diagnostic tests undergone by their patient(s). The survey will be distributed and completed online using the Bristol Online Surveys tool (https://www.onlinesurveys.ac.uk/).

Cost-effectiveness: The cost-effectiveness of the SCAN pathway will be assessed from the perspective of the NHS in England, using a within trial analysis. Each patient encounter from referral to SCAN up until a final diagnosis is made or excluded will be recorded. The outcome will be incremental cost-effectiveness compared to the pre-SCAN pathway, with effectiveness measured in unit reduction in time to diagnosis, and in additional diagnosis within 28 days. The comparison group will be the pre-SCAN patient cohort. Although the numbers of comparator patients should closely resemble those of patients referred to the pathway as the inclusion criteria are identical, we expect comparator patient numbers to be lower as GPs are requested to take time to complete the referral forms with no tangible benefit to their patients. Due to the expected lower response rate we will supplement comparator data from GPs with an audit of Oxfordshire surgeries with the appropriate data sharing agreement, approximately 60 practices, up to March 2017. The resource use of patients in the SCAN pathway and its comparator will be estimated from the database and costed using national unit costing databases.(39) In addition, patients will be asked to complete the UK Cancer

Costs Questionnaire (40) to record on going financial and opportunity costs. Sensitivity analyses will be carried out on the key assumptions of the evaluation, including resource use assumptions, the impact of adjusting for baseline characteristics, and extending the analysis to cost utility.

Eligible patients not referred to SCAN

The phased introduction of the SCAN pathway affords comparison with outcomes under the previous standard of care for patients meeting SCAN referral criteria. This will include patients with SCAN eligible symptoms identified by their GPs and diagnosed via alternative routes, for example by 2ww pathways, non-urgent specialist referral, or by emergency presentation. Robust statistical comparisons between SCAN and the period prior to SCAN may be limited dependent on gathering data on a sufficient number of patients with symptoms meeting SCAN referral criteria who are not referred to SCAN, which is in turn dependent on GPs completing the comparator referral forms. Therefore, the data collected on patients not referred to SCAN provided by GPs will be supplemented with an audit of the primary care record and will be presented in tables with descriptive statistics, only comparing SCAN and pre-SCAN outcomes when appropriate.

Sample Size

In order to have power >80% (alpha = 5%) and if the SCAN pathway halves the average length of the diagnostic interval compared to usual care (Hazard ratio = 2), we would need at least 43 patients diagnosed with cancer during the pre-SCAN period and at least 173 patients diagnosed with cancer following the introduction of the pathway. (41) If 15% of patients presenting to their GP with non-specific symptoms have cancer (12) we need to recruit at least 1460 patients.

Data handling and data management

A data management plan (DMP) is in place outlining in detail the specific procedures to ensure that high quality data are produced for statistical analysis. The DMP was reviewed and signed off by all relevant parties prior to data management activities commencing.

Data will be collected electronically in OpenClinica (https://www.openclinica.com/) and data validation is achieved through electronic programmed checks or through manual review of listing outputs. All discrepancies generated by electronic validation checks or manual listings will be reviewed by the data manager.

ETHICS AND DISSEMINATION

Evaluation of a newly established service/adopted pathway does not require research governance as such activity falls outside of the definition of research as set out by the Health Research Authority (HRA) and would not be considered research in the NHS. As such, this study is not subject to the Department of Health's Research Governance Framework for Health and Social Care (2005). This opinion can be reviewed by reference to the HRA's algorithm, available at http://www.hra-decisiontools.org.uk/research/ and attendant leaflet, Defining Research, or by reference to The Health Care Quality Improvement Partnership (HQIP)'s Guide for Clinical Audit, Research and Service Review.(42) In addition, a Privacy Impact Assessment concluded that individual patient consent was

not necessary to collect data on the comparator patients. The primary reason for this was that obtaining consent was likely to cause unnecessary distress to patients who were not yet able to make use of the new pathway. Instead, a data sharing agreement was signed by all participating GP surgeries and all comparator data will be sent electronically to the CCG Commissioning Support Unit (CSU) and pseudonomised before being shared with the SCAN team.

The results of this evaluation will be reported in peer-reviewed journals and on the websites of the various ACE Wave 2 funding bodies. Abstracts for oral or poster presentations will be submitted to national and international conferences. Data resulting from this study will be made available following a request to the authors.

STRENGTHS AND LIMITATIONS

This is the first published protocol for the evaluation of a MDC pathway based in the UK. The evaluation outlined will provide detailed information on the diagnostic yield and time to diagnosis for comparison of the MDC model with existing routes to diagnosis in the NHS. Our focus on incidental findings and cost-effectiveness will add valuable evidence about the value of early CT scanning of patients with non-specific symptoms, especially in response to concerns about overdiagnosis.

Our evaluation, however, has some limitations. First, due to the pragmatic nature of SCAN's implementation the evaluation has had to take into account resource constraints and logistical realities of Oxfordshire's health system. Consequently, we have been unable to randomise individual patients or GPs to the SCAN pathway, nor could we randomise the sequence of a stepped-wedge rollout of SCAN across CCG regions. Secondly, collection of comparator data is reliant upon local GPs opting to do so as an additional task in an already busy health service without additional financial incentive. We are supplementing this approach with a retrospective review of primary care records to identify eligible pre-SCAN patients. The method of symptom capture using this approach is in development but may be limited to retrospective electronic coded entries. Due to these factors the generalisability of our findings outside of Oxfordshire will be limited.

CONCLUSION

Cancer prognosis improves with early diagnosis but the UK lags behind many European countries in terms of the proportion of patients diagnosed at an early stage. For this reason, the Independent Cancer Taskforce has highlighted the need for alternative routes to diagnosis to be explored and has made specific reference to MDC based pathways. The SCAN pathway is such an MDC based pathway which has been adopted in Oxfordshire with the aim of reducing the time from initial presentation of non-specific but concerning symptoms to diagnosis, and increasing the proportion of cancers diagnosed at an early stage. We will evaluate the ability of the SCAN pathway to meet these aims over two years, will assess the patient experience of the diagnostic pathway, and appraise the cost-effectiveness of the pathway.

FUNDING STATEMENT

This work is supported by Cancer Research UK, Macmillan Cancer Support, NHS England, and the Department of Health's Policy Research Units. As part of the ACE programme, CRUK put out a research brief and specified some areas on which the pathways should be evaluated. The funders

had no role in the design of the pathway, writing of this protocol, nor the decision to submit for publication. Going forward, the funders will have no role in data collection, management, or interpretation.

STATEMENT OF CONTRIBUTION

The clinical pathway was designed by FG, SH, SA, BDN, TM, ZK, and DL. BDN, JO, and LA designed this pathway evaluation. The patient information leaflet was developed by BDN and reviewed by JL, JAP, JO, and SH. BDN, CFS, IG, and SK designed and oversaw the building of the SCAN database. BDN, CFS, and ZK designed and set up the procedures for the audit of clinical records for comparator data. BDN, JO and CFS wrote this protocol, all authors reviewed and gave comments. All authors will be involved in the running of this evaluation study and the analysis of the results. All authors have read and approve this protocol.

COLLABORATORS

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COMPETING INTERESTS

The authors declare no competing interests.

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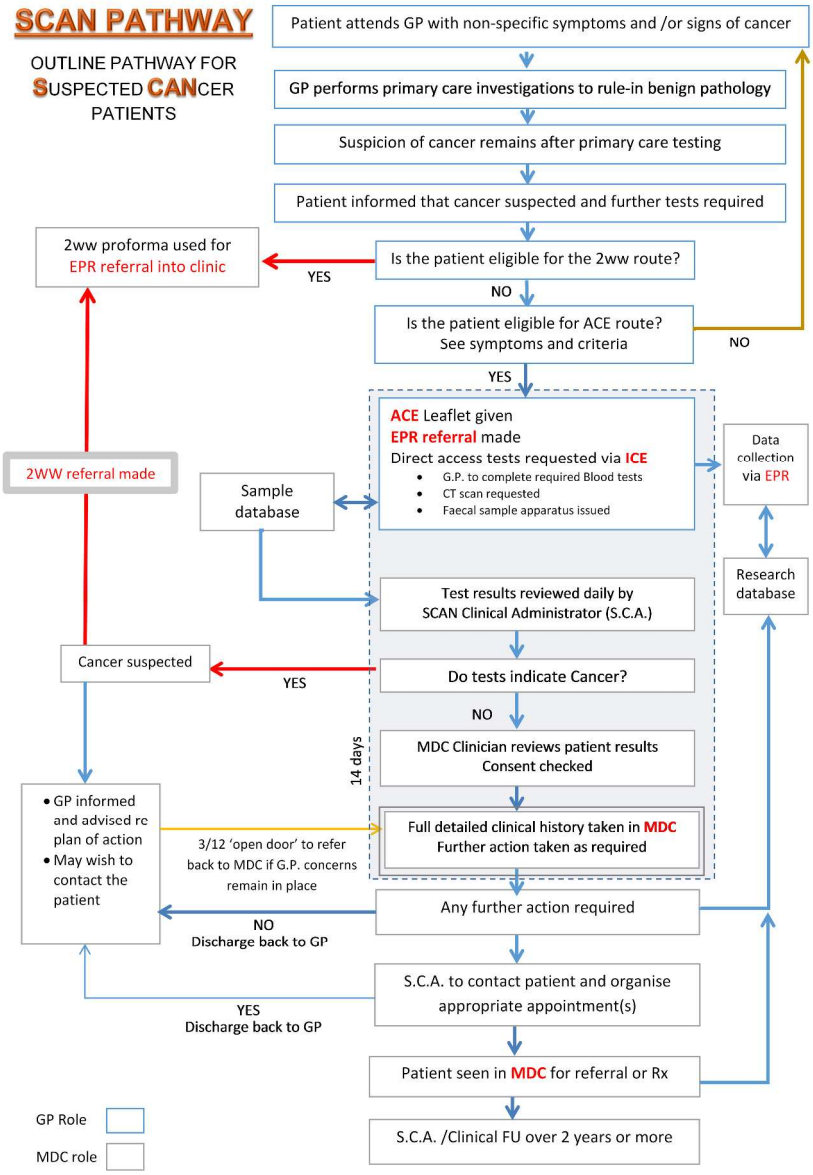

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Oxfordshire SCAN Pathway for Non-Specific-Symptoms of Cancer or Serious Disease

GP Pro Forma Oxfordshire

v3.1 EMIS Web
August 2017

Please email to **orh-tr.ace2scan@nhs.net** - please request a Read Receipt when sending

Pathway Information

The **SCAN Pathway** is part of a national programme designed to assess the rapid investigation of "vague" or "non-specific" symptoms and clinical signs that could represent cancer or serious disease, but that do not already have a designated pathway for urgent investigation or referral

Within 7 days of referral, a CT Neck, Thorax, Abdomen, and Pelvis and a broad panel of laboratory investigations will be completed and the results reviewed by a virtual Multidisciplinary Clinic (MDC) for non-specific symptoms.

If there is high suspicion of a specific diagnosis (cancer or non-cancer) from the CT the MDC will automatically refer your patient to an urgent referral pathway, a specialist clinic, or for further specialist testing (e.g. colonoscopy). If doubt remains following initial testing, the patient will be reviewed in person at the MDC for non-specific symptoms. Your patient will be referred back to you with a diagnosis or management plan once all investigations are completed. You will automatically receive the results of all blood tests and CT performed.

If you have already referred a patient to a pre-existing cancer pathway, and these tests are negative, and you wish the patient to be referred to the ACE Pathway, then if you have checked the box below, this will happen automatically – and you will be informed.

Patient's details				**Patient's background and culture**		
Forenames	**Given Name**			Ethnicity	**Ethnic Origin**	
Surname	**Surname**			1st Language	**Main Language**	
Known As	**Calling Name**					
NHS No	**NHS Number**			Interpreter required?	Y ☐ N ☐	
DOB	**Date of Birth**	Age	**Age**			
Sex	**Gender(full)**			**GP details**		
Title	**Title**			Referring GP		
Address & Postcode	**Home Full Address (single line)**			GP Address	**Organisation Name** **Organisation Full Address (single line)**	
				GP Tel No	**Organisation Telephone Number**	
				GP Fax No	**Organisation Fax Number**	
Hospital No	**Hospital Number**			Practice Email	**Organisation E-mail Address**	
Home Tel	**Patient Home Telephone**			Referral Date	**Short date letter merged**	
Work Tel	**Patient Work Telephone**			Date received		
Mobile Tel	**Patient Mobile Telephone**					
Email	**Patient E-mail Address**					
Patient's preferred contact number				☐ Home	☐ Work	☐ Mobile
Patient agrees to telephone message being left?				☐ Yes	☐ No	

Referral Criteria						
Checklist	☐	There is no other urgent referral pathway for this clinical scenario				
	☐	≥40 years of age				
	Y ☐ N ☐	Do you suspect cancer?				
	weeks	When did the patient first attend primary care with this problem?				
Referral Criteria *Tick all that still apply* ***after primary care assessment***	☐	**GP Clinical Suspicion of cancer or serious disease / GP "gut feeling"**				
	☐	**Persistent nausea or appetite loss**				Duration weeks
	☐	**Unexplained Weight Loss**	**Details**			
			Measured	☐		
			Patient Reported	☐		
	☐	**Severe unexplained fatigue**	TSH	**Single Code Entry: Plasma TSH level...**		
	☐	**New atypical pain** (e.g. diffuse abdominal pain or bone pain)	Description:			
	☐	**Unexplained laboratory test findings** (e.g. anaemia, thrombocytopenia, hypercalcaemia)	Details:			
In your opinion, what is the % risk of cancer in this patient?						
☐	**Please tick here if you are sending any additional documents.** The referral narrative should be typed onto this form, not in a separate letter					
Clinical Narrative (If necessary)						

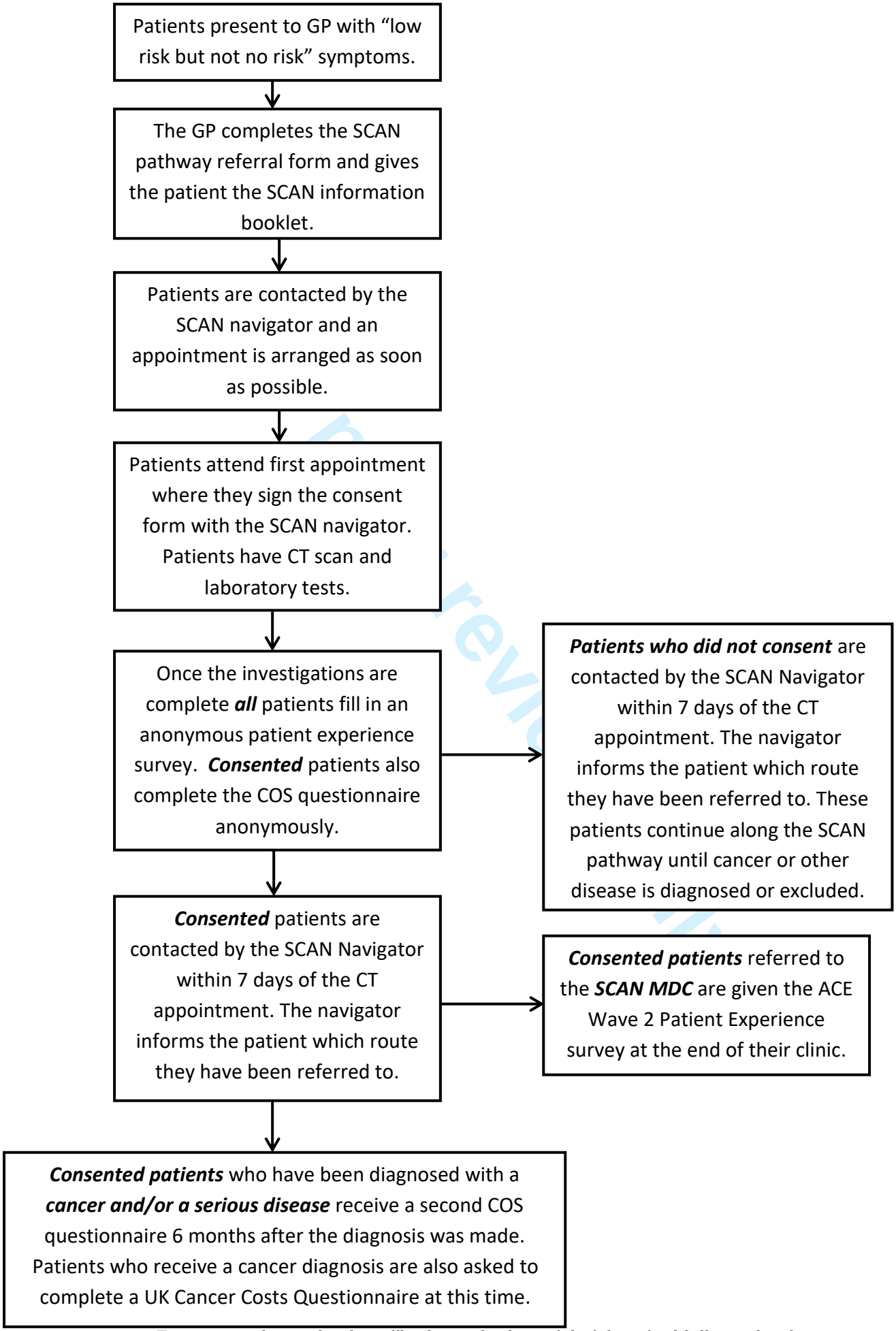
Automated Data		
	Automated Data	Manual Data Entry
Height	**Single Code Entry: O/E - height**	
Current Weight	**Single Code Entry: O/E - weight**	
Last Weight but 1	**Single Code Entry: O/E - weight**	
Last Weight but 2	**Single Code Entry: O/E - weight**	
Last Weight but 3	**Single Code Entry: O/E - weight**	

Smoking
Alcohol Consumption
Family History
Medication
Problems
Allergies
Consultations
Values and Investigations

Title Given Name Surname
NHS Number Date of Birth

Having a problem with this pro forma? Please email us at OCCG.GPproformas@nhs.net

Appendix 3. Patient journey in SCAN Pathway



Oxfordshire SCAN Pathway for Non-Specific-Symptoms of Cancer or Serious Disease

v0.3.2 EMIS Web
September 2017

COMPARATOR COHORT DATA COLLECTION FORM

Please email to **SCWCSU.ACESCANOCCG@nhs.net** - please request a Read Receipt when sending

Anonymised patient details	
Age	**Age**
Sex	**Gender(full)**
Ethnicity	**Ethnic Origin**
NHS No	**NHS Number**
GP Postcode	**Organisation Postcode**
Date of referral	**Short date letter merged**

Pathway Information

The **SCAN Pathway** is part of a national programme designed to assess the rapid investigation of "vague" or "non-specific" symptoms and clinical signs that could represent cancer or serious disease, but that do not already have a designated pathway for urgent investigation or referral.

Before SCAN is opened in Oxfordshire, a period of data collection is required to allow the numbers that will be referred to be estimated and as a comparison cohort when the service has started.

Please use this simplified form to send those patient details who meet the criteria below to the SCAN team.

NOTE: These patients will **not** be investigated through the SCAN pathway and **still require referral as usual by you.** We will follow-up these patients to identify to which diagnostic pathways they are currently being referred.

Referral Criteria

Checklist	☐	There is no other urgent referral pathway for this clinical scenario
	☐	≥40 years of age
	Y ☐ N ☐	Do you suspect cancer?
	weeks	When did the patient first attend primary care with this problem?

Referral Criteria *Tick all that still apply* ***after primary care assessment***						
	☐	**GP Clinical Suspicion of cancer or serious disease / GP "gut feeling"**				
	☐	**Persistent nausea or appetite loss**				Duration weeks
	☐	**Unexplained Weight Loss**	**Details**			
			Measured	☐		
			Patient Reported	☐		
	☐	**Severe unexplained fatigue**	TSH	**Single Code Entry: Plasma TSH level...**		
	☐	**New atypical pain** (e.g. diffuse abdominal pain or bone pain)	Description:			
	☐	**Unexplained laboratory test findings** (e.g. anaemia, thrombocytopaenia, hypercalcaemia)	Details:			

In your opinion, what is the % risk of cancer in this patient?	
☐	**Please tick here if you are sending any additional documents.** The referral narrative should be typed onto this form, not in a separate letter
Clinical Narrative (If necessary)	

Automated Data	
Automated Data	Manual Data Entry

Having a problem with this pro forma? Please email us at occg.gpproformas@nhs.net

NHS Number Date of Birth

Height	**Single Code Entry: O/E - height**	
Current Weight	**Single Code Entry: O/E - weight**	
Last Weight but 1	**Single Code Entry: O/E - weight**	
Last Weight but 2	**Single Code Entry: O/E - weight**	
Last Weight but 3	**Single Code Entry: O/E - weight**	

Smoking
Alcohol Consumption
Family History
Medication
Problems
Allergies
Consultations
Values and Investigations

NHS Number Date of Birth

Having a problem with this pro forma? Please email us at occg.gpproformas@nhs.net

Oxford University Hospitals NHS
NHS Foundation Trust

Suspected CANcer (SCAN) Pathway

Information for patients

Your GP has advised you may benefit from investigation via the **SCAN** pathway.

The **SCAN** pathway is part of a national programme called ACE (Accelerate, Co-ordinate and Evaluate). It is coordinated by Cancer Research UK and supported by NHS England's National Clinical Director for Cancer.

ACE was established to pilot a new diagnostic pathway for people with 'non-specific but concerning symptoms'. This uses a Multidisciplinary Diagnostic Centre (MDC), which allows people to undergo several diagnostic tests in one location.

Further information about the ACE programme can be found online at:

www.cancerresearchuk.org/health-professional/early-diagnosis-activities/ace-programme

Thank you for reading this information sheet. Do take time to talk to your family and friends about it. If you decide to take part you will be asked to sign and date a consent form at your first appointment.

What is the purpose of the SCAN pathway?

Many people visit their GP with 'vague' symptoms, such as weight loss and tiredness. These symptoms are called 'non-specific', as they affect the whole person. Often the cause of these symptoms remains unclear after your GP has assessed you, and sometimes there is a minor cause for such symptoms. However, there is a small chance that they could be the signs of a serious illness, such as cancer. Therefore, these symptoms are often called 'low-risk but not no-risk symptoms'.

At present, GPs do not have a way to get rapid investigations for people with 'non-specific' symptoms. People may go back and forth between their GP and the hospital many times until a diagnosis is made, all of which takes time. As a result there could be delay in diagnosis and treatment, which may have a negative effect on the person's health and the overall outcome.

Although the risk of serious disease is low, the cause of these symptoms can be difficult to diagnose. As a result, there are some people for whom earlier scans and tests could diagnose the cause more quickly, allowing treatment to be started sooner. **SCAN** may enable doctors and the NHS to better understand which people would benefit from early scanning, highlighting the need for more efficient access to radiology services.

As part of the ACE programme the **SCAN** project will carry out a service evaluation of a diagnostic pathway for people in Oxfordshire with 'non-specific symptoms'. This involves:

- rapid diagnostic imaging (Computed Tomography or CT scan)
- laboratory tests (blood and stool (faeces) tests)
- further testing or an appointment with a specialist, depending on the results.

The aim is that people on the **SCAN** pathway will have a diagnosis and be able to begin treatment faster than the previous pathways allowed.

Why have I been referred to SCAN?

Your GP has assessed you as having one of the 'non-specific' symptoms for which **SCAN** has been developed.

Do I have to take part?

No. Taking part in **SCAN** is entirely voluntary. It is up to you to decide if you want to be investigated by the **SCAN** pathway.

If you choose not to take part in the **SCAN** pathway, you will continue to receive care following the standard local guidelines agreed by Oxford University Foundation Hospital NHS Trust (OUHFT), Oxfordshire Clinical Commissioning Group (OCCG), and National Institute for Health and Clinical Excellence (NICE) guidelines.

What will I have to do if I take part?

Your GP will send the ACE team detailed information about your clinical problem, your symptoms, examination findings, medical history and any recent test results.

If you have any questions at this point, please contact the **SCAN** team.

Email: **scanpathway@ouh.nhs.uk**

Tel: **01865 227 780**
(8.30am to 4.30pm, Monday to Friday)

You will be asked to come for an appointment at the Radiology department in the Churchill Hospital in Oxford, within one week of the referral for a CT scan. You will need to collect a stool sample in the blue-topped specimen pot provided in the **SCAN** information envelope, the day before your **SCAN** appointment.

Following your first appointment, the clinical information received from your GP and all of your test results will be reviewed

by the **SCAN** team (a group of specialist doctors skilled in managing 'non-specific' symptoms).

Depending on your results, within one week the **SCAN** team will do one of the following:

1. refer you to a specialist clinic in Oxford
2. refer you for further rapid testing (within two weeks) in Oxford
3. invite you for a clinic appointment with the SCAN team in Oxford
4. refer you back to your GP with advice.

Taking part in the SCAN pathway

Please take any time you need to discuss this with your family and friends.

Before you sign the consent form at your **SCAN** appointment, you will be given time to ask questions to help you decide whether or not to take part.

When we ask you to sign the consent form, a member of our team will sign it too.

The consent form will confirm that you have read and understood the information in this leaflet. It will confirm that you have had a chance to ask questions and that these questions have been answered.

There will be another consent form which will confirm whether you agree to your blood being stored for research purposes. This is optional and does not affect your eligibility to use the **SCAN** pathway.

You can still change your mind after you have signed the consent form. You are free to withdraw from the pathway at any time, without giving a reason. This will not affect the standard of care you receive.

The SCAN Pathway

Before the start of the pathway

Your GP will discuss the **SCAN** pathway with you and will give you this information sheet.

You will be contacted by telephone by a member of the **SCAN** team, who will offer you an appointment for a CT scan and blood and stool tests.

You will have time to discuss the **SCAN** pathway in more detail and to ask any questions either at the first appointment, by telephone (01865 227 780), or by email (scanpathway@ouh.nhs.uk). Research staff may ask you some further questions during this discussion.

At your first appointment

Please bring your stool sample in the blue topped pot. You will be asked to:

1. sign a consent form to say you agree to continue on the **SCAN** pathway (see enclosed form)
2. sign a consent form to say you agree to your blood and urine samples being stored for research (see enclosed form). This is optional.
3. possibly have further blood taken and sent to the laboratory
4. hand in your filled blue-topped stool specimen pot
5. have a CT scan of your chest, abdomen, and pelvis
6. fill out a questionnaire about your experience.

Preparing for the CT scan

Please do not have anything to eat two hours prior to your appointment, as this may affect the results of the scan. You may drink water or clear fluids (no milk) up to the time of your scan. You do not need to have a full bladder.

During your scan you will have an injection of a special dye, called contrast, to enhance the scan quality. The CT scan will take approximately 20 minutes. A further information leaflet is included to give you more details about the CT scan.

Follow-up

Your follow-up care will be based on your medical history and test results. The various options are shown in the flowchart on page 10. If the results from the CT scan and other tests do not show that further evaluation is needed, the **SCAN** team will write to your GP with information and treatment suggestions.

If you take part in the **SCAN** pathway, the information collected during your follow-up care will be included in the SCAN database and will be used to help develop more effective pathways to diagnose people with non-specific symptoms. All of the information we collect will be kept strictly confidential.

At the end of the SCAN pathway

You will not be required to have any more appointments, tests or scans. You may be asked to fill out a further questionnaire about your experiences of the **SCAN** pathway.

Data from your medical records will be collected on the outcome of your investigations and any further diagnoses or treatments that you have over the next two years. Your GP or specialist will discuss with you any further NHS treatments, care, monitoring or testing that may be necessary. If you move away or change Health Authority, data will be collected about your health status from the Health and Social Care information Centre and other NHS bodies.

What if there is a problem during the course of the pathway?

Every care will be taken during the course of the pathway. If you have a concern about any aspect of the pathway, you should ask to speak with the **SCAN** team, who will do their best to answer your questions.

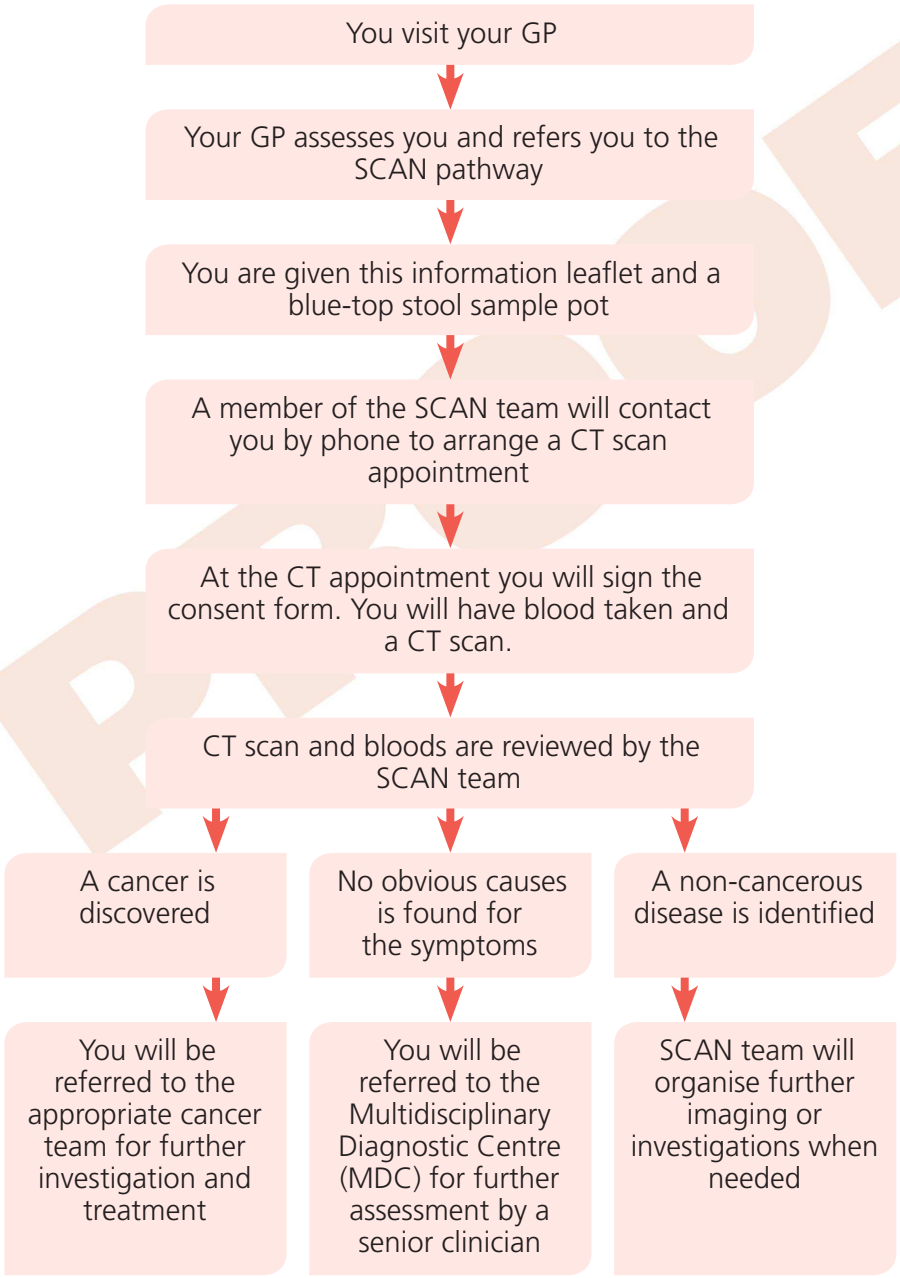
Tel: **01865 227 780**

Email: **scanpathway@ouh.nhs.uk**

If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Additional information is available from your local Patient Advice and Liaison Service office.

Email: **www.pals.nhs.uk**

Summary of SCAN pathway



page 10

Will my taking part in this service evaluation be kept confidential?

If you join the **SCAN** pathway, all information which is collected about you during the course of the research will be kept strictly confidential. Documents relating to you will be kept by the OUHFT and at the University of Oxford, Nuffield Department of Primary Health Sciences, in secure areas and on a password protected computer and database.

You will be entered into the **SCAN** database. All data collected about you will be linked with your NHS number and year of birth. Your medical records and the data collected for the pathway will be looked at by authorised persons involved in your care or the service evaluation. Authorised people from OUHFT may also check them to make sure that the service evaluation is being carried out correctly.

Oxford Imaging Trials Unit (OITU) at the Churchill Hospital will also keep your current and previous names, date of birth and NHS number, to find out if you were diagnosed by **SCAN** or an alternative pathway as part of the service evaluation. Any test results received will have been anonymised at site; this involves blacking out/removing any personal information.

Responsibility for compliance with national and international data protection standards lies with the Oxford University Hospital NHS Foundation Trust.

What will happen to any samples I give?

The blood and stool samples that you give as part of this pathway will be analysed immediately in the laboratory of Oxford University Hospitals.

In addition, we would like to collect blood and urine samples for research purposes, to investigate tests for cancer or other diseases in people with non-specific symptoms. This may sometimes involve diagnostic companies or researchers, who have developed specialist tests for these symptoms. There would be no financial gain for the **SCAN** team in relation to these samples. The additional consent form asks you to consent to the use of your samples in this way.

What will happen to the results of the SCAN pathway service evaluation?

The combined anonymised results of the SCAN pathway will be analysed by the SCAN researchers, shared with other ACE pilot projects, the Department of Health, Macmillan Cancer Support, Cancer Research UK, and published in medical journals.

The service evaluation will take 2-4 years to complete and the results should be available and published after 2019. If you are interested in the results, please look up ACE Wave 2 on the Cancer Research UK website or contact the SCAN team at scanpathway@ouh.nhs.uk

If the results show conclusively that rapid investigation of non-specific symptoms leads to earlier diagnosis of cancer, they may be used to influence future NHS guidelines.

Who is sponsoring this pathway?

The SCAN pathway is funded by the Department of Health, Macmillan Cancer Support, and Cancer Research UK. The pathway is supported by Oxford University Hospitals NHS Foundation Trust, the Oxfordshire Clinical Commissioning Group (OCCG) and the University of Oxford. It is being carried out by the Oxford Imaging Trials Unit and the OCCG.

Contact details

If you have any further questions about the SCAN pathway, please contact:

Julie-Ann Phillips (SCAN Navigator)

Tel: **01865 227 780**
(8.30am to 4.30pm, Monday to Friday)

Email: **scanpathway@ouh.nhs.uk**

Thank you for reading this information booklet. If you decide to take part in this pathway you must personally sign and date the consent form.

We will give you a copy of this information sheet and your signed consent form.
We will keep a second copy of this document with the service evaluation records on and will place a third copy in your radiology records.

This pathway is being supported by:

- Oxfordshire Clinical Commissioning Group
- Cancer Research UK
- NHS England
- Macmillan Cancer Support
- Nuffield Department of Primary Care Health Sciences
- Oxford University Hospitals NHS Foundation Trust

If you have a specific requirement, need an interpreter, a document in Easy Read, another language, large print, Braille or audio version, please call **01865 221 473** or email **PALS@ouh.nhs.uk**

Author: Julie-Ann Phillips, SCAN Navigator
March 2017
Review: March 2020
Oxford University Hospitals NHS Foundation Trust
Oxford OX3 9DU
www.ouh.nhs.uk/information

OMI 14548P

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Page where met
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1,2
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	NA
	2b	All items from the World Health Organization Trial Registration Data Set	NA
Protocol version	3	Date and version identifier	NA
Funding	4	Sources and types of financial, material, and other support	3, 12
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1, 13
	5b	Name and contact information for the trial sponsor	NA
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	12
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	11, 13
Introduction			

Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3
	6b	Explanation for choice of comparators	11
Objectives	7	Specific objectives or hypotheses	4
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	4 – 7
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	4
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	5
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	6, 7
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	NA
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	NA
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	NA

Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	8
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	8, 9
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	11
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	NA
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	NA
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	NA
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	6, 7 (enrolment of participants, all else NA)

Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	NA
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	7, 8
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	NA
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	7, 8, 11
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	9-11
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	9, 10
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	NA
Methods: Monitoring			

Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	11
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	NA
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	9
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	NA
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	2, 11
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	NA
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	6
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	6
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	7, 8
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	13

Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	11, 12
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	11
	31b	Authorship eligibility guidelines and any intended use of professional writers	NA
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	NA
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Online material 1
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.