NICE guidelines

- Our guidelines are based on the best available evidence. Our recommendations are put together by experts, people using services, carers and the public.
- NICE guidelines make evidence-based recommendations on a wide range of topics, from preventing and managing specific conditions, improving health, and managing medicines in different settings, to providing social care and support to adults and children, and planning broader services and interventions to improve the health of communities.
- Each guideline is developed according to a process that starts from the topic being chosen and extends to any future guideline updates.
- When exercising their judgement, professionals and practitioners are expected to take guidelines fully into account, alongside the individual needs, preferences and values of their patients or the people using their service

NICE

For more information please see Developing NICE guidelines: the manual: https://www.nice.org.uk/process/pmg20/chapter/introduction

13 principles underpin our work

1. Produce guidance and standards that reflect national priorities for health and care
2. Describe and regularly review our approach
3. Work with independent advisory committees to develop recommendations
4. Consider the advice and experience of a wide range of people
5. Offer an opportunity to comment on and influence our recommendations
6. Use relevant, reliable and robust evidence
7. Make recommendations based on an assessment of population benefits and value
8. Support innovation in the provision and organisation of health and social care services
9. Aim to reduce health inequalities
10. Consider if appropriate to make different recommendations for different groups of people
11. Propose new research questions and data collection to resolve uncertainties in the evidence
12. Publish recommendations and encourage their adoption
13. Assess the need to update our recommendations in line with new evidence

NICE

NICE guideline development

Topics chosen
Topics referred from NHS England, Department of Health and Social Care, Department of Education

Scope produced
- Why there is a need
- Areas covered and not covered
- Intended achievements

Guideline developed
- Review questions
- Literature search
- Summary of evidence
- Impact considered
- Committee reviews evidence

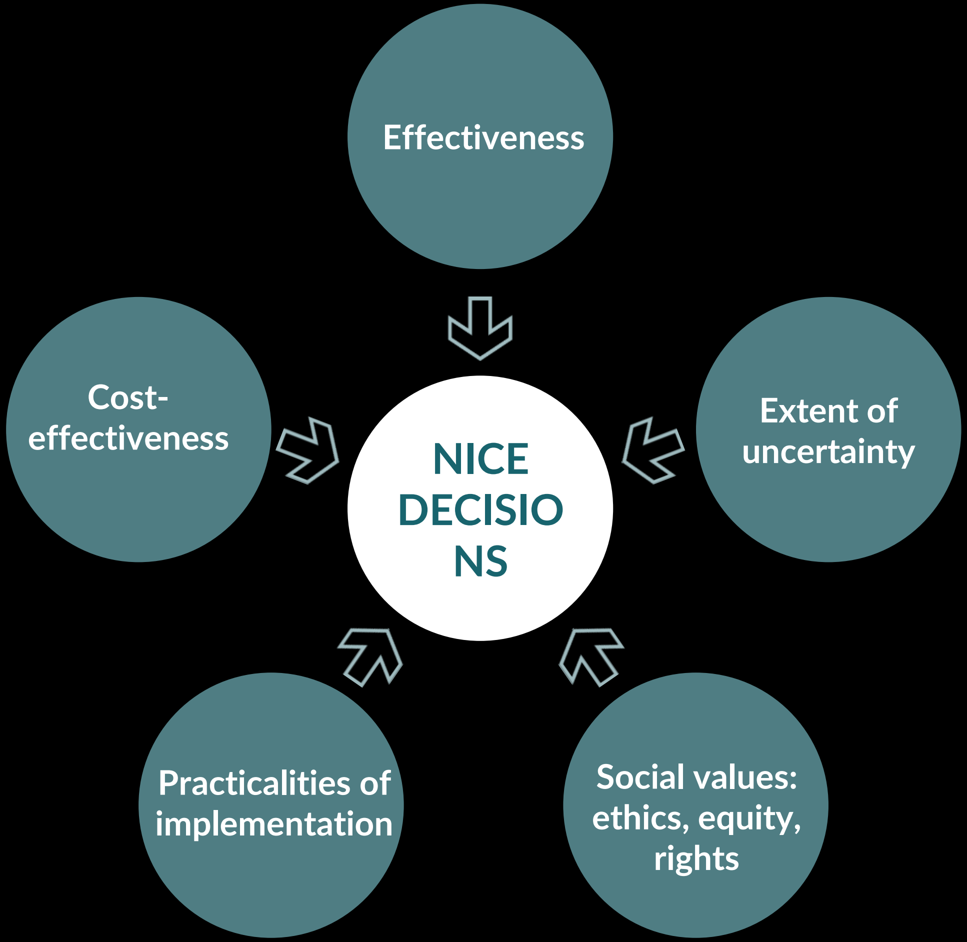
Draft guideline sent for consultation
Draft version sent to stakeholders

Comments considered, guideline revised
Guideline developer considers comments from stakeholders

Guideline signed off and published
Sign off by Guidance Executive

Updating guidelines
Our guidelines are regularly updated and maintained

What is considered in guidance development



Effectiveness

Cost-effectiveness

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Extent of uncertainty

Practicalities of implementation

Social values: ethics, equity, rights

NICE ME/CFS guideline

NICE

Committee Composition

Non-Expert Chair and Vice Chair

- helps the committee to work collaboratively,
- ensures everyone is heard *and* listened to,
- ensures meetings finish on time.

Lay members

- Representing a range of experience, including young person, parent/carer.

Practitioner and professional members

- Three clinical leads for ME/CFS services
- General Practitioners, Paediatricians, Physicians – all with an interest and expertise in ME/CFS
- Physiotherapy, Occupational Therapy, Nursing. Social Work, Clinical Psychology, Dietetics – all with an interest and expertise in ME/CFS

What lay members contribute to committees

Lay members serve an important role on committees at NICE. Their contributions have proven invaluable to our guidance. Lay members:

- Challenge the experts and evidence about what really matters to people.
- Ensure that the patient, carer, service user or community perspective is represented in the guidance.
- Help to ‘nudge’ the committee into remembering the bigger picture.
- Ask important questions that set the framework for discussion.
- Influence the wording of the recommendations.
- Identify and encourage research recommendations.
- Contribute a different, non-medical perspective.

Committee Meetings

The Committee met 31 times from 6th February 2019.

- First 14 meetings in person (to January 2020), subsequent meetings by video conference
- Break in Committee work from March 2020 to mid July 2020 due to Covid

For each of the twelve Review Questions identified in the scope, the committee discussed and approved a review protocol (this was done before looking at the evidence).

The evidence was reviewed at a subsequent meeting and recommendations drafted.

Evidence considered

The twelve review questions were based on the following frameworks:

- population, intervention, comparator and outcome (PICO) for reviews of interventions
- population, index tests, reference standard and target condition for reviews of diagnostic test accuracy
- population, setting and context for qualitative reviews.

Full literature searches, critical appraisals and evidence reviews were undertaken for each review question

Three Topic Experts

- Dr Jonathan Edwards (Difficulties of intervention trials in ME/CFS)
- Dr Nina Muirhead (Information, education and support for health and social care professionals)
- Dr Mujtaba Husain (Different models of multidisciplinary care)

Two commissioned focus groups

- University of Manchester Centre for Primary Care (Severe ME/CFS)
- Oxford Clinical Allied Technology and Trial Services Unit (Involving children and young people)

Calls for evidence

Evidence considered

Scope area	Source of additional evidence
Children and Young people	Focus Group
People with severe ME/CFS	Focus Group
Diagnosis of ME/CFS	Call for evidence • Management strategies before diagnosis
Management of ME/CFS	Expert testimony • Conducting intervention trials for the treatment of ME/CFS • The composition of multidisciplinary teams Call for evidence • Experience of interventions
Monitoring and review	Call for evidence • Monitoring and review in people with ME/CFS
Information, education and support for health and social care professionals	Expert testimony • Medical education

Methodological approach

- Methods used are those described in ‘Developing NICE guidelines: the manual’ 2018 version and specifically in NG201: Methods.
- The evidence for outcomes from the included RCTs were evaluated and presented using the ‘Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox’
- Review findings from the included qualitative studies were evaluated and presented using the ‘Confidence in the Evidence from Reviews of Qualitative Research’ (CERQual) Approach developed by the GRADE-CERQual Project Group, a subgroup of the GRADE Working Group.
- Decisions on whether a recommendation could be made, and if so in which direction, were made on the basis of the committee’s interpretation of all the available evidence, taking into account the balance of benefits, harms and costs between different courses of action.

Diagnosis – what the guideline says

The guideline includes recommendations for both suspecting and diagnosing ME/CFS. ME/CFS should be diagnosed in someone if all of the following 4 symptoms have persisted for 3 months and are not explained by another condition:

- **Debilitating fatigue**
- **Post exertional malaise**
- **Unrefreshing sleep**
- **Cognitive difficulties**

Diagnosis – why we’ve said it

- A range of different diagnostic criteria have been used to diagnose ME/CFS.
- There is no clearly identified ‘gold standard’ so it is not possible to assess the validity of each set of criteria
- The committee identified the features that are common to all or most of the criteria. They also considered the usability of the criteria as a clinical tool and the balance between over- and under-diagnosis.
- The Institute of Medicine (IOM) 2015 criteria were judged to provide a good balance.
- With the IOM criteria, the person must have one of either cognitive impairment or orthostatic intolerance. The committee identified that cognitive difficulties are included in 7 of the 9 reviewed criteria and are commonly reported so felt it was an essential feature.

Diagnosis – why we've said it

- The IOM criteria indicate a minimum symptom duration of 6 months.
- The committee were concerned about delays to diagnosis with some people waiting years.
- A minimum length of symptom duration is built in to avoid misdiagnosis and to rule out short-lived fatigue.
- The committee agreed that a 3-month minimum duration struck the right balance in allowing for prompt diagnosis while avoiding mis-diagnosis.
- For children and young people, the evidence available for this population broadly aligned with the adult evidence. They recognised the importance of referral to a paediatrician for assessment and diagnosis.

Diagnosis – impact on reviewing

- NICE uses GRADE to assess the quality of evidence for each outcome in a study
- Studies are assessed against different criteria including ‘indirectness’. Evidence in a study is ‘indirect’ if the population doesn’t match the population in the protocol
- With the protocol population defined by the diagnostic criteria, if studies included a different population or were unclear about the population, they were downgraded.
- This does not mean that studies were excluded from the review, just that their quality assessment was downgraded.
- This is a standard approach across all NICE guidelines

Graded Exercise Therapy

1. Definition
2. Evidence and Effectiveness
3. Experience of interventions
4. Overall

Graded exercise therapy (GET) – what we mean

Graded exercise therapy is defined in this guideline as therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in [the evidence review]

Graded exercise therapy – PACE definition

Graded exercise therapy was done on the basis of deconditioning and exercise intolerance theories of chronic fatigue syndrome. These theories assume that the syndrome is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity……… [GET] consisted of establishment of a baseline of achievable exercise or physical activity, followed by a negotiated, incremental increase in the duration of time spent physically active.

***Lancet* 2011; 377: 825**

Graded exercise therapy – Cochrane definition

Graded exercise therapy is characterised by establishment of a baseline of achievable exercise or physical activity, followed by a negotiated, incremental increase in the duration of time spent physically active followed by an increase in intensity

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Graded exercise therapy – CG53 definition

GET is an evidence-based self-management approach to CFS/ME involving appropriate physical assessment, mutually negotiated meaningful goal setting and education. It involves setting an achievable baseline of physical activity, followed by individually tailored and planned increases in duration of exercise. This is followed by an increase in intensity when able; taking into account a patient’s preferences and objectives, current activity patterns, sleep, setbacks, and emotional factors; with the objective of improving CFS/ME symptoms and functioning aiming towards recovery.

Evidence

Evidence from 12 randomised controlled trials were identified for graded exercise therapy.

Six studies compared graded exercise therapy to usual care, two studies to flexibility/relaxation, and single studies compared graded exercise therapy to heart rate variability feedback, adaptive pacing, intermittent exercise, and activity dairies.

Qualitative Review - Evidence was identified for both adults' and children/young people's experiences of GET

The quality of the evidence ranged from low to very low quality.

Significant methodological concerns with some studies reported by some commentators

Differences in outcomes were small and not maintained on long term follow-up

Interpretation

- The committee were not confident about the positive findings for GET. The outcomes showing benefit were mainly measured at short follow-up points and the results were not sustained over longer time periods. There was also inconsistency in the findings.
- Taking this into account, along with the harms identified in the qualitative findings and the committee's own experience, the committee made a negative recommendation
- However, they recognised the importance of energy management programmes and made positive recommendations for what those programmes should involve. They also made positive recommendations for physical activity or exercise programmes for those people with ME/CFS who want to undertake them.

Exercise & energy management – what we've said

- Do not offer people with ME/CFS:
    - any therapy based on physical activity or exercise as a cure for ME/CFS
    - generalised physical activity or exercise programmes – this includes programmes developed for healthy people or people with other illnesses
    - any programme that does not follow the approach in recommendation 1.11.13 or that uses fixed incremental increases in physical activity or exercise, for example, graded exercise therapy
    - physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories as perpetuating ME/CFS. *(1.11.14)*

Exercise & energy management – what we've said

- Help people with ME/CFS develop a plan for energy management as part of their care and support plan. Support them to establish realistic expectations and develop goals that are meaningful to them. (*1.11.13 – the recommendation also lists a range of elements to include in the plan*)
- Work with the person to establish an individual activity pattern within their current energy limits that minimises their symptoms. For example:
    - agree a sustainable level of activity as the first step, which may mean reducing activity
    - plan periods of rest and activity, and incorporate the need for pre-emptive rest
    - alternate and vary between different types of activity and break activities into small chunks. *(1.11.4)*

Exercise & energy management – why we've said it

- The committee recognised that energy management is one of the most important tools people with ME/CFS have to support them in living with the symptoms.
- It is important to help people to manage their energy effectively so as to avoid post-exertional malaise and a worsening of symptoms.
- It also supports people to increase their activity if possible, while maintaining their health.

Exercise & energy management – what we’ve said

- Refer people with ME/CFS to a physiotherapist or occupational therapist working in an ME/CFS specialist team if they:
  - have difficulties caused by reduced physical activity or mobility (also see the sections on physical functioning and mobility and care for people with severe or very severe ME/CFS) or
  - feel ready to progress their physical activity beyond their current activities of daily living (see the section on physical activity and exercise) or
  - would like to incorporate a physical activity or exercise programme into managing their ME/CFS (see the section on incorporating physical activity and exercise). *(1.11.8)*

Children and Young People – what we said

- Emphasis on child-centred approach and age appropriate communication
- Earlier time for suspecting (4 weeks) to reflect importance of timely support.
- Early referral to paediatrics and involvement of education/training.
- Care and support plan developed by paediatric ME/CFS specialist team
- Outlook thought to be better in children and young people than in adults
- Offer children and young people with ME/CFS a review of their care and support plan at least every 6 months – more frequently if needed

Safeguarding – what we said

Risk of symptoms of ME/CFS being considered indicative of abuse or neglect, ie:

- physical symptoms that do not fit a commonly recognised illness pattern
- more than 1 child or family member having ME/CFS
- disagreeing with, declining or withdrawing from any part of their care and support plan.
- Reduced or non-attendance at school

Follow the NICE guidelines on child maltreatment and child abuse and neglect.

Education – what we said

- Work with training and education services to
    - provide information about ME/CFS and the needs and impairments of CYP with ME/CFS
    - discuss the child or young person's care and support plan
    - discuss a flexible approach to training and education.
- Give parents and carers information about education, health and care (EHC) plans
- Advise children and young people with ME/CFS and their parents or carers (as appropriate) that:
    - training or education should not be the only activity they undertake
    - they should aim to find a balance between the time they spend on education or training, home and family life, and social activities.

CBT – what we said

- Discuss cognitive behavioural therapy (CBT) with adults, children and young people with ME/CFS (and their parents or carers, as appropriate). Explain:
    - its principles, including that it may help them manage their symptoms but it is not curative and
    - any potential benefits and risks. *(1.12.28)*
- Only offer CBT to adults, children and young people with ME/CFS if, after discussing it (see recommendation 1.12.28), they would like to use it to support them in managing their symptoms. *(1.12.29)*
- For children and young people with ME/CFS who would like to use CBT:
    - involve parents or carers (as appropriate) in the therapy wherever possible
    - adapt the therapy to the child or young person's cognitive and emotional stage of development. *(1.12.30)*

CBT – what we said

- Explain that CBT for people with ME/CFS:
    - aims to improve their quality of life, including functioning, and reduce the distress associated with having a chronic illness
    - does not assume people have ‘abnormal’ illness beliefs and behaviours as an underlying cause of their ME/CFS, but recognises that thoughts, feelings, behaviours and physiology interact with each other. (*1.12.32*)

CBT – why we've said it

- There were some positive findings for some outcomes with CBT but the quality of the evidence was all graded as low or very low and the findings were inconsistent.
- The committee acknowledged criticisms of CBT in the qualitative studies where it was used as a cure for ME/CFS.
- Based on the findings, the committee made a negative recommendation for the use of CBT as a cure for ME/CFS, but recognised that it has a role to play in managing the impacts of ME/CFS as a chronic condition, particularly in manging symptoms such as sleep, depression and dietary issues
- The guideline recommends discussing CBT with people and allowing them to make an informed decision about CBT.