REVIEW

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Strategies to accelerate diagnosis of primary brain tumors at the primary–secondary care interface in children and adults

David Walker^{*1}, Willie Hamilton², Fiona M Walter³ & Colin Watts⁴

Practice Points

- Is the time right to apply UK health strategy to promote early diagnosis in brain tumors across all ages?
- Primary brain tumors represent a serious health risk for populations as a result of the high risk of disability and early mortality.
- Novel treatment approaches are improving outcomes, particularly in children.
- Low-grade tumors (benign) in children account for 40% and are associated with >90% long-term survival, although many have focal disability.
- Low-grade (grade 2) tumors in adults are more accurately described as premalignant and are associated with a high risk of malignant transformation within 1–7 years.
- The public's top priority is to improve diagnosis; its speed and accuracy, the way it is communicated and access to specialist services.
- Studying factors affecting the total diagnostic interval will identify the blocks to diagnosis.
- Raising professional and public awareness, providing reassurance, identifying pathways of referral and monitoring impact upon practice against a target can lead to service improvement.
- Alarm symptoms alone are poor indicators for selecting patients for scanning to diagnose brain tumors.
- Direct access to brain imaging from primary care may accelerate diagnosis if effective selection criteria are developed.

SUMMARY This article presents a shared view from practitioners with special interests in diagnosing and managing primary brain tumors in both primary and secondary care, in adult and pediatric disciplines; it examines the complexity of identifying whether it would be of benefit and feasible to try to identify those with brain tumors earlier, how this could be achieved and what evidence exists to justify such an approach. The experience of the

¹Children's Brain Tumor Research Centre, Queen's Medical Centre, Nottingham, NG7 2UH, UK

²University of Exeter, Veysey Building, Salmonpool lane, Exeter, EX2 4SG, UK

³General Practice & Primary Care Research Unit in the Department of Public Health & Primary Care, University of Cambridge, Cambridge, UK

⁴Cambridge University, Department of Clinical Neurosciences, Division of Neurosurgery, ED Adrian Building, Forvie Site, Robinson Way, Cambridge, CB2 0PY, UK

*Author for correspondence: david.walker@nottingham.ac.uk

HeadSmart Campaign in childhood brain tumor, using awareness as a method for driving service change, is used to illustrate how diagnostic practice can be changed across the primary and secondary care interface. This article highlights the importance of focusing upon the needs of patients with primary brain tumors as they represent a significant set of life-threatening and disabling diseases with significant implications for cancer and palliative services.

Promoting early diagnosis of all cancer is a recognized UK health strategy [1,2]. This article explores how this is being applied to accelerate diagnosis of CNS tumors in children (<18 years of age) and how it could be approached in adults. Here, we focus on primary brain tumors, which classically present *de novo*, while secondary tumors, although at least as common as primary brain tumors, are usually heralded by the prior cancer diagnosis.

■ Brain tumors as a population health risk

Brain tumors present across all age groups from infancy to old age with a bimodal distribution

peaking in childhood and old age (incidence curves in Figure 1). In the UK, approximately 450 childhood CNS tumors, which are almost exclusively primary tumors, are diagnosed each year affecting children up to 15 years of age. They are the most common solid tumor of childhood, accounting for 27% of all malignancies [3,4]. Involvement of the brain is a risk for 55% of childhood malignancy, with 30% accounted for by acute leukemias.

In adulthood, over 4000 new primary malignant brain tumors are diagnosed annually affecting approximately seven individuals in 100,000 of the general population [5]. The

Figure 1. Average number of new cases of brain and CNS (C70-72) tumors in the UK and age-specific incidence rates per 100,000 between 2006 and 2008.

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lifetime risk for brain cancer is one in 160. Although brain tumors account for less than 2% of all primary neoplasms, the high mortality means they rank as the third-leading cause of cancer-related death among men aged 15–54 years and the fourth-leading cause of cancer-related death among women between 15 and 34 years of age [6].

Across the age groups, brain tumors are the most common cause of cancer-related deaths in children and people up to 40 years of age. Brain involvement with malignancies is a risk for up to 55% of all cancer cases across the age groups. Effective treatment of secondary CNS malignancies is recognized as the rate-limiting step to cure in most cancers that respond to systemic therapies.

There is a health service disconnect between the rarity of primary brain tumors and their high ranking among causes of cancer deaths that causes concern to both the public and specialists, especially when they are diagnosed in young or middle-aged people who have families, partners and are in full-time employment [3,4,7–8,101].

Clinical outcomes: children & adults

In childhood, modern treatments offer 5-year survival rates of up to 75%, with over half surviving long term. The majority are offered treatment within clinical trials, which emanate from European and international trial collaborations, many led by UK translational researchers [9]. This means that treatments are evidence based and evolving. Despite this, 60% of survivors experience moderate or severe life-long disability [10,11], which, with current first-world life expectancy, means that every new patient represents 65 life years at stake. With long-term survival of at least 50% expected in the UK, 14,652 life years are estimated to be lost and gained, annually. For those gained, the 60% disability rate (moderate or severe) means that an estimated 8775 life years, each year, are associated with moderate or severe life-long disability, with the societal and health demands that this creates.

In adulthood, population-based survival statistics are rare and tend to report patients with primary intrinsic tumors. These heterogeneous cancers include pilocytic astrocytomas (WHO grade 1), which occur in children and have a 10-year survival rate of 96%, and do not undergo malignant transformation into a more aggressive clinical phenotype. WHO grade 2 gliomas include astrocytomas

(median survival: 5.6 years), oligodendrogliomas (median survival: 11.6 years) and mixed oligoastrocytomas (median survival 6.6 years). On the other hand, these latter tumors undergo malignant transformation into a more aggressive clinical phenotype. The mechanism of transformation is poorly understood, but care should be taken to avoid thinking of these cancers as benign and nonthreatening. They are ‘pre-malignant’ and are part of a phenotypic spectrum that includes high-grade disease. Anaplastic astrocytoma (median survival: 1.6 years) and anaplastic oligodendrogliomas (median survival: 3.6 years) represent WHO grade 3 high-grade cancers and WHO grade 4 glioblastoma multiforme represents the malignant extreme with a median survival of just 0.4 years [12]. Since brain cancer covers a broad age spectrum, the average years of life lost by patients is estimated to be 20.1 years compared with a mean of 12.6 years for all cancers [13].

Raising concerns about children & young people

Over the past decade, in the UK, public concern that delays in diagnosis for brain tumors are disadvantaging children and young people were repeatedly expressed to practitioners, through complaints processes, in the courts, in the media and in parliament. The National Health Service did not seem responsive to their needs. The 2005 NICE Suspected Cancer Referral Guideline focused on selecting patients for a secondary care referral within the 2-week wait scheme rather than directly accessing brain imaging [14]. It has had no discernible impact in children and young people. More recently, public concerns about cancer in children and young adults, and brain tumors in particular, were prioritized in a national manifesto, presented in the UK Houses of Parliament by a consortium of brain tumor charities, and were the subject of concern in young people affected with cancers of all types, and brain tumors in particular [8,101].

■ Are delays in diagnosis a problem in adult practice?

The National Patient Safety Agency (NPSA) ranked brain tumors eighth for adverse event reporting linked to cancer-related diagnostic delay, accounting for 3% of all diagnostic delays and 2% of high-risk presentations [7]; few other studies have been published. The main public concerns surrounding diagnosis are related to

the shock of the diagnosis, the methods of communication and poor prognosis for the majority of patients, as well as the lack of new treatments or clinical trials within the UK.

Accelerating diagnosis

It is not possible to reliably diagnose any brain tumor without a brain scan and, in the vast majority of cases, a histological diagnosis. The symptomatology is dictated by the key elements of medical and family history, the age of the patient, the anatomical location of the tumor and the identification of symptoms or signs of raised intracranial pressure, and/or signs of focal neurological deficit. The progressive enlargement of any tumor within the brain puts the patient at risk of incremental neurological damage due to compression or invasion, or sustained elevated intracranial pressure due to tumor growth or secondary hydrocephalus.

Reducing the time to diagnosis of primary brain tumors would offer the opportunity to:

- Intervene earlier in the disease's progress and reduce the risk of acquired neurological disability due to tumor-related brain injury prior to, or at the time of, surgery or radiation therapy;
- Reduce the number of initial operations conducted as urgent or emergency procedures owing to severe raised intracranial pressure with the associated enhanced mortality and morbidity risks;

- Reduce patients' and families' anxieties about the consequences of avoidable delays in diagnosis, whether they are due to patient and family delays, or physician and health system delays;

- Enhance the public's confidence in the health services.

■ Total diagnostic interval

The time from symptom onset identified by the patient and/or family until the date of diagnosis and commencement of treatment after diagnosis, is called the total diagnostic interval (TDI). The components of the interval are specified in the recently published the Aarhus Statement (Box 1 & Figure 2) [15,16]. These definitions were developed using systematically reviewed international evidence, and the expertise of researchers and practitioners from primary care and adult practice. They are yet to be validated in pediatric practice. It is notable that, in younger children, the parent plays the key role as observer and advocate in reporting signs and symptoms and seeking advice regarding referral.

Strategies aimed at reducing the TDI require each interval component to be addressed specifically, with a view to their minimization. In their thematic review 'Delayed Diagnosis of Cancer', the NPSA scoped the safety issues, identified possible solutions and made patient, practitioner and policy-maker safety recommendations [7].

Box 1. Aarhus definitions.

- At the patient level, the appraisal and health-seeking interval occurs while the patient and family become aware of symptoms and decide whether to seek advice from their GP
- At a primary health system level, the GP (recognition of symptoms) interval is while the primary care practitioner assesses symptoms and makes an assessment to justify investigation or referral, plus the processes associated with the initiation of investigation or referral
- The secondary healthcare system interval is the time taken to make arrangements for assessment, physician/surgical recognition of symptoms and the processes of performing diagnostic investigations
- The pretreatment interval is the time taken to initiate the first treatment after diagnosis; in brain tumors this is normally the time until the date of primary surgery

GP: General practitioner.

Childhood & teenage & young adult brain tumors (<25 years): a specialist view point

In childhood, the distribution of tumors differs anatomically from adult counterparts, as nearly 60% present in the posterior fossa, involving the brainstem or cerebellum with symptomatology linked to those structures and the risk of obstructive hydrocephalus (Figure 3). Headache in children and young people, while important as a symptom, affects only 33% of cases at presentation and is rare in very young children under 2 years of age who cannot verbalize, and whose unfused skull bones can accommodate raised intracranial pressure. The combination of symptoms of raised intracranial pressure with one or more new-onset focal neurological deficits, such as visual disturbance of eye movements or function, head tilt, accelerated head growth in infants and other motor signs, are the most common combinations heralding a diagnosis. The low-grade/benign tumors, which constitute the largest group (40%), commonly involve the

Figure 2. Overall milestones and time intervals in the route from first symptom until start of treatment.

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hypothalamus, optic pathways and cerebellum. Sustained raised intracranial pressure can cause global brain injury, causing blindness owing to optic atrophy or cortical injury, and impairing subsequent cognitive capacity, which, if it occurs in early life, can profoundly affect global development. Delayed diagnosis, therefore, can cause increased mortality and threaten life-long neurological and cognitive function.

■ Enhancing pathways of secondary care in adults

Primary brain tumors in adults are more commonly supratentorial in location. Headache due to focal brain swelling and raised intracranial pressure is a common, but late symptom. Patients with these symptoms are not generally selected for brain scanning until there is clear evidence of focal neurological deficit, epilepsy or symptoms or signs of raised intracranial pressure. They, therefore, present a diagnostic challenge to discern brain tumor as a cause from the many other headache syndromes. Many patients are diagnosed as ‘emergencies’, rather than via the 2-week wait referrals, and wait in their referring hospital until a neurosurgical bed is available, at which point they are transferred, often for surgery the following day. Streamlining such referrals via dedicated preparatory neurosurgical oncology clinics at

this early stage has been piloted (Figure 4) and found to be efficient and cost effective [17]. The alternative pathway of diagnosis is linked to observing patients with low-grade tumors (grades 1 and 2) who have presented with less acute neurological problems and are under surveillance for evidence of tumor growth or transformation. Therefore, these low-grade tumors do not present acutely. Evidence for the benefits of surgery, medical therapy or radiotherapy remains under investigation [18].

Along with enhanced organization of patient pathways, tackling the prevailing pessimism towards the efficacy of surgery for high-grade glioma, including glioblastoma, is essential to promote timely initiation of treatment after diagnosis. These elements of the process of care complement a policy of aggressive clinical intervention, including attempted maximal resection over biopsy or subtotal resections when it is safe to do so. Recent evidence has clearly demonstrated that substantial gains in survival are possible with such intensified surgical techniques and oncological management [19,20]. The UK NICE, in its Improving Outcomes Guidance for people with brain and other CNS tumors, has made such recommendations [18]. The concentration of surgical expertise in fewer surgeons can be anticipated to enhance outcomes as has been seen in other cancers (e.g., breast and

Figure 3. Ranked tumor symptoms by anatomical region in the brain.

colon) [21,22]. Pediatric neurosurgeons treating high caseloads of children with posterior fossa tumors obtain better rates of gross tumor resection, a major predictor of survival, and lower associated morbidity [23]. The introduction of new technologies through integrated research is an essential step to include in such service redesign [17,24].

General practitioner viewpoint on diagnosing brain tumors across the age groups

As general practitioners (GPs), attempting to respond to the specialists' viewpoints and the stark consequences for individuals ultimately diagnosed with a brain tumor, it places us in the challenging position to develop strategies to identify patients at risk and broach such a serious diagnosis, whilst conducting a busy clinic. It is not surprising that some shrink from the task. To feel that one may have contributed to an avoidable delay is the last experience anyone would want. Childhood cancer can affect any system and is every GP's nightmare. It is a once in a career diagnosis, so individual GPs have no

chance at all of building up experience of the disease. Worse still, brain tumors account for less than a quarter of childhood cancers, so a single GP will be extremely unlikely to encounter such a child. However, the risk for the child is one in 600 for any cancer and one in 2400 for brain cancer. GPs do know that some childhood brain tumors have a good prognosis – but only if identified early. We also see a lot of ill children in GP surgeries, and for the vast majority a brain tumor never even enters the list of diagnostic possibilities. We face similar diagnostic challenges for adults with brain tumors where symptoms such as headache are common, but a brain tumor is a rare diagnosis.

To try and approach the challenges for primary care in a systematic way, the Aarhus framework was developed to assist with breaking down the elements of the TDI so that strategies could be developed to influence each component [16]. The overlap with the NPSA recommendations is reassuring. By reviewing available evidence, covering the primary care elements of the TDI, we hope to identify strategies to influence this interval.

■ Symptom appraisal & help seeking: approaches to reduce patient delay

Delays in cancer diagnosis have been attributed to patient, as well as healthcare system, factors [25–27]. The National Awareness and Early Diagnosis Initiative, launched in 2008 by Cancer Research UK with the Department of Health, aims to improve the public's awareness of the signs and symptoms of cancer, and encourage those with symptoms to seek help earlier [1,2]. A number of sociodemographic, psychosocial and clinical factors have been associated with speed of diagnosis in other cancers, with older age, male gender, living alone and lower educational level as contributory to longer TDIs [28,29]. Psychosocial factors such as fears about the diagnosis of cancer and the consequences, nondisclosure of a symptom and self-medication have also

been shown to contribute to patient delay [30,31]. The nature of symptoms is an important predictor of help-seeking behavior; pain or bleeding is associated with shorter intervals, but nonspecific symptoms, or those that do not interfere with daily activities, tend to present later [29]. Failure to recognize the seriousness of symptoms or misattributing them to existing conditions or another more common cause has been previously described [29]. It is likely that a combination of these factors also affects presentation with primary brain tumors. Furthermore, a meta-ethnography of patient help-seeking experiences in relation to delays in cancer diagnosis confirmed strong similarities across patients with different cancer types, and highlighted the recognition and interpretation of symptoms as of key importance [32].

Figure 4. Pathway of care.

MDT: Multidisciplinary team.

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Figure 5. Model of pathways to treatment.

HCP: Healthcare provider.

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Little is known about the processes of symptom detection, help-seeking decisions and experiences of pathways to presentation of patients with brain tumors. There have been no prospective studies relating to brain tumors. Where retrospective studies have been carried out, none have included children, whose parents play a critical role in the appraisal phase. A theoretical model of pathways to treatment has been recommended by a recent international consensus group (Figure 5) [33]. A UK qualitative study exploring patient factors found that, for brain tumor patients, neurocognitive symptoms such as dysarthria, alterations in perception, seizures and hallucinations were the primary symptoms that patients complained about [34].

The help-seeking interval was most influenced by changes in health affecting daily living activities; this was particularly noted among people with brain cancer for whom neurocognitive symptoms, such as an inability to dress, prompted help-seeking. Such studies using interviews must be interpreted with caution in

view of the risk of recall bias, particularly for people with long delay periods or whose diagnosis and/or treatment were traumatic, or where the symptoms had an impact on daily living activities.

■ GP recognition of symptoms interval

Several relevant epidemiological studies have been reported in the last year, and they serve to underline the problems that UK primary care has with the diagnosis of brain tumors across all age groups. In an analysis of the 2010 National Cancer Patient Experience Survey in England, Lyratzopoulos *et al.* reported that all patients with brain tumors (children, teenage and young adults [TYAs], and adults) were much more likely to report symptoms to their GP than many of those with other cancers (odds ratio for brain vs rectal tumors: 1.9; 95% CI: 1.5–2.6) [35]. People with brain tumors are also more likely to have a long primary care interval compared with all other common cancers [36,37]. Lyratzopoulos *et al.* identified that people with

brain tumors (again, adults as well as younger patients) are also more likely than those with other cancers to have their tumor diagnosed after an emergency presentation with a seizure, and some of these presentations may occur after an initial symptomatic presentation that did not lead to suspicion of brain cancer [38]. Indeed, only 1% of adult brain tumors are diagnosed following fast-track GP referral for suspected cancer [39]. It would seem from these data that the diagnosis is rarely being considered in primary care and diagnosis results from an emergency or investigations initiated in secondary care. GPs in the UK have not routinely had a direct ability to request brain imaging. Recent discussions have proposed that this will change in the future [40].

Research into symptomatology

Researching the diagnosis of primary brain tumors at the primary care level using the Clinical Practice Research Datalink (CPRD) with historical GP records for over 13 million patients available, offers currently the best research tool. It avoids recall bias. However, it misses symptoms that patients have not reported, those unrecorded by the GP and, in the case of children, it misses the concerns expressed by parents, who are most knowledgeable about their child's and

their family's well-being and medical history. Thus, it is not a perfect research medium.

■ Headache in children

Studies in a cohort study of 48,574 children with new-onset headache aged 5–17 years inclusive compared with a group of the same size without new-onset headache found only 13 malignant brain tumors (0.03% of children) in the year following presentation with only one case in the comparator group [41]. When the GP diagnosed a primary headache (cluster, migraine or tension), no patients developed a tumor. In a meta-analysis of brain tumor symptomatology at presentation, Wilne *et al.* identified headache in only 33% of childhood brain tumor presentations, underscoring the importance of casting the symptomatic net wider than headache alone in children [42].

■ Other symptom clusters

A recent study examined 'alert' symptoms and the recommendation that three unexplained visits to general practice warrant consideration of pediatric cancer (not just brain tumors; although 270 of the 1267 cases had a brain tumor) [43]. However, individual symptoms and consultation patterns had very low positive predictive values (PPVs) for cancer in primary care (out of

Figure 6. Hand-off diagram of the short referral pathway.

DOB: Date of birth; GP: General practitioner.

Figure 7. Hand-off diagram of the medium referral pathway.
A&E: Accident and emergency; DOB: Date of birth; GP: General practitioner; NHS: National Health Service.

10,000 children with a recorded alert symptom, approximately six will be diagnosed with cancer within 3 months). PPVs for ‘neurological symptoms’ (a composite variable created to include relevant symptoms such as weakness) were tiny – 0.08%, as was headache at 0.06% [43]. A Danish case series also found ‘alarm symptoms’ to be rare in primary care cancer patients, with only a fifth of children with cancer having one [44]. Against that, a study in a Scottish GP surgery of teenagers and young adults identified alarm symptom reporting to be remarkably common, with 4% of the ‘healthy’ population reporting one to primary care [45]. Another UK study used the same data set with 13 age-, sex- and practice-matched controls. The highest PPV for brain tumors was for abnormalities of movement, at 0.1%. The other classical symptoms reported at presentation included visual symptoms, vomiting, headache, generalized pain and seizures, and these had even lower PPVs [46]. An audit project of specialist pediatric neurological and brain tumor referral practice, conducted in 2010, used the ‘handoff diagram(s)’ (Figures 6–8) to illustrate the healthcare attendances (lines linking home and points of healthcare contact) and

time from first clinical contact to CNS imaging (scale). There were some limitations to the methods (e.g., a single-center cohort, recall bias and incomplete validation of time points) [47]. It is clear that compliance with existing guidelines for investigation of childhood epilepsy and brain tumors, and the time points defined within them, was low.

While analysis of TYA cancer presentations in CPRD also identified higher consultation rates (median of three consultations) in the 3 months leading up to diagnosis for all cancer types, comparing the likelihood of brain tumor, against acne referrals, were 55.69 for seizures (95% CI: 19.09–162.52); 34.04 for headache (95% CI: 17.95–64.55); and 27.3 for vomiting (95% CI: 9.58–77.37); data were not supplied for visual disturbance [48]. Further work using linked CPRD-Hospital Episode Statistics (HES)–Cancer Registry data sets of childhood brain tumor cases identified that emergency secondary care consultations rose in the 6 months prior to diagnosis, indicating a more complex multistep referral process in the childhood and TYA group [49]. Taken together, the audit and this CPRD work would suggest

that, on an individual case analysis, the interval between first symptom and diagnosis, referral pathways, and service costs vary significantly and the longer delays are associated with many referrals between primary and secondary care before diagnosis (Figures 1–3) [47], thus, challenging the applicability of the Aarhus serial step model.

■ Adult studies

In similar adult studies using CPRD, it was confirmed for the first time that symptoms reported to secondary (or tertiary) care were also relevant in primary care [50]. The PPV for cancer was 1.2% for new-onset seizures, 3% for weakness and only 0.09% for new-onset headache. Disappointingly, we were unable to identify secondary symptoms in the headache group that would have boosted the PPV to a level that GPs could reasonably consider referral for a suspected cancer.

These studies only provide a partial explanation of the problem. They are limited in their scope by the nature of the evidence, in children in particular; ‘alarm features’ of childhood cancer are common in noncancer patients, and not sufficiently common in cancer patients on their

own. The evidence excludes the expertise of the parent, developmental, medical and family history. They do not provide evidence to develop expert diagnostic systems. The NPSA recommendations suggest that to minimise delays in diagnosis it is necessary to:

- Have a diagnostic tool for use in primary care, adapted to meet clinical guidelines;
- Identify, review and disseminate current good practice in the processes of ordering, managing and tracking tests and test results;
- Review and develop methods for empowering patients on a cancer diagnostic pathway;
- Develop a model for stronger leadership and improved safety reporting and learning, including significant event audit at a local and national level;
- Improve routine monitoring of delayed diagnosis.

Creating evidence-based clinical guidance

Having experienced the distress of children and their families, we were moved to initiate a project seeking evidence for a new guideline seeking to change clinical referral practice at

Figure 8. Hand-off diagram of the long referral pathway.

A&E: Accident and emergency; DOB: Date of birth; GP: General practitioner.

the primary–secondary care interface. A limited center cohort study in 2007 confirmed that the previously published NICE Cancer Referral Guideline had not changed the TDI of a median of 12–14 weeks compared with previously published UK single-center cohorts. A systematic review and meta-analysis of international reports of symptomatology at diagnosis and reporting

of TDI found the UK to be low in the international rankings [17]. It summarized the age-related symptomatology of over 4000 reported cases. Using this source material and a Delphi consensus process, involving over 150 experienced practitioners and parents, a series of consensus statements were developed into a clinical guideline, using AGREE criteria, which was

This card is designed to help you know and spot the signs and symptoms of brain tumours in children and young people.

Fortunately brain tumours in children and young people are rare, but they happen.

- ⚡ A quarter of childhood cancers occur in the brain
- ⚡ Early diagnosis of brain tumours can improve the outcome
- ⚡ If you are worried you / your child has a brain tumour, SAY this to your doctor
- ⚡ The website www.headsmart.org.uk can provide further information, support and reassurance

Any child or young person with symptoms that are unusual for him or her, or are persistent or unexplained, should be seen by a GP. If you are worried make an appointment with your doctor.

Please remember any child or young person needing urgent medical help should be taken to the nearest emergency department or dial 999.

The HeadSmart Campaign is run by a partnership between the Children's Brain Tumour Research Centre (CBTRC) at The University of Nottingham, The Brain Tumour Charity and the Royal College of Paediatrics and Child Health (RCPCH). It is funded and promoted by The Brain Tumour Charity.

If you would like to talk to someone about brain tumours, or the HeadSmart campaign, please contact the Support & Info Line at The Brain Tumour Charity on:

Freephone 0808 800 0004
Free from landlines and most mobiles
or email info@headsmart.org.uk

CBTRC Charitable Status Inland Revenue Number: X15294
The Brain Tumour Charity Registered Charity no: 1150054 (England and Wales) SC042096 (Scotland)
RCPCH Registered Charity no: 1057744
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HEADSMART
be brain tumour aware

This card will give you all the information you need to be brain tumour aware.

www.headsmart.org.uk

Under 5
Preschool

Brain tumours happen...
Symptoms include:

- ⚡ Persistent / recurrent vomiting
- ⚡ Balance / co-ordination / walking problems
- ⚡ Abnormal eye movements
- ⚡ Behaviour change, particularly lethargy
- ⚡ Fits or seizures (not with a fever)
- ⚡ Abnormal head position such as wry neck, head tilt or stiff neck

**If your child has one of these, see your doctor
If two or more, ask for an "urgent referral"**

5 - 11
Children

Brain tumours happen...
Symptoms include:

- ⚡ Persistent / recurrent headache
- ⚡ Persistent / recurrent vomiting
- ⚡ Balance / co-ordination / walking problems
- ⚡ Abnormal eye movements
- ⚡ Blurred or double vision
- ⚡ Behaviour change
- ⚡ Fits or seizures
- ⚡ Abnormal head position such as wry neck, head tilt or stiff neck

**If your child has one of these, see your doctor
If two or more, ask for an "urgent referral"**

12 - 18
Young People

Brain tumours happen...
Symptoms include:

- ⚡ Persistent / recurrent headache
- ⚡ Persistent / recurrent vomiting
- ⚡ Balance / co-ordination / walking problems
- ⚡ Abnormal eye movements
- ⚡ Blurred or double vision
- ⚡ Behaviour change
- ⚡ Fits or seizures
- ⚡ Delayed or arrested puberty, slow growth

**If your child has one of these, see your doctor
If two or more, ask for an "urgent referral"
Especially if growth or puberty is slow**

Figure 9. HeadSmart campaign.

Figure 10. Symptom interval monitoring of UK brain tumor referral practice 2007–2012.

accredited by National Health Service Evidence in 2011 [51,52]. The guideline focuses on selecting patients for timely imaging to exclude or diagnose brain tumors. This was endorsed by the Royal College of Paediatrics and Child Health (UK) and published in 2007 with support from other Royal Colleges [53].

■ HeadSmart: Be Brain Tumor Aware

Simply publishing a guideline was recognized to be no guarantee of its dissemination or impact in practice. The HeadSmart: Be Brain Tumor Aware [102] campaign targeting the public and professionals through the media and professional networks was initiated by a consortium of the Children's Brain Tumor Research Center [103], the Royal College of Paediatrics and Child Health [104] and the Brain Tumor Charity (formerly Samantha Dickson Brain Tumour Trust) [105], and supported by the Health Foundation [106]. It was launched in June 2011 [101]. It focused on age-related symptoms and selection of children for reassurance, review or referral. It was designed around a symptom checklist and a public and professional access website (Figure 9).

Reassurance was the most likely action, given the rarity of the condition. This campaign was supported by a network of clinical and community champions, motivated by quality improvement

data, collected contemporaneously in treatment centers linked to the Children's Cancer and Leukemia Research Network as part of the National Institute for Health Research Cancer Research Network, as well as promoting the campaign in pediatric multiprofessional regional networks. Community champions approached schools, public groups, general practices and community services to reinforce HeadSmart messages in person and in social media [107]. They continue to do so. The Royal College of General Practitioners have recently launched a relevant web-based training package, with excellent reviews [108], and they will join the HeadSmart Campaign by distributing its messages directly to its membership (>46,000 GPs) in 2013 and 2014.

■ HeadSmart impact

The campaign was successful in establishing awareness of HeadSmart in public and professional surveys in an estimated 11% of the population and a representative sample of pediatricians [53]. Over 70% of the pediatricians within 4 months of the launch reported that they were confident in selecting patients for scanning, rising from 54% who were confident prelaunch. Awareness and confidence among GPs, however, did not change. The most common professional feedback was that HeadSmart material was valuable in offering reassurance to those who did

not need a brain scan. No reports of increased imaging demands have been received. TDI data, collected by clinical champions, showed that the median TDI prior to the project was 14.4 weeks (mean: 35.4 weeks) in 2006; prior to the project campaign's launch, in early 2011, the median was 9.3 weeks (mean: 22.9 weeks); after the launch, between 2011 and 2013, it was 6.9 weeks (mean: 20.4 weeks; $p = 0.001$) (Figure 10). In early 2011, prelaunch, the median primary care consultation to diagnosis interval was 3 weeks (mean: 15.2 weeks) and 2.3 weeks (mean: 10.3 weeks) in late 2011, which reduced to 1.0 weeks (mean: 13.3 weeks) in 2012 ($p = 0.026$). Formal evaluation, using CPRD data linked to HES and Cancer registries, is required to confirm or refute this preliminary observation. The prelaunch phase of this is complete [49]. This awareness campaign, targeting children, meets almost all of the recommendations of the NPSA. The National Cancer Intelligence Network has announced that TDI data, as part of national brain tumor registration in childhood, will be collected from July 2013 onwards as part of this strategy.

Adult brain tumors: a new challenge?

Low-grade gliomas predominate in younger adults, and early detection, followed by accurate diagnosis and effective surveillance, remain significant challenges in view of the risk of malignant transformation. High-grade gliomas predominate in elderly patients, who represent a growing demographic within the UK population. As treatment of systemic cancers improves, cerebral metastatic disease involves a growing number of patients and represents a rapidly expanding area of clinical neuro-oncology activity. These factors combine to make brain cancers in adults a growing health problem and a rising economic burden costing the European community nearly €5.2 billion annually [54].

Hence, early detection and successful management of this poorly recognized disease will require changes in the process of care in parallel with evolution in clinical practice. Work is needed to establish whether access to an earlier diagnosis should be set as a new health priority for this group generally. A recent initiative to allow GPs direct access to brain imaging, may contribute to changes in practice; although further training for patient selection for brain scanning will be needed to support GPs in this

role, as well as clear lines of responsibility for feeding back results and ongoing referrals [55].

Conclusion & future perspective

Public dissatisfaction with the current level of awareness of brain tumors as a possible diagnosis and barriers to accessing high-quality specialist services is driving a strong professional and political agenda to make changes through translational research. Making the diagnosis is inevitably the first step to get right. The experiences from pediatric practice show that it is possible to change practice by raising awareness without causing unnecessary alarm. Setting a quality improvement target for total diagnostic interval for the health system and providing evidence-based reassurance for those who do not need scanning seem the important components of an awareness campaign for a rare condition such as brain tumor. Clinical diagnosis will always be imperfect. However, as risk factors are identified novel methods will be developed to screen populations, reducing the reliance on clinical detection; although the wide age range and diverse tumor subtypes may mean that progress to achieve such advances will be gradual and require careful introduction across age groups.

Disclaimer

W Hamilton is the clinical lead for the current revision of the National Institute for Health and Care Excellence (NICE) 2005 guidance on 'Referral for Suspected Cancer'. His contribution to this article is in a personal capacity and is not to be interpreted as representing the view of the Guideline Development Group or of NICE itself.

Financial & competing interests disclosure

All authors have completed the International Committee of Medical Journal Editors uniform disclosure form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author). W Hamilton has received several research grants for studies on cancer diagnosis, including one from Colonix Ltd (Cambridge, UK), a commercial firm. He has received travel support to give lectures and attend conferences, plus occasional speaker's fees, from conference organisers in the charitable and educational sector, but none from commercial sources. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

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