# THE DIAGNOSIS OF BRAIN TUMOURS IN CHILDREN

QUICK REFERENCE GUIDE

An evidence based NICE accredited guideline to assist healthcare professionals in the assessment of babies, children and teenagers presenting with signs and symptoms that may be due to a brain tumour.

headsmart.org.uk



The complete guideline including methodology, evidence base and references can be viewed and downloaded from headsmart.org.uk.

The initial guideline was published in June 2008, the current version (version 2) was published in January 2017. The guideline is due for review in January 2022.

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# 1. GUIDELINE BACKGROUND, AIM AND SCOPE

This quick reference guide summarises the recommendations in the Diagnosis of Brain Tumours in Children guideline. The complete guideline including methodology, evidence base and references can be viewed and downloaded from headsmart.org.uk.

## **Background**

Approximately 450 children are diagnosed with a brain tumour each year in the UK. Brain tumours are the most common cause of cancer related death, with an annual mortality of nine per million (80 to 100 children annually in the UK). 60% of survivors are left with a life-altering disability.

It can be difficult for healthcare professionals to recognise when a child presents with the signs and symptoms of a brain tumour. Childhood brain tumours are relatively rare and have a very varied presentation. The signs and symptoms that precede diagnosis are diverse, fluctuate in severity and differ according to the tumour location and the developmental stage of the child. Many of the initial signs and symptoms of brain tumours are non-specific and mimic other more common and less serious disorders.

Children with brain tumours are frequently unwell for a prolonged period before the diagnosis is made. In the UK, the median symptom interval (time between symptom onset and diagnosis) for childhood brain tumours was over three months, this is longer than that experienced by children in other countries.

A prolonged symptom interval for childhood CNS tumours is associated with an increased risk of life-threatening and disabling neurological complications at presentation and a worse cognitive outcome in survivors. It has a detrimental effect on professional relationships

with patients and their families, and their subsequent psychological well-being.

The Diagnosis of Brain Tumours in Children guideline was written to support healthcare professionals in the recognition and assessment of children and young people presenting with signs and symptoms that could be due to a brain tumour. It aims to reduce prolonged symptom interval experienced by many UK children diagnosed with a brain tumour.

# Aim of the guideline

The guideline advises on the following:

- **1.** The signs and symptoms that may occur in children with a brain tumour.
- 2. Assessment of children presenting with these signs and symptoms.
- **3.** Indications and waiting times for imaging children with these signs and symptoms.

## Scope

#### Patient inclusion criteria

The guideline is applicable to all children aged 0-18 years who present with signs and/or symptoms that could result from a brain tumour and are being reviewed by a healthcare professional.

#### **Guideline users**

The guideline is intended to support the assessment and investigation by healthcare professionals of children who may have a brain tumour.

The guideline has been developed following careful consideration of the available evidence and has incorporated professional expertise via a Delphi consensus process. Healthcare professionals should use it to support their decision making when assessing children who may have an intracranial tumour.

It does not however override the responsibility of a healthcare professional to make decisions appropriate to the condition of individual children. > Statements in red text advise

Statements in the blue box advise on presentations frequently associated with misdiagnosis.

A one-page Sub-specialty summary is shown in Figure 2 on page 10. Downloadable version available at headsmart.org.uk/clinical

# 2. BEST PRACTICE

There are 94 recommendations in total with 48 strong recommendations. Levels of evidence and forms of recommendations are listed in the full guideline and are taken from SIGN, Scottish Intercollegiate Guideline Network (2015).

#### Consultation

- Parents and their carers should be asked explicitly about their concerns in any consultation.
- If a parent/carer expresses concerns about a brain tumour or symptoms attributable to a brain tumour this should be reviewed carefully. If a brain tumour is unlikely, the reason why should be explained with reference to the symptoms card/decision support tool and appropriate safety netting advice given.
- If a child warrants a review, the timing of this review should comply with national diagnosis of all cancers (currently, diagnosis or all clear should be given to the patient within four weeks).
- If the patient, parent/carer and healthcare professional are not fluent in a common language an interpreter must be used for the consultation (languageline.co.uk).
- Low parental educational level, social deprivation and lack of familiarity with the UK healthcare system may be associated with diagnostic delay.
   Care must be taken for appropriate safety netting with a multi-disciplinary approach for these families (for example health visitor liaison).

#### Referral

- A primary healthcare professional who has a high index of suspicion regarding a possible brain tumour should discuss their concerns with a secondary healthcare professional the same day.
- A child referred from primary care in which the differential diagnosis includes a possible space-occupying lesion should be seen in a rapid-access clinic or similar service (i.e. within two weeks).

# **Imaging**

- A child in whom CNS imaging is required to exclude a brain tumour (potential diagnosis but low index of suspicion) should be imaged and reported within four weeks to meet Department of Health recommendations.
- MRI is the imaging modality of choice for a child who may have a brain tumour.
- If MRI is not available a contrast enhanced CT should be performed.
- Imaging results should be interpreted by a professional with expertise and training in central nervous system MR and CT imaging in children.
- The need to sedate or anaesthetise a child for imaging should not delay diagnosis and should be compliant with Department of Health guidance.

# **Predisposing factors**

 Some predisposing factors (personal or family history of brain tumours, leukaemia, sarcoma and early onset breast cancer; prior therapeutic CNS radiation; NF1/2; tuberous sclerosis) are associated with an increased risk of childhood brain tumours.

Patients/parents should be specifically asked about these factors in consultation as their presence may lower the threshold for referral and investigation.

#### **Headaches**

- Consider a brain tumour in any child with a new, persistent\* headache
- · Headache in isolation, unlikely to be a brain tumour
- Brain tumour headaches occur at any time of day
- Children aged younger than 4 years may not be able to describe a headache observe behaviour

#### CNS imaging required with

- · Persistent headache that wakes a child from sleep
- Persistent headache that occurs on waking
- Persistent headache in a child under 4
- Confusion or disorientation with a headache
- Persistent headache with 1 or more other symptoms

#### Common pitfalls

 Failure to reassess a child with a migraine or tension headache when the headache character changes

\*Persistent = continuous or recurrent headache present for more than 4 weeks

#### Nausea and vomiting

- Consider a brain tumour in any child with persistent\* nausea and/or vomiting
- Head circumference should be measured and plotted in children under 2 with persistent vomiting

#### CNS imaging required with

- Persistent vomiting on waking (NB: exclude pregnancy where appropriate)
- Persistent nausea/vomiting with 1 or more other symptom

#### Common pitfalls

- · Failing to consider a CNS cause for persistent nausea and vomiting
- \*Persistent = nausea and/or vomiting present for more than 2 weeks

#### Visual signs and symptoms

- · Consider a brain tumour in any child with persistent\* visual abnormality
- · Visual assessment requires assessment of:
- · visual acuity
- eye movements
- pupil responses
- · optic disc appearance
- visual fields (>/= 5 yrs)
- Pre-school and unco-operative children should be assessed by hospital eye service within 2 weeks of referral
- · Parent concern alone warrants referral for visual assessment

#### CNS imaging required with

- Papilloedema
- Optic atrophy
- New onset nystagmus
- · Reduction in visual acuity not due to refractive error
- · Visual field reduction
- Proptosis
- New onset paralytic squint
- Visual symptom with 1 or more other symptom

#### Common pitfalls

- Failure to fully assess vision REFER IF NECESSARY
- Failure of communication between community optometry and primary and secondary care
- \*Persistent = visual abnormality present for more than 2 weeks

## Referral from primary care

- High risk of tumour SAME DAY referral
- Lower risk\* specialist assessment with

## **Imaging**

- High risk of tumour URGENT CNS imagi
  - Lower risk\* CNS imaging within 4 week
- \*Lower risk = CNS tumour in differential diagn

#### CONSIDER A BRAIN TUMOUR I

- Headache
- Nausea and/or vomiting
- Visual symptoms and signs: reduced visual acuity and/or field abnormal eye movements abnormal fundoscopy
- Motor symptoms and signs: abnormal gait abnormal co-ordination focal motor weakness
  - Growth and endocrine symptoms:
    growth failure (weight/height)
    delayed, arrested or precocious p
    galactorrhoea
    primary/secondary amenorrhea
- · Increasing head circumference
- · Behavioural change
- · Diabetes insipidus
- Seizures (see www.nice.org.uk/guidano
- Altered consciousness (see www.nottin Guidelinealgorithm.pdf)

#### Assess these children with

- History: associated symptoms, any predisposing factors
- Examination of:

visual system motor system height and weight head circumference (<2yrs)

pubertal status

IF TWO OR MORE SYMPTOMS - SCAN

This guideline has the support of the RCPCH following a rigorous assessment of the guideline development methodology and a full endorsement is expected upon completion of a full stakeholder consultation.

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#### I: A GUIDELINE FOR HEALTHCARE PROFESSIONALS

•

to secondary care in 2 weeks

osis, low index of suspicion

## N ANY CHILD PRESENTING WITH

uberty

:e/qs27) gham.ac.uk/paediatric-guideline/

# Ask about common predisposing factors

- Personal or FH of brain tumour, sarcoma, leukaemia or early onset breast cancer
- Neurofibromatosis
- Tuberous sclerosis
- Other familial genetic syndromes

#### Assessment pitfalls

- Initial symptoms of brain tumour can mimic other common illnesses
- Symptoms frequently fluctuate resolution then recurrence does not exclude a brain tumour
- A normal neurological examination does not exclude a brain tumour
- Language difficulties use interpreter

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#### **Head circumference**

- Consider a brain tumour in any child under two years with an increasing head circumference outside the normal range in comparison to their height and weight
- Careful assessment of other signs and symptoms of a brain tumour should be undertaken in these babies

#### CNS imaging required with

- · Rapid rate of head circumference growth crossing centiles
- · Increasing head circumference with any other associated symptoms

#### **Common pitfalls**

 Failing to measure and monitor head circumference in a baby or young child with persistent vomiting

#### Motor symptoms and signs

- · Consider a brain tumour in any child with persisting\* motor abnormality
- · Motor assessment requires history or observation of:

sitting and crawling in infants

walking and running

handling of small objects

handwriting in school age children

 Brain tumours can cause a loss or change in motor skills and this can be subtle e.g. ability to play computer games

#### **CNS** imaging required with

- · Regression in motor skills
- · Focal motor weakness
- Abnormal gait/co-ordination (unless local cause)
- Bells palsy with NO improvement within 4 weeks
- · Swallowing difficulties (unless local cause)
- Head tilt/torticollis (unless local cause)
- Motor symptom with 1 or more other symptom

#### **Common pitfalls**

- Attributing abnormal gait/balance to middle ear disease with no corroborating findings
- Failure to identify swallowing difficulties and aspiration as a cause of recurrent chest infections.

\*Persistent = motor abnormality present for more than 2 weeks

#### **Growth and endocrine**

- Consider a brain tumour in any child with any combination of growth failure, delayed/arrested puberty and polyuria/polydipsia
- Early specialist assessment if required for:

precocious puberty/delayed or arrested puberty

growth failure

galactorrhoea

primary or secondary amenorrhoea

#### **CNS** imaging required with

• Growth or endocrine symptom with 1 or more other symptoms

#### **Common pitfalls**

- · Failing to consider a CNS cause in children with weight loss and vomiting
- Failure to consider diabetes insipidus in children with polyuria and polydipsia

#### **Behaviour**

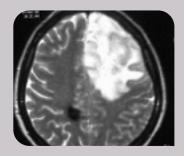
 Consider a brain tumour in any child with new onset lethargy, mood disturbance, withdrawal or disinhibition

#### **Common pitfalls**

Failing to consider a physical cause for behavioural symptoms

# **PRESENTING SYMPTOMS O**

# 4. SUB-SPECIALTY SUMMARY (FIGURE 2)



Supratentorial tumours can cause change in personality, mood or disinhibition. They can also cause symptoms of anorexia. A brain tumour needs to be considered as part of the differential diagnosis.

# **PSYCHIATRY**

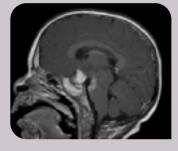


- Behavioural change
- Depression



COMMUNITY

- Developmental de
- Developmental reg



Central tumours such as optic pathway glioma are slow growing and will present with progressive visual symptoms that may present to an ophthalmologist.

## OPHTHALMOLOGY



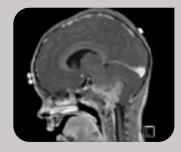
- Decreased visual acuity
- Nystagmus/parinauds
- Diplopia
- Squint
- Visual field defect





Nausea and vomit

Abdominal pain



Head tilt or torticollis can be caused by a posterior fossa tumour. These symptoms may present to ENT specialists as head tilt and torticollis have other common ENT causes.

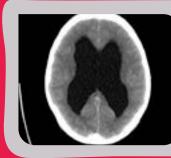
# EAR, NOSE AND THROAT

- Dizziness
- Vertigo
- **Torticollis**
- Head tilt
- Hearing loss
- **Tinnitus**



# GASTROENTEROLO

- Reflux



# F BRAIN TUMOURS BY SUB-SPECIALTY

A young child with hydrocephalus caused by a brain tumour will have an increasing head circumference and developmental delay or regression.



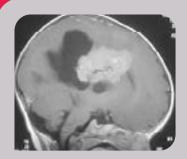
lay

gression

## NEUROLOGY

- Seizures
- Motor weakness
- CN palsies





A supratentorial cortical tumour will present with focal neurological signs such as weakness.

#### **ENDOCRINOLOGY**

- Growth problem
- Hypo-pit/pituitary dysfunction
- Diabetes insipidus
- Precocious or delayed puberty
- Menstrual irregularities
- Galactorrhoea



Central tumours such as a craniopharyngioma are slow growing and will present with abnormal growth or precocious or delayed puberty. These children may also have visual symptoms.

# )**G**Y ing



# RESPIRATORY



- Recurrent chest infections



A child with hydrocephalus caused by a brain tumour will have persistent vomiting. In infants where the sutures are not yet fused there will be no other signs of hydrocephalus aside from macrocephaly.

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Recurrent respiratory infections can occur secondary to aspiration caused by a bulbar palsy. This MRI shows a brainstem tumour which causes cranial nerve palsies.

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# ASSESSMENT OF A CHILD WITH A POTENTIAL BRAIN TUMOUR

# Presenting signs and symptoms

The following signs and symptoms are all associated with childhood brain tumours. Their presence should alert the clinician to this possibility.

#### Headaches

Nausea and/or vomiting

Increasing head circumference (crossing centiles)

#### Visual signs and symptoms including:

- Reduced visual acuity
- Reduced visual fields
- Abnormal eye movements
- Abnormal fundoscopy

#### Motor signs and symptoms including:

- Abnormal gait
- Abnormal co-ordination
- Focal motor abnormalities
- Head tilt/torticollis

# Growth and endocrine abnormalities including:

- · Growth failure
- · Delayed, arrested or precocious puberty
- Galactorrhoea
- Primary/secondary amenorrhoea

#### Behavioural change including:

- New onset mood disturbance
- New onset pervasive lethargy
- New onset withdrawal
- New onset disinhibition

#### Diabetes insipidus

#### Seizures

(see www.nice.org.uk/guidance/qs27)

#### Altered consciousness

(see www.nottingham.ac.uk/
paediatric-guideline/Guidelinealgorithm.pdf)

Signs and symptoms in childhood brain tumours may occur singularly or in combination.

## **History**

- Take detailed history and enquire specifically about:
  - Other symptoms

     (as listed on previous page)
  - Predisposing factors
  - Family history

#### **Assessment**

- Assess:
  - Visual system
  - Motor system
  - Height and weight
  - Head circumference if under two years
  - Pubertal status
- The initial symptoms of a brain tumour frequently mimic those that occur with many common childhood conditions.
- Symptoms frequently fluctuate in severity

   resolution and then recurrence does not exclude a brain tumour.
- Presentation depends upon the age of the child.
- A normal neurological examination does not exclude a brain tumour.

It is important to note that due to the nonspecificity of the symptoms, some children may be referred to sub-specialty doctors. A detailed history and assessment is required in these children if the cause of the symptoms is not clear. Figure 2 on page 10 shows the signs and symptoms in relation to the system/specialty.

# 6. SIGNS AND SYMPTOMS IN A CHILD WITH A POTENTIAL BRAIN TUMOUR

#### **Headaches**

A headache is a common symptom and is very rarely, in isolation, due to a brain tumour.

Any child presenting with a persistent headache (a persistent headache is defined as occurring on most days for four weeks or more) should be assessed carefully for the other symptoms of a brain tumour, as listed in the presenting symptoms section of this guideline.

A child with a headache without a clear cause requires careful review, the timing of which needs to be mindful of the differential diagnoses.

Brain tumour headaches can occur at any time of the day or night.

Children aged younger than four years, or those with communication difficulties, are frequently unable to describe the headache. Their behaviour (e.g. withdrawal, holding head) may indicate a headache.

In a child with a known migraine or tension headache a change in the nature of the headache requires reassessment and review of the diagnosis.

For more information regarding headaches there is a NICE guideline called "Headaches in over 12s: diagnosis and management" www.nice.org.uk/guidance/cg150/chapter/recommendations

Delayed diagnosis has been associated with:

Failure to reassess a child with a migraine or tension headache when the headache character changes.

# CNS imaging required for:

- Persistent headaches that wake a child from sleep.
- Persistent headaches that occur on waking.
- A persistent headache occurring at any time in a child younger than four years.
- Confusion or disorientation occurring with a headache.
- A persistent headache with one or more other signs/symptoms associated with a brain tumour (i.e. nausea/vomiting, visual symptoms, increasing head circumference, motor symptoms, growth and endocrine symptoms, behavioural change).

# Nausea and vomiting

Early specialist referral for consideration of underlying causes including CNS causes is required for a child with persistent nausea and/or vomiting.

(Nausea and/or vomiting that lasts for more than two weeks should be regarded as persistent).

Babies and young children under the age of two who may not be able to communicate other symptoms of raised intracranial pressure should have their head circumference measured, plotted and compared with previous measurements.

Delayed diagnosis has been associated with:

Attributing persistent nausea and vomiting to an infective cause in the absence of corroborative findings (e.g. contact with similar illness, pyrexia, diarrhoea).

# CNS imaging required for:

- Persistent vomiting on awakening (either in the morning or from a daytime sleep).
- Persistent nausea and/or vomiting with one or more other signs/symptoms associated with a brain tumour (i.e. headache, visual symptoms, increasing head circumference, motor symptoms, growth and endocrine abnormalities, behavioural change) require CNS imaging.
- · NB: exclude pregnancy where appropriate.

#### **Head circumference**

A rapidly increasing head circumference (crossing centiles) can be a sign of an underlying brain tumour and requires referral to secondary care.

In all babies with an increasing head circumference (crossing centiles), careful assessment of other signs and symptoms associated with a brain tumour should be undertaken.

In babies in whom a head circumference is crossing centiles and a brain tumour is suspected an MRI is the imaging modality of choice within the appropriate timescale.

Delayed diagnosis has been associated with:

Failure to measure head circumference in babies with unexplained persistent vomiting.

# CNS imaging required for:

- A rapidly increasing head circumference crossing centiles.
- An increasing head circumference with one or more other signs/symptoms associated with a brain tumour (i.e. headache, nausea/vomiting, visual symptoms, motor symptoms, endocrine or growth symptoms, behavioural change) require CNS imaging.

# Visual signs and symptoms

Consider a brain tumour in any child presenting with a persisting visual abnormality (any visual abnormality lasting longer than two weeks should be regarded as persistent).

Parental/carer concern alone (including nursery staff) regarding a baby or young child's vision should be taken seriously and a referral for visual assessment should be made.

# Visual assessment must include assessment of:

- Pupil responses
- Visual fields in school age children
- Eye movements
- Optic disc appearance
- Visual acuity

If the assessing healthcare professional is unable

to perform a complete visual assessment the child should be referred for assessment.

Children referred for visual assessment with signs or symptoms suggestive of a brain tumour should be seen in a rapid access clinic or similar service (i.e. within two weeks).

Community optometry should refer any child with abnormal eye findings suggestive of a possible brain tumour directly to secondary care.

Consideration should be given to the appropriate place of assessment. If appropriate community optometry expertise is not available, pre-school and uncooperative children should be assessed by the hospital eye service.

A child with a new onset non-paralytic (concomitant) squint should have early ophthalmological assessment for consideration of underlying causes (including CNS causes).

# Delayed diagnosis has been associated with:

Failure to fully assess vision in a young or uncooperative child.

Failure of communication between community optometry and primary and secondary care.

## **CNS imaging required for:**

- Papilloedema.
- · Optic atrophy.
- New onset nystagmus.
- Reduction in visual acuity not attributable to an ocular cause.
- Visual field reduction not attributable to an ocular cause.
- · Proptosis.
- New onset paralytic (non-concomitant) squint.
- Visual abnormality with one or more other signs/symptoms associated with a brain tumour (i.e. headaches, nausea/ vomiting, increasing head circumference, motor symptoms, growth and endocrine abnormalities, behavioural change) require CNS imaging.

# Motor signs and symptoms

Consider a brain tumour in any child presenting with a persisting motor abnormality (any motor abnormality lasting longer than two weeks should be regarded as persistent).

A history of a change or deterioration in motor skills may indicate a brain tumour e.g. change in hand or foot preference, developmental regression, changes in gait, difficulties with balance.

History should enquire into subtle changes in motor skills e.g. loss of learned skills (computer games, sport, handwriting).

Assessment of a child's fine motor and visual-motor skills should include questioning or observation of:

- Handling of small objects e.g. cup, spoon, small toy.
- Handwriting in older children.

Delayed diagnosis has been associated with:

Attributing abnormal balance or gait to middle ear disease in the absence of corroborative findings.

Failure to identify swallowing difficulties as the cause of recurrent chest infections or "chestiness".

# CNS imaging required for:

Any child with focal neurological signs, for example:

- Regression in motor skills.
- Abnormal gait or co-ordination unless attributable to a non-neurological cause.
- · Focal motor weakness.
- Swallowing difficulties, without a local cause.
- Abnormal head position, without a local cause.
- A motor abnormality with one or more other signs/symptoms associated with a brain tumour (i.e. headache, nausea/ vomiting, visual symptoms, increasing head circumference, growth and endocrine abnormalities, behavioural change) require CNS imaging.

#### **Growth and endocrine**

Consider a brain tumour in any child presenting with any TWO of the following:

- Growth failure
- Delayed or arrested puberty
- Polyuria and polydipsia
- Galactorrhoea
- Primary/secondary amenorrhoea

If the history raises any concern, including parental concern, about any aspect of growth, the child's height, weight and head circumference (if under two years of age) should be measured and plotted on a growth chart.

A child with a height or weight outside the normal range (<0.4th or >99.8th centiles, crossing centiles due to increased or decreased velocity outside that expected for age/pubertal stage or parental target range) should be referred to secondary care for assessment of their growth (see centile charts).

Brain tumours can present with rapid weight loss or faltering growth, however the differential diagnosis when presented with this symptom is wide. If a young person presents with rapid weight loss, the other signs and symptoms of a brain tumour should be specifically looked for as part of the assessment.

Early referral to secondary care is required for children presenting with precocious puberty, delayed or arrested puberty, growth failure, galactorrhoea, primary/secondary amenorrhoea or polyuria/polydipsia.

Tumours affecting the midline supratentorial part of the brain can also affect vision. Children presenting with the above symptoms require a full visual assessment.

Delayed diagnosis has been associated with:

Attributing impaired growth with vomiting to gastrointestinal disease in the absence of corroborative findings.

Failure to consider diabetes insipidus in children with polyuria and polydipsia.

Failure to consider a brain tumour in young people with symptoms suggestive of an eating disorder.

Failure to assess vision in children presenting with these symptoms.

# CNS imaging required for:

 An endocrine or growth abnormality with one or more other signs/ symptoms associated with a brain tumour (i.e. headaches, nausea/ vomiting, visual symptoms, motor symptoms, increasing head circumference, behavioural change) require CNS imaging.

# **Behaviour**

Brain tumours can manifest with neuropsychiatric symptoms including:

- New onset mood disturbance
- Withdrawal
- Disinhibition
- Pervasive lethargy

If a child or young person presents with these symptoms, the other signs and symptoms of a brain tumour should be specifically looked for as part of the assessment.

Environmental context is important when assessing lethargy: a child who is lethargic in situations in which they are normally active requires further assessment.

Delayed diagnosis has been associated with:

Attributing behavioural change to "normal adolescent behaviour" and/or attributing mood disturbances to a psychiatric cause without full physical assessment.

#### **Further information**

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NICE has renewed accreditation of the process used by the Children's Brain Tumour Research Centre, University of Nottingham to produce The Diagnosis of Brain Tumours in Children guideline. The renewed accreditation is valid until January 2022. More information on accreditation can be viewed at www.nice.org.uk/accreditation.