Institute of Health & Society
NATTINA Study Launch Event
6th November 2014, 15:00 – 17:00 hours
Lumley Seminar Room, The Royal College of Surgeons of England

Present: Janet Wilson (JW), Ken McKenzie (KM), Simon Prowse (SP), Elsie Green (EG), Lorraine McSweeney (LM), Peter Wilson (PW), Isabel Rubie (IR), Scott Wilkes (SW), Claire Hopkins (CH), Musheer Hussain (MH), Chris Raine (CR)

By teleconference: Jill Morrison (JM), John Birchall (JB), Sean Carrie (SC), Nick Steen (NS), Lisa Mole (LM2), Nikki Rousseau (NR)

Apologies: Katie Haighton (KH), Kim Ah-See (KAS), Andrew Coatesworth (AC), James O'Hara (JOH), Hisham Mehanna (HM), June Jones (JJ)

Secretary: None present

Item		Responsible
1.	Welcome and introductions to the coordinating team and collaborators.	
2.	<u>Introduction and explanation of the background to the NATTINA trial by JW.</u> JW explained there were two substantial strands in the background to NATTINA. One included a randomised controlled trial of tonsillectomy in childhood which was in many ways a successful trial in terms of recruitment and in terms of primary outcome. There was a demonstrable benefit of tonsillectomy shown in terms of stopping tonsillitis. JW advised there were two aspects of the trial which were not so successful and summarised the reasons. Firstly, patients were not stratified very well at baseline for severity. This gave an over-representation of severe cases in the group who volunteered to have tonsillectomy. The participants in the group who preferred to have tonsillectomy were more generally affected than those who received medical treatment. Secondly, there was insufficient follow up data. With this information coupled with some information regarding the importance of the timing of surgery – as some patients crossed over from medical treatment into surgery but it was unclear when the surgery had taken place. It was up to NS, the trial statistician to try to analyse the impact of tonsillectomy in all	

	participants regardless of randomisation, it was difficult to establish when surgery had occurred. A researcher led proposal was made to the HTA suggesting a mirror trial for Adults with patient preference arms. It was apparent that not everyone would like to be randomised in and out of surgery. The HTA did not embrace the idea of patient preference arms and the trial was not taken forward. However, the concept of the trial was still supported by the Birmingham collaborator as part of the HTA Review Board and a short time later the trial became a commissioned call for research with some tight criteria. The number of sore throat days was to be the primary outcome and there was no desire to fund preference arms. JW confirmed this design was followed and successfully bidding a tightly contest bid. It was confirmed that a nine centre study has been set up and the event today would allow discussion of the detail which will be outlined in the presentation by IR. JW reported that the other factor catalysing the development of trial was the changing demographics of tonsillitis and tonsillectomy. JW noted for interest that there was another paper published in the latest Annals from Norfolk and Norwich, commenting on the change in demography. Although they did not notice any change in tonsillectomy rates they have noticed a substantial increase in admissions with tonsillitis. When looking at the national data there's been a general decline in the instances of tonsillectomy and a definite increase in acute hospital admissions with tonsillitis and quinsy. There may be a number of factors for this in that it may relate to changes in antibiotic prescribing and limitations on GPs for prescribing antibiotics and also to changing rates in tonsillectomy. It may also be related to the pattern of care. Referring back to the most recent paper from the College Annals, depending on which hospital episode statistics are looked at and allowing for the increase in population, the paper advises there was a 181% increase in acute tonsillitis admissions over a decade up to 2012/13. JW noted that this is a substantial increase and has big financial implications. JW noted this comes back to the clinical guidance with NICE. There is no indication that this is the correct guidance for	

	tonsillectomy as there is no level-one evidence base. Furthermore, one of the things which could potentially be a problem in the past and was maybe a problem with NESTAC was the inability to model alternative ways of selecting patients as selection was on the basis of sore throat episodes that would qualify for tonsillectomy. JW advised that to some extent within the study must randomise people who are eligible by the clinically agreed criteria in the study but on the other hand as there is now the tonsil outcome inventory 14, which is a continuous variable of severity, in terms of health economics this gives more flexibility of modelling i.e. what if tonsils were removed in more of the less severely affected people or what if tonsils were removed in the more severely affected would it become more or less cost effective in terms of what happens when tonsils are not removed. Alternatively are the guidelines correct and is there an alternative reason tonsillitis has increased. JW invited comments as to why tonsillitis admissions have dramatically increased over the decade. <u>Resulting discussion:</u> <u>Why have tonsillitis admissions risen by 181% in a decade?</u> JM agreed with JW's points with regards change in pattern of GP care combined with under use of NHS 24 and NHS 111 (previously NHS Direct). Patients visit A&E in lieu of their GP and there is potential influence of reduced antibiotic prescription. JW summarised discussion thus far and further noted that beyond the conclusion that tonsillectomy provision has been overcut, pathways of acute illness could be investigated i.e. junior doctors assessing patients out of hours and opting not to discharge. SP raised issue of treatment failure: potential rate of increased resistance to penicillin v and agrees with observation of junior doctors being more likely to admit patients over night in absence of an ENT doctor. SW added from perspective of patient, during out of hours A&E is 'path of least resistance' to access care, and flagged current shortage of GPs (16,000 according to BMJ) means patients might not even be seeing GP in normal hours. JB asked whether walk-in centres contribute to this increase. JM pointed out there are no walk-in centres in Scotland and that GPs are more readily equipped to monitor and manage illness of	

3.	known patients in comparison to risk aversion of A&E doctors who know they may not see a patient again. KM asked whether analysis of length of stay, and not just hospital admission had been done. JW answered that hospital episode statistics do give median length of stay – so a big change would show. Adding this could be investigated in the NATTINA study so as not to miss patients' backstories. SW flagged the increased rate of oropharyngeal carcinoma, whilst not suggesting this is caused by reduced rate of tonsillectomy, pointed out the high number of cancers with tonsil primaries which cannot develop post tonsillectomy. <u>Presentation on Trial Information and Design by IR</u> Resulting discussion included: <u>Collecting and defining adverse trial events</u> Question from CH: why is the study only collecting adverse events relating to the surgery and why an admission with tonsillitis in the conservative group would not trigger an adverse event for the study? JW clarified that IR's inclination was to include this consideration into the study. However, technically it is not in the frame of adverse events, so would result in arbitrary decisions being made due to the absence of information on the natural history of tonsillitis management. JW affirmed that the study expects instances of tonsillitis in the control group (there would be something very wrong with the randomisation process if this did not occur) just as there will be potentially unnecessary surgery for those patients in the surgical arm of the trial. CH followed pointing out that each unit's threshold for readmitting with a tonsillectomy is very variable. Equally, different departments' threshold for admitting with tonsillitis and quinsy might differ. Therefore the study will only be collecting variation from one side. JW noted that the study will be able to document the inter site variation in admission of 300 people in 9 centres. Some data may relate to the geographic dimension or the demographic of the population being served. JW added her own anecdotal feedback is 8% re-admission	

	(rather than 4%). SW noted readmission with severe tonsillitis or quinsy is a clinical outcome of the patient and not necessarily a trial adverse event. Underlined difficulty of defining a trial adverse event in the NATTINA study is not quite as simple as administering a drug and observing an adverse reaction to that drug. CH pointed out that post-tonsillectomy haemorrhage is also a potential consequence of practice rather than the trial and therefore if readmission is classified as the adverse trial event, it can occur in both arms. PW pointed out the study will be collecting all of this data for analysis so the information will not be lost. CH noted that readmission will only be collected through GP linkage rather than the participating site. IR clarified the study will be collecting adverse events for both arms through weekly alert responses from patients and GP linkage data at the end of the trial, and emphasized that the study does need live moment-to-moment feedback. JW pointed out a learning outcome from NESTAC, that patients need to be reminded that STAR forms are not fed back to their clinician but collected in an anonymous way for research purposes. KM noted that returned GP data will provide only consistent data as patients could be readmitted into non-participating hospitals, potentially generating false low returns of hospital admission. JB asked whether time of readmission will be captured. To enable analysis of out of hours admission followed by discharge the following morning. JW confirmed electronic case support form does not currently require time, but could be added. SP concurred importance of differentiating between expected symptoms and patients with genuine need for readmission. <u>Screening log data</u>	Jill Morrison

	KM asked how data captured from patients declining participation in the study would be stored. IR clarified the screening log records of those declining would be kept in hard copy form in the site file and an electronic copy would also be available for clinicians to print off. KM conjectured it might be easier to have this in electronic form in the clinic. JW asked PW to advise from perspective of filling in the screening log from another trial. PW expressed no preference for electronic or hard copy. JW asked EG whether paper copies are more efficient in a clinic setting. CG concurred it is quicker. KM flagged his practice records are entirely electronic. JW noted EG's preference, in light of high volume of patients to be screened and randomised, and affirmed that these could be transferred to electronic formats later. <u>GP consent for access to collection data</u> JM asked how the study proposed to ensure GP consent and involvement in the study with regards access to patient records. IR has spoken to members of the North East & North Cumbria CRN to compile following method: • GPs will receive initial letter alerting them to their patient's involvement in the trial. • NCTU will then contact GP directly to provide governance approval and to offer copy of patient's consent form. • If GPs cannot or do not wish to collect the information directly, the local CRN can send a facilitator or research nurse to the GP practice to collect the data. • IR admitted there is a chance the GP might not allow access to data, and if having been shown governance approval letter, patient's consent form and affirmation of CRN's ability to collect data themselves the GP still declines access, the study cannot make any further claim. JW sought to clarify JM's question toward how the study should proactively work to engage GPs rather than the mechanisms for data collection. JM explained that in Glasgow there is not a strong history of	

	CTU having engagement with GP practices (ceding it may be different in Newcastle and other areas). Therefore GPs may not respond positively to contact from CTU and posited the Scottish Primary Care Network as an alternative. However without guarantee of 100% participation and JW forecasted a significant number of practices declining access to data due to the disruption caused (citing Bell's Palsy study), JM summarised there are issues to address with both the process and a charm offensive to GPs to underline importance of the question of the study and how the study will be minimally disruptive. JM also offered to begin this work with a meeting with the Scottish Primary Care Research Network week commencing 10 November 2014. IR clarified that the form sent to GPs is estimated to take 30 minutes to complete and GPs will be paid for their time, and proposed that practice nurses could collect this information for the GP. JM followed that GPs are unlikely to participate for the money. Finance sends a positive message however JM posited if GPs see it as an important research question they are more likely to participate. SW concurred that in England financial incentive would also be negligible. Context for English practices – around 1 in 6 GP practices are Research Site Initiative (RSI) sites ready willing and able to conduct NIHR portfolio trials. However 1 in 2 practices recruit to NIHR portfolio trials. SW proposed that if studies can provide GP practices with an NIHR portfolio number and service support costs to pay for opportunity cost, GPs are likely to fully participate in research. SW also agreed GPs tend to take a view about how much time they can afford to spend compared to the financial gain. IR confirmed the grant allocates £40 per patient compared to the standard primary care research costing template, which it is hoped will provide more of an incentive. SW underlined double pronged approach to collect data at 24 months: 1) Trial unit approaching GPs with portfolio number and service support costing 2) Ask LCRN primary care research staff to do the work for GP. JM observed difference in funding channels for research in	

	Scotland compared to England and maintained their may need to be a discrete approach to Scottish practices. JW explained there is a large amount in the Scottish budget which is not directly allocated, and as collection data is so key, this could potentially be redistributed as an incentivising per capita payment. Noting that approximately a third of the patients in the study and 3 of 9 centres will be in Scotland. SW addressed how to advertise the study. Positing that prior knowledge of the study before GPs receive a letter alerting them to their patient's participation in the study could be helpful. Since the changes to LCRN in April 2014, individual LCRNs have bespoke websites nominating CCG GP research champions who oversee around 50 practices. SW identified this as a potential channel to advertise the study to GPs. JM affirmed this infrastructure is not available in Scotland. There are four nodes of the Scottish Primary Care Research Network, which don't reach every practice. RCGP have an estimated reach of 50% of practices.	
4.		
	KM proposed that research nurse or recruiting surgeons could contact GPs directly.	
5.		
	JM and the rest of the group agreed this to be the most pragmatic way of approaching the issue in Scotland. <u>NATTINA DVD</u> (to be shown to patients on their first clinic visit prior to consented participation in the trial) <u>Qualitative sub-study presentation by LM</u> <u>Initial questions and discussion:</u> JM asked how many GPs need to be recruited to the sub study. LM requires 10 in total, ideally distributed across all sites and confirmed she is still recruiting patients until the end of November 2014. JW asked for more detail on case based or theme based analysis. LM described theme base as a matrix style of analysis compared to analysing individuals and the sub study will use a combination of approaches.	

6.	PW asked if the data analysis is iterative or end collected and whether LM could give any insight into findings to date. LM confirmed the data collection is iterative. Feedback concerns include: - Patients who have English as a second language. - Contamination from GPs – giving patients expectation that they will be put forward for a tonsillectomy. <u>Managing patient expectations:</u> MH pointed out patients expectations of receiving surgery naturally occur upon being referred to a tonsil clinic. JW tied this observation into proposing a mini launch to appraise GPs of this. CR asked if there is a way to say NATTINA is challenging current guidelines. JW clarified that adults in the feasibility study appeared to be open to deferment of surgery which is why the 24 month usual care arm is being defined as deferred surgery. <u>Identifying potential patient participants in the feasibility study:</u> SC reported that he has had a couple of potential patients through clinic for the feasibility study but had not yet contacted LM, and reassured he should be able to provide patients imminently.	
7.	PW concurred he has identified possible patients at SC's site and SP reported a strong lead in Bradford. MH offered anecdotal evidence that 1 in 3 patients are willing to be randomised. JW noted the cumbersome consent process potentially limiting numbers of patients participating in the feasibility study. <u>Website, Facebook and Twitter presentation by IR</u> IR confirmed she can upload recruitment figures to the website and will primarily be using Facebook and Twitter for this function. JW confirmed intention to have a patient engagement group which could include patients not participating in the trial.	

8.	Question and Answer Session: Questions to NS regarding statistical analysis: NS confirmed he will be supervising a junior statistician (Tony Fouweather) throughout the trial. Recruiting trial nurses: MH asked about funding for a nurse for one session a week. JW confirmed the HTA release funds in quarters and will not release first quarter until there is actual recruitment. IR explained the start date was extended from April 2014 to July 2014 and consequently contracting and first payment has been delayed. JW confirmed that NATTINA is currently funded for a clinic every other week from a consultant perspective and advised recruiting a nurse once a week to process administrative work in addition to clinic hours. KM advised the Glasgow site has recruited a research-funded tenant nurse with the expectation she will carry out all administration associated with the trial. JM asked whether this nurse would keep the site files and highlighted this could be a difficulty for hospital nurses but not for tenant nurses. JW proposed establishing a teleconference among nurses in the study once every two weeks or monthly, to share experience of practicalities and as a motivational tool. PW concurred nurse presence keeps study moving forward within clinics. A.O.B IR reported on first final draft for BMC trials Journal which is almost ready for circulation and submission. Meeting closed with thanks by JW.	
