Study Title: Experience of a Health Website Evaluated in a Research Study (EXPERT): An exploratory study to assess feasibility and measure the impact of online health information, (experiential and fact-based) for self-management of asthma, motivation to stop smoking, and preparedness for caring for someone with multiple sclerosis.

Ethics Ref: Liverpool East 13/NW/0162

Trial Registration Number:

Date and Version No: 31st October 2013, version 3.0

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Sponsor: University of Oxford

Funder: NIHR

Signatures:

Investigator Agreement

"I have read this protocol and agree to abide by all provisions set forth therein.
I agree to comply with the International Conference on Harmonisation Tripartite Guideline on Good Clinical Practice."

Principal Investigator (Print Name)	Investigator Signature	Date

Co-Investigator (Print Name)	Investigator Signature	Date
Co-Investigator (Print Name)	Investigator Signature	Date
Co-Investigator (Print Name)	Investigator Signature	Date
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Confidentiality Statement

This document contains confidential information that must not be disclosed to anyone other than the Sponsor, the Investigator Team, host NHS Trust(s), and members of the Research Ethics Committee.

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AMENDMENT HISTORY

Amendment No.	Protocol Version No.	Date issued	Author(s) of changes	Details of Changes made
(1)	V1.1	03/06/2013	A Naughten Trial Manager	Changes to the recruitment method of MS Carers to include Primary Care.

Protocol amendments should be submitted to CTRG as sponsor before submission to the ethics committee.

1 SYNOPSIS

Study Title	Experience of a Health Website Evaluated in a Research Study (EXPERT): An exploratory study to assess feasibility and measure the impact of online health information, (experiential and fact-based) for self-management of asthma, motivation to stop smoking, and preparedness for caring for someone with multiple sclerosis.
Internal ref. no.	JP/EXPERT/0005
Study Participants	Males and Females over 18 living in the UK with internet access and one of three conditions: someone self-managing their asthma; someone who smokes but has a willingness to quit; or someone who is a carer of a person with multiple sclerosis.
Planned Sample Size	Approximately 300 participants
Follow-up duration	Two weeks from recruitment to final follow-up measure (questionnaire).
Planned Study Period	Seventeen months (January 2013 to May 2014)
Primary Objective	To estimate the feasibility issues in an online randomised study providing an active and comparator information based website intervention.
Secondary Objectives	1. To assess the efficacy of two types of online health information (patient experience accounts compared with non-experience based information) on a range of self-reported outcomes. 2. To measure the impact of the intervention and comparator websites using the eHealth Impact Questionnaire (eHIQ) 3. To explore whether the interventions have differential effects on pre-specified subgroups of participants.

Primary Endpoint	The feasibility endpoints are as follows: • Number of participants providing consent • Total recruitment (number of participants randomised to a website allocation) • Number of participants with complete records/measurements (completed all baseline and follow up measures and at least one website log in recorded) • Number of participants with partial records/measurements (completed at least one baseline or follow up measure and/or at least one website log in recorded) • Usage of intervention and comparator sites (total number of log ins, total number of pages visited, total usage duration). • Number of participants lost to follow up or withdrawn
Secondary Endpoints	Our outcome measures for efficacy (comparing change from baseline to 2-week follow-up between intervention and comparator groups) are as follows: 1. Asthma: Partners in Health (PIH, 12-item) 2. Smoking: Motivation To Stop Scale (MTSS, single item, 8 point scale) 3. Caring: Preparedness for Caregiving Scale (PFCS, 8-item) Our secondary outcome measures are: 1. For all participants: eHealth Impact Questionnaire (eHIQ); SF36 physical dimension and mental dimension summary scores; and the following SF36 subscales: mental health (also known as the MHI-5), physical functioning, role physical, bodily pain, general health perceptions, vitality, social functioning, and role emotional. 2. Additionally for Asthma: Chronic Disease Self-efficacy Scale (6-item); Single-item control question. 3. Additionally for Smoking: Abstinence rates (single

	question); quit attempts (single question); Smoking Abstinence Self-efficacy Questionnaire (SASEQ, 6-item)

2 ABBREVIATIONS

AE	Adverse event
AR	Adverse reaction
CRF	Case Report Form
DMC	Data Monitoring Committee
eHIQ	Electronic Health Impact Questionnaire
GCP	Good Clinical Practice
GP	General Practitioner
IB	Investigators Brochure
ICF	Informed Consent Form
ICH	International Conference of Harmonisation
NIHR	National Institute for Health Research
NRES	National Research Ethics Service
PC-CTU	Primary Care – Clinical Trials Unit
PEx	Patient Experience
PI	Principal Investigator
PIS	Participant/ Patient Information Sheet
R&D	NHS Trust Research and Development Department
REC	Research Ethics Committee
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SOP	Standard Operating Procedure
TMC	Trial Management Committee
TMF	Trial Master File

TSC	Trial Steering Committee

3 BACKGROUND AND RATIONALE

The provision of reliable, relevant and timely health information for the public and patients is fundamental to the delivery of the National Health Service. “High Quality Care for All” (2008) stresses the importance of an NHS that gives patients and the public more information and choice, and has quality of care at its heart,’ (1). The Department of Health’s strategy “The Power Of Information: Putting all of us in control of the health and care information we need” (2012) (2) recognises the change in the way people access information and sets out a ten year framework to ensure information and new technologies are harnessed to achieve high quality care and improve outcomes for patients and service users. The NHS has already recognised the potential of internet patient experiences (PEx). The NHS Choices website includes videos of individual experiences as well as explanations of treatments and conditions.

Traditionally, authoritative health information has been based on facts and figures, not on the experiences of patients. However, people facing a new diagnosis or health related decision, or living with a long term condition, often feel that they need to know how others have experienced what they are going through (3). People seek knowledge about their health from others who have been through the same experiences (4-6). They now routinely do this via the internet (7). Sharing experiences is part of a wider shift in the relationship between lay and medical expertise (8, 9) but not all groups engage with online patient experiences in the same way (10).

Hearing other patients’ experiences has the potential to affect decision-making, one’s sense of isolation or support, and adjustment to the illness or health condition (11). At the same time there are concerns that testimonials, or unmoderated comments, may combine a powerful and memorable delivery with a misleading message (12). Experiential information is not an alternative to existing medical evidence and may influence different, complementary health related domains, such as support, decision-making, knowledge, self-care, coping and anxiety. Our current work indicates a range of domains that could be affected by exposure to online PEx. These include: finding information, feeling supported, maintaining relationships with others, affecting behaviour and experiencing health services, a further two (learning to tell the story and visualising disease) are less acknowledged but important features of online resources (13). However, we know relatively little about how people use and evaluate online PEx; there are no generic assessment tools sensitive to measure the impact of PEx, and thus we remain unsure whether, when and how the NHS should provide information based on other patients’ experiences. The provision of PEx for NHS users needs as firm an evidence base to support its collation and provision as all other health information (14). This evidence needs to be embedded in clinical practice, where feasibility and acceptability are crucial and evaluated in a randomised controlled study.

In this study we are therefore proposing to evaluate the impact of online health information websites containing information derived from patients' experiences (their narrative accounts of health and illness) in three exemplar conditions, and compare this impact with that of three comparator websites which contain facts and figures (and information from health professionals) but no experiential information from patients. Our three exemplar conditions have been chosen to assess the impact of experiential information on (1) confidence to self-manage a chronic disease (asthma); (2) motivation to change an unhealthy behaviour (smoking); (3) preparedness to undertake a caring role (carers of people with multiple sclerosis). Our theoretical work suggests that these are three of the several ways in which experiential information may be beneficial. We are also measuring the impact of all six websites using a new bespoke tool, the eHealth Impact Questionnaire, and examining any changes on mental health scores and quality of life scores. This research proposes an exploratory study; that is, our main aim is to establish the feasibility of undertaking this research and to identify any emergent evidence of efficacy or harm. Our intention is to use the knowledge from this study to inform further, more pragmatic, effectiveness research in future.

4 OBJECTIVES

4.1 Primary Objective

To evaluate the feasibility issues in an online randomised study providing health information websites containing patient experience information compared with matched health information websites that do not contain experiential information.

4.2 Secondary Objectives

1. To assess the efficacy of two types of online health information (patient experience accounts compared with matched health information websites that do not contain experiential information) on a range of self-reported outcomes.
2. To measure the impact of the intervention and comparator websites using the eHealth Impact Questionnaire (eHIQ)
3. To explore whether the interventions have differential effects on pre-specified subgroups of participants.

5 STUDY DESIGN

5.1 Summary of Study Design

This is a randomised, controlled single-blind study. We have chosen three exemplar conditions – asthma, smoking cessation and carers of individuals with multiple sclerosis. For each condition we have created two websites, one containing patient experience information (active intervention) and

the other containing information based solely on facts and figures and no experienced based information (comparator). Recruitment of participants eligible for the asthma and smoking cessation arms of the study will be through primary care. In addition we would like to recruit smokers willing to quit by placing adverts in newspapers, online and in public places where smokers are likely to see them. Participants eligible for the carers of people with multiple sclerosis arm will be recruited through various routes including neurology clinics, newspaper adverts, website adverts, voluntary groups, online forums and social networking sites. All eligible participants will be sent a patient information sheet and consent form by post to be signed and returned to the research office. Participants will be asked to provide baseline measures prior to the allocation of the intervention or comparator website. They will then be given the opportunity to create a unique user ID and password which will allow them unlimited access to their allocated website for two weeks. Participants' website use will be tracked so we will be able to tell how many times a participant accessed the site, the number and type of pages viewed, the amount of time spent using the website, as well as any search terms used to find information on the site. After two weeks, participants will be asked to provide follow up measures and they will no longer have access to their website. A selection of participants will be invited for interview after completion of the study. Interviews will be conducted by an experienced qualitative researcher in the participant's home or at another suitable location acceptable to the participant. Most communication with participants will be via email but we may also telephone participants to request they complete follow up questionnaires. Those participants invited for interview will be contacted by telephone or email and the interview itself will be conducted in person.

5.2 Primary Endpoints/Outcome Measures

The primary outcome measures in this exploratory study concern feasibility, and will be assessed regularly during the recruitment period and at the end of the study as totals and split by the three conditions asthma, smoking cessation, and carers, to include:

- Number of participants providing consent
- Total Recruitment (number of participants randomised to a website allocation)
- Number of participants with complete records/measurements (completed all baseline and follow up measures and at least one website log in recorded)
- Number of participants with partially completed records/measurements (completed at least one baseline or follow up measure and/or at least one website log in recorded)
- Usage of intervention and control sites
- Number of participants lost to follow up or withdrawn (lost to follow up defined as randomised participants who can no longer be contacted or do not respond to requests from the research team and withdrawn defined as participants who have asked not to be contacted).

5.2.1 Secondary Endpoints/Outcome Measures

Our secondary endpoints comprise outcome measures for efficacy (comparing change from baseline to 2-week follow-up between intervention and comparator groups). The primary measures for efficacy are as follows:

1. Asthma: Partners in Health (PIH, 12-item)
2. Smoking: Motivation To Stop Scale (MTSS, single item, 8 point scale)
3. Caring: Preparedness for Caregiving Scale (PFCS, 8-item)

Our secondary measures for efficacy are:

1. For all participants:
    a. eHealth Impact Questionnaire (eHIQ);
    b. SF36 physical dimension and mental dimension;
    c. SF36 subscales (mental health, physical functioning, role physical, bodily pain, general health perceptions, vitality, social functioning and role emotional.
2. Additionally for Asthma:
    a. Chronic Disease Self-efficacy Scale (6-item);
    b. Single-item control question.
3. Additionally for Smoking:
    a. Abstinence rates (single question);
    b. Quit attempts (single question);
    c. Smoking Abstinence Self-efficacy Questionnaire (SASEQ, 6-item)

5.3 Study Participants

5.3.1 Overall Description of Study Participants

Study participants will be male or female, over the age of 18, resident in the UK and with access to the internet. They will either have asthma, be smokers with a willingness to quit, or be carers of a person with multiple sclerosis. Participants who match more than one condition can only be included once. Only one participant per household can be included.

5.3.2 Inclusion Criteria

1. Smokers
    a. People who are current smokers, who have been smokers for at least a year, and who indicate some willingness to quit, including those referred to smoking cessation services.
    b. Male or female aged 18 or over.

c. Willing and able to give informed consent for participation in the study.
d. Live in England.
e. Have access to the internet and able to use websites.

2. People with asthma
    a. People who have been clinically diagnosed asthma as coded in their primary care electronic record, and who have been prescribed inhaled corticosteroids for at least 3 months in the previous year.
    b. Male or female aged 18 or over.
    c. Willing and able to give informed consent for participation in the study.
    d. Live in England.
    e. Have access to the internet and able to use websites.

3. Carers of people with multiple sclerosis
    a. People who identify themselves as a caregiver for another person who has a diagnosis of multiple sclerosis.
    b. Male or female aged 18 or over.
    c. Willing and able to give informed consent for participation in the study.
    d. Live in England.
    e. Have access to the internet and able to use websites.

5.3.3 Exclusion Criteria

1. Smokers
    a. People who are terminally ill.
    b. People who cannot understand English.
    c. People who have previously entered the study.
    d. People who have another significant disease or disorder which, in the opinion of the GP, may either put that person at risk because of participation in the study, or may influence the result of the study, or affect that person's ability to participate in the study.

2. People with asthma
    a. People who are terminally ill.
    b. People who cannot understand English.
    c. People who have previously entered the study.
    d. People who have another significant disease or disorder which, in the opinion of the GP, may either put that person at risk because of participation in the study, or may influence the result of the study, or affect that person's ability to participate in the study.

3. Carers of people with multiple sclerosis
    a. People who are terminally ill.
    b. People who cannot understand English.
    c. People who have previously entered the study.
    d. People who have a significant disease or disorder which, in the opinion of the Principal Investigator, may either put that person at risk because of participation in the study, or may influence the result of the study, or affect that person's ability to participate in the study.
    e. People whose only caring role is in a professional (paid) capacity.

5.4 Expenses and Benefits

There are no financial costs to participants in taking part in the study and we will therefore not be reimbursing expenses or providing other financial benefits. It is hoped that participants will benefit from the health information provided in their allocated website. For participants who take part in the interviews, we will reimburse travel expenses for an interview not conducted in their own home. Interview participants will not receive any other payments.

5.5 Study Procedures

5.5.1 Recruitment

For the asthma and smoking cessation study arms, we will work with the Primary Care Research Network to identify GPs at practices who would be interested in taking part. We will then contact practice GPs with information about the study and ask them to identify eligible participants based on the inclusion and exclusion criteria specified in this protocol. We will request that they screen for eligible patients via database searches and knowledge of their patient population. We will provide the GP with study documents to send to eligible participants to include: a covering letter, patient information sheet, consent form, contact details form and reply-paid envelope. In addition we would like to recruit smokers willing to quit by placing adverts in newspapers, online and in public places where smokers are likely to see them. These advertisements will invite interested potential participants to contact the research office for further information and provide their contact details. The Trial Manager will then send them the study documents as described above.

For carers of people with multiple sclerosis, we will have an open recruitment process with advertisements for study participants placed in secondary care clinics, venues for community and carers groups, newspapers, and in charity and NHS newsletters, websites and in online social media aimed at carers. These advertisements will invite interested potential participants to contact

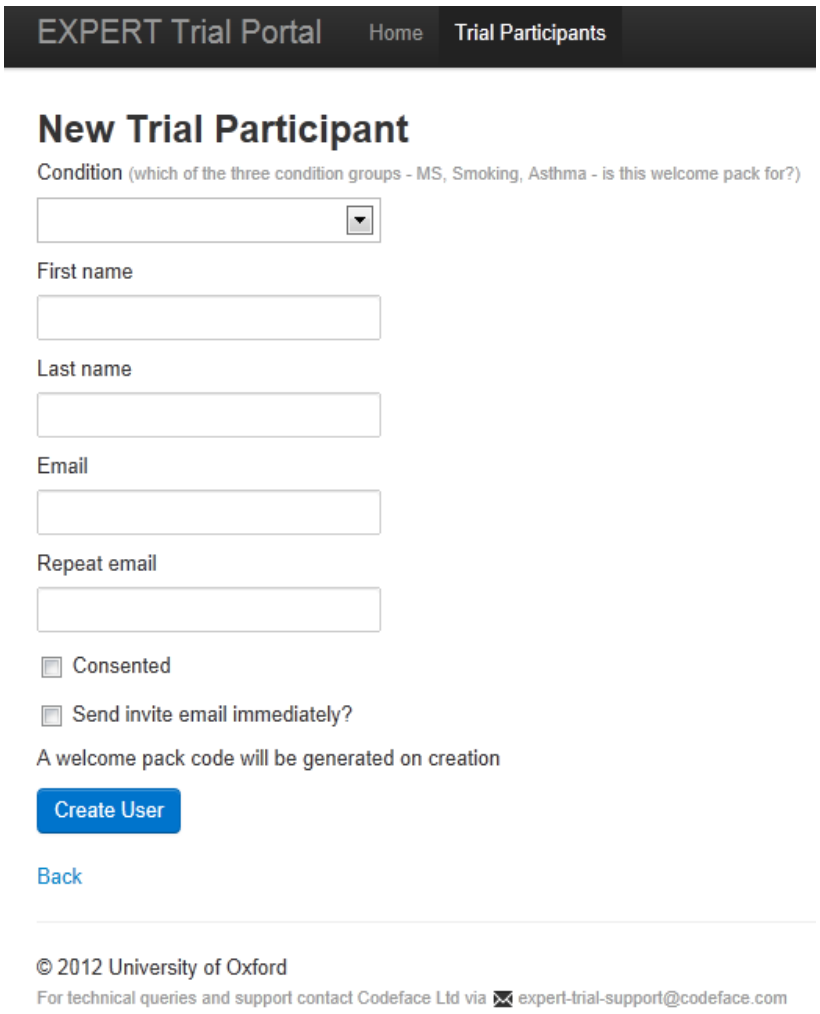
the research office for further information and provide their contact details. The Trial Manager will then send them study documents as outlined above.

We will also recruit carers of people with Multiple Sclerosis through Primary Care in GP practices who are willing and able to participate. We will provide the GP with study documents to send to eligible participants to include: a covering letter, patient information sheet, consent form, contact details form and reply-paid envelope. We will ask that the GP does not contact anyone that meets the exclusion criteria for MS Carers.

5.5.2 Informed Consent

For all recruitment methods, potential participants will be invited to read the patient information sheet and discuss the study with others before deciding whether to take part and to contact the research team with any questions (contact details will be provided in the information sheet). If the participant agrees to take part, they will be asked to complete the consent and contact details form and return this to the research office in a reply-paid envelope. The information sheet outlines the purpose of the study and details what will happen to the participant if they consent to take part. It also states that the participant is free to withdraw from the study at any time for any reason and with no obligation to give the reason for withdrawal and that this will not affect their future care. There is no time limit between participants receiving the Patient Information Sheet and providing consent within the recruitment period. A copy of the signed Informed Consent will be retained by the participant and a copy sent to the participant's GP if they were recruited through primary care.

Once a completed consent and contact details form is received by the research office, the Trial Manager (or other appropriate member of the research team), will enter the participant's details into a secure, password-protected online Trial Management Portal (see screen-shot below), to include condition (asthma, smoking cessation or carer), first name, last name, email address, consent form received.



5.5.3 Collection of baseline measures

A unique 'Welcome Code' will be generated and automatically sent by email to the participant with a link to the study registration webpage. The Trial Manager will be emailed confirmation that the participant has been sent their Welcome Code. If after one week the participant has not used their Welcome Code, a reminder will be sent by automatic email inviting them to visit the study registration page. If the participant no longer wishes to take part they can simply ignore this reminder. If the participant does wish to take part they can use the link in the email to access the study registration page where they will be asked to complete some online questionnaires. Whilst completing these questionnaires participants can navigate back and forth through the sections to make any amendments as required. They will also be prompted if questions are left blank but they are not required to answer all the questions before proceeding.

5.5.4 Allocation to intervention or comparator, and blinding

Once the participant submits their questionnaire answers (baseline data) by clicking 'finish' they are randomised into the study and allocated a website. Participants will be randomised in a 1:1 ratio between the intervention and comparator websites in each of the three study arms.
They will be invited to create a unique User ID and Password and will be provided with an on-screen link to their allocated website as well as being sent email confirmation. Access to the website will be available for two weeks for each participant.

Because of the nature of the intervention and comparator (information-based websites) it is not possible to completely blind participants. However in the information for participants we will only explain that our intention is to find out whether or not people find health information websites useful and if so, how best to provide health information online. In this way we hope that participants will not be aware of our primary hypothesis regarding the differential effect of experiential information. The investigators looking at questionnaire data will be blind to the allocation of intervention or comparator during study recruitment, administration of interventions, and analysis. The website usage data and qualitative interviews will be reviewed and analysed separately by researchers based in the Health Experiences Research Group who will not be blind to allocation due to the nature of the data.

5.5.5 Reminders, usage data, and follow-up outcome measures

At 2, 6 and 10 days after completing baseline data all participants will be sent automated email reminders to visit their allocated website. Any visits to the website will be recorded and tracked. At the end of the two week period the participant will be emailed to request that they complete the follow up questionnaires and will be given a link to the questionnaires website. At this point access to the allocated information website is withdrawn. Participants who do not complete follow up questionnaires will be sent reminders by email every day for up to two days after the due date (a maximum of two reminders). After completion of follow up questionnaires participants will be emailed to thank them for taking part and reminded that we may contact them again to invite them for interview. The Trial Manager will be sent details of participants who have not completed follow up questionnaires after receiving two reminders. The Trial Manager or other designated member of the research team will contact these participants by telephone to request they complete follow up questionnaires. Any participants withdrawn or lost to follow up will be flagged appropriately.

5.6 Follow-up interviews

A subset of study participants will be invited to be interviewed by an experienced qualitative researcher from the Health Experiences Research Group, Department of Primary Health Care Sciences, University of Oxford. These interviews will be undertaken to explore with participants

their attitudes and behaviour in relation to their allocated websites and other sites they may use, as well as their views on participating in the research. Participants selected will be contacted by telephone or email; those who agree to be interviewed will be sent a separate Patient Information Sheet and consent form and arrangements will be made for when and where the interview will take place. The participants will be selected for maximum variation to give us as diverse a sample as possible. For each of the six websites, we will include people of both genders and of different age brackets, people who demonstrate a high and low usage of their allocated website and questionnaire responders and non-responders. The sampling method seeks to achieve representation of the diversity of experiences, rather than numerical representation. Analysis and data collection will proceed simultaneously during the recruitment period and continue until 'data saturation' is reached to ensure that the widest practical range of experiences has been included. Participants will be contacted as soon as possible after the deadline for submission of follow up questionnaires. We hope to interview 20 to 30 people.

5.7 Definition of End of the Study

The end of the study is the date when the last participant submits their follow up questionnaires or the last participant is interviewed, whichever is later.

5.8 Discontinuation/ Withdrawal of Participants from the Study

A participant may withdraw from the study at any time without providing a reason. Participants can notify the research team of their wish to withdraw by contacting the research office. If a participant does withdraw from the study they may also request that any data already provided by them is deleted. This is explained in the Patient Information Sheet. If a participant does not complete follow up measures and does not respond to reminders or requests to complete follow up measures they will be considered lost to follow up. Any data from participants lost to follow up will continue to be used in the study. The Principal Investigator may withdraw a participant from the study at any time if necessary in accordance with Good Clinical Practice.

5.9 Source Data

Source data will include baseline and follow up questionnaires (electronic format) as well as consent and contact forms. It will also include website usage data.

6 DETAILS OF STUDY INTERVENTION

6.1 Description of study intervention

The intervention is a password protected, multi-media internet site based on guidelines developed as part of the NIHR funded programme grant RP-PG-0608-10147. For each condition (asthma,

smoking cessation, carer) two websites have been developed one containing patient experience information and the other containing information solely based on facts and figures with no experience-based content. Participants will be randomised to have access to one or other of these websites within the relevant condition. The comparator sites share the design and multimedia (such as video) features of the intervention sites but the content excludes any accounts of personal experience. They use source material from the national health information portal NHS Choices with all experiential information removed.

6.2 Assessment of use of the website

User activity will be tracked by both page views (number and type) and interaction with web pages e.g. if a participant views videos or listens to audio clips. We will also track whether participants use the search facility and what search words they use. The recorded data will be linked to baseline and follow-up questionnaire data by a unique participant ID number. IP addresses will not be stored.

Tracking data will be collected in the following ways by individual user:

- Total visits to site (including times and date stamps)
- Total time spent on site
- Total number of page views
- Breakdown of session times (start and finish)
- Breakdown of page type visited and time spent on each. There will be eight page types: home page; topic summary page; categories page; interviewee page; video clip page; audio clip page; text only clip page; text only glossary page
- Breakdown of clips viewed and length of time they were viewed for, split by the three formats: video, audio, and text only
- If a user has JavaScript disabled in their browser this will be recorded

6.3 Measures to guard against contamination

There is a theoretical risk of contamination (i.e. patients allocated to one of the websites viewing the other website). In this study the websites have been developed specifically for the study and are only available to study participants, accessible only with username and password. Nevertheless it is possible that people with access to one of the websites might share their login details with others, or might otherwise copy the content and share it outside the study setting. We will ask participants not to divulge their individual username and password, or otherwise allow other people access to the website or its content. We will not recruit people who share a household. We will explain that we are monitoring participants' use of the site, and that giving access to other people will make it

difficult to interpret the data. We will ask about possible contamination in our qualitative interviews with a subset of participants and in a single question to all participants at follow-up.

7 SAFETY REPORTING

The intervention and comparator websites delivered in this study are low-risk information-only interventions and do not require any change in standard clinical management of the patients recruited to this study. Participants who have concerns about their health after viewing information provided on their allocated website will be advised to contact their GP or NHS Direct. Participants will be able to comment on the website content that they are asked to view and these comments will be reviewed regularly by a member of the research office. Any concerns expressed about website content will be reported to the Trial Steering Committee for review.

8 STATISTICS

Analysis and reporting of results will conform to CONSORT guidelines, as follows:

- Study flow will be reported using a CONSORT diagram.
- Any deviations from the protocol will be reported, with reasons.
- We will report dates of recruitment and follow-up.
- We will report baseline characteristics of both groups (intervention and comparator).
- Analyses will be on an intention to treat basis, and the number of included participants will be clearly stated.
- For each primary and secondary outcome measure, a summary of results for each group will be reported, together with the estimated effect size and its precision.
- We will report any other analyses performed, including subgroup analyses and adjusted analyses. These will be highlighted as hypothesis generating instead of hypothesis testing analyses in the final report
- We will report any concerns expressed by participants as detailed in section 7 Safety Reporting above.

A detailed statistical analysis plan is to be produced separately by the Primary Care Clinical Trials Unit statistician. Our primary objective is to establish the feasibility issues in this study. For this analysis the focus will be on determining overall feasibility parameters for the whole study and not on comparisons between intervention arms (secondary endpoints/outcomes of effectiveness). These parameters are:

- Number of participants providing consent
- Recruitment rates (number of participants randomised to a website allocation)
- Number of participants with complete records/measurements (completed all baseline and follow up measures and at least one website log in recorded)

- Number of participants with partially completed records/measurements (completed at least one baseline or follow up measure and/or at least one website log in recorded)
- Usage of intervention and control sites
- Number of participants lost to follow up or withdrawn (lost to follow up defined as randomised participants who can no longer be contacted or do not respond to requests from the research team and withdrawn defined as participants who have asked not to be contacted).

Except for usage of intervention and control sites, all these will be summarized using rates reported as a percentage with 95% confidence intervals. Usage will be summarized using means and standard deviations or if deemed highly skewed median and interquartile ranges. Use of the search facility and search terms will be reported using multiple descriptive statistics (frequency of terms used). We will carry out exploratory comparisons between groups which will be based on percentages, means of continuous normally distributed variables or medians for skewed data, to evaluate unexpected differences between the arms which could impact on feasibility. Appropriate measures of dispersion will be reported.

Our secondary objective is to compare change from baseline to 2-week follow-up between intervention and comparator groups on a range of self-reported measures, as follows:

1. Asthma:
    a. Primary outcome
        i. Partners in Health (PIH, 12-item)
    b. Secondary outcomes
        i. Chronic Disease Self-efficacy Scale (6-item);
        ii. Single-item control question.
        iii. eHealth Impact Questionnaire (eHIQ);
        iv. SF36 physical dimension and mental dimension;
        v. SF36 subscales (mental health, physical functioning, role physical, bodily pain, general health perceptions, vitality, social functioning and role emotional).
2. Smoking:
    a. Primary outcome
        i. Motivation To Stop Scale (MTSS, single item, 8 point scale)
    b. Secondary outcomes
        i. Abstinence rates (single question);
        ii. Quit attempts (single question);
        iii. Smoking Abstinence Self-efficacy Questionnaire (SASEQ, 6-item)
        iv. eHealth Impact Questionnaire (eHIQ);

v. SF36 physical dimension and mental dimension;
vi. SF 36 subscales (mental health, physical functioning, role physical, bodily pain, general health perceptions, vitality, social functioning and role emotional)

3. Caring:
   a. Primary outcome
      i. Preparedness for Caregiving Scale (PFCS, 8-item)
   b. Secondary outcomes
      i. eHealth Impact Questionnaire (eHIQ);
      ii. SF36 physical dimension and mental dimension
      iii. SF36 subscales (mental health, physical functioning, role physical, bodily pain, general health perceptions, vitality, social functioning and role emotional).

We will also, in a cross-sectional analysis, compare the scores on the eHealth Impact Questionnaire (eHIQ) at the 2 week follow-up point between the two groups.

Outcomes will be compared using chi-square tests of significance for categorical data (including binary data) and t-tests for continuous data. For binary data logistic regression will be used to explore potential confounding and to investigate explanatory variables. Categorical outcomes will be dichotomized and logistic regression will be used as well. For continuous outcomes, these analyses will be based on linear regression models (if necessary after transformation of data to comply with normality and homoscedasticity assumptions). ANCOVA based on adjustment for non-evenly distributed characteristics between the groups at baseline will be used to test for differences in outcomes between intervention and control groups.

For all outcomes we will investigate interactions with age, sex, ethnicity, educational attainment, internet use and ability, measures of disease severity, general health status, level of social support, level of health literacy, life orientation score (LOT-R), baseline mental health score, and usage of the intervention.

We will include descriptive statistics to characterise participants in terms of baseline characteristics; CONSORT diagram of the flow of participants through the study, and proportion who completed each stage to study entry; and usage of intervention in terms of total visits to site, total time on site, and total number of website pages visited.

We will undertake pre-specified subgroup analyses on the following subgroups:

- High self rated internet ability versus low self-rated
- High level of self reported social support versus low
- High self-rated health literacy versus low
- High educational attainment versus low educational attainment groups
- Optimism versus pessimism trait according to LOT-R instrument

The baseline data of those who entered the study but did not complete follow up according to the study protocol, and those who did, will be compared to determine how representative the study results are and to investigate any potential threats to validity from differential losses to follow up in each arm.

The investigators undertaking analysis will be blind to the allocation of intervention or comparator.

Qualitative Component

Interview transcripts will be analysed by the qualitative researcher responsible for the data collection. The transcripts will be coded and entered into a specialist software package such as NVivo10 which will be used to organise and analyse anticipated and emergent themes using the method of constant comparison.

8.1 The Number of Participants

We are aiming to recruit a total of 300 participants – 100 in each of the three groups (smoking cessation, asthma and MS carers). The focus of the study is to assess feasibility which could usually be addressed using a smaller sample (30-40 per condition ref). However, this sample size would provide enough power to estimate acceptability judged by engagement with the PEx components of the site with a precision of plus or minus 14% within each condition/arm (50 participants) and 8% for the whole study /per arm (150 participants). This is based on a worst case scenario of acceptability being of 50%. Assuming acceptability to be in the region of 80%, we estimate that with 150 patients in the PEx group for each of the three conditions a 95% confidence interval would have a lower limit of 73% and a higher limit of 87%.

Based on a balanced randomisation to active:control groups in a ratio of 1:1 (i.e. 50 intervention, 50 comparator) we should be able to detect potential large effects of the PEx component. For dichotomous outcomes these are equivalent to relative risks of 2.1 or above for a baseline rate of 30% or less given an alpha of 0.05 and 90% power; while for continuous outcomes these detectable differences would be of the order of .4SDs based on the same power and significance. We anticipate

that these differences in questionnaire measures between the groups would translate into small to moderate effect size differences on a clinical outcome in a larger pragmatic trial.

8.2 The Level of Statistical Significance

The primary analysis will be contingent on achieving P=0.05. Pre-specified secondary analyses will also be powered at P=0.05.

8.3 Criteria for the Termination of the Study.

It is not thought that the study will need to be terminated early due to safety concerns. Any concerns about website content and the safety of participants that arise during the course of the study will be reviewed by the Trial Steering Committee and we will act on their advice as appropriate.

8.4 Procedure for Accounting for Missing, Unused, and Spurious Data.

We have not defined any procedures a priori to account for missing, unused or spurious data. As part of the primary objective of assessing feasibility, the rate of missing values is highly relevant and will be an important outcome included in the final report. We will therefore report data on attrition rates, compliance (website visit) and completion of outcome measures, which should help to define these procedures for the full study. A detailed description will be included in the Statistical Analysis plan (SAP) as specified in the PC-CTU's SOP "Statistical Analysis Plan".

8.5 Procedures for Reporting any Deviation(s) from the Original Statistical Plan

We do not anticipate any deviation from the statistical plan outlined above. However, provision for alternative methods and changes to analyses will be included in the SAP.

8.6 Inclusion in Analysis

We will analyse our data using an intention to treat analysis. All eligible, randomised and evaluable participants will be included in the analysis. Details of this primary analysis and secondary analyses (per-protocol population) will be included in the SAP.

9 DIRECT ACCESS TO SOURCE DATA/DOCUMENTS

Direct access will be granted to authorised representatives from the sponsor and host institution to permit study -related monitoring, audits and inspections.

10 QUALITY CONTROL AND QUALITY ASSURANCE PROCEDURES

The study will be conducted in accordance with the current approved protocol, ICH GCP, and PC-CTU SOP "Quality Management". A risk assessment has been conducted in conjunction with PC-

CTU Quality Assurance Manager and a monitoring plan agreed. Monitoring will be carried out by the PC-CTU Quality Assurance Manager, Trial Manager or other appointed person. PC-CTU data will be evaluated for compliance with the protocol and accuracy in relation to source documents where possible. Following PC-CTU SOP "Monitoring of Clinical Trials", the monitor(s) will verify that the study is conducted in compliance with GCP and the study protocol.

The Trial Management Committee (TMC) will be responsible for the monitoring of all aspects of the study's conduct and progress and will ensure that the protocol is adhered to and that appropriate action is taken to safeguard participants and the quality of the study itself. The TMC will be comprised of individuals responsible for the study's day to day management and will meet regularly throughout the course of the study.

A Trial Steering Committee (TSC) will be convened to provide independent oversight of the study and ensure its conduct is in accordance with the protocol. As this study involves a low-risk intervention, it is not considered necessary to convene a separate DMC so members of the TSC will perform this role and review the data.

11 ETHICS

Due to the type of intervention used in this study we do not believe that there are any significant ethical issues.

11.1 Declaration of Helsinki

The Principal Investigator will ensure that this study is conducted in accordance with the principles of the Declaration of Helsinki.

11.2 ICH Guidelines for Good Clinical Practice

The Principal Investigator will ensure that this study is conducted in accordance with the principles of the ICH Guidelines for Good Clinical Practice (July 1996).

11.3 Approvals

All study material will be submitted to an appropriate Research Ethics Committee (REC), relevant R&D departments and host institution(s) for written approval.

The Principal Investigator will submit and, where necessary, obtain approval from the above parties for all substantial amendments to the original approved documents.

11.4 Participant Confidentiality

The study staff will ensure that participants' anonymity is maintained. Patient contact details will be collected and stored separately from baseline and follow up data and according to PC-CTU guidelines. Participant's personal data will be stored electronically in an encrypted and password protected file and only accessible by authorised study personnel. All paper documents will be stored securely in locked filing cabinets in the Department of Primary Health Care Sciences, University of Oxford. Participants will be allocated a unique study reference number which will be used in the study database and linked to the data provided via the online questionnaires so this can be analysed anonymously. This database will be stored on a secure University of Oxford server and will be password protected.

12 DATA HANDLING AND RECORD KEEPING

Consent and contact details will be collected on paper forms and sent to the research office by the participant using reply-paid envelopes. Paper forms will be stored according to PC-CTU SOP "Document Control". MS Carers who respond to advertisements may provide their name and contact details via email in which case the data will be entered and stored in a secure, password protected electronic file and the original email will be deleted. Baseline and follow up data will be collected electronically via secure forms on a password protected website portal and then be transferred to a clinical database management system (CDMS), OpenClinica. This database will be held on a secure University of Oxford server and be password protected. The collection, transfer and storage of personal data will comply with the Data Protection Act, clinical trial guidelines and PC-CTU Standard Operating Procedures relating to Data Management. Data completeness will be monitored regularly by the PC-CTU Data Manager. At the conclusion of the study all essential documents will be archived in accordance with the PC-CTU SOP "Archiving" and stored for at least five years from the end of the study. The Principal Investigator is responsible for authorising retrieval and disposal of archived material.

13 FINANCE AND INSURANCE

The study is funded until the end of January 2015 and forms part of a larger programme grant awarded by the NIHR (reference number RP-PG-0608-10147).

13.1 Compensation for harm

Negligent Harm: Indemnity and/or compensation for negligent harm arising specifically from an accidental injury for which the University is legally liable as the Research Sponsor will be covered by the University of Oxford. The NHS will owe a duty of care to those undergoing clinical treatment, with Trust Indemnity available through the NHS Litigation Authority Scheme.

14 PUBLICATION POLICY

The Investigators will be involved in reviewing drafts of the manuscripts, abstracts, press releases and any other publications arising from the study. Authors will acknowledge that the study was funded by the NIHR Programme Grant (RP-PG-0608-10147). Authorship will be determined in accordance with the ICMJE guidelines and other contributors will be acknowledged.

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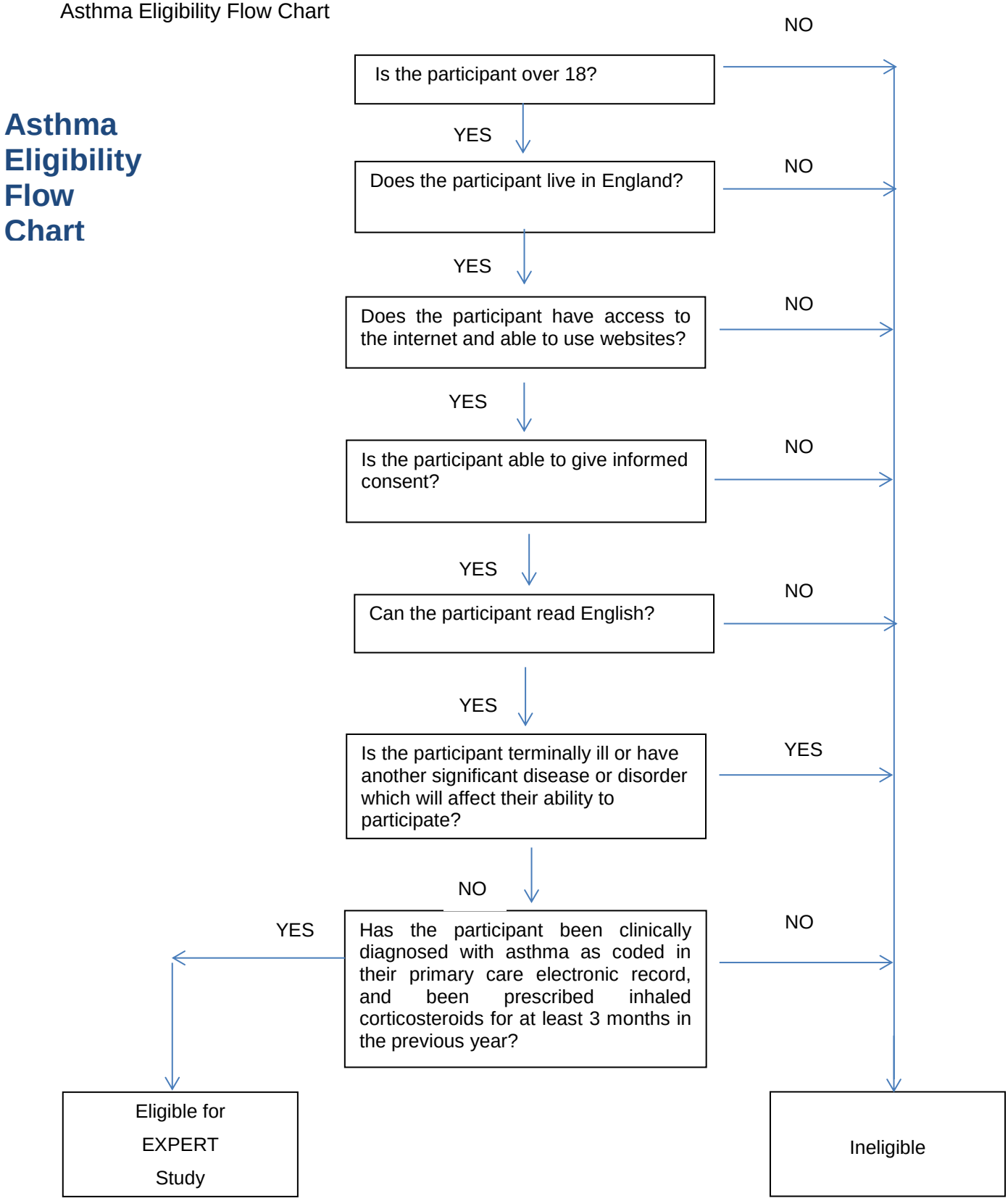
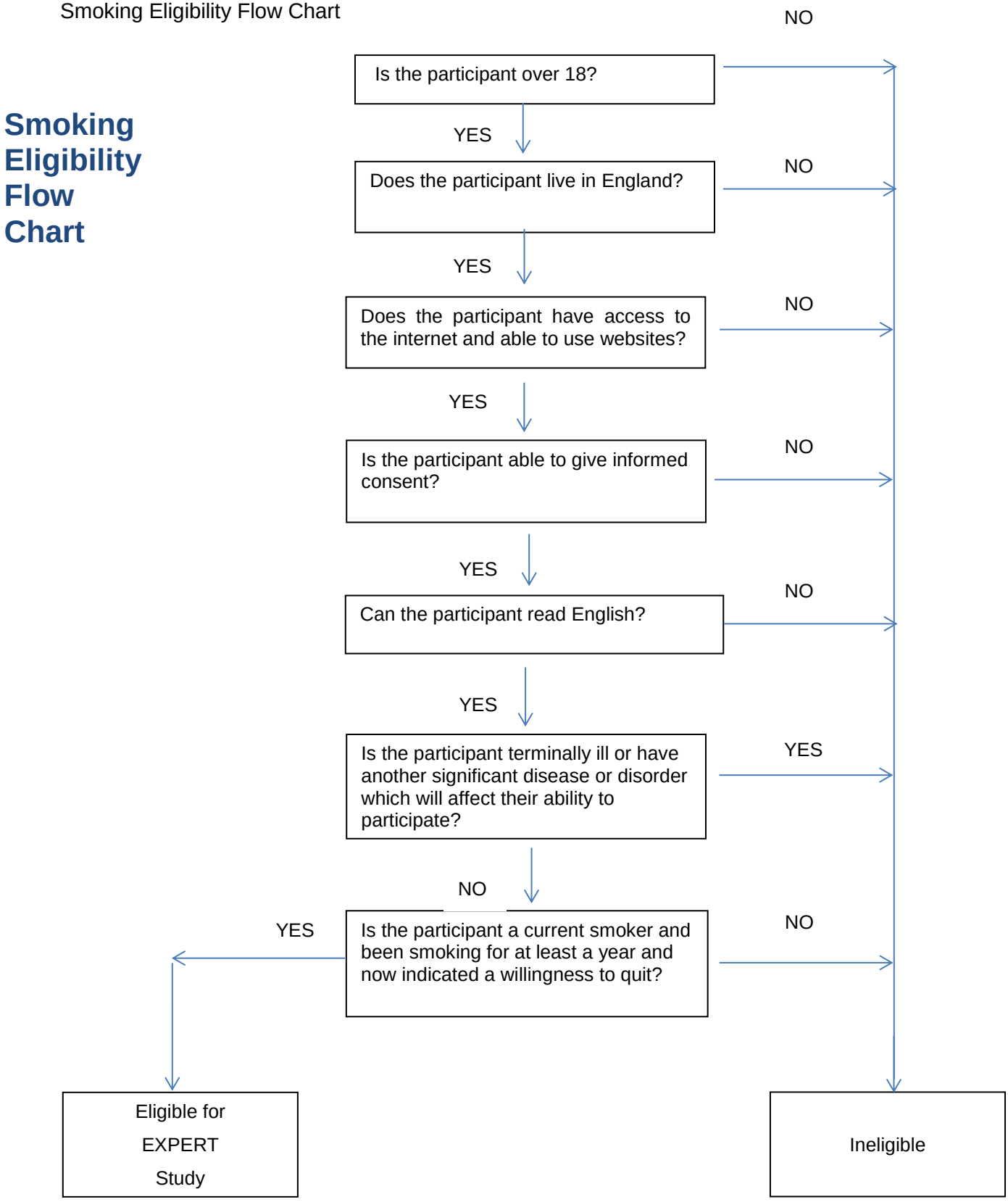
16 APPENDIX 1

Asthma Eligibility Flow Chart



17 APPENDIX 2

Smoking Eligibility Flow Chart



18 APPENDIX 3

MS Carers Eligibility Flow Chart

MS Carer Eligibility Flow Chart