QUALITY IMPROVEMENT IN CYSTIC FIBROSIS: WHAT CAN WE LEARN FROM EACH OTHER?

Research proposal version 3
12 August 2013

Applicants: **Dr Stephanie J MacNeill (PI)**
Dr Paul Cullinan (CI)
National Heart and Lung Institute, Imperial College London
Dr Diana Bilton (CI)
Dr Siobhan Carr (CI)
Royal Brompton Hospital
Dr Jonathan Boote (CI)
University of Sheffield
Ms Katherine Collins (CI)
National Services Scotland
Dr Caroline Elston (CI)
King's College Hospital
Mr Steve Harrison (CI)
Dr Martin Wildman (CI)
Sheffield Teaching Hospital
Dr Mohammed A Mohammed (CI)
University of Birmingham
Ms Joanne Osmond (CI)
CF Trust

BACKGROUND AND RATIONALE

CF. CF is a common genetic disease affecting approximately 9000 patients in the UK (1). The genetic mutation leads to mucus obstruction and infection in the lungs (2). As well as the lungs, other organs such as the liver, intestines and pancreas are affected (3) which in turn leads to poor nutrient absorption and malnutrition. The prognosis for patients with CF has improved dramatically over the years and it was recently shown that there has been a clear increase in the median age at death from the early 1970s (4). In 2009, the median predicted survival for UK patients reached 38 years (1).

Patients with CF are treated at specialist centres which offer dedicated paediatric or adult care; transition to adult care usually occurs after children's 16th birthday. Care involves daily treatments which can include drugs to clear mucus and prevent lung infections, pancreatic enzymes to aid in digestion and physiotherapy.

The CF Trust – the national UK charity for CF - maintains a national registry database (UK CF Registry) of detailed clinical and demographic information on all patients attending these specialist centres. Patients are invited to attend annual reviews at their specialist centre and based on these data the Trust produces annual reports describing the health of patients. The reports are available on the CF Trust website to be accessed by patients and clinicians alike (https://www.cysticfibrosis.org.uk/about-cf/publications/cf-registry-reports.aspx).

Centre comparisons. Since 2008, the annual reports published by the CF Trust have included comparisons between centres in terms of key clinical outcomes using simple rankings. An example of the type of comparisons presented in the report is included in the appendix of this protocol. While these comparisons give a sense of the distribution of outcomes between centres, they encourage the reader to assume, for example, that centres with the highest lung function measures are "better" than those with lower values. This is misleading on two grounds:

1) *The rankings make no allowances for the differences in the intake of patients*. It could be argued, for example, that centres with younger patients would have improved lung function compared to those with older patients since lung function declines with age in CF patients. As such, between-centre comparisons that do not account for the age of patients risk not detecting good outcomes in centres where patients are older. Similarly, poor outcomes in centres with younger patients may not be detected.
2) *The rankings include no formal tests comparing centres*. Without formal comparisons we cannot say that there is evidence that outcomes are better at one centre than another let alone conclude that any observed differences are related to the process of care.

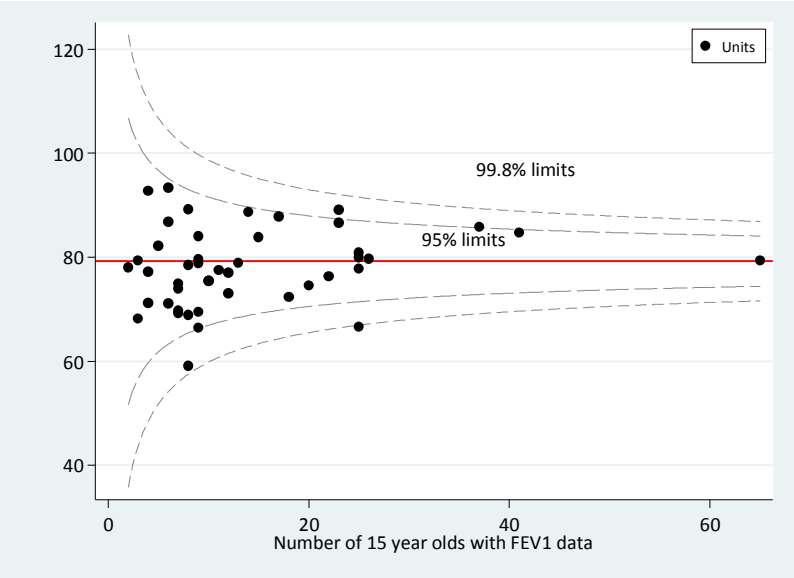
Such short-comings are important if the reader interprets the graphs as league tables. Marshall and Speigelhater (5) showed that league tables – even after adjustment for the intake of patients – are unreliable in identifying poor performance. Furthermore, Lilford et al (6) suggest that league tables – where one's position could be due to a host of reasons ranging from differences in definitions and data quality between providers, chance, inadequate case-mix adjustment to differences in institutional management – can generate undue tension as blame is attributed without identification of the reason. After all, the very nature of a league table is that one provider is ranked bottom whether care is poor or not and that ranking may simply be due to chance (7). Without providing any explanation for observed differences we are no further forward in knowing how to improve care *which should be the ultimate aim of any institutional comparisons*.

Quality improvement in CF: what this study adds. Quality improvement programs of varying sorts are not new in CF and have a long history in the US (8, 9) and have recently been described in Germany

(10). In the UK, however, there has not yet been work testing the hypothesis that there are key differences in the delivery of care which affect outcomes. We therefore propose to adopt a "quality improvement" approach to understanding whether differences between centres are related to the processes of care which builds upon and improves on existing methodologies in CF. Here we will consider ***all*** centres in our analyses and use statistical process control (SPC) charts to determine whether there are meaningful differences. These charts were developed as a means of studying the variability of "processes" over time (11) and have been shown to be useful when comparing healthcare providers (whether hospitals, clinics or primary care practices) as well as outcomes of single providers over time (such as Harold Shipman) (12).

SPC charts function by plotting summary outcome measures for individual units over time or size of the unit with control limits (either at 2 or 3 standard deviations). It is anticipated that there will be some variability between units which is intrinsic to the process itself; referred to as "common cause variation" (12). SPC charts are designed to highlight where there is variability caused by factors *outside* the process; referred to as "special cause variation". Centres whose summary measures are outside the control limits (either higher or lower) are said to exhibit special cause variation.

An example of a SPC chart is presented below. In this chart, each dot represents a different CF unit and they are being compared in terms of the mean FEV_1 in children aged 15 years with the size of the unit on the horizontal axis. The dashed lines represent the control limits. Units located between the limits are said to show "common cause variation" and those outside the limits "special cause variation". 95% limits are equivalent to 2 standard deviations and 99.8% limits to 3 standard deviations.



AIMS AND OBJECTIVES

The aim of this project is to determine whether there are meaningful differences in key health outcomes between CF centres in the UK and to determine the processes of care driving such differences.

Our objectives are to:

1. Establish a framework to allow future comparisons of key measures of quality in terms of care structures and processes

2. Develop statistical models using data from the national CF Registry database which allow us to adjust clinical outcomes at centres for the patient case-mix
3. Compare centres using SPC charts to determine whether important differences exist between centres on key clinical outcomes
4. Consult with experts in CF care to turn existing care guidelines (13) into maps of the structures, policies and processes required to deliver good outcomes and to identify factors that could facilitate or hinder these from being successful
5. Consult with CF patients to ascertain what patients feel are the factors that could facilitate or hinder these structures, policies and processes from being successful
6. Collect data from individual centres and describe the structures and processes of care at these centres based on the SPP mapping exercise
7. Explore how the structures, policies and processes of care differ between centres with exceptional outcomes and the rest. This will be done by exploring the data collected from the centres as well as performing site visits to a sample of centres and surveying their patients

METHODS

In order to address our research objectives we identified a number of work-packages and sub-packages. At the end of each work package a short report will be written and shared with the rest of the collaborators and patient representatives for discussion and feedback.

WP1: Centre comparisons

In this work-package we will use data from the CF Registry to compare CF centres in the UK on key clinical outcomes.

Data source. Annual review data (2007 to 2011 inclusively) from the CF Registry database will be used for all analyses.

Outcomes. Consultation with members of the CF Registry steering committee and with centre directors identified a number of respiratory and nutrition outcomes deemed clinically meaningful for both paediatric and adult centres. For paediatric centres the proposed outcomes are:

1. Forced expiratory volume (FEV_1) at age 12 years. Here we will consider patients who were 12 years old at the time of their annual review between 2007 and 2011.
2. FEV_1 at age 15 years. Here we will consider patients who were 15 years old at the time of their annual review between 2007 and 2011.
3. FEV_1 change from ages 13 to 15 years. We will consider patients who were 13 years old at the time of their annual review between 2007 and 2009.
4. Body mass index (BMI) centile at age 15 years. As with FEV_1 at age 15, patients who were 15 years old at the time of their annual review between 2007 and 2011 will be studied.

For adult centres:

1. FEV_1 change from ages 18-21 years. Here we will consider patients who were 18 years old at the time of their annual review in 2007 or 2008.
2. BMI change from 18 to 21 years as described above.

We will also conduct a subgroup analysis of 16 to 17 year old patients. The outcomes of interest for these patients are:

1. FEV_1 at ages 16 and 17. Here we will consider patients who were 16 or 17 years at the time of their annual review in 2007-2011.
2. BMI at ages 16 and 17 as described above.

Candidate variables for case-mix adjustment. Case-mix adjustment involves adjusting outcomes for non-modifiable factors that are known to be associated with healthcare outcomes and differ between centres. By adjusting outcomes for the patient case-mix, we eliminate from our between-centre comparison factors that the centre has no control over. In the case of this study, candidate variables include the patient's CF genotype, sex, whether or not they have sufficient pancreatic function to digest food without supplements, socio-economic status (based on Townsend deprivation scores), age (measured in months) and age at diagnosis (measured in months). For patients at adult clinics we will also look at the model of paediatric care they received prior to attending the adult clinic and whether they were chronically colonised with *Pseudomonas aeruginosa* prior to transfer to adult care.

Inclusion criteria. In the first instance we will consider all centres and all patients with annual review data between 2007 and 2011. At the individual level, all patients within the age ranges stated above at the time of their annual review will be considered eligible for the analysis. For outcomes relating to changes in FEV_1 and BMI over time, we will require that patients have data at the same centres during the periods under study. Patients who transfer between centres during the study period and those who have missed annual reviews during this period will not be included in the analysis. We will reconsider these inclusion criteria if they prove too prohibitive resulting in small sample sizes.

The data comparison analyses will be divided into three sub-packages:

WP1.1: Data preparation (leads: Stephanie MacNeill, Diana Bilton, Siobhan Carr, Mohammed Mohammed and TBA statistician)
This work will involve a statistician exploring the longitudinal and cross-sectional data and identifying eligible patient cohorts as described above.

Centres will also be described in terms of data completeness. While the proportion of patients attending annual reviews has increased year-on-year to approximately 85% in 2010 (14) it is known by the CF Registry Steering Committee that some centres have been more successful than others in capturing annual review data from their patients. Investigators will collaborate to define minimum criteria for completeness and will then compare those centres not meeting these criteria in terms of available data. The aim of this is to assess whether centres with low completion rates differ substantially from those with more complete data.

WP1.2: Case-mix adjustment (leads: Stephanie MacNeill, Paul Cullinan, Mohammed Mohammed, Martin Wildman and TBA statistician)
This work will follow, in the first instance, the analysis plan adopted by O'Connor et al (15) in their case-mix adjustment for the evaluation of mortality in CF in the US. The first step in this analysis will involve describing how the candidate variables differ by centre and performing relevant tests depending on data type. Next, tests for associations will be performed to assess which variables are associated with each of the studied outcomes. For each of the outcomes, those candidate variables that differed by centre and were associated with the outcome were retained for the case-mix adjustment.

WP1.3: SPC chart analysis (leads: Stephanie MacNeill, Paul Cullinan, Mohammed Mohammed, Martin Wildman and TBA statistician)

In this sub-package we aim to assess whether, after removing the impact of un-modifiable factors (WP1.2) there is evidence of special cause variation in outcomes by CF centre. For this work we will use SPC charts for the different outcomes under study. Control charts for continuous measures will be used. This will include the funnel charts proposed by Spiegelhalter (16) which function much in the same way as funnel plots for meta-analyses. As recommended by Spiegelhalter we will use 99.8% and 95% prediction limits (equivalent to approximately 3 and 2 standard deviations, respectively) to identify special cause variation. 95% prediction limits will act as warning limits and 99.8% limits will act as action limits.

Additionally, we will consider the use of SPC charts to determine whether there is evidence of special cause variation in the rates of missing data by centre.

WP2: Consultation to identify factors that would help to understand variability
WP2.1: Development of structures, policies and processes (SPP) maps and CF experts focus group (leads: Steve Harrison, Jonathan Boote and Martin Wildman)
It is recognised that the study of systems to understand quality is most successful when clearly focused on the most important determinants of outcomes (17). WP2 is designed to identify the range of determinants considered to be important to CF care professionals.

We will conduct two one-day workshops with multi-disciplinary groups of CF experts. One workshop will be conducted for experts in paediatric CF care and another for adult CF care. At each workshop will be a group of consultants, specialist nurses, physiotherapists, psychologists and dieticians. We aim to recruit up to 10 participants in each workshop with at least one person representing each discipline. These disciplines were selected as covering all key roles in the delivery of CF care in adult and paediatric centres. From their own professional experience and contacts in the CF community, the research team will identify a number of potential participants from the different disciplines. If unable to recruit all of these proposed participants we will recruit more broadly using a variety of means including invitations distributed through relevant professional networks.

The morning of each workshop will involve Steve Harrison (co-investigator and expert in quality improvement) leading a consultation to understand the structures, policies and processes that are considered to enable best outcomes. This will be used to produce SPP maps that help visualise the important determinants of good quality outcomes.

The afternoon of each workshop will involve a focus group facilitated by Jonathan Boote (co-investigator and expert qualitative researcher) to identify what the group feel are the major factors that would facilitate or hinder these SPPs from being successful in clinical practice. Focus groups were selected as the most appropriate qualitative data collection method for pragmatic reasons: it makes financial and practical sense to run these groups in the afternoon of the consultation event, rather than to invite attendees to participate in separate one-to-one interviews. Also, the different professional groups present will have the chance to hear and debate different points of view and hear about different professional experiences.

Following the workshops, the outcomes of each will be shared with participants to provide the opportunity to comment on the synthesis of the data collected and providing the opportunity for final refinements.

The analysis of the focus group data will be guided by the principles of interpretative thematic analysis (18), whereby the transcripts will be thoroughly read by the researcher, and codes and

categories will be assigned to sections of the text to highlight key thematic areas with regard to factors that hinder or facilitate structures, processes and policies. In addition, a form of content analysis – an assertions analysis (19) - will be undertaken of each transcript to examine the frequency with which particular barriers or facilitators are characterized in a particular way.

WP2.2: Consultation with patients (leads: Jonathan Boote and Martin Wildman)
The aim of WP2.2 is to ascertain what *patients* feel – from their own experiences - are the factors that influence the best possible outcomes (as outlined in WP1). The primary purpose of this work is to develop a questionnaire to be issued to patients at selected centres involved in site visits in WP4.

This work will also allow us to investigate the patients' views on the key SPPs identified in WP2.1 to assess if these are important to them as well as to clinicians. This work-package will therefore identify where patients' and clinicians' priorities differ and overlap.

To do this, we will conduct a focus group with the team of 7 clinical care patient advisors who are tasked by the CF Trust to promote high quality care. The focus group will be held during one of the advisors' regularly scheduled teleconferences.

The focus group will be conducted by Jonathan Boote and will comprise of two components. The first will focus on the patients' own experiences of CF care. The second will ask participants to consider, from their own experiences, factors that could facilitate or hinder the SPPs identified in WP2.1 from being successful and their views on the importance of these clinician-defined SPPs.

The focus group schedule of questions for WP2.2 will be developed with input from the study steering committee as well as patient clinical care advisor Dominic Kavanagh who was involved in the development of this project.

Analysis of the patient focus groups will be conducted using the same techniques of thematic analysis and assertions analysis as described above in WP2.1.

WP3: Describing care structures (leads: all partners and TBA statistician)
The aim of this work-package is to carry out a survey to quantify structures, processes and policies adopted in individual centres using a questionnaire.

We will administer online questionnaires to centre directors of all specialist CF centres in the UK – as well as their multi-disciplinary teams. The questionnaires will incorporate both quantitative and qualitative components in order to assess the care structures. The questionnaire will be developed from the workshops conducted in WP2.1. Additionally, we will enquire about: staffing levels, number of patients treated each year, income received, how the centre is funded (either on a yearly banded tariff or as part of a block contract; it is widely felt that the former provides better funding), restrictions on the use of key CF therapies and how patients are followed-up after treatment. The latter is explored since there is evidence, for example, that the best outcomes occur in those centres with frequent reviews (20).

The survey questionnaire will enquire about current practices and whether there have been changes since 2007. Where there have been changes we will collect details. The collected survey data will be supplemented with any available current and historic resource data from the CF Trust.

Results of the survey will be analysed using the appropriate techniques for quantitative and qualitative data. A statistician – under the supervision of Stephanie MacNeill - will be responsible for the quantitative components and Jonathan Boote will describe the qualitative results. The qualitative data from the survey questionnaires will be analysed using the Framework method (21).

WP4: Identify the "processes" that differ (leads: all partners and TBA statistician)
The control chart analyses in WP1.3 will have potentially identified centres exhibiting special cause variation with respect to specified outcomes. In the current work-package we aim to understand the explanations for outcome differences.

It is important to take a structured approach in this work and the SPP maps and focus groups in WP2.1 and WP2.2 will provide a suitable structure. The questionnaires sent out to individual centres in WP3 already will have provided some information about the SPPs, barriers and facilitators at the centre-level. This work-package will involve comparative analysis of these data which will then provide a starting point for discussions in a sample of individual centres. In these discussions – facilitated by Steve Harrison using the SPP maps and the information from the centre questionnaires – we will seek to understand the SPPs associated with the centres' performances. Additionally, we will also conduct questionnaire surveys of patients at these centres in order to gain the patients' perspective on the care they receive.

Hence, the understanding of processes of care that has been developed from the SPP maps, barriers and facilitators (WP2.1 and WP2.2) and questionnaires sent to individual centres (WP3) will produce a working understanding of the determinants of outcomes and this understanding will be further refined by the individual site visits and patient surveys conducted in WP4.

Comparative analysis. For each outcome, centres will be classified according to whether or not they exhibited special cause variation in the analyses in WP1.3. We will then attempt to determine whether these disparities are related to the care delivered. The aspects of clinical care that will be explored include those identified as important in the workshops of WP2.1 and patient focus group in WP2.2.

Each centre will have provided data about important structures, processes and policies and the barriers and facilitators to these aspects of care by returning the questionnaire in WP3. Additionally, for each centre we will collect data from the CF Registry relating to the characteristics of care proposed as potentially important by the collaborators of this study. These will include the proportion of patients with chronic pseudomonas on nebulised antibiotics, rhDNase treatment rates and patients with low BMI on percutaneous endoscopic gastrostomy (PEG) feeds, for example. These data will be merged in to a single database and tabulated for each centre. This will allow us to look for patterns to see whether outlying units have clear differences in their structures, processes and policies. From this we can develop hypotheses about the important structures, processes and policies that can be explored in the site visits.

Site visits. We will also perform site visits at a sample of 6 adult and 6 paediatric centres (2 centres with outlying "negative" outcomes, 2 centres with average outcomes and 2 centres with outlying "positive" outcomes) and conduct cross-sectional surveys of patients at these centres in order to get patients' perspectives on the care they receive. The site visits will involve meeting with the centre's CF specialist multi-disciplinary team and conducting a facilitated focus group lead by Steve Harrison and involving adult/paediatric consultants from our research group. Members of the research group involved in the visits will be blind to the centre's results from WP1.3. This blinding will be

communicated to the centres so that they are aware of our intentions to reduce any potential sensitivities that may arise. The centres participating in these visits, however, will know how their own results from the centre comparisons (although they will not know the results of other centres). As such, they will have the opportunity to reflect on potential reasons for the results obtained.

The visits will be structured and designed based on the outcomes of WP2.1 and WP3. They will build upon the information produced by the SPP maps generated in WP2.1, focus groups in WP2.1 identifying potential facilitators and barriers associated with these SPPs and survey of centre directors and their multi-disciplinary teams in WP3. This previous work will ensure that visits are focused on the most important aspects of SPPs and associated barriers and facilitators. Steve Harrison, as a Microsystems coach, has extensive experience in exploring how teams deliver care and the SPP maps will be used to facilitate discussions in individual centres. Through these site visits, he will produce unit-specific SPP maps. These can then be compared with the SPP maps produced in WP2.1 and the SPP maps of the other outlier units that are studied. This allows a pictorial and quantitative comparison of the structures, processes and policies in highly performing, average and low performing units.

Patients at these centres will be sent an anonymised questionnaire to ascertain their perspective on the care they receive. For paediatric centres these will be sent to the parents or guardians and in the adult centres these will be sent to the patients themselves. The questionnaire will be developed by Jonathan Boote based on the outcome of the focus group with the clinical care patient advisors in WP2.2. To ensure that patient confidentiality is maintained, the centres themselves will administer the mail-out of the questionnaire themselves and we will not collect identifiable information.

The centres will be selected based on the outcome of the SPC analyses in WP1.3.

Data analysis. Using Registry data and data collected from the centre survey (WP3), the TBA statistician will make quantitative comparisons between outlying centres and the rest using simple descriptive statistics. Jonathan Boote will analyse the qualitative components of the patient questionnaires using the Framework method as discussed in WP3.

WP5: Dissemination (leads: all partners and TBA statistician)

We have consulted widely within the CF community in developing this protocol and as a result the centre directors are well acquainted with our aims and objectives. When the study begins in 2013, we will have an information session with the centre directors to discuss the study aims and provide training in the interpretation of SPC charts. This session will be offered by Mohammed Mohammed who has extensive experience of working with healthcare providers in studies making institutional comparisons. It will take the form of a presentation to the centre directors within an existing meeting co-ordinated by the CF Trust. We will also email the directors a PDF guide for future reference.

At the end of this study our final results will be communicated to patients/carers, clinicians, centre directors, service commissioners and the wider research community to provide all with evidence to make informed decisions about how the quality of healthcare services can be improved.

Dissemination will be tailored to the individual stakeholder groups. For patients and their families, we will publish our work on the CF Trust's website and in its in-house magazine *CF Today*. We also aim to present our findings at the CF Trust's annual parents' meeting which patients and their families are invited to attend. Patients do not participate in such meetings due to the risk of cross-infection and therefore we will make our results accessible in a web-based forum.

For CF care providers we will present our findings at CF Trust organised conferences as well as at a specially-organised meeting for centre directors in London. Final written reports and shorter centre-specific summary reports (PDF) will be provided to commissioners and centre directors. The aim of this will be to share what we have learned and highlight where we have identified successful practices and where improvements can be made thus benefitting patients.

To communicate our findings to the wider research community we aim to present at relevant conferences and write at least two scientific papers to be published in peer-reviewed journals. These publications will present our final results and we also hope to publish work on discrete, stand-alone components of our work as we progress in the study. By sharing our results widely we will be sharing our gained knowledge of successful care practices. Additionally, our experience will provide a useful example for quality improvement exercises in other chronic conditions where there exists a clear framework for care thus potentially improving service delivery in other areas within the NHS.

ANTICIPATED DIFFICULTIES

1. The study period (2007 onwards) was selected to ensure we used the most complete data on the CF Registry. Despite this we anticipate that there will be some missing data and will therefore incorporate a study of predictors of missing data within WP1.

   To assess potential bias, sensitivity analyses will be performed to assess the impact of including and excluding centres with high rates of incomplete data. If necessary and time permitting, we may also add an additional year of data (2012) to increase sample sizes. If no significant differences are found between centres we may consider comparing centres with recognised and accepted target values.

2. Information on the care structures at the centres and permission for site visits will only be forthcoming if centres are supportive and engage with the project. To encourage their support and engagement in the study we have already begun to work with the centres by seeking their perspective on our study design and project aims. We have visited three of the major centres (Birmingham Heartlands Hospital (adult clinic) and Royal Brompton Hospital (adult and paediatric clinics)) to get their feedback on our plans.

TIMELINE

WP1: Centre comparisons

This work will begin in July 2013. We envisage that extracting, preparing and analysing the data will take 18 months.

WP2: Consultation to identify factors that would help to understand variability

This work will begin in June 2013 and we anticipate having the two one-day workshops with CF experts in autumn 2013. The focus group session with the CF Trust's team of clinical care patient advisors will take place in spring 2014.

WP3: Describing care structures

This work will begin after the workshops in WP2 in November 2013. A template questionnaire will first be piloted at two centres before a wider survey in January 2014. The results of the survey will be analysed and a report describing the methods and results will be completed by June 2014.

WP4: Identify the processes that differ between centres

Planning this work will begin in January 2015 where we will classify centres as centres with outlying "negative" outcomes, "average" outcomes and outlying "positive" outcomes based on the results of WP1. From these we will recruit 2 adult and 2 paediatric sites from each group. We will seek approval from the relevant local committees when these sites are identified. Site visits will take place between May and October 2015. Patient surveys will be conducted at these sites during this same period. Analysis comparing centres in terms of process measures using data from WP3 and the CF Registry will take place between May and October 2015. Analysis and synthesis of the data collected at site visits and in patient surveys will be complete by December 2015.

WP5: Dissemination
We will be communicating with the centres throughout the study at regular annual meetings for centre directors organised by the CF Trust. We will develop, consult and disseminate our final results to centre directors, CF care commissioners and healthcare providers between January and March 2016. We will develop, consult and disseminate our final results for patients and their families between February and May 2016. We will disseminate our results to the wider scientific community in research papers and at scientific conferences. For discrete stand-alone components of this project we aim to submit for publication when these are complete. Our final results will be disseminated in the final stages of the grant.

STAFFING
We form a multi-disciplinary team of academics, NHS clinicians, patient representatives and CF care commissioners. Our combined skills ensure that we have the infrastructure required for a successful project.

Statistics and epidemiology. Dr. Stephanie MacNeill, the lead applicant, is a medical statistician at Imperial College London (IC). She will provide statistical guidance at all stages, act as lead on WP1, act as project manager and manage a TBA statistician who will perform the statistical analyses. Paul Cullinan is a consultant respiratory physician at the Royal Brompton Hospital (RBH) and chair in occupational and environmental respiratory disease at IC. He will provide the project with epidemiological oversight.

CF Care - paediatric. Dr. Siobhan Carr is a consultant physician in paediatric CF care at RBH and will be involved in all aspects of the study relating to paediatric centres.

CF Care - adults. Three consultant physicians in adult CF care will contribute their experience and expertise: Dr. Diana Bilton at RBH, Dr. Caroline Elston at King's College Hospital (London) and Dr. Martin Wildman at Northern General Hospital (Sheffield). They will be involved in all aspects of the study relating to adult centres including consultations with experts.

Quality improvement and qualitative research. Four members of the research team bring unique and essential skills in quality improvement research to the project. Dr. Mohammed Mohammed is a senior lecturer at University of Birmingham with interests in health care quality, league tables and case-mix adjustment. He will advise on the centre comparison work in WP1 and contribute to the design and interpretation of data in WP3 and WP4. Steve Harrison is a service improvement manager at Northern General Hospital specialising in quality improvement using Clinical Microsystems. He will lead WP2.1, design the questionnaire for WP3 and lead the site visits in WP4. Dr Jonathan Boote is an experienced health services researcher at the University of Sheffield, with specific expertise in the conduct and analysis of qualitative research. He will lead WP2.2, be involved in WP3 and design the patient questionnaire in WP4 and analyse all qualitative data. As well as being a CF consultant, Dr. Martin

Wildman is also an honorary senior lecturer in health services research at University of Sheffield and has experience in applying case-mix adjustment methods. With this experience he will advise on the centre comparisons in WP1, participate in the design, running and analysis of the consultation with CF experts and focus groups in WP2.1, participate in the survey in WP3 and participate in the site visits in WP4.

Patient and care representation. To incorporate the interests of the CF community and commissioners, Jo Osmond, Director of Clinical Care and Commissioning at the CF Trust, and Katherine Collins, CF care commissioner, will participate in the project. Dominic Kavanagh, a clinical care patient advisor at the CF Trust, will be consulted regularly to ensure that patient needs and interests are considered.

PROJECT MANAGEMENT

Stephanie MacNeill will be responsible for the overall delivery and reporting of the project's main aims as well as financial management. Responsibilities for the conduct and delivery of each work-package are devolved as described in the research plan. A project management group comprised of all the co-investigators – including Jo Osmond, Director of Clinical Care at the CF Trust, and Katherine Collins as CF care commissioner – will meet twice annually to plan, coordinate and assess the progress of the project. Other meetings and teleconferencing will be arranged as necessary to address issues arising in each of the work-packages.

To ensure that patient needs and interests are considered and that we get their input and advice we will invite Dominic Kavanagh – one of the Trust's clinical care patient advisors – to participate in regular telephone conferences. He participated in the development of the project proposal and is fully aware of its aims. As well as offering his own perspective he can seek advice from his fellow clinical care patient advisors at their regular teleconference meetings within the existing structure of the CF Trust without requiring extra meetings.

In keeping with NIHR regulations we will establish an independent study steering committee. Their role is to provide overall supervision for the project on behalf of the Project Sponsor and Project Funder and to ensure that the project is conducted to the rigorous standards set out in the Department of Health's Research Governance Framework for Health and Social Care and the Guidelines for Good Clinical Practice.

ETHICAL ISSUES

We identified a small number of potential ethical issues in our project and have described how we have addressed them:

1. Within WP1 we will be making use of anonymised patient data from the CF Registry database. Patients have consented to their data being added to the database and to be used for research purposes. Ethical approval for the CF Registry was obtained from the Huntingdon Research Ethics Committee in 2007 (REC reference number: 07/Q0104/2). As their data are fully anonymised patients will not be identifiable.

2. In WP2.1 we will be conducting workshops with multidisciplinary teams of CF experts (1 workshop for adult care and 1 for paediatric care). Participants in these workshops are NHS employees engaged in CF care and they will be asked about their professional practice. As such, we do not feel that these workshops will give rise to any undue anxiety or worry on the part of participants. Participants will be contacted on their work email/address and we will seek their consent for participating in the sessions. They will be reminded at the start of the session and in the information sheet that they do not have to take part in the study and may

withdraw at any time or choose not to answer certain questions. Also, they will be reminded that all information collected during the course of the study will be kept strictly confidential and that participants will not be personally identifiable in any reports or papers produced by the research team.

3. In WP2.2 we will be conducting focus groups by teleconference with the CF Trust's team of clinical care patient advisors to gain patient's perspectives on what makes a good centre. They will be contacted via the CF Trust and we will seek their consent for participating in the sessions. During the course of the focus group they may wish to discuss instances of poor care which may be potentially upsetting for them. To address this potential for upset we will adopt the following strategies:

    a) Participants will be reminded at the start of the focus group and in the information sheet that they do not have to take part in the study and that they may withdraw at any time or choose to answer certain questions. Participants will be informed that we will, however, use whatever data are collected in the focus group prior to their withdrawal.

    b) Participants will be reminded at the start of the focus group that they are free to temporarily leave the focus group by going on "mute" should they become upset. Another member of the research team will be available to speak to them by telephone to help them if they wish.

    c) We will establish from the start that this is a research project about good quality care and that while we recognise that there might be some overlap with poor care, we are not able to take complaints further. We will in these instances direct them to the clinical care patient advisors at the CF Trust as described in the patient information sheet.

    d) We will remind participants at the start of the focus group and in the information sheet that the session is being audiotaped so that the discussion can be later transcribed. All recordings, however, will be deleted after transcription.

    e) Participants will be reminded at the start of the focus group and in the information sheet that all data collected by the researchers will be kept strictly confidential. Patients will not be personally identifiable in any reports or papers produced as a result of this research.

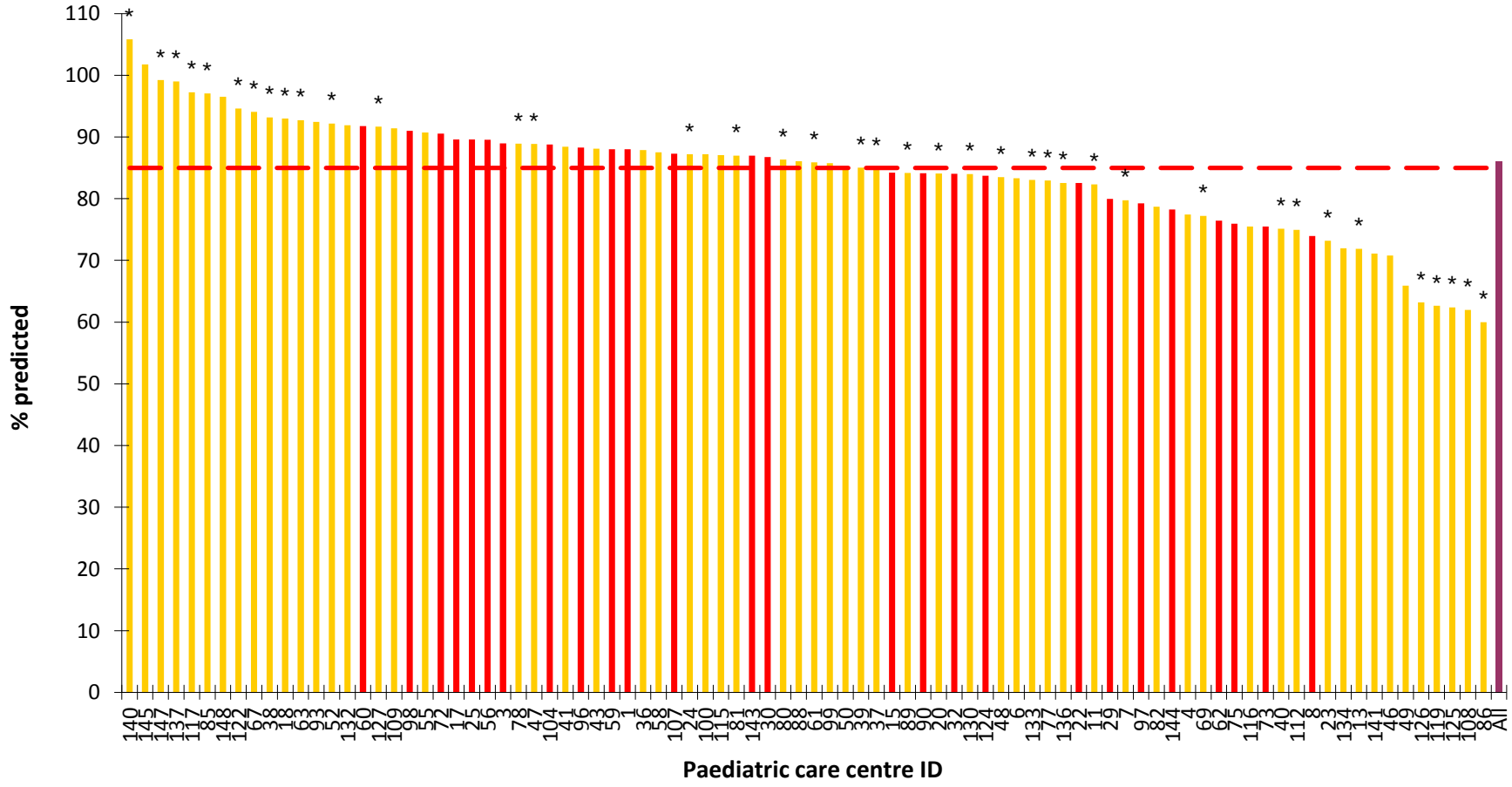
4. In WP3 we will be surveying centre directors and their multi-disciplinary teams regarding the processes of care at their centres. We are not seeking to collect personal data on patients or staff. We will communicate with centre directors through their work email/telephone. Then, we will communicate with the centre directors' personal assistants or secretaries who will pass on the details of the online survey to the members of the multi-disciplinary team as specified by the centre director.

5. In WP4 we will be performing site visits at a sample of centres where we will meet with the centre director and members of their multidisciplinary team to discuss their processes of CF care. The centres chosen for this work will be based on the outcome of the centre comparisons in WP1 and the discussion will be based upon the outcomes of WP2 and WP3. Our questions will relate uniquely to the processes of care and we will not collect personal data on patients or staff. Members of the research group involved in this work will be blind to the centres' results from WP1. This blinding will be communicated to the centres so that they are aware of our intentions to reduce any potential sensitivities that may arise. We will

stress to directors that this work is not designed to be punitive and that individual centres will not be identifiable in our dissemination materials. We will approach centre directors to participate in this work and, for those agreeing to participate, we will apply to the centre's relevant research governance department for approval.

6. We will also conduct an anonymised patient survey at those centres agreeing to participate in the site visits in WP4. The survey is designed to ascertain patients' perspectives on the care they receive and the questions asked will be based on the information gathered in WP2.1, WP2.2 and WP3. At adult centres the questionnaire will be directed to the patient themselves. At paediatric centres, the questionnaire will be directed to the parents or guardians of the patient. To maintain patient confidentiality, we will provide the centres with all of the questionnaire materials and they will administer the mailout without the research team having access to patient details. Questionnaires will not include patient names or hospital numbers and will be returned to the researchers. We will apply for local approval for this work when the consenting centres have been identified and questionnaire finalised.

Appendix: **Current centre comparisons (Median FEV1 % predicted by paediatric centre)**



References

1. Cystic Fibrosis Trust. UK CF Registry Annual Data Report 2009. London: 2011.
2. Ratjen FA. Cystic fibrosis: pathogenesis and future treatment strategies. Respiratory care. 2009;54(5):595-605. Epub 2009/04/28.
3. Davis PB. Cystic fibrosis since 1938. American journal of respiratory and critical care medicine. 2006;173(5):475-82. Epub 2005/08/30.
4. Barr HL, Britton J, Smyth AR, Fogarty AW. Association between socioeconomic status, sex, and age at death from cystic fibrosis in England and Wales (1959 to 2008): cross sectional study. BMJ. 2011;343:d4662. Epub 2011/08/25.
5. Marshall EC, Spiegelhalter DJ. Reliability of league tables of in vitro fertilisation clinics: retrospective analysis of live birth rates. BMJ. 1998;316(7146):1701-4; discussion 5. Epub 1998/06/20.
6. Lilford R, Mohammed MA, Spiegelhalter D, Thomson R. Use and misuse of process and outcome data in managing performance of acute medical care: avoiding institutional stigma. The Lancet. 2004;363(9415):1147-54.
7. Adab P, Rouse AM, Mohammed MA, Marshall T. Performance league tables: the NHS deserves better. BMJ. 2002;324(7329):95-8.
8. Quon BS, Goss CH. A story of success: continuous quality improvement in cystic fibrosis care in the USA. Thorax. 2011;66(12):1106-8.
9. Kraynack NC, McBride JT. Improving Care at Cystic Fibrosis Centers through Quality Improvement. Semin Respir Crit Care Med. 2009;30(05):547-58.
10. Stern M, Niemann N, Wiedemann B, Wenzlaff P. Benchmarking improves quality in cystic fibrosis care: a pilot project involving 12 centres. International journal for quality in health care : journal of the International Society for Quality in Health Care / ISQua. 2011;23(3):349-56. Epub 2011/04/21.
11. Shewart WA. Economic control of quality of manufactured product. London: D. Van Nostrand Company Inc; 1931.
12. Mohammed MA, Cheng KK, Rouse A, Marshall T. Bristol, Shipman, and clinical governance: Shewhart's forgotten lessons. Lancet. 2001;357(9254):463-7. Epub 2001/03/29.
13. Cystic Fibrosis Trust. Standards for the Clinical Care of Children and Adults with Cystic Fibrosis. London: Cystic Fibrosis Trust, 2011.
14. Cystic Fibrosis Trust. UK CF Registry Annual Data Report 2010. London: 2012.
15. O'Connor GT, Quinton HB, Kahn R, Robichaud P, Maddock J, Lever T, et al. Case-mix adjustment for evaluation of mortality in cystic fibrosis. Pediatric pulmonology. 2002;33(2):99-105. Epub 2002/01/22.
16. Spiegelhalter DJ. Funnel plots for comparing institutional performance. Statistics in medicine. 2005;24(8):1185-202. Epub 2004/11/30.
17. Baxter PJ, S. Qualitative case study methodology: study design and implementation for novice researchers. The Qualitative Report. 2008;13(4):544-59.
18. Miles MH, M. Qualitative Data Analysis. Beverly Hills, US: Sage; 1994.
19. Stewart DWS, P.N.; Rook, D.W. Focus groups. 2nd ed: Sage; 2007.
20. Johnson C, Butler SM, Konstan MW, Morgan W, Wohl ME. Factors influencing outcomes in cystic fibrosis: a center-based analysis. Chest. 2003;123(1):20-7. Epub 2003/01/16.
21. Ritchie J, Spencer L. Qualitative data analysis for applied policy research. In: Bryman A, Burgess RG, editors. Analysing qualitative data. London: Routledge; 1994.