

## Appendix

**Table 1. NICE 2005 schematic for suspected brain and CNS cancer referral guideline, illustrating the complexity of referral**

Patient presents with	Action
New unexplained headache or neurological symptoms	Should prompt neurological examination (absence of papilloedema does not exclude possibility of brain tumour)
CNS related symptoms including: <ul style="list-style-type: none"> <li>• progressive neurological deficit</li> <li>• new onset seizures</li> <li>• headaches</li> <li>• mental changes</li> <li>• cranial nerve palsy</li> <li>• unilateral sensorineural deafness</li> </ul> In whom CNS malignancy is suspected	Urgent referral
Suspected recent onset seizures (detailed history, physical exam and developmental assessment should be carried out where appropriate).	
Rapid progression of any of the following: <ul style="list-style-type: none"> <li>• Subacute focal neurological deficit</li> <li>• Unexplained, cognitive impairment or behavioural disturbance or slowness or a combination of these.</li> <li>• Personality changes confirmed by witnesses with no reasonable explanation.</li> </ul>	
Recent onset headaches with symptoms of raised intra cranial pressure (vomiting, drowsiness, postural related headache, headache with pulse synchronous tinnitus) or focal/non-focal neurological symptoms (blackout, change in personality or memory)	
New, qualitatively different unexplained headache becoming progressively severe	Discuss with a specialist or nonurgent referral
Recent onset unexplained headache $\geq$ 1 month without features of raised intracranial pressure.	

**Table 2. CNS tumours with age, sex, past medical history, presenting symptoms, neurological**

<b>Tumour</b>	<b>Age</b>	<b>Sex</b>	<b>Past medical history</b>	<b>Presenting symptoms</b>	<b>Neurological Examination</b>	<b>MRI Findings</b>
Glioblastoma Multiforme	51	F	Left nephrectomy for renal cell carcinoma	Visual disturbance, headache, visual field loss, memory loss, disorientation	Right homonymous hemianopia	Left temporal space occupying lesion
Glioblastoma Multiforme	64	M	Hypothyroidism, type 2 diabetes mellitus, thyroid cancer	Foot drop and leg weakness, hemisensory disturbance	Left hyper-reflexia and hypertonia	Right cerebral space-occupying lesion
Right cerebellar metastasis	53	F	Breast cancer, lung cancer	Headache with features of raised intracranial pressure, nausea	Not provided	Right cerebellar metastasis causing obstructive hydrocephalus
Cerebral metastasis	82	M	Metastatic pancreatic cancer	Double vision, left sided forehead numbness	Right 6 <sup>th</sup> nerve and left 5 <sup>th</sup> nerve palsy	Cerebral metastasis, epidermoid cyst
Meningioma	53	F	Behcet's disease	Forgetfulness, poor appetite and weight	Left homonymous hemianopia and right hearing loss	Right temporal lobe tumour
Meningioma	39	F	Caesarean section	Headache with features of raised intracranial pressure, left sided tinnitus, hearing loss and facial sensory disturbance, unsteadiness	Romberg's positive	Meningioma
Meningioma	74	F	Hypercholesterolaemia, eczema	Right ear ache	Not provided	Incidental craniocervical junction meningioma
Meningioma	70	F	Previous meningioma	Unsteady gait and tremor	Parkinsonism	Small incidental parafalcine meningioma
Pituitary adenoma	50	F	Acromegaly	Visual disturbance	Signs of acromegaly, bitemporal hemianopia	Pituitary tumour
Pituitary adenoma	70	F	Hemithyroidectomy for mass	Visual disturbance, found to have bitemporal quadrantanopia by optometrist	Bitemporal quadrantanopia	Small high signal lesion within pituitary

**examination findings and MRI findings**

**Table 3. End diagnosis (in order of frequency)**

<b>Diagnosis</b>	<b>Frequency</b>	<b>%</b>
<i>Primary headache disorder</i>	85	55.6
Migraine (unspecified)	38	24.8
Migraine with aura	22	14.4
Cerebrovascular disease	8	5.2
Non-specific headache	8	5.2
Migraine without aura	7	4.6
Peripheral neuropathy	6	3.9
Medication overuse headache	5	3.3
Epilepsy	5	3.3
Multiple sclerosis	5	3.3
Parkinson disease	5	3.3
Syncope	5	3.3
Meningioma	4	2.6
Tension Headache	3	2.0
Isolated sensorineural hearing loss	3	2.0
Benign paroxysmal positional vertigo	3	2.0
Non-neurological diagnosis	3	2.0
Motor neuron disease	2	1.3
Vestibular dysfunction	2	1.3
Musculoskeletal pain	2	1.3
Cerebral metastases	2	1.3
Pituitary Adenoma	2	1.3
Glioblastoma multiforme	2	1.3
Cluster Headache	1	0.7
Primary coital cephalgia	1	0.7
Subdural haematoma	1	0.7
Vestibular neuronitis	1	0.7
Cerebellar syndrome of unknown aetiology	1	0.7
Functional neurological disorder	1	0.7
Post-traumatic disorder	1	0.7
Migraine with incidental arachnoid cyst	1	0.7
Anosmia due to otolaryngorhinological disorder	1	0.7
Alzheimer's disease	1	0.7
Occipital cortical dysgenesis	1	0.7
Retinal scarring	1	0.7
Anxiety	1	0.7
Cervical disc herniation	1	0.7

Four patients were given more than one end diagnosis

**Table 4. Presenting symptoms (in order of frequency) and predictive values for CNS cancer**

Symptom	Frequency	%	CNS Cancer	PPV % [95% CI]	NPV % [95% CI]
<i>Headache</i>	96	62.7	2	2.1 [0.8, 5.4]	96.5 [91.0, 98.7]
With features of raised ICP	45	29.4	1	2.2 [0.4, 11.2]	97.2 [95.2, 98.4]
Without features of raised ICP	51	33.3	1	2.0 [0.3, 10.5]	96.1 [94.8, 97.5]
Visual disturbance	49	32.0	2	4.1 [1.5, 10.4]	98.1 [95.0, 99.3]
Nausea and vomiting	42	27.5	1	2.4 [1.8, 3.1]	100.0
Dizziness	33	21.6	0	0.0	96.7 [96.4, 96.9]
Ataxia	24	15.7	0	0.0	96.9 [96.7, 97.1]
Limb weakness	19	12.4	1	5.3 [1.0, 24.3]	97.8 [96.1, 98.7]
Photophobia	18	11.8	0	0.0	97.0 [96.7, 97.2]
Sensory loss	15	9.8	1	6.7 [1.2, 29.5]	97.8 [96.2, 98.8]
Paraesthesia	12	7.8	0	0.0	97.2 [97.0, 97.3]
Tinnitus	11	7.2	0	0.0	97.2 [97.1, 97.3]
Memory loss	10	6.5	1	10.0 [1.8, 40.5]	97.9 [96.6, 98.9]
Gait abnormalities	9	5.9	1	11.1 [2.0, 43.7]	97.9 [96.4, 98.8]
Hearing loss	9	5.9	0	0.0	97.2 [97.1, 97.3]
Dysarthria	8	5.2	0	0.0	97.2 [97.1, 97.3]
Seizures	7	4.6	0	0.0	97.3 [97.2, 97.4]
Blackout	7	4.6	0	0.0	97.3 [97.2, 97.4]
Weight loss	6	3.9	0	0.0	97.3 [97.2, 97.4]
Altered mental state	6	3.9	0	0.0	97.3 [97.2, 97.4]
Fatigue	6	3.9	0	0.0	97.3 [97.2, 97.4]
Tremor	6	3.9	0	0.0	97.3 [97.2, 97.4]
Falls	5	3.3	0	0.0	97.3 [97.2, 97.4]
Dysphasia	5	3.3	0	0.0	97.3 [97.2, 97.4]
Cranial nerve palsy	4	2.6	1	25.0 [4.2, 71.8]	98.0 [96.5, 98.9]
Neck or back pain	4	2.6	0	0.0	97.3 [97.2, 97.4]
Personality change	2	1.3	0	0.0	97.4 [97.3, 97.4]
Hallucinations	2	1.3	0	0.0	97.3 [97.3, 97.4]
Epistaxis	1	0.7	0	0.0	97.4 [97.4, 97.4]