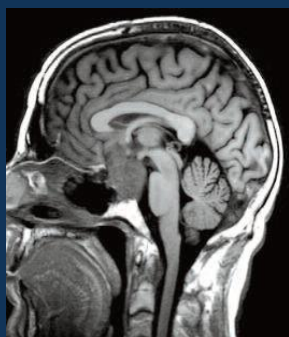




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Painting pictures of the brain with numbers

Neurology for Insurers
Dr Ian Cox & Adele Groyer
Gen Re

Overview

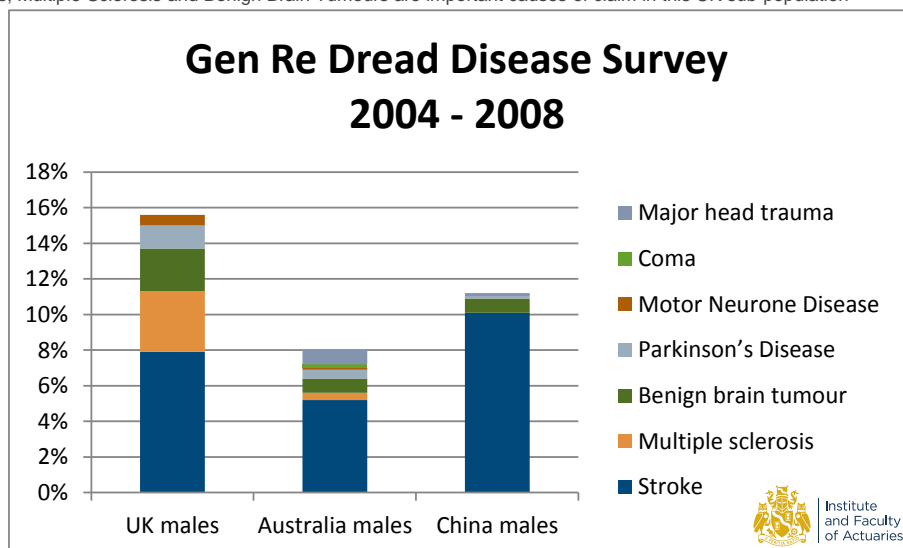
- Critical Illness Product Background
 - Why should we be interested in neurology?
- Consult our doctor
 - How your brain works (assuming it does)
 - White matter and grey matter (and whether it matters)
 - How we can we look at the Central Nervous System
 - Changes in the way doctors diagnose and manage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



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Critical Illness Neurological cause of claim

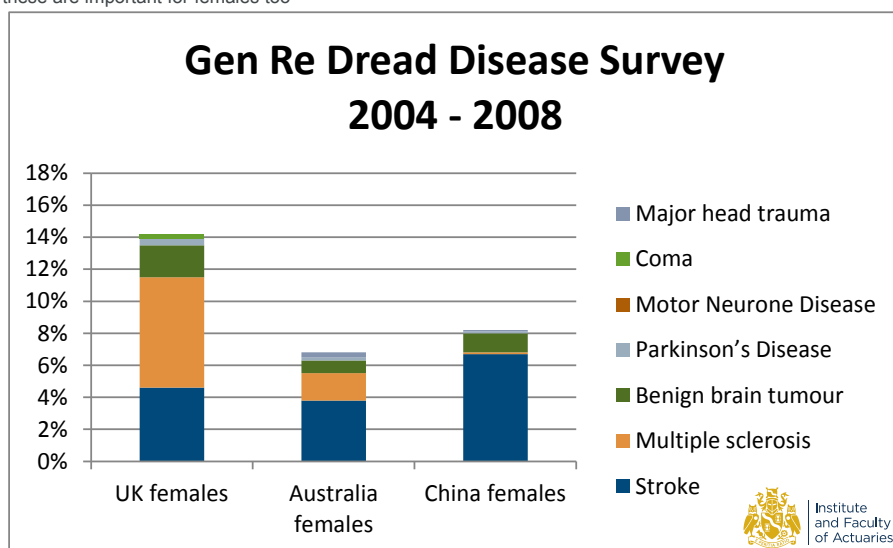
Strokes, Multiple Sclerosis and Benign Brain Tumours are important causes of claim in this UK sub-population



3

Critical Illness Neurological cause of claim

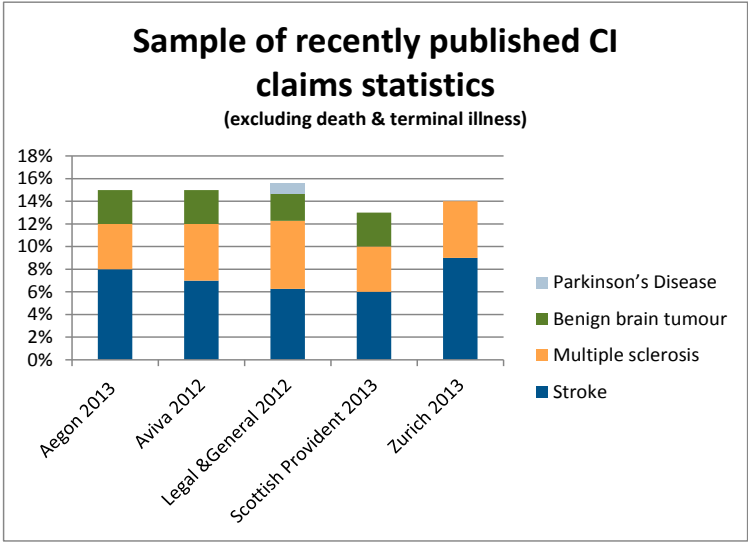
... and these are important for females too



4

2012/2013 Claims statistics - a similar picture

Neurological causes still account for around 15% of CI claims



Zurich reported only on a few top causes of claim

5



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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



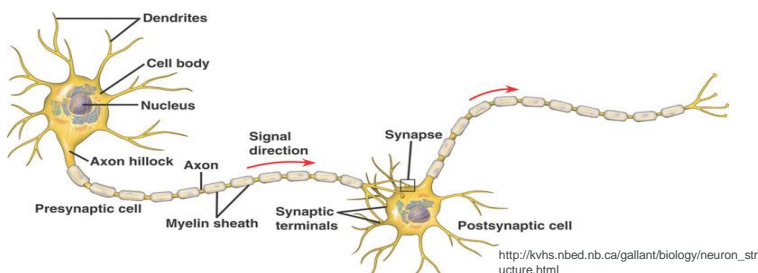
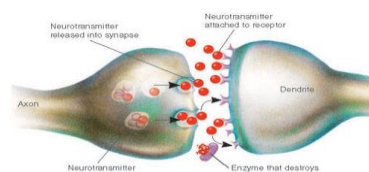
Neurons

Axons and dendrites - transport electrical and chemical messages

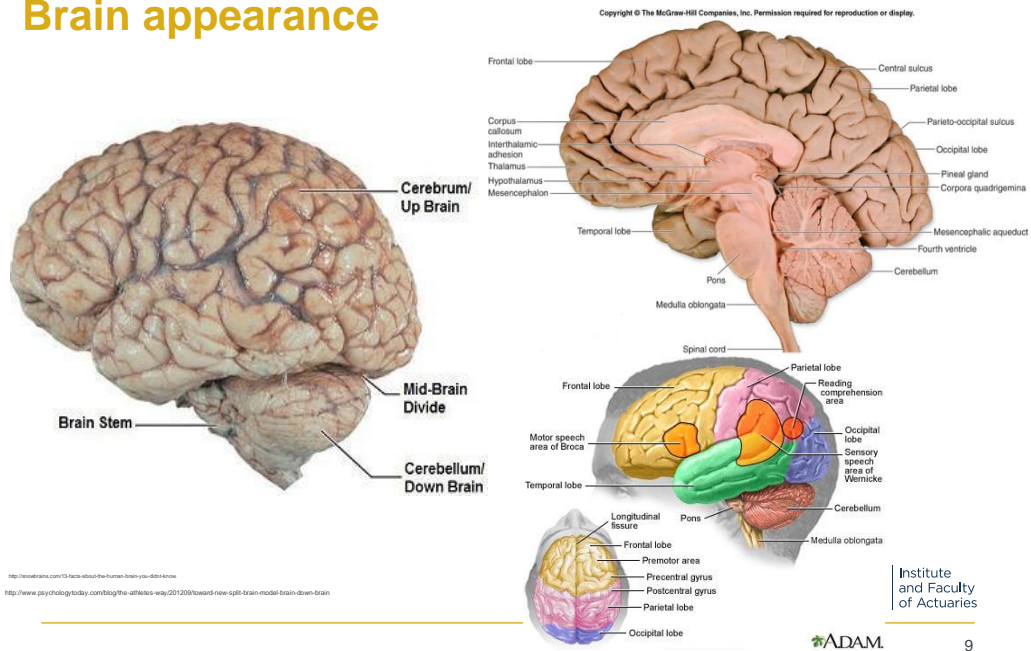
Axons covered by segment like myelin sheath

This assists speed of conduction

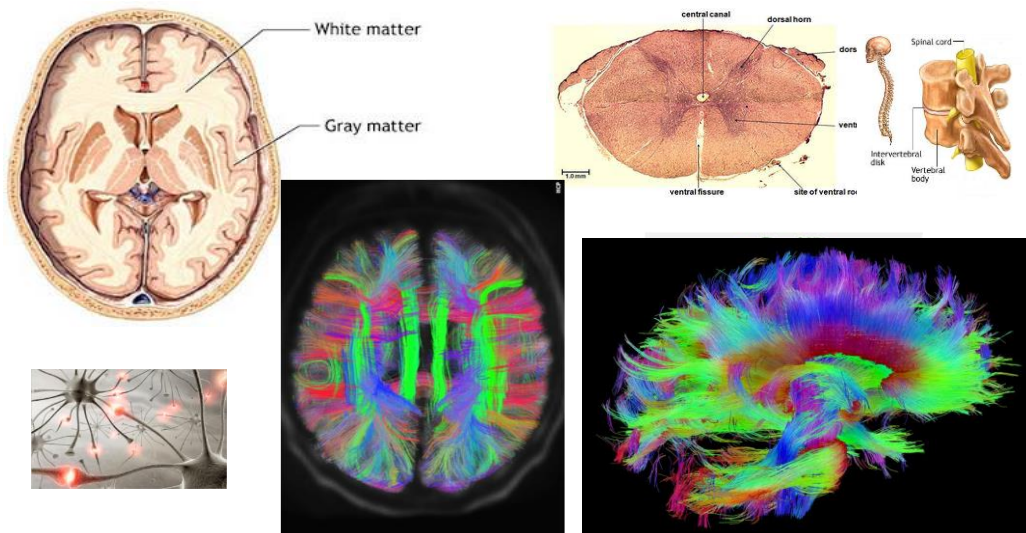
Connects brain to muscles (motor) and to sensory cells



Brain appearance



Grey Matter, White Matter



How can we look at the Nervous System?

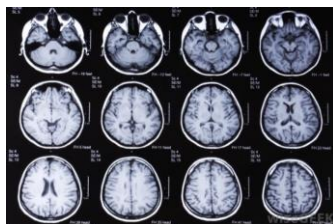
- Symptoms – reported
- Clinical Examination of individual
- Test transmission of nerves
 - Nerve conduction
 - Visual evoked responses
- Imaging
 - X-Ray
 - CT
 - MRI
 - Functional imaging



CT or MRI ?

CT

- Was more available
- Quicker
- Cheaper
- Possible with metal in body
- But radiation



MRI

- Now more available
- Longer process
- More expensive
- Claustrophobia in most machines
- Not possible with metal in body
- Different images possible (not just 'MRI')
- No radiation



MS diagnosis

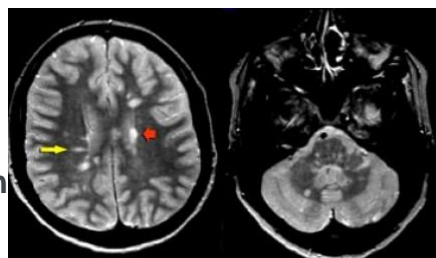
MacDonald Criteria

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

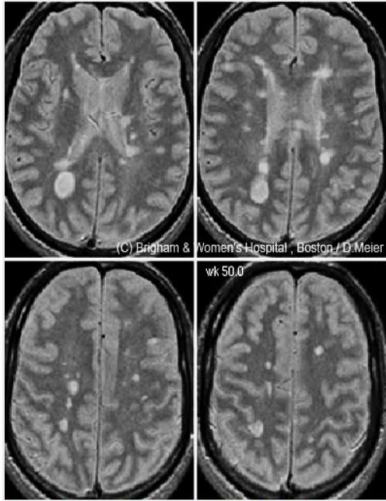


MS lesions on MRI over one year

according to the clinical measures, stable during that year," Guttmann says.

Contents of this article

- Sensitive in some ways, imprecise in others
- Diagnosing MS faster
- MRI for monitoring and treating MS: A work in progress
- Predicting MS outcomes: A tough quest marked by dissension
- A shortcut to speed drug development
- Revealing what's below the tip of the MS-pathology iceberg
- Can next-generation methods help fill in the gaps?
- Getting coordinated in the MS field
- Visualizing the future of MS imaging



(C) Brigham & Women's Hospital, Boston / D. Meier

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

The Next Frontier

MS attacks cause early inflammation – swelling and leakage of immune cells into area.

Leaving scars - gliosis

- » Partnership and Consent in MS Decision-Making
- » More Than Meets the Eye
- » Genetic Associations
- » Discriminatory Disease
- » Altered Immunity, Crippled Neurons

SEE FULL LIST »

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Category: ALL

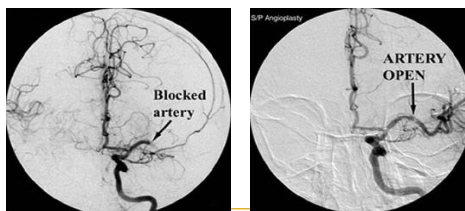
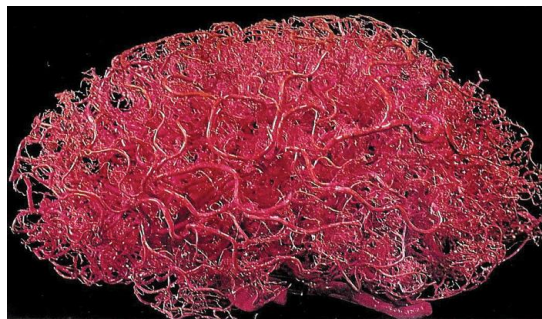
☐ CLINICAL RESEARCH ☐ MEETINGS ☐ DRUG DEVELOPMENT ☐ METHODS ☐ LABORATORY RESEARCH ☐ PEOPLE

Posting date

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'

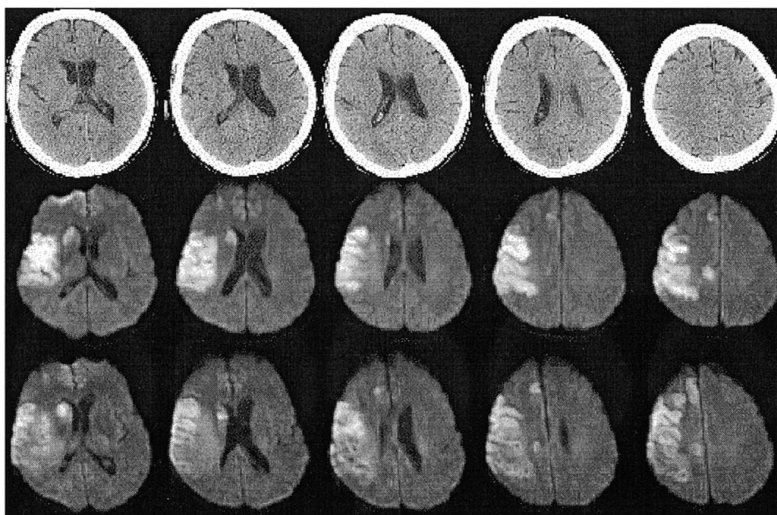


<http://www.wellcomecollection.org/full-image.aspx?page=3586&image=cast-of-blood-vessels>

Stroke Vs Transient Ischaemic Attack (TIA)

- TIA: Change diagnosis to 'tissue based' diagnosis
- No time – 24 hrs no longer relevant
- Scans vital
- CT scan: not sensitive for haemorrhage
- **Transient ischemic attack (TIA): a transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction**
- TIA signs and symptoms seen within 3-6 hrs and virtually all are seen in 24 hours. The sensitivity 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'*

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



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% (12-23)	83% (77-88)
>12 h	135	22% (14-33)	91% (82-96)	16% (9-27)	92% (83-97)
3-12 h	131	29% (19-41)	81% (70-89)	20% (12-33)	81% (69-90)
<3 h	90	27% (17-40)	76% (64-86)	12% (5-24)	73% (59-84)
Specificity					
All	356	98% (93-99)	97% (92-99)	98% (94-99)	96% (92-99)
>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% (85-100)	96% (79-100)	100% (89-100)	92% (78-98)

Data in parentheses are 95% CI.

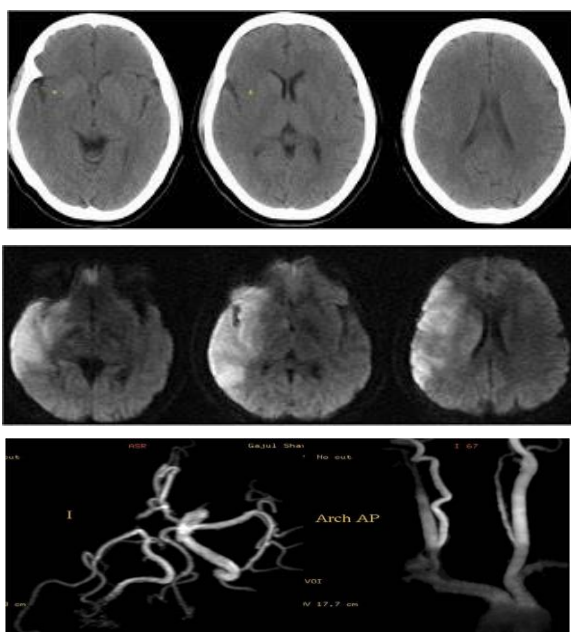
Lancet. Jan 27, 2007; 369(9558): 293-298.
doi: [10.1016/S0140-6736\(07\)60151-2](https://doi.org/10.1016/S0140-6736(07)60151-2)



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Stroke

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



20

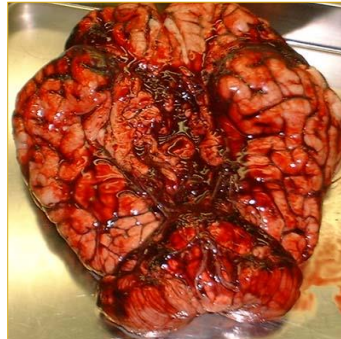
Cerebral aneurysm & Subarachnoid Haemorrhage



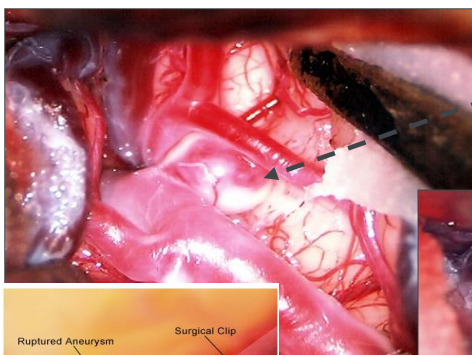
Dilatation of a blood vessel

Risk is that this may:

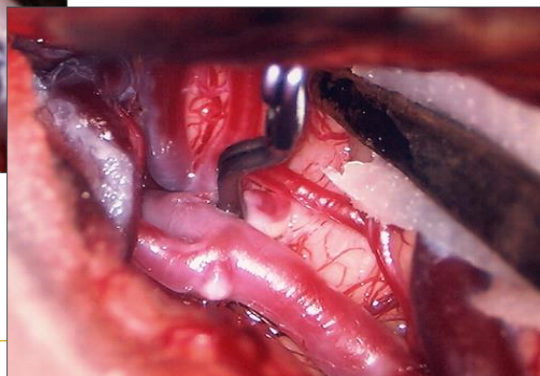
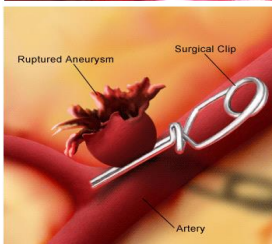
burst – causing haemorrhage
cause pressure on surrounding
brain tissue



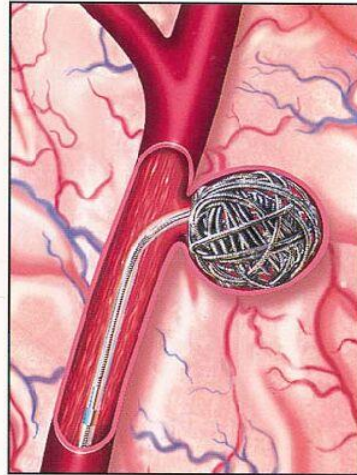
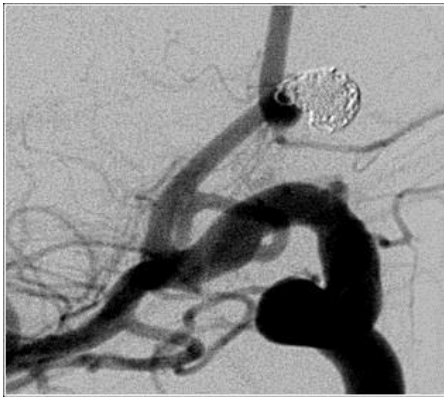
Clipping of cerebral aneurysm



Aneurysm



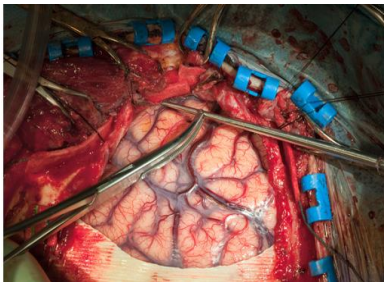
Coiling of aneurysm



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Brain covering layers – meninges - BBT

No classification of Benign Vs Malignant!!

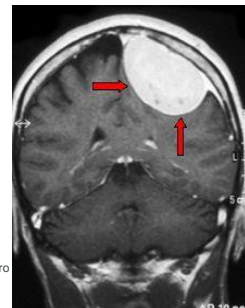


<http://heartautopsy.com/?p=1175>



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

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?

theguardian

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News UK news

Brain age tests to be offered to middle-aged in battle against dementia

Experts welcome computer-based examination, that analyses patients' lifestyle to calculate risk to brain health

Mark Tran
The Guardian, Monday 3 November 2014 13:29 GMT
Jump to comments (59)



More than 800,000 people in the UK have dementia, according to estimates. Photograph: Roxana Wegner/Getty Images/Flickr RF

Doctors are to offer middle-aged patients the opportunity to take a computer-based test designed to show how their "brain age" compares with their biological age as a way of encouraging them to pursue healthier lifestyles.

UK news

Society
Dementia · Mental health
Health · GPs · NHS
Doctors · Alcohol · Smoking

Science
Ageing

Life and style

More news

More on this story

Major brain pathway rediscovered
A massive white matter tract at the back of the brain, overlooked for the past century, might be crucial for skills such as reading



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Dementia

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

NEWS HEALTH

Home World UK England N.Ireland Scotland Wales Business Politics Health Education SciEnv

22 October 2014 Last updated at 13:03

GPs to be paid £55 for each dementia diagnosis

COMMENTS (1186)



Family doctors in England are to be paid £55 for each patient they diagnose with dementia, NHS bosses say.

NHS England said the aim of the six-month £5m scheme was to increase the number of sufferers who receive treatment for the condition, which causes a decline in brain function.

It is estimated up to 90,000 patients are living with undiagnosed dementia.

Related Stories

Putting parents in care "haunts me"

The dementia timebomb

PM urges global push on dementia

MailOnline



Doctors 'leaned on' to diagnose dementia cases: GPs are told they will lose money if they don't meet their NHS targets

- Leading GP Dr Martin Brunet, from Godalming, Surrey, voiced view in BMJ
- Jeremy Hunt has said it is important to increase diagnosis and detection
- Dr Brunet: GPs with few cases will be desperate to escape a low ranking
- He argues 'naming and shaming' could lead doctors to 'up the numbers'

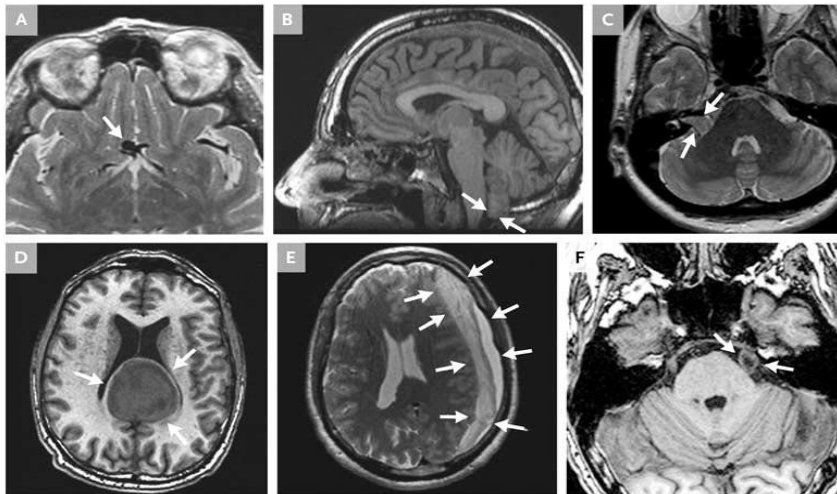
By JENNY HOPE MEDICAL CORRESPONDENT
PUBLISHED: 00:00, 2 April 2014 | UPDATED: 00:06, 2 April 2014



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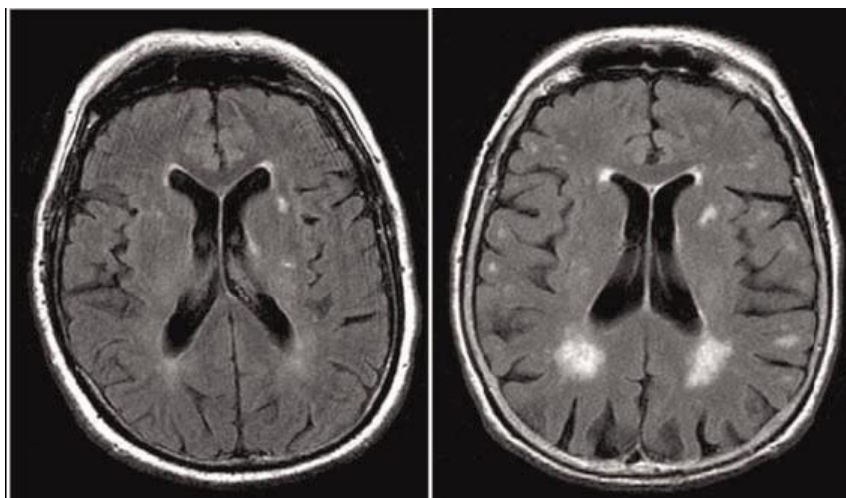
Incidental MRI findings



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

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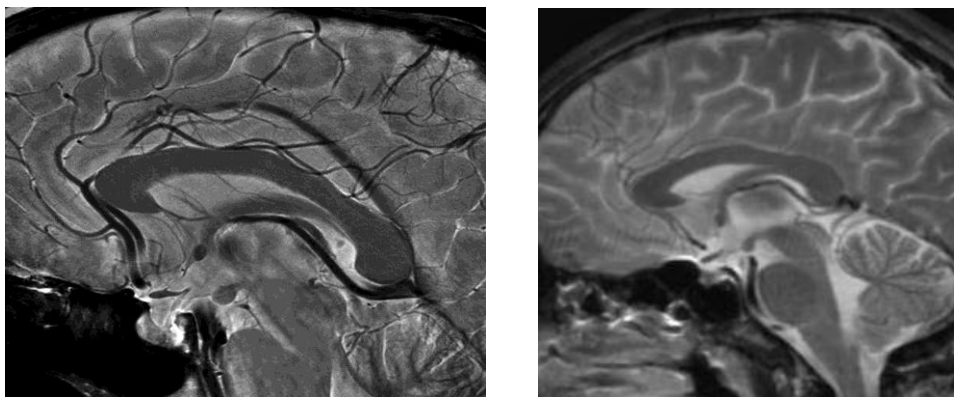
White matter lesions on scan



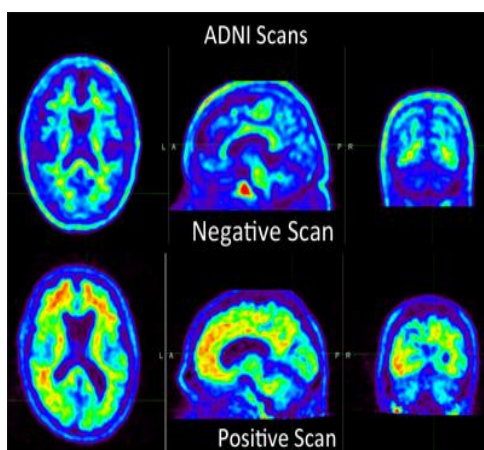
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Future changes in neurological imaging

7T vs 1.5T MRI scan



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



Detects β -amyloid
deposition in brain

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 (typically 100% pay)

The list is long and includes many similar illnesses

ABI/ABI+	Non-standard full benefits
Stroke	Devic's Disease
Multiple sclerosis	Benign Spinal Cord Tumour
Benign Brain Tumour	Progressive Supranuclear Palsy
Parkinson's Disease	Multiple System Atrophy
Alzheimer's Disease	Dementia
Motor Neurone Disease	Bacterial Meningitis
Coma	Encephalitis
Traumatic head injury	Creutzfeldt-Jakob Disease

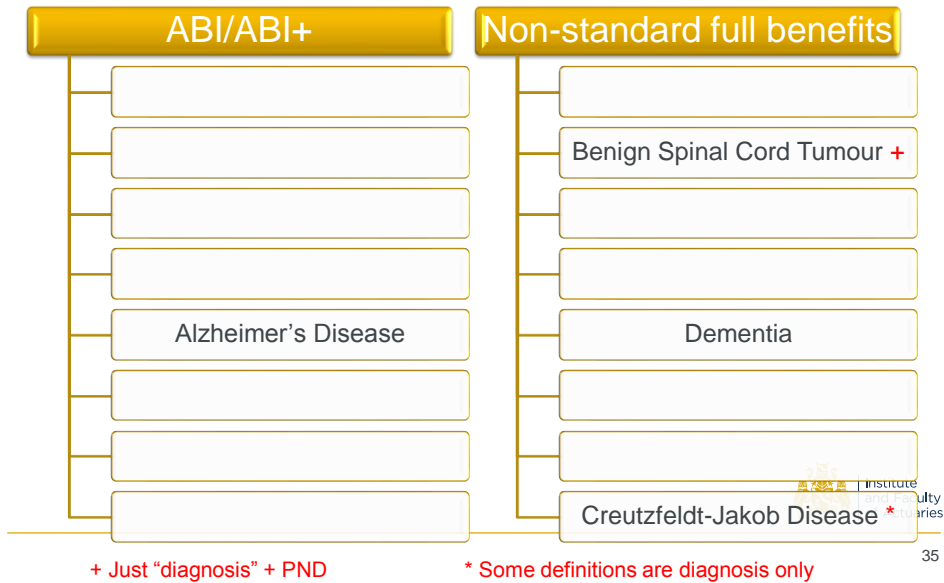
33

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

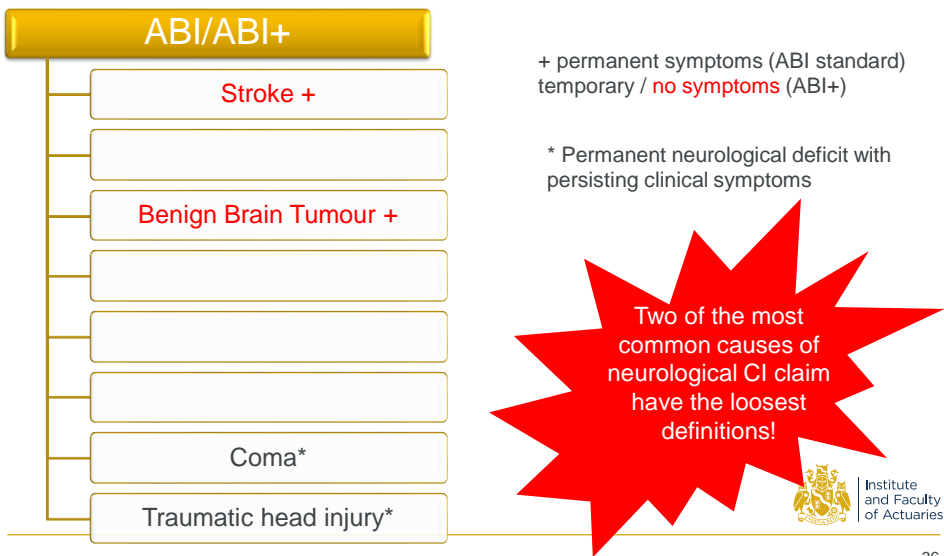
ABI/ABI+	Non-standard full benefits
	Devic's Disease
Multiple sclerosis	
	Progressive Supranuclear Palsy
Parkinson's Disease	Multiple System Atrophy
Alzheimer's Disease	Dementia
Motor Neurone Disease	Bacterial Meningitis
	Encephalitis

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

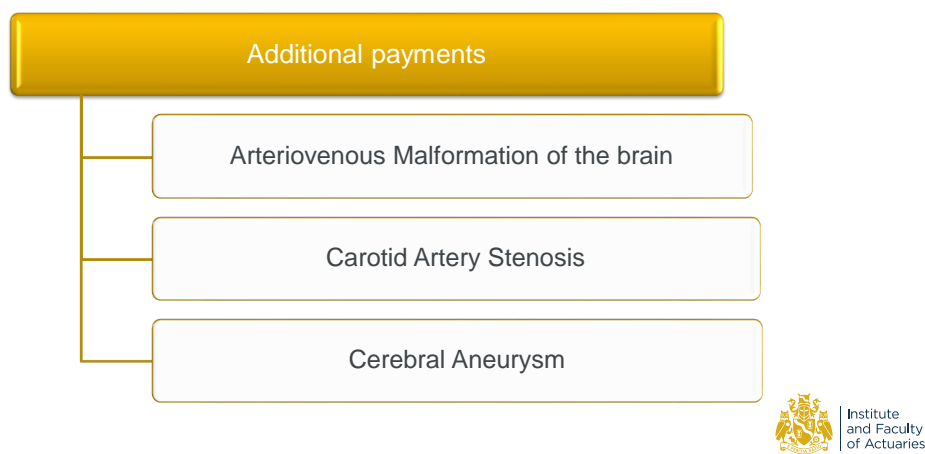


No specification of who makes the diagnosis



Neurological CI claims triggers

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



How representative is the past data we see?

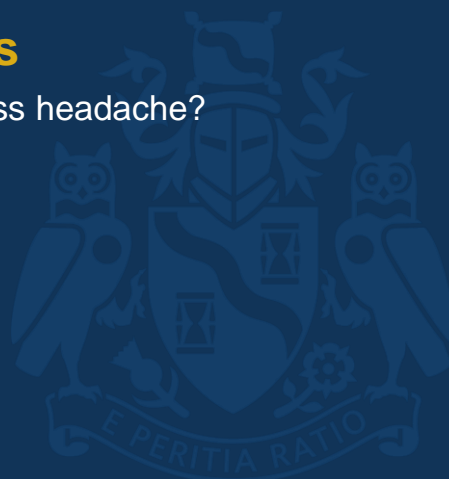




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Incidental MRI findings

Do the statistics suggest an illness headache?



[Presentation Title] | [Name of Presenter] | [MM/DD/YYYY]

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3

Context

Some rough tools to estimate impact of increased neurological claim rates on total Accelerated Illness 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 UK insured lives experience 2003-2006



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MRI findings

Morris Z et al, "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

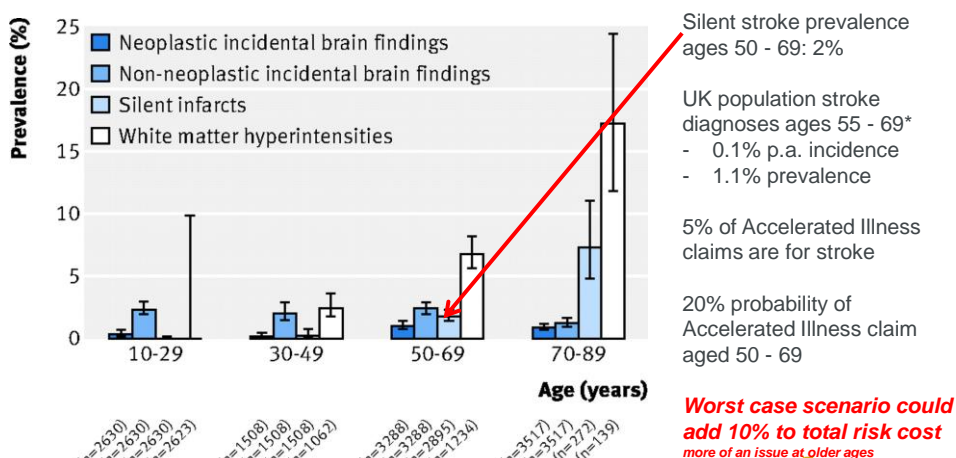
- White matter hyperintensities
- Silent (asymptomatic) brain infarcts
- Brain microbleeds



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MRI findings: Silent stroke

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



* 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

42

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

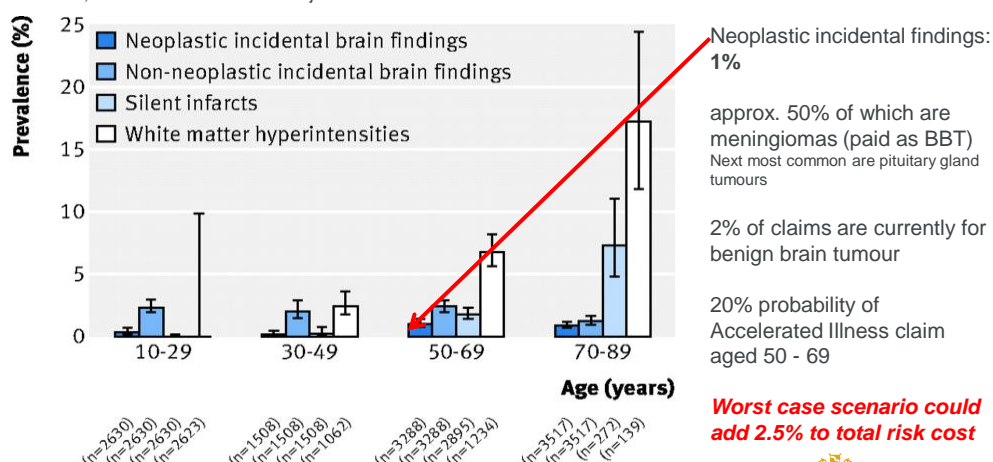
Trial was conducted in the 1990s



- 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*

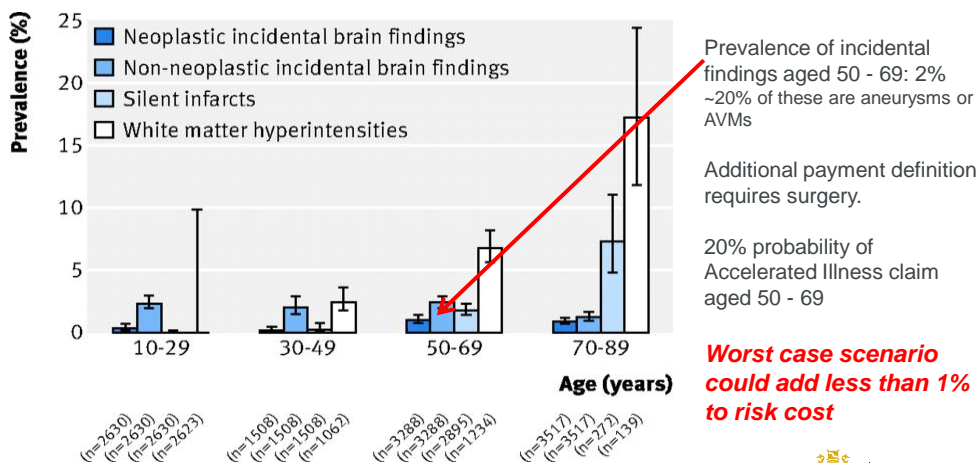
MRI findings: Benign Brain Tumours

Morris Z et al, “Incidental findings on brain magnetic resonance imaging: systematic review and meta-analysis”, BMJ 2009;339:b3016 doi:10.1136/bmj.b3016



MRI findings: aneurysms and AVMs in the brain

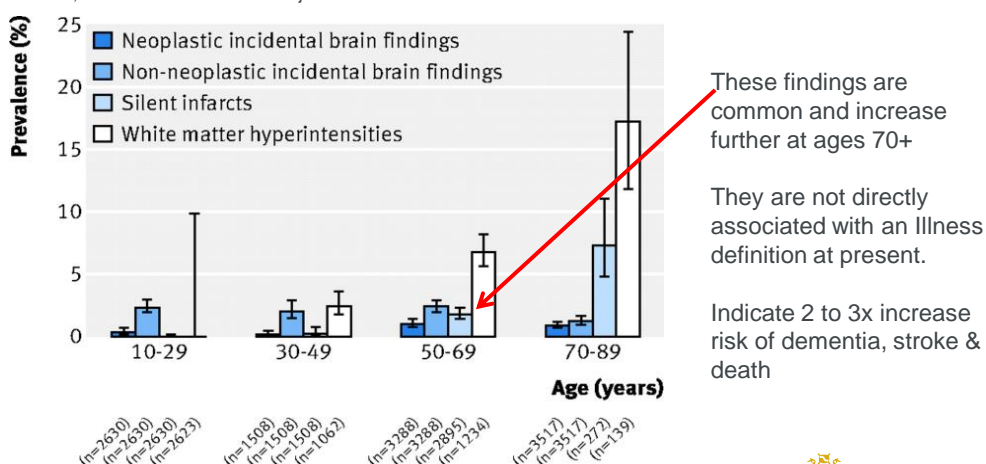
Morris Z et al, "Incidental findings on brain magnetic resonance imaging: systematic review and meta-analysis", BMJ 2009;339:b3016 doi:10.1136/bmj.b3016



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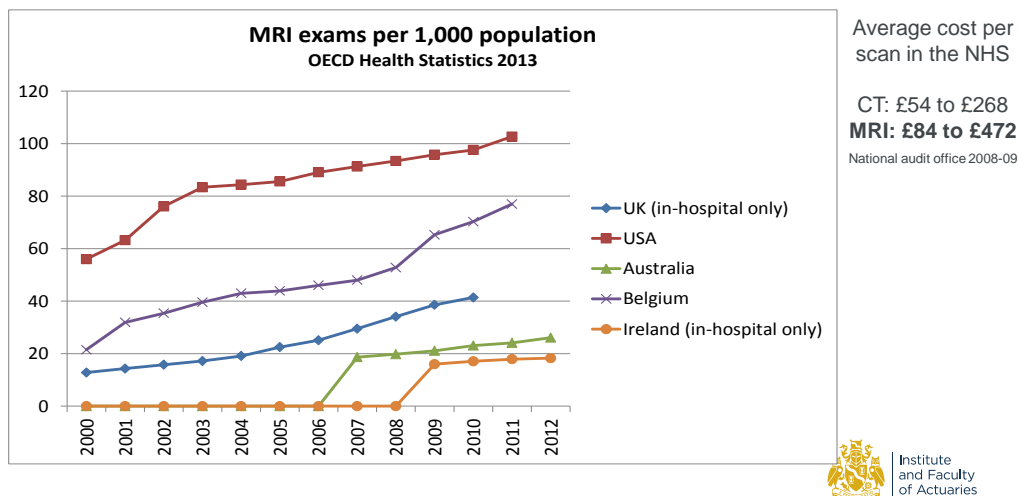
MRI findings: white matter hyperintensities

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



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MRI scans are being done more often



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BMJ

RESEARCH

Insufficient evidence to justify asymptomatic screening

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

Zoe Morris, senior clinical fellow in neuroradiology,¹ William N Whiteley, CSO clinical academic fellow,¹ W T Longstreth Jr, professor of neurology and epidemiology,² Frank Weber, consultant neurologist,³ Yi-Chung Lee, attending physician,⁴ Yoshito Tsushima, associate professor of diagnostic radiology,⁵ Hannah Alphas, medical student,⁶ Susanne C Ladd, consultant radiologist,⁷ Charles Warlow, emeritus professor of medical neurology,¹ Joanna M Wardlaw, professor of applied neuroimaging,^{1,8} Rustam Al-Shahi Salman, MRC clinician scientist and honorary consultant neurologist¹

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²Departments of Neurology and Epidemiology, Harborview Medical Center, Seattle, WA, USA

³German Air Force Institute of Aviation Medicine, Department of Neurology, Fuerstenfeldbruck, Germany

⁴Department of Neurology, Taipei Veterans General Hospital, Taiwan

⁵Department of Diagnostic Radiology and Nuclear Medicine, Guma University Hospital, Japan

⁶Department of Radiology and Radiological Sciences, Johns Hopkins Hospital, Baltimore, MD, USA

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 findings was 37. The prevalence of incidental brain findings was higher in studies using high resolution MRI sequences than in those using standard resolution sequences (4.3% 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.

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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 worst case scenarios appear less catastrophic than other triggers



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.