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Health Technology Assessment Programme
National Institute for Health Research
Evaluation, Trials and Studies Coordinating Centre
University of Southampton, Alpha House
Enterprise Road, Southampton, SO16 7NS

tel: +44(0)23 8059 5586
fax: +44(0)23 8059 5639

email: hta@hta.ac.uk
web: www.hta.ac.uk

Clinical effectiveness and patient perspectives of different treatment strategies for tics in children with Tourette syndrome: An evidence synthesis

Protocol

Chief Investigator: Professor Chris Hollis[1]

Trial Co applicants: Professor Tim Kendall[2]

Dr Craig Whittington[3]

Mrs Suzanne Dobson[4]

Professor Georgina Jackson[5]

Professor Mary Robertson[6]

Dr Tara Murphy[7]

Dr Hugh Rickards[8]

Dr Jeremy Stern[6]

Dr Isobel Heyman[9]

Dr Madeline Groom[10]

Dr Penny Bunton[11]

Dr Tammy Hedderly[12]

Dr Cris Glazebrook[5]

1. The University of Nottingham, Developmental Psychiatry, South Block, E Floor, Queen's Medical Centre, Nottingham NG7 2UH

2. National Collaborating Centre for Mental Health, Royal College of Psychiatrists Research Unit, Floor 4, 21 Mansell Street, London E1 8AA

3. National Collaborating Centre for Mental Health (CORE UCL), Research Department of Clinical, Educational and Health Psychology, University College London, Gower Street London WC1E 6BT

4. Tourettes Action, Kings Court, 91 - 93 High Street, Camberley, Surrey GU15 3RN

5. Behavioural Sciences, Division of Psychiatry, The University of Nottingham, A Floor, South Block Queen's Medical Centre, Nottingham NG7 2UH

6. Department of Neurology, Atkinson Morley's Wing, St George's Hospital, Blackshaw Road, Tooting, London SW17 0QT

7. Department of Clinical Neuropsychology, Level 4, Frontage Building Great Ormond Street Hospital NHS Trust, London WC1N 3JH

8. Department of Neuropsychiatry, South Birmingham Mental Health NHS Trust Barberry Building, 25 Vincent Drive, Edgbaston Birmingham B15 2FG

9. Maudsley Hospital South London and Maudsley NHS Trust & Institute of Psychiatry, De Crespigny Park, London SE5 8AF

10. University of Nottingham, Developmental Psychiatry, South Block E Floor, Queen's Medical Centre, Nottingham NG7 2UH

11. University of Manchester & Guy's & St Thomas' NHS Foundation Trust (GSTT), University of Manchester

12. Evelina Childrens Hospital and Kings Health Partners St Thomas' Hospital, Westminster Bridge Road, London SE1 7EH

Email addresses:

Professor Chris Hollis (PI) c/o Angela.Finnemore@nottingham.ac.uk

1. Study Identifiers

1.1 Full project title

Clinical effectiveness and patient perspectives of different treatment strategies for tics in children with Tourette syndrome: An evidence synthesis

Short Title: Treatment of tics in children with Tourette syndrome

1.2 PROSPERO Reference

CRD42012002059

1.3 HTA reference

10/142/01

2. Project overview

2.1 Research objectives

The overarching aim of the project is to effect a step change in the quality of care provided by the NHS to children and young people with Tourette syndrome (TS). The primary objective is to answer the question: what works for whom and when? We will produce an evidence-based care pathway and research recommendations as the result of a synthesis of diverse sources of evidence that include:

i) a systematic review of the clinical effectiveness of treatments for tics in children and young people led by the National Collaborating Centre for Mental Health (NCCMH). This review will extend beyond efficacy trials to include observational studies of adverse effects, predictors of outcome and qualitative studies of patient experiences of treatment.

ii) a qualitative research study to elicit young people's views on their experiences of treatment and what outcomes they value most. This extends an existing research collaboration between the University of Nottingham and *Tourettes Action*.

In order to undertake an evidence synthesis we will establish an expert advisory group; the **Tourette Expert Group** (TEG) involving leading UK clinicians/ researchers and service users/ carers nominated by *Tourettes Action*. The TEG will define the key review questions and synthesise diverse sources of evidence including the systematic review, review of grey literature, service user/carer survey and qualitative interviews with young people. We will describe in the form of a care pathway the level of evidence underpinning important clinical management decisions for young people with TS. The care pathway model will be used to illustrate review questions in a logical sequence spanning the initial presentation of TS to management of complex and co-morbid cases. Key clinical decisions include the order in which drug and behavioural/psychological treatments should be offered and how they should be combined based on both clinical severity and co-morbidity. Where high level evidence is lacking (e.g. RCTs or meta-analyses) the TEG will use discussion and informal consensus to identify current best practice. Where gaps in evidence are identified in the pathway, the TEG will make primary research recommendations to address relevant review questions.

3. Study Background

3.1 Clinical features

Tourette syndrome (TS) is a common neuropsychiatric disorder characterised by chronic motor and vocal tics. Tics are typically brief, rapid movements (e.g. blinking or grimacing) or vocalisations (e.g. grunting or squeaking) but can include more complex movements or vocalisations. Tics begin in childhood, with a peak onset around age 7 to 9 years, often increasing in severity until mid-teens and then declining (but usually not disappearing) in late adolescence and young adult life. Tics follow a fluctuating (waxing and waning) course and may be exacerbated by stress, tiredness or boredom and improved by focussed mental activity. Tics are commonly preceded by an uncomfortable sensory premonitory urge, with the performance of the tic resulting in relief from the urge. Although involuntary, older children and adolescents may be able to briefly suppress or postpone a tic at the expense of an increased urge to complete the tic and/or increased anxiety.

3.2 Epidemiology

Tics are common, with up to 20% of children experiencing transient mild tics (usually lasting less than 3 months). Tourette syndrome (TS), defined by the presence of both motor and vocal tics lasting for more than 12 months is more common than previously thought, with an estimated prevalence of 6 to 10 per 1000 (approximately 1%) in school age children [1].

3.3 Co-morbidity

Tourette syndrome (TS) commonly occurs together with other neurodevelopmental disorders (co-morbidity), including attention deficit hyperactivity disorder (ADHD)[2], obsessive compulsive disorder (OCD)[3], learning disability (LD) and autism spectrum disorder (ASD). Co-morbidity can be described as 'simple' e.g. TS+ADHD or TS+OCD or 'complex' e.g. TS+ADHD+ASD or TS+ASD+LD. The presence of co-morbidity is associated with increased impairment and greater complexity of management.

3.4 Impairment and Quality of Life

The experience of TS is frequently distressing and associated with significant social impairment and can be detrimental for personal, social, educational and occupational functioning. A child with TS may experience teasing and bullying from other children and inappropriate sanctions from teachers who don't appreciate the involuntary nature of tics. This may lead to social isolation, low self-esteem and sometimes depression. Severe motor tics may also result in physical pain, fatigue and self-injury. The chronic, unexpected and intrusive nature of tics can lead to high levels of family stress, which itself may further exacerbate tics in a child or young person.[4]

3.5 Current Clinical Practice

There is considerable variation in both services and treatments for children with TS in the UK. This may result in part from the lack of national evidence-based guidelines (e.g. NICE Guidance or Technology Appraisal). The needs of children with TS may not be well served by either mainstream community paediatric/ paediatric neurology services or by child and adolescent mental health services (CAMHS). Of particular concern is the lack of availability of services offering non-pharmacological interventions for tics (personal communication; survey carried out by *Tourettes Action* in 2009). It is recognised that not all children with TS require or wish for specific treatment. In children with mild tics and mild/moderate impairment, explanation and education about the condition provided in an age appropriate manner for the child, family and school is frequently sufficient.

3.5.1 Drug treatments

The current mainstay of treatment for all people with TS (with moderate/severe tics) are medications including the older 'typical' antipsychotic drugs; such as haloperidol, sulpiride and pimozide; the newer 'atypical' antipsychotics such as risperidone, aripiprazole, olanzapine and quetiapine; and alpha 2 adrenergic agonists such as clonidine and guanfacine and dopamine agonists such as tetrabenazine. In children with moderate/severe tics, the most commonly used medications in the U.K. are clonidine and the newer atypical antipsychotics including risperidone and aripiprazole. In a recent survey of clinicians specialising in the treatment of TS conducted by the European Society for the Study of Tourette Syndrome (ESSTS), drugs were ranked in the following order of preference for treatment of tics in children and adolescents; risperidone, clonidine, aripiprazole, pimozide, sulpiride, haloperidol and tetrabenazine[5]. Given the frequent co-morbidity with other conditions (e.g. ADHD or OCD), children with TS may also receive drugs such as atomoxetine with the aim of reducing both ADHD symptoms and tics, or fluoxetine/ despimipramine with the aim of reducing OCD symptoms and tics. In children with TS, the primary aim of treatment should be to minimise tic-related impairment (personal, social and educational), with the secondary aim being the reduction (rather than elimination) of tics to a tolerable level.

3.5.2 Behavioural and psychological treatments

These include; habit reversal training (HRT), exposure and response prevention (ERP) therapy, family intervention, psychoeducation, self-hypnosis, relaxation training and many others. Probably the best evaluated behavioural intervention is HRT, where children are trained to initiate a competing response to the tic when they experience a premonitory urge. HRT is typically embedded within a broader psychological/ behavioural treatment package. Behavioural and psychological treatments – often addressing broader tic-related impairments - can be highly valued by patients and carers. However, provision of these therapies for children and young people in the U.K. is variable and largely limited despite the growing evidence base.

3.5.3 Neuro-therapeutic interventions

These offer promise in TS as they are based on intervening in the presumed patho-physiological mechanisms of the disorder, or training compensatory neural processes. Examples include deep brain stimulation (DBS), transcranial magnetic stimulation (TMS), EEG neurofeedback and transcranial direct current stimulation (tDCS). However, the evidence base for these interventions is limited, especially in children, and they remain largely experimental. Important questions remain unanswered about the safety, acceptability and long term benefits and harms of these interventions.

4. Existing Research Evidence

4.1 Drug treatments

There is limited evidence for the efficacy of antipsychotic drugs and other medications in children and young people with TS. All medications except haloperidol are unlicensed for the treatment of TS in children in the U.K. Where randomised controlled trials (RCTs) do exist, they typically measure only short term effects, ranging from 4 to 8 weeks. There are also concerns that children and young people may be more sensitive than adults to the potential adverse effects of antipsychotics, including weight gain, metabolic adverse effects (e.g. hyperglycaemia/ type II diabetes and hyperlipidaemia/ hypercholesterolaemia) and movement disorders [6].

The European Society for the Study of Tourette Syndrome (ESSTS) Guideline Group have recently publish a series of clinical guidelines for assessment [7], pharmacological [5], behavioural/ psychological treatments [8] and deep brain stimulation (DBS). The review of pharmacological treatment identified only a small number of randomised controlled trials, most involving small numbers and mixed samples of adults and children. Although this review did not adopt a formal GRADE approach to evaluate the quality of evidence; five drugs: clonidine, risperidone, ziprasidone, haloperidol and pimozide were given an 'A' ranking (i.e. evidence of benefit in at least two controlled randomised trials). Of these five drugs, ziprasidone has been withdrawn from the U.K. due to concerns about QTc prolongation and pimozide has been associated with sudden cardiac death and requires careful cardiac monitoring. Risperidone is the most widely used drug for children and young people with tics among a survey of ESSTS members, and has been shown to be superior to placebo in two RCTs[9, 10] and showed superiority compared to clonidine in TS patients with obsessive compulsive symptoms[11] .

Outcomes used in treatment studies of children and young people with TS typically focus on reduction in tic frequency/ severity as measured by scales such as the Yale Global Tic Severity Scale (YGTSS). However, tic reduction may be a less important outcome to young people and families than improving educational attainment, psychological wellbeing and peer relationships. Furthermore, a reduction in tics may not necessarily predict an improvement in broader outcomes including quality of life (QoL).

4.2 Behavioural and psychological treatments

In a recent ESSTS Guideline Group review of behavioural and psychological treatments for tics and TS [8], the very limited evidence base favoured habit reversal training (HRT) [12] and exposure response prevention (ERP) [13] over a range of other interventions including CBT, massed practice, contingency management etc. One parallel group study compared HRT and ERP and found no difference [14]. The ESSTS Guideline recommends that behavioural interventions should be given as first line treatments – although there have been no studies directly comparing behaviour therapies with drug treatment. Furthermore, most studies of behaviour therapy for tics include a substantial group of patients who remain on drug treatment. These studies are generally not powered to assess moderating or interaction effects between treatments. Finally, most behaviour therapy packages in trials are quite intensive (e.g. weekly one hour sessions for 8 -10 weeks). There are no studies evaluating cost effectiveness or maintenance effects over longer periods of follow-up.

5. Research methods

5.1 The Evidence Synthesis: Scope

This scope defines what the evidence synthesis will (and will not) cover, and what the systematic review team will consider. The scope is based on the HTA call no. 10/142. It will be refined by the study team (TEG: Tourette Expert Group).

The areas that will be addressed by the systematic review and evidence synthesis are described in the following sections.

5.1.1 Population

Groups that <u>will be</u> covered:

1. Children and young people (younger than 18 years) who have a clinical diagnosis of Tourette syndrome (including Tourette disorder and chronic motor tic disorder, or chronic vocal tic disorder).

2. Children and young people with TS and a comorbid disorder including ADHD, OCD, ASD and learning disability.

Groups that will not be covered:

1. Adults (aged 18 and older).
2. Children and young people with a transient tic disorder (duration less than 12 months).

5.1.2. Healthcare setting

Care that is received in primary care, secondary and tertiary CAMHS, paediatric services (including community/general paediatrics and paediatric neurology clinics) and specialist Tourette Clinics, from healthcare professionals who have direct contact with, and make decisions concerning the care of, children and young people with TS.

The transition from CAMHS and paediatrics to adult services, and the treatment and care received during transition.

The evidence synthesis will also be relevant to the work of, but will not cover the practice of, healthcare professionals and others working in acute medical departments, accident and emergency (A&E), paramedic services, services for the homeless, prison medical services, the police and those who work in forensic services and criminal justice. It will also be relevant to professionals who work in education e.g. schools, colleges and other educational settings; and to those who work in social care e.g. with looked after children.

5.2 Clinical management

5.2.1 Key clinical issues that will be covered

The clinical effectiveness of any medication licensed for use in North America, Europe or Australasia, including;

Antipsychotics: such as haloperidol, sulpiride, olanzapine, risperidone, quetiapine, arpipiprazole.

Other medications: such as clonidine, tetrabenazine, fluoxetine, clonazepam

Other dietary interventions: such as fish liver oil.

The clinical effectiveness of psychological or behavioural psychosocial interventions:

1. Habit reversal training (HRT)
2. Exposure and response prevention (ERP)
3. Counselling and supportive psychotherapy
4. Cognitive behavioural therapy
5. Family interventions (including family therapy)
6. Psychoeducation
7. Physical activity/ exercise
8. Relaxation training
9. Self-hypnosis

The clinical effectiveness of physical interventions; including acupuncture, botulinum toxin, TMS, DBS, tDCS and EEG neurofeedback for tics in children with Tourette's syndrome.

Whether the clinical effectiveness of the treatment of tics (either by medication, behavioural treatment or both) is moderated by the presence of a co-morbid disorder (e.g. ADHD, OCD, ASD or LD), age or tic severity?

Whether behavioural treatment (e.g. HRT) is as effective when delivered alone or only in combination with medication?

What are the views of patients and carers regarding the choice of treatments available and what outcomes are considered most important and meaningful?

What evidence is there that combining behavioural treatment with medication increases engagement and adherence with treatment?

5.2.2 Clinical issues that will not be covered

1. Cost effectiveness of different treatments.
2. The clinical effectiveness of different treatments in adults.

6. Research Components

6.1 Tourette Expert Group (TEG)

A **Tourette Expert Group (TEG)** will be formed to undertake the evidence synthesis and work with the systematic review team and qualitative study team [Fig 1.]. The TEG will agree the final scope of the review including identifying review questions, interventions and outcomes. The methodology will be that used in the development of NICE Clinical Guidelines without exhaustive external consultation. The systematic review team will be managed by the National Collaborating Centre for Mental Health (NCCMH), which has extensive experience in developing NICE Guidelines.

The TEG will comprise of experts in the fields of clinical practice, research and user/carer experience with TS. The TEG will consist of UK clinical experts drawn from the disciplines of child and adolescent psychiatry (paediatric neuropsychiatry), paediatric neurology and clinical neuropsychology. In addition, the TEG will include academics and clinical neuroscientists with expertise in neurotherapeutics, evidence-based practice, qualitative research and systematic review methodology (from the NCCMH). This expert group encompasses basic neuroscience, clinical care, academic groups and service user group representation.

The TEG will develop the review protocol, including terms to be used in the search strategy. The TEG will evaluate the evidence produced by the systematic review team to produce clinical evidence summaries for each intervention. The TEG will then develop a stepped care pathway for management based on best evidence. Where evidence is lacking to support clinical decisions in the pathway, recommendations will be made for primary research to answer specific review questions.

6.2 Patient and carer perspectives

These will form a central part of the evidence synthesis. Firstly, there will be two user/carer representatives on the TEG nominated by *Tourettes Action* (TA). Secondly, evidence about experiences of treatment will be obtained from the anonymised records of the national TA helpline. Thirdly, we will conduct, in partnership with *Tourettes Action,* an on-line survey of parents of children with TS exploring their experience of their child's treatment and services. Fourthly, we will conduct qualitative interviews with up to 50 young people with TS identified by parents via the on-line survey. The interviews with young people will explore the range of treatments offered (drug and behavioural), experiences of different treatments (both positive

and negative), acceptability of different treatments and what outcomes are viewed as most important and meaningful.

6.2.1 QuEST: Qualitative study of Experiences of Services and Treatment: Young people's perspective on treatment for tics

6.2.1.1 Background

There is significant variation in the treatments and interventions available to children and adolescents with Tourette syndrome (TS). In evaluating the clinical effectiveness of different treatment strategies, the actual experiences of patients with TS should be examined. A recent UK study using focus groups with young people suggests TS can be a distressing and disabling condition and that the struggle to control tics can have a negative impact on quality of life, particularly at school [15]. To our knowledge, research to date has not focused on young people's experience of treatment for tics. What are the views of patients and carers regarding the choice of treatments available, what are the positive and negative experiences of care received, and what outcomes are considered most important and meaningful?

6.2.1.2 Rationale

The rationale for the QuEST research is based upon a need to better understand the experience of treatment of tics and what outcomes are most important from the perspective of young people with TS.

This study will build on research currently being carried out in partnership with *Tourettes Action* at The University of Nottingham exploring young people's experience of TS and their educational and psychosocial needs. The study will thus make use of an on-going research partnership with *Tourettes Action* and in-house expertise in qualitative methodology and interviewing.

6.2.1.3 Methods

Stage 1: On-line National Survey

We will conduct an online survey of parents of children with TS, recruited through the *Tourettes Action* website and newsletters. Inclusion criteria will be children with tics aged under 18 years whose parents have reported their child has a diagnosis of TS. The aim of the survey is to explore parents' perceptions of the treatment their child has received for tics, including perceptions of effectiveness and acceptability. The survey will also use treatment vignettes to explore parents' perceptions of unfamiliar treatments, or those which parents may not have had direct experience of. The online survey will correspond to quality markers for surveys adapted from Parker et al.[16] and have a minimum target sample size of 300 respondents. The sampling frame will be determined to achieve maximum coverage of recipients with experience of different treatment approaches. Parents will be approached through the TA website, the TA newsletter or direct contact from the TA (TA members). Responses to open-ended questions will be analysed using content analysis [17,18] and deductive analysis will be guided by the emerging findings from the systematic review. This analytical approach allows us to obtain parent views without constraint or bias, but also allows for classification and quantification of responses. This will enable us to determine the prevalence of types of views about treatment and the factors influencing parent perceptions.

Stage 2: In-depth Qualitative Interviews

Participating parents of young people aged 11 to 17 years will be asked if their child would be interested in taking part in an interview to discuss their feelings about the treatment they have had for their tics. Children will be purposively sampled from consenting parents to capture experience of a range of treatments (i.e. different drug and behavioural therapies). It

is anticipated that a substantial number of participants will have a comorbid disorder (e.g. ADHD, OCD) in addition to TS.

Interviews will be conducted either by Skype or by telephone, or, where practical, by face to face interview. Interviews will be audiotaped and transcribed in full. In the interview, participants will be asked about their experiences of treatment for tics. The questions will examine issues including their positive and negative experiences of treatments, their perceived treatment needs and what they hope to gain from treatment (i.e. what outcomes are important to them).

Interviews will be analysed using theme analysis[19], with themes identified inductively (i.e. emerging from the interview transcripts) and deductively (guided by evidence from the systematic review). In accordance with Boyatzis[19], each theme will be given a conceptually meaningful label, a definition, a description of how to know when the theme occurs, a description of any qualifications or exclusions to the application of the theme and examples of positively and negatively coded extracts from the data. This will form the basis of a coding frame from which to assess the reliability of the data coding.

The sample size will be flexible and will include up to 50 young people depending on the number needed to achieve saturation of the themes. This qualitative approach is particularly suited to exploring the experiences and views of young people regarding treatment for tics.

The findings of this study will be presented to the Tourette Expert Group (TEG) in a summary report. This study will provide information on the patient and carer perspective and thus make a valuable contribution to the existing evidence base (e.g. identify gaps in treatments and services offered) and inform subsequent recommendations and guidelines (e.g. choice of outcome measures in trials).

6.3 Systematic review of clinical evidence

6.3.1 Systematic review search strategy

A stepwise, hierarchical approach will be taken to locating evidence, based on methods used for developing clinical guidelines for the National Institute for Health and Clinical Evidence (NICE), and complying with the CRD's guidance for undertaking reviews.

The following databases will be searched (accessed through University College London's MetaLib – a service which enables cross-searching of up to ten databases at once):

- AMED [allied and alternative medicine]
- CINAHL Plus [nursing, allied health, biomedicine, and healthcare]
- EMBASE [pharmacological and biomedical database]
- MEDLINE / MEDLINE In-Process [medicine, nursing, dentistry, veterinary medicine, the health care system, and the preclinical sciences]
- PsycINFO [psychology and related]

In addition, the Cochrane Library will be searched to retrieve Cochrane and other reviews, clinical trials, technology assessments, and economic evaluations.

Strategies will be built up through a number of trial searches, and discussions of the results of the searches with the review team and the TEG. In order to assure comprehensive coverage, search terms will purposely be kept broad to help counter dissimilarities in database indexing practices and thesaurus terms, and imprecise reporting of study populations by authors in the titles and abstracts of records. No age limits will be placed on the search given the relative paucity of evidence [21].

In addition, the following search methods will be utilised: 1) scanning the reference lists of all eligible publications for more reports; 2) sending lists of eligible studies to subject experts (identified through searches and the TEG) and asking them to check the lists for completeness, and to provide information of any published or unpublished research for consideration; 3) checking the tables of contents of key journals for studies that might have been missed by the database and reference list searches; 4) tracking key papers in the Science Citation Index (prospectively) over time for further useful references. Finally, we will contact authors of potentially relevant studies if further information is needed to assess their eligibility for inclusion in the review, i.e. for randomised controlled studies of mixed populations (children and adults), in an attempt to obtain data restricted to children/young people.

6.3.2 Review strategy

Review protocols will be used to set out the review strategy, including the eligibility criteria (PICO: population, intervention, comparison, outcome) that must be met for studies to be included as evidence, the review question(s), the criteria used for quality assessment, and the method of evidence synthesis.

Studies acquired in full will be re-evaluated for eligibility at the time they are being entered into Review Manager Version 5 (Cochrane Collaboration). For each study, appropriate study characteristics and patient important outcomes will be extracted, depending on advice from the TEG. A second reviewer will double-check the abstracted data, with discrepancies resolved through discussion with the TEG.

For review questions concerning effectiveness, eligible studies will be assessed for quality using the methods outlined in the Cochrane Handbook. The eligibility of each study will be confirmed by at least one member of the TEG.

Where appropriate, meta-analysis will be used to synthesise evidence using a random-effects model. Where this is not appropriate or possible, methods of narrative synthesis will be used that are based on the work of Popay and colleagues[20]. For review questions that concern intervention effectiveness, non-randomised studies will only be included if good quality RCTs do not exist. For questions about adverse effects, randomised and non-randomised evidence will be utilised. Once the evidence is synthesised, the GRADE approach (www.gradeworkinggroup.org/) will be used to assess the quality of the evidence for each outcome.

For review questions regarding the views of patients and carers, qualitative studies and the results of the qualitative interview study of experiences of services and treatment (QuEST) will be the primary source of evidence.

For each intervention, clinical evidence summaries and GRADE evidence profiles will be produced by the systematic review team and presented to the TEG to aid interpretation of the evidence.

6.3.3 Design

The approach taken will broadly follow the methodology used in the development of a NICE clinical guideline (http://www.nice.org.uk/), without the necessity for extensive external stakeholder consultation (n.b. patients and carers will be included both on the expert group and as part of the review of patient experience). After the Tourette Expert Group (TEG) is formed, the key steps will include:

1. Identify existing reviews related to the topic
2. Agree the scope and parameters of this review with the TEG
3. Refine the review questions based on advice from the TEG

4. Develop review protocols for each of the key clinical issues
5. Conduct the systematic review
6. Synthesise the evidence including narrative data
7. Use the GRADE approach to assess the quality of the evidence
8. Develop narrative evidence summaries
9. TEG produces consensus recommendations for each of the key clinical issues/ pathway (specifying quality of evidence at each step)
10. TEG produces primary research recommendations

7. Ethical arrangements

Ethical approval will be sought from the University of Nottingham Medical School Ethics Committee.

Participants will be recruited from the membership of *Tourettes Action* (in excess of 700). The study will only commence once full ethical approval is in place.

8. Service users/ public involvement

Tourettes Action (TA) leads on engaging service users in the project. Tourettes Action is a charity working to make life better for people with Tourette Syndrome. The charity has identified a number of ways in which to engage with people living with TS to inform this project. The TA Helpline, website and online forum can be used for service user consultations to inform the project at key stages. TA also hold several service user meetings each year which could be used as another way to gather information and check initial findings as part of the ongoing process.

Lay experts have been recruited via Tourettes Action to represent service users on the Tourette Expert Group (TEG). Service users will therefore play an important part in the decision model throughout the course of the review.

9. Research Governance

9.1 Funding

Funding has been secured from the National Institute of Health Research – Health Technology Assessment programme (reference 10/142/01).

9.2 Steering group

A Steering group has been set up to drive study progress and to set the agenda for the TEG meetings. The Steering group is chaired by the facilitator of TEG (Professor Tim Kendall). The group will also include the Principal Investigator, the Project Manager, the Systematic Reviewers and other key study collaborators. The Steering group will meet prior to each TEG meeting.

9.4 Responsibilities of the team members

National Collaborating Centre for Mental Health (NCCMH) - Systematic Review Team:

Professor Tim Kendall – Director: Provides high level leadership for the project. Oversees project management, act as bridge between technical team and the TEG, facilitate TEG meetings and act as guarantor of the process, review draft report.

Dr Craig Whittington, Chief Systematic Reviewer: Helps draft the review protocol, provide training and supervision to the technical team, draft the evidence review outline, review draft report.

Dr Mary Pennant, Systematic Reviewer, National Collaborating Centre for Mental Health: Helps draft the review protocol, attend all meetings, conduct systematic review and synthesise evidence, draft evidence review.

Dr Linnea Larsson, Project Manager: Main contact point for project. Co-ordinates the overall project and appointment of research staff, set up steering group meetings and liaise with TEG, oversees project workplan with milestones, take working notes at each meeting, draft outline of final report.

Qualitative Study Team

University of Nottingham

Professor Cris Glazebrook, Division: Behavioural Sciences, Responsible for design and supervision of the qualitative study (QuEST).

Mr Jose Cuenca, Research Assistant: Responsible for on-line survey design and data analysis and the qualitative interviews and analyses carried out under the supervision of Professor Cris Glazebrook.

Tourettes Action UK

Mrs Suzanne Dobson, CEO: will lead on patient recruitment and involvement (PPI).

Tourette Expert Group members:

Professor Chris Hollis (Chair), Professor Tim Kendall (facilitator), Dr Craig Whittington, Mrs Suzanne Dobson, Professor Georgina Jackson, Professor Mary Robertson, Dr Tara Murphy Dr Jeremy Stern, Dr Isobel Heyman, Dr Madeline Groom, Dr Penny Bunton, Dr Tammy Hedderly, Dr Cris Glazebrook, Dr Hugh Rickards, Ms Seonaid Anderson, Mr Nick Bingham and Mr David Jones.

Undertakes the evidence synthesis and will work with both the systematic review team and the qualitative study team. Develops the review protocol, evaluate the evidence produced by the systematic review team to produce clinical evidence summaries for each intervention. Responsible for developing a stepped care pathway for management based on best evidence. Where evidence is lacking to support clinical decisions in the pathway, recommendations will be made for primary research to answer those.

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