Health Technology Assessment Programme

National Institute for Health Research

NIHR HTA Programme

09 July 2013

The NIHR Evaluation, Trials and Studies Coordinating Centre (NETSCC), based at the University of Southampton, manages evaluation research programmes and activities for the NIHR

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The University Of Sheffield. Clinical Trials Research Unit.

NIHR Health Technology Assessment programme funded project

CPRD MORE DIMENSIONS TO DATA

Clinical Practice Research Datalink

PLEASANT

Preventing and Lessening Exacerbations of Asthma in School-age children Associated with a New Term

RESEARCH PROTOCOL
(Version 1.8)

REC:
Authorised by:

Preventing and **L**essening **E**xacerbations of **A**sthma in **S**chool-age children **A**ssociated with a **N**ew **T**erm

PLEASANT

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1. Lay Summary

In the UK there is a pronounced increase in the number of visits to the doctor by school age children with asthma in September. It is thought that that this might be caused by the return to school, when children with asthma will be mixing with many other children again and picking up bugs which can affect their asthma and make them poorly.

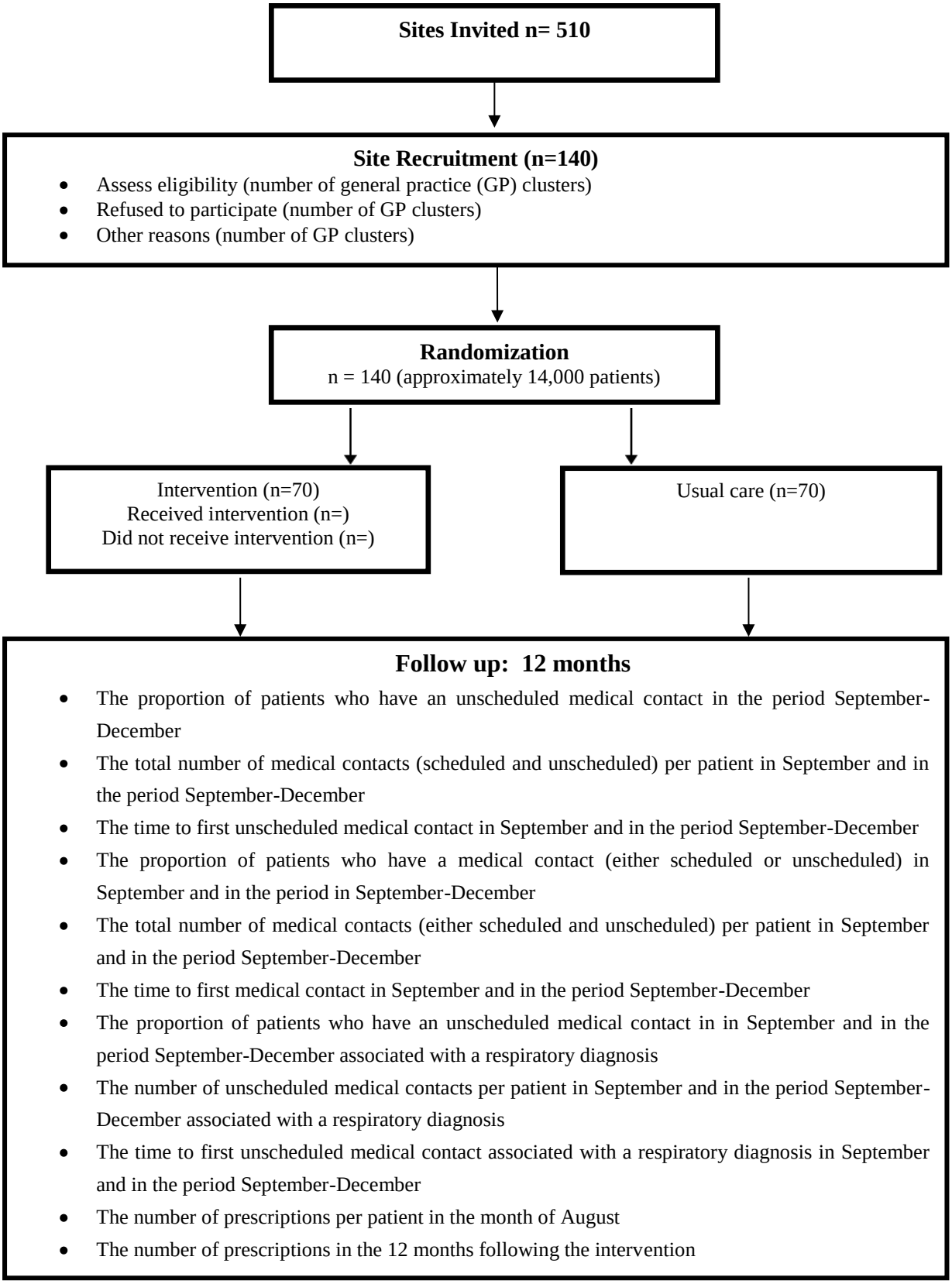
During the summer holidays there is a drop in the number of prescriptions collected. August is a good month to be an asthmatic – children with asthma are not mixing with many other children and the pollen count is quite low – therefore children with asthma might not take their medication as they should or allow their medication to run low.

We hope that a simple letter from the GP, reminding children with asthma to take their medication or to collect their prescriptions, can help prevent them being poorly in September. The letter itself will say that returning to school can increase the chance of a child with asthma being poorly. It will suggest that parents ensure their children's medication is fully up to date and they take their medication daily if they need to for at least 2 weeks before going back to school.

To see if the letter works we will ask some GPs to send it out to the parents of school aged children with asthma, and some GPs will not, so that we can compare whether the letter has had any effect. We will be looking at a number of factors including whether children who get the letter see their GP less in September. In addition to the number of visits made to their doctor we will be looking at the number of prescriptions children with asthma have and the effect on costs to the NHS.

Figure 1

Trial summary



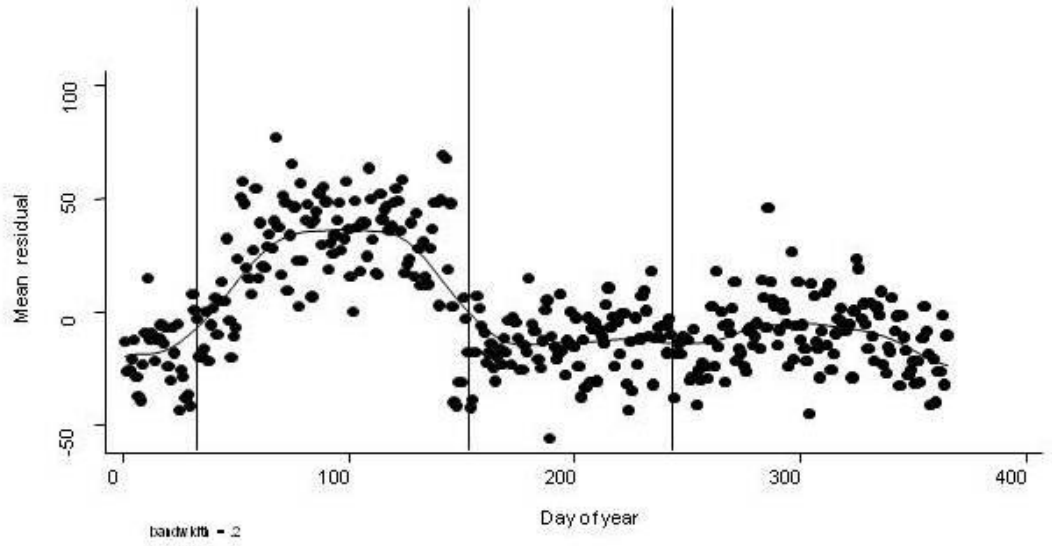
2. Background

Asthma episodes and deaths are known to be seasonal.[1] A number of reports have shown peaks in asthma episodes in school aged children associated with the return to school following the summer vacation[2-10]. These studies mainly report hospital admissions, although one study has reported peaks both in hospital admissions and all medical contacts[10].

Children returning to school are exposed to a variety of novel respiratory insults including allergens and viruses, at a time of changing climactic conditions. It has previously been shown that viral infection and allergen exposure in allergen sensitised asthmatics are associated with increased hospital admissions for acute asthma. The same study demonstrated the protective effect of inhaled corticosteroids on acute asthma exacerbations in a paediatric asthma population[11].

In previous research by the team a random sample of around 75,000 school age (5-16 years) children were observed, using a data set from selected general practices within the General Practice Research Database (now the Clinical Practice Research Datalink[12]), who had a documented medical diagnosis of asthma. Age (within 2 years) and sex matched controls from the same practice were also taken[13].

Figure 1: Mean residuals for excess medical contacts for children with asthma for over controls in England. The vertical lines represent, from left to right, the 1st September, 1st January and 1st April.

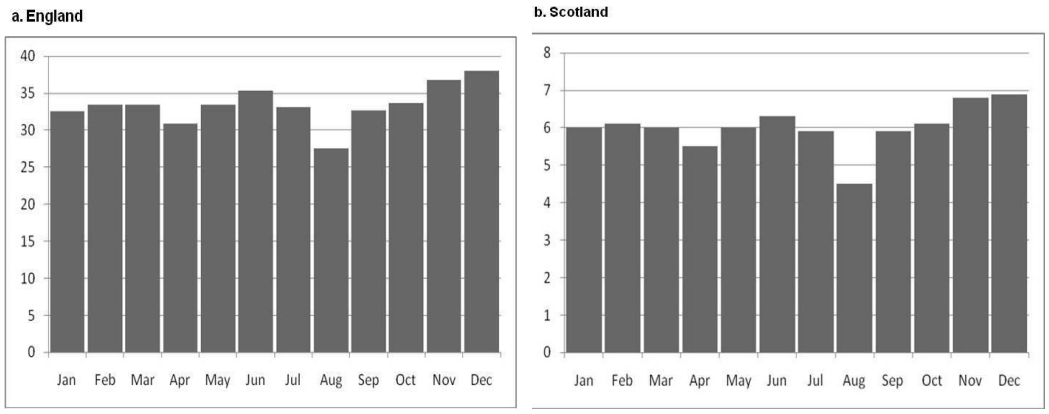


This investigation confirmed the increase in unscheduled medical contacts in children with asthma throughout the year with an approximate doubling in medical contacts compared to non-asthmatic children. Regression analysis shows that children with asthma are

approximately twice as likely as controls to have unscheduled medical contact and are more likely to see their doctor around the return back to school. If asthmatic children were at a constant increased risk of medical contacts throughout the year Figure 1 would show a random scatter of the residuals in England. However, around the return to school there is a pronounced positive increase in the value of residuals (a similar pattern was observed for Scotland). This indicates that at this time there is a greater than expected increase in the number of contacts by children with asthma compared to controls.

We suggest that July and August are periods of reduced viral exposure (due to reduced contact with other children because of the holidays) and reduced pollen (antigen) exposure for asthmatic children. It could therefore be argued that this is a good time to have asthma; the pollen season is in the main over, school age children are not at school and so have less opportunity to pick up any viral infections that are going through population.

Figure 2: Average daily prescriptions by month for England and Scotland.



We also observed a drop in prescriptions for inhaled steroids in August immediately preceding the return back to school with 25% fewer prescriptions in August compared to July and September[13] (see figure 2). This drop in prescriptions precedes the viral challenge of a return back to school. We further showed that patients who received a prescription for inhaled corticosteroid had 0.14 fewer contacts per patient (95% CI 0.12 to 0.16, P<0.001, England; 95% CI 0.10-0.18, P<0.001, Scotland) than those who did not receive an August prescription.

To interpret the figure of 0.14: hypothetically imagine a cohort of 200 children with asthma on inhaled corticosteroid, where 100 receive an August prescription and 100 do not. If the 100 patients with a prescription make a total of 50 unscheduled medical visits (0.5 mean visits/patient) then 64 unscheduled medical contacts would be made by those not receiving a prescription (0.64 mean visits/patient; difference 0.14). Hence, per 100 children with asthma on inhaled corticosteroid not receiving a prescription in August there is an excess of 14 unscheduled medical contacts.

It is therefore possible that children who stop taking or reduce their inhaled corticosteroids over the summer months and/or run low of other medications and fail to restart them before the return to school, render themselves more vulnerable to acute asthma exacerbation.

Unplanned medical contacts cost the NHS: £36 for a contact in surgery; £121 for a GP home visit[14]; £59 to £142 for an emergency department contact if not admitted and £74 to £249 if admitted; £385 for a non-elective short stay for asthma without complications[15] The intervention/letter therefore has the potential to benefit the health and quality of life of children with asthma while also improving the effectiveness of NHS services by reducing NHS use in one of the busiest months of the year.

3. Aims and objectives

3.1 Primary research objective

The aim of the study is to assess if an NHS delivered public health intervention (a letter sent from the GP to parents/carers of school aged children with asthma) reduces the number of unscheduled medical contacts after the school return.

The primary objective of the study is to assess whether the intervention reduces the September peak in total medical contacts.

3.2 Outcome measures

3.2.1 Primary outcome measure*:*

- The proportion of patients aged between 5-16 who have an unscheduled medical contact in September

3.2.2 Secondary outcome measures*:*

- The proportion of patients who have an unscheduled medical contact in the period September-December
- The total number of medical contacts (scheduled and unscheduled) per patient in September and in the period September-December
- The time to first unscheduled medical contact in September and in the period September-December
- The proportion of patients who have a medical contact (either scheduled or unscheduled) in September and in the period September-December
- The total number of medical contacts (either scheduled and unscheduled) per patient in September and in the period September-December
- The time to first medical contact in September and in the period September-December
- The proportion of patients who have an unscheduled medical contact in September and in the period September-December associated with a respiratory diagnosis

- The number of unscheduled medical contacts per patient in September and in the period September-December associated with a respiratory diagnosis
- The time to first unscheduled medical contact associated with a respiratory diagnosis in September and in the period September-December
- The number of prescriptions per patient in the month of August
- The number of prescriptions in the 12 months following the intervention
- The proportion of patients who have a scheduled medical contact (for example asthma review) in August
- The proportion of patients who have a scheduled medical contact (for example asthma review) in the 12 months following the intervention.

The above analyses will be undertaken on patients aged 5-16, since asthma is difficult to diagnose in children below this age[16-17]; patients aged <5 will be analysed separately to these (see section 10.2).

3.3 Health economic objectives and resource use

An exploratory economic evaluation will be undertaken to compare the incremental cost per quality adjusted life year (QALY) of the reminder letter versus standard care. The perspective of the analysis will be that of the NHS and Personal Social Services. Data on the number and type of medical contacts avoided in the intervention group will be collected, and will be combined with PSSRU unit costs and Department of Health reference costs to assess any cost savings associated with preventing exacerbations. This will be compared to the additional cost of sending out reminder letters and any additional costs arising from an increase in prescription rates as a result of the reminder letters.

We will make assumptions on the cost of sending out the reminder letters based on the national costing template from the National Institute for Health Research (NIHR) Primary Care Research Network (PCRN). This template breaks down general practice activity, for the purposes of costing NHS service support, and as such should give an indication of what this activity would cost if it was done within usual care.

4. Trial Design

The study is a cluster randomised trial; 70 GP practices undertaking the intervention and 70 control practices of "usual care" (n=140 general practices in total). The randomisation will be stratified by size of GP practice to ensure that there is an equal sample size – in terms of number of school age children with asthma – in each arm of the trial. The randomisation will be undertaken by a statistician within the Clinical Trials Research Unit, in line with the randomisation plan.

The data for the trial will be extracted using the Clinical Practice Research Datalink (CPRD). This database records all medical contacts a patient will make from unscheduled medical contacts – because they are ill – to scheduled medical contacts – for asthma reviews or repeat prescriptions. It records the type of medical contact and the diagnosis, if appropriate, for the contact.

For the treatment as usual arm, GP practices need do nothing as we can extract the medical contact details through the CPRD with no further need to contact the practices.

Data will be collected at baseline, then 1 month and 12 months following the intervention.

5. Selection of sites and site recruitment

The setting will be in primary care with general practices that are currently part of Clinical Practice Research Datalink (CPRD).

Invitation letters will be sent out, via CPRD, to all current active GP CPRD sites. We would expect to reach the target of 140 sites recruited within 3-6 months, based on past CPRD experience of recruiting GP sites to research trials[12].

CPRD will liaise with practices that have expressed interest in participation and details passed on to the study team. The study team will contact the practice to discuss the study at which time the practice will be randomised to either the intervention or control (care as usual) arm. Intervention practices will then be sent GP packs which will include the GP letter template and instructions for participation.

We will access support from the Primary Care Research Network to advertise the trial. Any interested practices will be forwarded further information regarding the practicalities of delivering on the study including sign up to CPRD as this will be a requirement for participation.

5.1 Site Randomisation

The study is a cluster randomised trial; 70 general practices (GPs) undertaking the intervention and 70 control practices of "usual care". The randomisation will be stratified by size of GP to ensure that there is an equal sample size – in terms of number of school age asthmatic children – in each arm of the trial. Subsequent to their agreeing to take part, practices will be randomised to one of the two arms. GPs randomised to intervention will be asked to send a letter to eligible patients; GPs randomised to control will not be required to do anything further.

5.2 Site compliance

A member of the study team will be responsible for site set up and maintaining on-going contact with the GP setting. Site set up will be done either via telephone or video conferencing. For those sites that prefer a face-to-face contact the study team will either do the visit (if within a reasonable distance) or liaise with the appropriate Local Primary Care Research Network to do the visit on their behalf.

An electronic GP study information pack will be sent out to all sites with a flow chart to show progress through the trial period, timing of intervention, information required from sites and subsequent NHS service support cost payments.

5.3 Withdrawal

Practices are free to withdraw from the trial at any time. This will be documented on a site withdrawal form. Any data already collected during the course of the trial up to the point of withdrawal will be used in the final analysis. We will ask the site for their permission to continue to collect data.

6. Trial Intervention

6.1 Target population for intervention

The population targeted for the intervention will be school aged asthmatic children (aged between 4 and 16) registered with a general practitioner. The CPRD will identify eligible participants based on pre-agreed diagnostic codes for asthma and the inclusion/exclusion criteria

6.2 Inclusion criteria

Children

- between 4 and 16 years of age as of 1st September 2013

- with a coded diagnosis of asthma
- who have been prescribed asthma medication in the previous 12 months

6.3 Exclusion criteria

Children

- aged 4 and under as of age as of 1st September 2013 and 16 years and over as of 31st August 2013
- who are not considered appropriate for this intervention by their GP
- with asthma who are not receiving asthma medication
- with co-existing neoplastic disease

CPRD will send the list of eligible participants for the GPs to check and confirm.

6.4 Trial Intervention

The intervention is a letter sent, from a GP, to the parents/carers of children with asthma reminding them to maintain their children's medication and collect a prescription if they are running low. It will also advise that should their child have stopped their medication it should be resumed as soon as possible.

The letter template has been developed and based on standard letters already used in general practice, for example those used to invite for a routine asthma review. The wording of the letter has had input from the study team, which includes a GP, Health Psychologist and Consultant Respiratory Paediatrician and also discussed in detail at two patient and public events, that included school aged children with asthma and their parents.

The letters will be sent out w/c 29th July 2013 to obviate the distraction of planning for family holidays and yet leave enough time for parents and children to renew prescriptions and gain benefit from the medication.

6.5 Postal procedures

Practices will be encouraged to use DocMail service for sending the letters via a website to secure servers. This will reduce practice burden and allow the study team to monitor that practices have sent the letters, on what date, whilst also confirming the number of letters sent.

If practices prefer not to use this method, and hand post, as is their choice - we will then ask for confirmation that the letters have been posted, the date and numbers sent.

7. Data Collection

7.1 Clinical Practice Research Datalink

The Clinical Practice Research Datalink (CPRD) is a computerised database of anonymised longitudinal medical records from primary care. Currently data are being collected on about 5 million active patients of research standard. These are from around 625 general practices throughout the UK (510 in England and Wales). We plan to recruit and randomise practices who are part of CPRD and therefore to use CPRD for data collection.

The CPRD are able to capture all medical contacts, from prescription request through to out of hours contacts, along with the reason for the contact. This therefore negates the need to request this information from the GP, reduces practice burden, and ensures complete data sets. The study team will not have access to any patient identifiable data and will receive fully anonymised data from the CPRD.

We will collect data from CPRD at 3 time points; baseline and, at 1 month and 12 months post intervention.

7.2 Allocation of Scheduled vs Unscheduled contacts

Every NHS service contact is coded by the GP practice, captured within the practice database, which will then enable allocation to either scheduled or unscheduled contact.

We are defining a scheduled contact as any contact that is part of the planned care for the patient, for example an asthma review; a medical review; repeat prescription or immunisation. An unscheduled contact will be any contact not part of their care plan that is either patient initiated or as a result of illness.

To ensure the allocation of scheduled and unscheduled contacts are robust we will have an adjudication panel, consisting of 3 GPs, who will be blind and independently review the prescription and diagnosis codes allocating to scheduled or unscheduled contact.

8. Data handling and record keeping

The primary data source will be anonymised GP and NHS contacts extracted and forwarded by the CPRD to the CTRU. Data pertaining to the nature of the appointment will be forwarded to the adjudication panel for their review, who will in turn define appointments as being scheduled or unscheduled. This data will be handled and prepared within CTRU in preparation for the statistical analysis.

Detailed data management and data quality issues will be set out in a data management plan. Data will be retained in accordance with the Data Protection Act 1998 and CTRU data management SOPs.

All source documents and data will be retained for a period of at least 5 years following the end of the trial.

9. Access to source data

Monitoring and audit by the relevant health authorities will be permitted by the sponsor. These include the Research Ethics Committee and local R&D departments. The sponsor will be allowed to monitor and audit the trial. Access to source data will be via the CPRD and the sponsor will be able to access these records for audit purposes (source data will be minus patient identifiers).

10. Statistical analysis

10.1 Sample size

From previous research in the CPRD practice population 30% of school age asthmatic children had at least one unscheduled medical contact within the month of September[13]. We postulate that the intervention may reduce the number of children who have unscheduled medical contacts from 30% to 25% (i.e. an absolute reduction of 5%). We would have an effect size of 5%. The average practice size in the CPRD is 8,294. We thus anticipate circa 100 school age asthmatic patients per practice (based on 12% of a practice being school age children and 11% of school age children having asthma). Hence, to detect a difference of 5% with 90% power and two sided significance level of 5%, with an intra-class correlation (ICC) of 0.03 to account for clustering we require 70 practices per arm. The sample size of 140 practices would equate to approximately 14,000 school age asthmatic patients.

Ukoumunne et al[18] give estimates of ICCs for patients with respiratory symptoms in symptoms in General Practice. Based on the work of Ukoumunne et al an ICC of 0.03 is a conservative estimate. The power of the study for ICCs of 0.01, 0.02, 0.03, 0.04 and 0.05 is respectively 99.4, 96.0, 90.0, 83.1 and 76.2%

As a further sensitivity analysis we investigated the effect of practices not sending out the letter as planned. Suppose 10 practices failed to send out the letter, these would still be included in the primary analysis under the intent to treat principle. However, the effect that could be observed would be reduced to 4.3%. Under the sample assumptions (ICC=0.03 etc)

the power for the same sample size is reduced to 79.3%. This is a little under 80% but it does demonstrate that the study is reasonably robust to at least one deviation in the planned design.

10.2 Data analysis

The study periods are defined in three stages. The primary study period is 1st – 30th September 2013, since this is the period when the intervention is felt likely to impact. The extended study period is 1st September - 31st December 2013, since asthma-related appointments are more frequent in the entire period. The follow-up period is 12 calendar months from 1st September 2013 to 31st August 2014.

The primary analyses will be by intent to treat among patients aged 5-16 as of 1st September 2012. The primary endpoint (the proportion of patients who have an unscheduled medical contact in September) will be analysed by logistic regression in which the covariates will include the individual's age; gender; number of contacts the previous September; the trial arm (intervention or control); and the design/cluster effect of general practice as a random effect.

The same approach will be used for analyses based on the extended period. The proportion of patients who have an unscheduled medical contact, the proportion of patients who have any medical contact; and the proportion of patients who have an unscheduled medical contact associated with respiratory illness. The number of unscheduled medical appointments per patient in the extended period; the total number of medical contacts (scheduled and unscheduled) per patient in the extended period; the number of unscheduled medical contacts per patient associated with a respiratory diagnosis in the extended period; the number of prescriptions per patient in the month of August; and the number of prescriptions per patient in the 12 months following the intervention will be analysed in an analogous approach to the primary endpoint. A random effects negative binomial model will be fitted, including the same covariates as above. Further analyses will address the time to first medical contact (defined as the number of days from the start of school term to the date of first appointment, up to and including December 2013, the time to first medical contact up to and including December 2013, and the time to first unscheduled medical contact associated with a respiratory diagnosis will all be analysed using a random effects ("shared frailty") regression model including the same covariates as described previously.

Patients aged 4-5 will be analysed separately to those aged 5-16, since the diagnosis of asthma is more controversial in this age group; it is often not practical to measure variable airway obstruction below the age of 5 making diagnosis of asthma difficult[16-17]. The impact of the intervention in patients under 5 will be compared to that seen in the main analysis to assess whether the intervention appears to benefit younger children. Additional exploratory analyses will investigate whether the impact of the intervention is related to age or other characteristics of the patient.

A detailed description of the statistical analysis of efficacy and safety outcomes will be written in the trial Statistical Analysis Plan which will be finalised prior to receiving post-intervention data from GPRD. The trial will be reported using the principles highlighted in the CONSORT statement for reporting cluster RCTs[19].

11. Economic Evaluation

An exploratory economic evaluation will be undertaken to compare the incremental cost per quality adjusted life year (QALY) of the reminder letter versus standard care. The perspective of the analysis will be that of the NHS and Personal Social Services. The time horizon will be one year from the intervention and therefore no discounting will be applied.

Data on the number and type of medical contacts in the intervention and control arms will be collected through the CPRD, and combined with PSSRU unit costs and Department of Health reference costs to assess the cost of medical contacts in each arm. Unscheduled contacts in September will be included to capture the impact of any reduction in asthma exacerbations. Scheduled contacts in the year following intervention will be included to capture any change in health care resource use in response to the letter. These will be reported separately in addition to reporting the overall costs of medical contacts for each arm. Prescription costs will be assessed for the year following intervention by combining data on the number of prescriptions with unit cost data from the British National Formulary (BNF). The costs for prescriptions and medical contacts will be combined to give overall costs in the control arm, but in the intervention arm the overall cost will also include the cost of sending out the intervention.

A systematic review by co-applicant SD and colleagues[20] appraised published evidence of health-related quality of life in asthma and found evidence showing that asthma exacerbations have a significant impact on quality of life[21]. This review will be updated to identify more recent publications, and literature evidence will be used to determine the effects of the intervention, via reduced exacerbations, on health-related quality of life. We will assume that the intervention has no effect on survival and therefore any QALY gain will be wholly driven by improvements in quality of life.

This evidence will inform a simple decision-analytic model to estimate the mean costs and QALYs for the intervention and control groups. Univariate sensitivity analyses and probabilistic sensitivity analyses will be used to examine the uncertainty in the model, with results displayed using cost-effectiveness planes and cost-effectiveness acceptability curves.

12. Safety assessments

The trial and subsequent intervention is hoping to optimise usual clinical care and promote adherence to current prescribed medication. As a result we do not anticipate any adverse events as a result of the trial.

12.1 Reporting Procedures

The trial intervention is aiming to optimise usual asthma care and improve adherence to medications already prescribed by the GP, thus reducing potential exacerbation of asthma following return to school in September. Therefore involvement in the trial will not result in any adverse or serious adverse events as a result of participation.

Any asthma complications relating to the health of the child would be picked up by their GP or out of hours service and managed as per usual care. These unscheduled/emergency contacts with NHS services will be picked up as part of the routine outcome data and described within the final trial report. We are therefore not putting any formal reporting procedures, for adverse events or serious adverse events, in place.

However, practices randomised to the intervention will be provided with a short reporting template to inform the study team of any incidents they feel are related to the conduct of the trial.

12.2 Research Governance

Trial oversight:
Two committees are being established to govern the conduct of the study:
1. Trial Management Group (TMG)
2. Trial Steering Committee (TSC)

All committees are governed by Sheffield CTRU standard operating procedures. The TMG consists of the Principal Investigator, co-investigators and key staff within the CTRU. The role of the TMG is to implement all parts of the trial.

The TSC consists of the Principal Investigator, key staff within the CTRU (as non voting members), an independent chair and two independent members (including a statistician) and 2 lay members. The roles of the TSC are to provide supervision of the protocol and statistical analysis plan, provide advice on and monitor progress of the trial.

12.3 Monitoring arrangements

Once all research governance approvals are in place the study team will contact each GP site for a study set up meeting. This will be before randomisation in order to check the site has all the necessary information and staff in place before starting the study. Following the intervention there will be a one-off follow up meeting to monitor each GP site in order to ensure the intervention has been delivered within time and ascertain numbers of letters sent. No further contact will be required from the practices.

13. Ethical considerations

The trial will be conducted subject to Research Ethics Committee favourable opinion. The application will be submitted through the IRAS central allocation system. The approval letter from the ethics committee and copy of all approved study documentation will be present in the site files before initiation of the study and site recruitment.

This trial will be conducted in accordance with the Research Governance Framework for health and Social Care 2005.

14. Patient and Public Involvement

The PLEASANT trial research team is committed to the principles of patient and public involvement (PPI). Children with asthma and their parents were involved in the design of the trial and will be involved throughout the conduct of the study.

14.1 PPI in the design of the trial

During the design of the trial, a PPI consultation event was held in January 2011 with a group of children with asthma and their parents. This event was used to investigate whether the hypothesis underlying the trial was supported by children with asthma and their parents, to give an opportunity for the children and parents to discuss the wording of the intervention (the GP letter) and to give their views on to whom the letter should be addressed (i.e. should it be addressed to the child or to their parent/guardian). This initial PPI consultation event was written up as a University of Sheffield report[22].

14.2 PPI throughout the trial

PPI during the conduct of the study will have two components: (1) two further PPI consultation events will be held in September 2012 and December 2014/January 2015, involving up to 6 children and their parents/guardians; (2) two parents of children with asthma will be invited to become members of the Trial Steering Committee, which will meet twice in the first year and once in the final year of the study.

14.2.1 PPI consultation events

The September 2012 PPI consultation event was used to:

- Remind attendees of the purpose of the study and give feedback on outcome of the HTA application
- Discuss the children's adherence with their medication over the school holidays and subsequently since they have been back at school

- To present the GP letter that was discussed at the January 2011 consultation event and to show how it has changed as a result of the consultation and peer review, and to invite further discussion on how the wording of the letter could be improved.
- To invite any further comment on the design and endpoints to be used in the study, and in particular to invite comments on what, from their perspective, is a scheduled and unscheduled contact
- To discuss plans for PPI for the study, and to invite interested parents onto the Trial Steering Committee
- To discuss the ethics application and the research team's rationale for how the ethics of the study are being addressed in the REC application. To also invite comment on the lay summary of the REC and the PPI section
- Invite opinions on the study logo and the website.

The second PPI consultation event was written up as a University of Sheffield report[23].

The December 2014/January 2015 PPI consultation event will be used to consider the findings of the trial from the perspective of children with asthma and their parents. It will also provide an opportunity to discuss how the findings should best be disseminated to children and to parents.

For attending the consultation events, each child will be provided with a £20 gift voucher and their parents will be able to claim for their expenses such as travel.

14.2.2 PPI members of the Trial Steering Committee

Two parents of children with asthma will be recruited onto the Trial Steering Committee. Payment for time will be offered at a rate of £50 per meeting, plus travel expenses. A glossary of key research terms used in the study will be provided. The study's PPI lead will meet with the parent members of the Trial Steering Committee before or after each meeting to discuss the agenda items and any issues of concern, and will act as a mentor for them.

14.3 PPI outputs

A section of the PLEASANT website will contain details relating to PPI in the study, including the names of the children with asthma and their parents who are actively involved in the study. (All the children with asthma and their parents who are actively involved in the PLEASANT trial have agreed for their names to go on the study website). A report of each PPI consultation event will be produced by the study's PPI lead and these will be uploaded onto the study website. A paper reflecting on the PPI in the design and conduct of this study will be submitted to a peer-reviewed journal at the end of the trial.

15. Finance and indemnity

The trial has been financed by the NIHR Health Technology Assessment Programme and details have been drawn up in a separate agreement.

This is an NHS sponsored study. If there is negligent harm during the clinical trial when the NHS body owes a duty of care to the person harmed, NHS indemnity will cover NHS staff, medical academic staff with honorary contracts and those conducting the trial.

The University of Sheffield has in place insurance against liabilities for which it may be legally liable and this cover includes any such liabilities arising out of this clinical trial.

16. Reporting and dissemination

Results of the trial will be disseminated in peer reviewed scientific journals and clinical and academic conferences. A patient and public event will also be held to feedback to those involved in the development of the study protocol.

Details of the trial will also be made available on the study website. Summaries of the research will be updated periodically to inform readers of the on-going progress.

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