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Painting pictures of the brain with numbers

Neurology for Insurers

Dr Ian Cox & Adele Groyer (Gen Re)

Overview

- Critical Illness Product Background
  - Why should we be interested in neurology?
- Consult our doctor
  - How your brain works (assuming it does)
  - White matter and grey matter (and whether it matters)
  - How we can we look at the Central Nervous System
  - Changes in the way doctors diagnose and manage Stroke, MS and Alzheimer's Disease
- Critical Illness Pricing implications

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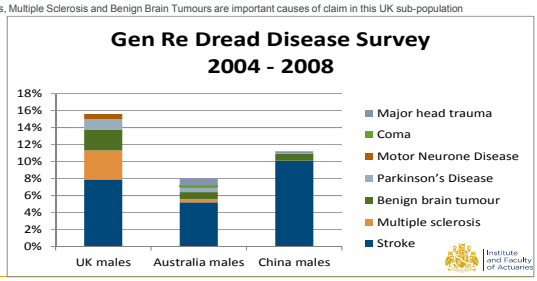
Critical Illness Neurological cause of claim

Strokes, Multiple Sclerosis and Benign Brain Tumours are important causes of claim in this UK sub-population



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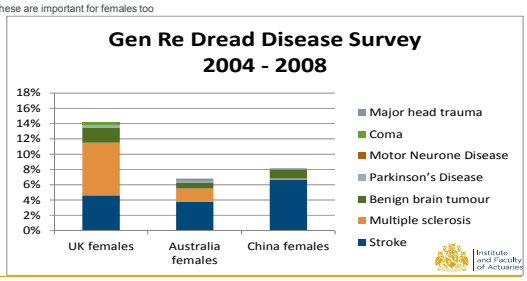
Critical Illness Neurological cause of claim

… and these are important for females too



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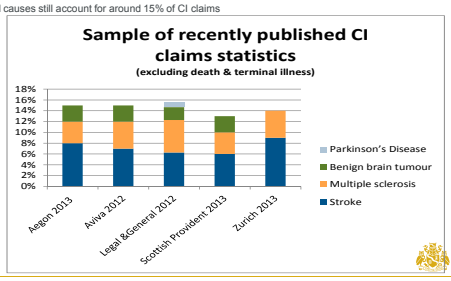
2012/2013 Claims statistics paint a similar picture

Neurological causes still account for around 15% of CI claims



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Zurich reported only on a few top causes of claim

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What matters……

The Brain

Neurons and other cells

- Basic functional unit of the nervous system
- 100 Billion cells in the brain
- 100 trillion synapses or connections
- Other supporting cells – Glial cells
  - Called astrocytes, oligodendrocytes

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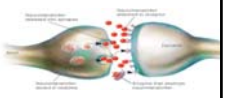
Neurons

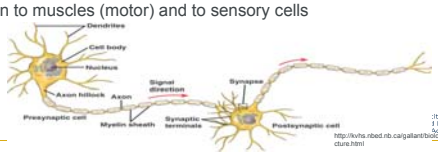
Axons and dendrites - transport electrical and chemical messages

Axons covered by segment like myelin sheath



This assists speed of conduction

Connects brain to muscles (motor) and to sensory cells



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http://kvhs.nbed.nb.ca/gallant/biology/neuron_structure.html

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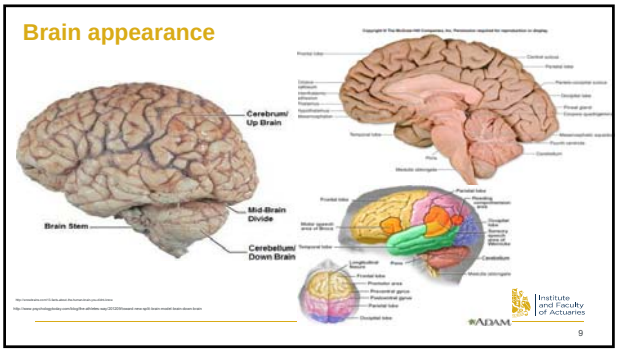
Brain appearance



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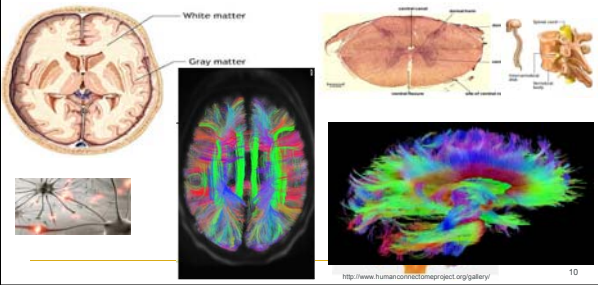
Grey Matter, White Matter



http://www.humanconnectomeproject.org/gallery/

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How can we look at the Nervous System?

- Symptoms – reported
- Clinical Examination of individual
- Test transmission of nerves
  - Nerve conduction
  - Visual evoked responses
- Imaging
  - X-Ray
  - CT
  - MRI
  - Functional imaging

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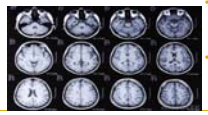
CT or MRI ?

CT	MRI
• Was more available	• Now more available
• Quicker	• Longer process
• Cheaper	• More expensive
• Possible with metal in body	• Claustrophobia in most machines
	• Not possible with metal in body
• But radiation	• Different images possible (not just 'MRI')
	• No radiation



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MS diagnosis

MacDonald Criteria

Clinical presentation (person presenting to neurologist)	Additional data needed for MS diagnosis
Two or more attacks; objective clinical evidence of two or more lesions	None
Two or more attacks; objective clinical evidence of one lesion	Dissemination in space shown on MRI **or** Up to two MRI detected lesions typical of MS plus positive cerebrospinal fluid* **or** Await a further relapse suggestive of dissemination in space (ie affecting another part of the body)
One attack; objective clinical evidence of two or more lesions	Dissemination in time demonstrated by MRI **or** Second clinical attack (relapse)
One attack; objective clinical evidence of one lesion (known as 'clinically isolated syndrome')	Dissemination in space demonstrated by MRI **or** Up to two MRI detected lesions typical of MS plus positive cerebrospinal fluid* AND dissemination in time demonstrated by MRI **or** Dissemination in time demonstrated by MRI (ie new lesion seen on MRI at least 3 months after the original scan) **or** Second clinical attack (relapse)
Insidious neurological progression suggestive of multiple sclerosis (typical for primary progressive MS)	Positive cerebrospinal fluid* **AND** dissemination in space, shown on MRI **or** Abnormal visual evoked potential plus abnormal MRI **AND** dissemination in time demonstrated by MRI **or** Continued progression for one year (determined retrospectively or by ongoing observation)

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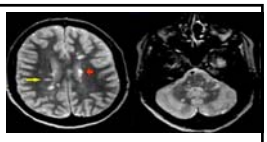
MS diagnosis



- **Disseminated in time and space**
- **Evidenced by clinical examination**
  - **More than one clinical lesion**
- **Evidenced by more than one lesion on MRI**
  - **Different lesions in position and/or duration**

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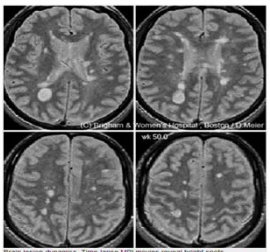
http://www.radiologyassistant.nl/en/p4556dea65cb62/multiple-sclerosis.html#45979814a5eb

MS lesions on MRI over one year



Brain lesion dynamics. Time-lapse MRI movies reveal bright spots representing multiple sclerosis brain lesions, that form and then grow, shrink, or disappear over 12 months in a man with RRMS—who experienced no flare-ups of symptoms in that period. Each video runs through 24 scans of a

MS attacks cause early inflammation – swelling and leaking of immune cells into area.
Leaving scars - gliosis

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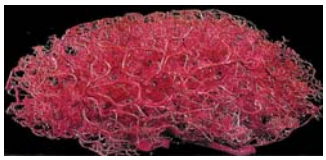
Blood supply in the brain

Stroke

- Haemorrhage or Infarct
- Infarct when blood vessel is blocked – thrombosis or embolus
- Treatment with clot busting drugs if infarct
- New concept of 'Brain Attack'



http://www.wellcomecollection.org/full-image.aspx?page=3586&image=cast-of-blood-vessels

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Stroke Vs Transient Ischaemic Attack (TIA)

- TIA: Change diagnosis to 'tissue based' diagnosis
- No time – 24 hrs no longer relevant
- Scans vital
- CT [illegible] haemorrhage
- O[illegible] within 3-6 hrs and virtually all are seen in 24 hours. Th[illegible]y of CT to diagnose stroke is 64% and the specificity is 85%
- 30% to 50% of classically defined TIAs show brain injury on diffusion-weighted magnetic resonance (MR) imaging (MRI).
- '***TIA patients should undergo neuroimaging evaluation within 24 hours of symptom onset, preferably with magnetic resonance imaging***'

Transient ischemic attack (TIA): a transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction

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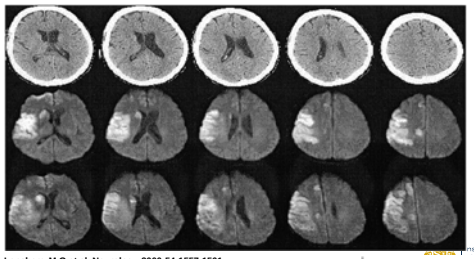
Acute CT scans (top row) 1.5 hours and MRI diffusion-weighted images (DWI) obtained 3.5 and 36 hours after stroke onset in a woman with left hemiparesis



Lansberg M G et al. Neurology 2000;54:1557-1561

AMERICAN ACADEMY OF NEUROLOGY

Sensitivity Specificity CT and MRI acute stroke

Sensitivity and specificity of blinded imaging diagnosis by time from onset to scan

	n	Acute stroke		Acute ischaemic stroke	
		CT	MRI	CT	MRI
Sensitivity					
All	356	26% (20-32)	83% (78-88)	16% (12-21)	83% (77-88)
<12 h	135	22% (14-31)	91% (82-96)	16% (9-27)	92% (83-97)
3-12 h	131	29% (18-41)	83% (70-89)	20% (12-33)	81% (68-90)
<3 h	90	27% (17-40)	78% (64-86)	12% (5-24)	73% (59-84)
Specificity					
All	356	98% (95-99)	87% (82-90)	98% (94-99)	96% (92-98)
<12 h	135	98% (89-100)	96% (86-99)	98% (90-100)	97% (88-99)
3-12 h	131	97% (87-99)	98% (90-100)	96% (87-99)	99% (91-100)
<3 h	90	100% (83-100)	96% (79-100)	100% (89-100)	92% (74-98)

Data in parentheses are 95% CI

Lancet. Jan 27, 2007; 369(9558): 293–298. doi: 10.1016/S0140-6736(07)60151-2

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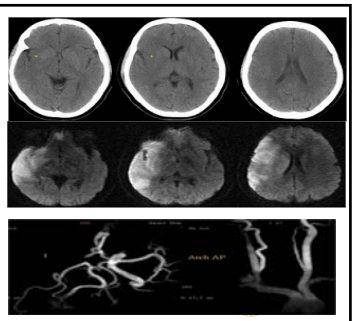
Stroke

- 55 year old man with weakness
- CT to rule out haemorrhage
- MRI next
- Angiogram



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Cerebral aneurysm & Subarachnoid Haemorrhage

Dilatation of a blood vessel
Risk is that this may:
- burst – causing haemorrhage
- cause pressure on surrounding brain tissue

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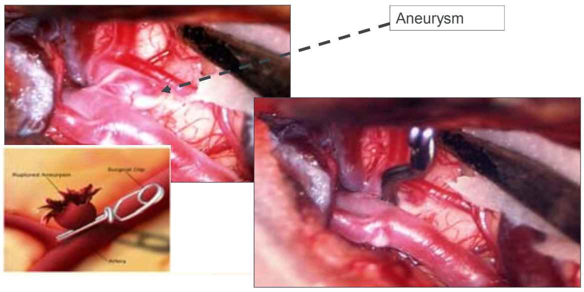
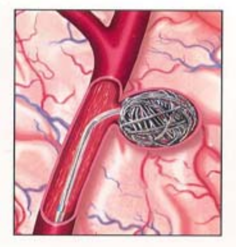
Clipping of cerebral aneurysm



Coiling of aneurysm



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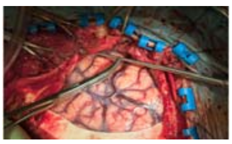
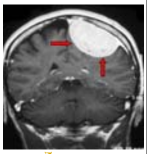
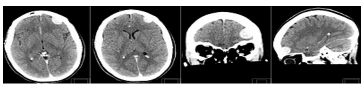
Brain covering layers – meninges - BBT

No classification of Benign Vs Malignant!!



http://heartautopsy.com/?p=1175





http://www.wellcomecollection.org/whats-on/exhibitions/brains/image-galleries/cutting-and-treating.aspx?view=brain-surgery

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http://www.neurochirurgia-ire.it/eng/5-8_Meningioma.shtml

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Dementia

- Continuum of increasing memory loss
- Diagnostic criteria not objective – rely on impairment of everyday functioning and questions answered by patient (clinical medicine)
- Where does mild cognitive impairment end and dementia start?

Ernest Saunders 1991
Convinced High Court that he had dementia and sentence reduced (Distillers Trial)
Within 12 months fully recovered re-entering commercial world

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Dementia

- Scans not diagnostic although supportive
- Clinical diagnosis
- Blood tests ?coming for early diagnosis
- Screening suggested - targets

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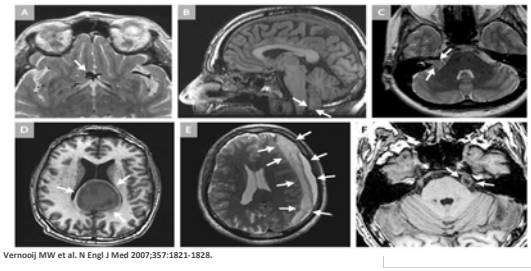
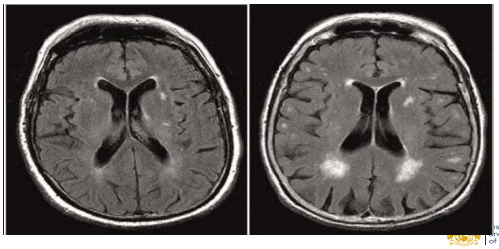
Incidental MRI findings



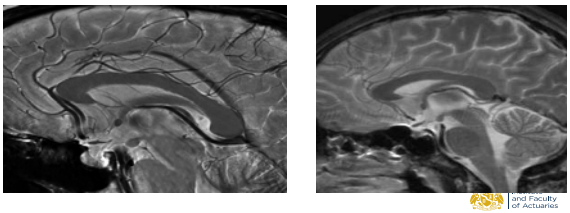
Vernooij MW et al. N Engl J Med 2007;357:1821-1828.

White matter lesions on scan

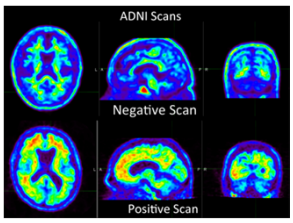


Future changes in neurological imaging

7T vs 1.5T MRI scan



Positron Emission Tomography (PET) Scanning with Florbetapir in possible Alzheimer's Disease



Detects β-amyloid deposition in brain

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Blood markers

- 'holy grail' of pharma/biomarker industry
- Massive investment ongoing
- Looking at:
  - Stroke
  - Dementia
  - MS
  - Huntington's

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Implications for insurance

Neurological CI claims triggers

The list is long and includes many similar illnesses

ABI/ABI+	Non-standard full benefits	Additional payments
Stroke	Devic's Disease	Arteriovenous Malformation of the brain
Multiple sclerosis	Benign Spinal Cord Tumour	Carotid Artery Stenosis
Benign Brain Tumour	Progressive Supranuclear Palsy	Cerebral Aneurysm
Parkinson's Disease	Multiple System Atrophy	
Alzheimer's Disease	Dementia	
Motor Neurone Disease	Bacterial Meningitis	
Coma	Encephalitis	
Traumatic head injury	Creutzfeldt-Jakob Disease	

Neurological CI claims triggers

Definite diagnosis by a Consultant Neurologist
PLUS Permanent Neurological Deficit or specific form of permanent impairment

ABI/ABI+	Non-standard full benefits	Additional payments
	Devic's Disease	
Multiple sclerosis		
	Progressive Supranuclear Palsy	
Parkinson's Disease	Multiple System Atrophy	
Alzheimer's Disease	Dementia	
Motor Neurone Disease	Bacterial Meningitis	
	Encephalitis	

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Neurological CI claims triggers

Definite diagnosis by a suitable / specified medical professional
PLUS specific form of permanent impairment

ABI/ABI+	Non-standard full benefits	Additional payments
	Benign spinal cord tumour+	
Alzheimer's Disease	Dementia	
	Creutzfeldt-Jakob Disease*	

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+ Just "diagnosis" + PND

* Some definitions are diagnosis only

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Neurological CI claims triggers

Does not specify who makes the diagnosis but requires specific surgery or procedure

ABI/ABI+	Non-standard full benefits	Additional payments
		Arteriovenous Malformation of the brain
		Carotid Artery Stenosis
		Cerebral Aneurysm

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Neurological CI claims triggers

And the rest

ABI/ABI+	Non-standard full benefits	Additional payments
Stroke +		
Benign Brain Tumour +		
Coma*		
Traumatic head injury*		

Two of the most common causes of neurological CI claim have the loosest definitions!

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+ permanent (ABI standard)
temporary / no symptoms (ABI+)

* Permanent neurological deficit with persisting clinical symptoms

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How representative is the data we see?

What constitutes "Definite Diagnosis" and how protective is this requirement?

Currently undiagnosed / asymptomatic cases

- Prevalence detectable by MRI
- Use of MRI
- Robustness of impairment requirements in insurance definition

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Incidental MRI findings

Do the statistics suggest a CI headache?

Context

Some rough tools to estimate impact of increased neurological claim rates on total Accelerated CI cost

- **Probability of death or CI claim by age 69 for someone aged 50**
  - Male non-smoker: 23%
  - Female non-smoker: 16%

CMI AC04 tables (Working Paper 50)

Based on insured lives experience 2003-2006

MRI findings

Morris z el at, "Incidental findings on brain magnetic resonance imaging: systematic review and meta-analysis", BMJ 2009;339:b3016 doi:10.1136/bmj.b3016

Incidental brain findings on magnetic resonance imaging

Potentially symptomatic or treatable abnormalities
- Neoplasms
- Cysts
- Structural vascular abnormalities
- Inflammatory lesions
- Other—for example, Chiari malformations, hydrocephalus

Markers of cerebrovascular disease
- White matter hyperintensities
- Silent (asymptomatic) brain infarcts
- Brain microbleeds

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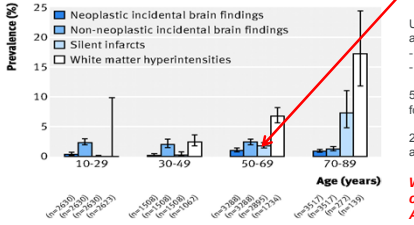
MRI findings: Silent stroke

Morris Z el at, "Incidental findings on brain magnetic resonance imaging: systematic review and meta-analysis", BMJ 2009;339:b3016 doi:10.1136/bmj.b3016



Silent stroke prevalence ages 50 - 69: 2%

UK population stroke diagnoses ages 55 - 69*
- 0.1% p.a. incidence
- 1.1% prevalence

5% of ACI claims are currently for stroke

20% probability of CI claim aged 50 - 69

Worst case scenario could add 10% to total ACI risk cost
more of an issue at older ages

* Lee S. et al, UK stroke incidence, mortality and cardiovascular risk management 1999–2008: time-trend analysis from the General Practice Research Database, BMJ Open2011;1:e000269

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Do patients "fully recover" after stroke?

- 19% of stroke survivors aged 50 – 69 were classified as "fully recovered" 6 months after stroke

adjusted for unknown statuses

Source: International Stroke Trial database US and UK statistics

Trial was conducted in the 1990s

- Changes from reclassification of some TIAs as strokes more recently
- *"fully recovered" label has been modified and incidental findings have been associated with poorer cognitive performance*

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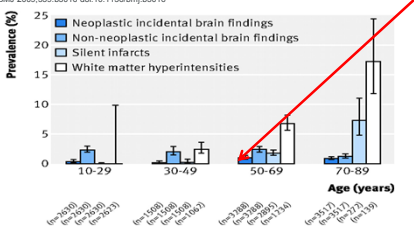
MRI findings: Benign Brain Tumours

Morris z el at, "Incidental findings on brain magnetic resonance imaging: systematic review and meta-analysis", BMJ 2009;339:b3016 doi:10.1136/bmj.b3016



Neoplastic incidental findings: **1%**

approx. 50% of which are meningiomas (paid as BBT)
Next most common are pituitary gland tumours

2% of claims are currently for benign brain tumour

20% probability of CI claim aged 50 - 69

Worst case scenario could add 2.5% to total ACI risk cost

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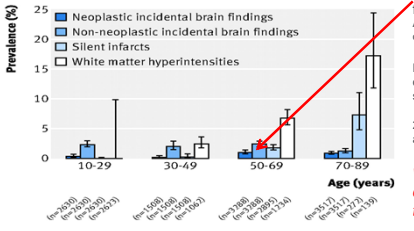
MRI findings: aneurysms and AVMs in the brain

Morris z el at, "Incidental findings on brain magnetic resonance imaging: systematic review and meta-analysis", BMJ 2009;339:b3016 doi:10.1136/bmj.b3016



Prevalence of incidental findings aged 50 - 69: 2%
Approx 20% of these are aneurysms or AVMs

New additional payment definition which requires surgery.

20% probability of CI claim aged 50 - 69

Worst case scenario could add less than 1% to total ACI risk cost

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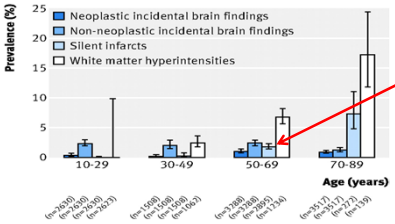
MRI findings: white matter hyperintesities

Morris z el at, "Incidental findings on brain magnetic resonance imaging: systematic review and meta-analysis", BMJ 2009;339:b3016 doi:10.1136/bmj.b3016



These are the most common findings and are very common age ages 70+

They are not directly associated with aCI definition at present.

Indicate 2 to 3x increase risk of dementia, stroke & death

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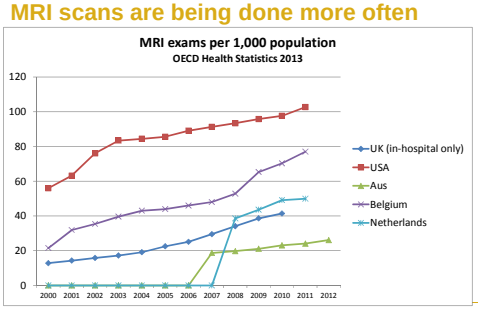
MRI scans are being done more often



National audit office 2008-09 the average cost per scan in the NHS

CT: £54 to £268
MRI: £84 to £472

Private MRI scan: £250

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BMJ

RESEARCH

Insufficient evidence to justify asymptomatic screening

Incidental findings on brain magnetic resonance imaging: systematic review and meta-analysis

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ABSTRACT

Objective To quantify the prevalence of incidental findings on magnetic resonance imaging (MRI) of the brain.

Design Systematic review and meta-analysis of observational studies.

Data sources Ovid Medline (1950 to May 2008), Embase (1980 to May 2008), and bibliographies of relevant articles.

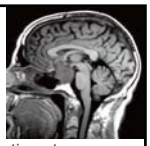
Review methods Two reviewers sought and assessed studies of people without neurological symptoms who underwent MRI of the brain with or without intravenous contrast for research purposes or for occupational, clinical, or commercial screening.

Main outcome measures Overall disease specific and age

silent infarcts, and microbleeds). The number of asymptomatic people needed to scan to detect any incidental brain finding was 17. The prevalence of incidental brain findings was higher in studies using high resolution MRI sequences than in those using standard resolution sequences (4.7% v 1.7%, P<0.001). The prevalence of neoplastic incidental brain findings increased with age

Conclusions Incidental findings on brain MRI are common, prevalence increases with age, and detection is more likely using high resolution MRI sequences than standard resolution sequences. These findings deserve to be mentioned when obtaining informed consent for brain MRI in research and clinical practice but are not sufficient to justify screening healthy asymptomatic people

Concluding thoughts



- Neurological CI definitions are complicated
  - Information sharing between disciplines helps
- Diagnostic criteria and technology in the clinical setting continue to change
  - Screening is a possibility but is not clearly beneficial now
  - Insurers need to remain vigilant and participate regularly in industry discussions
- There is some risk attached to the existing definitions
  - Especially the “diagnosis only” variety
  - But the worst case scenarios does not appear to be catastrophic

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Questions

Comments

Expressions of individual views by members of the Institute and Faculty of Actuaries and its staff are encouraged.

The views expressed in this presentation are those of the presenter.

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