

# Mild Cognitive Impairment (MCI) in the Older Population

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Future Leaders of Ageing Research (FLARE) Fellow (UK)



Wales Dementias and Neurodegenerative Diseases  
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# Defining the Window of Opportunity for the Treatment and Prevention of Dementia



- Prevention may only be possible prior to disease onset (reversal difficult if not impossible)
- A focus on the earliest identification of disease
- Are there any screening tools that accurately identifies those individuals at high risk of dementia?

# Continuum of Ageing

## Mild Cognitive Impairment (MCI)

- Transitional state between 'normal' ageing and pathological decline
- In clinical samples 10-20% with an MCI case diagnosis progress to dementia (/year) vs. 1-2% of healthy controls
- Is MCI predictive of dementia in the population?

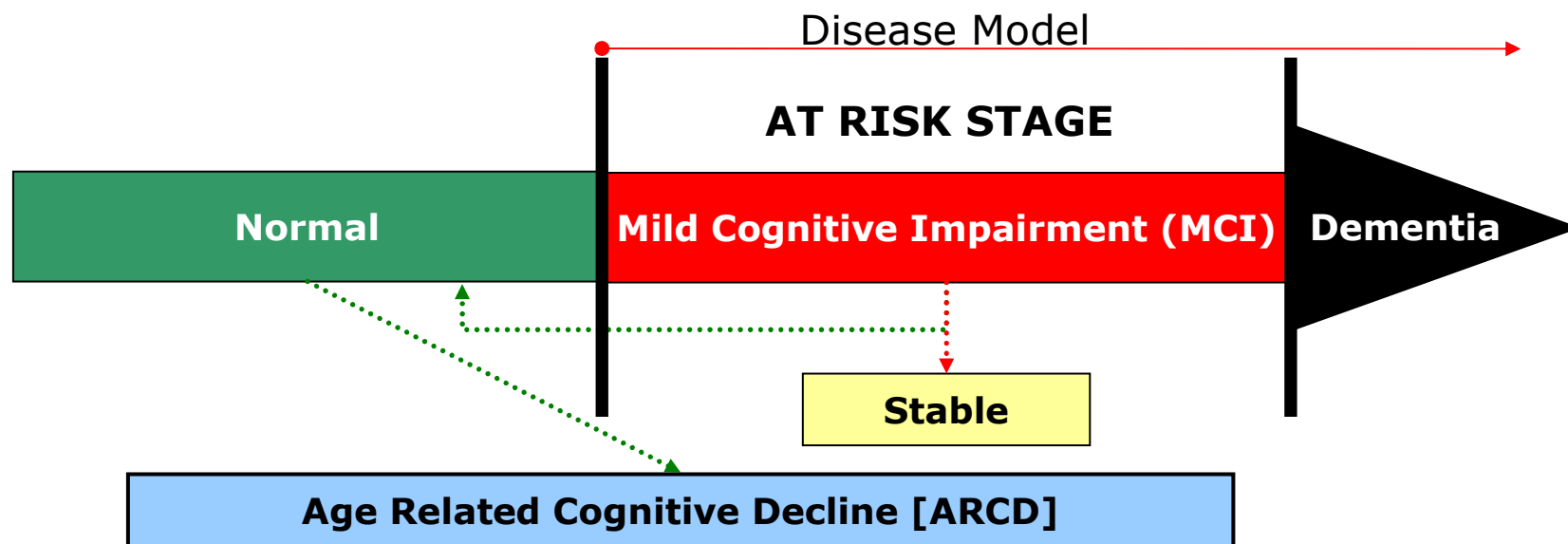


Figure. Cognitive Model of Ageing

# Defining MCI

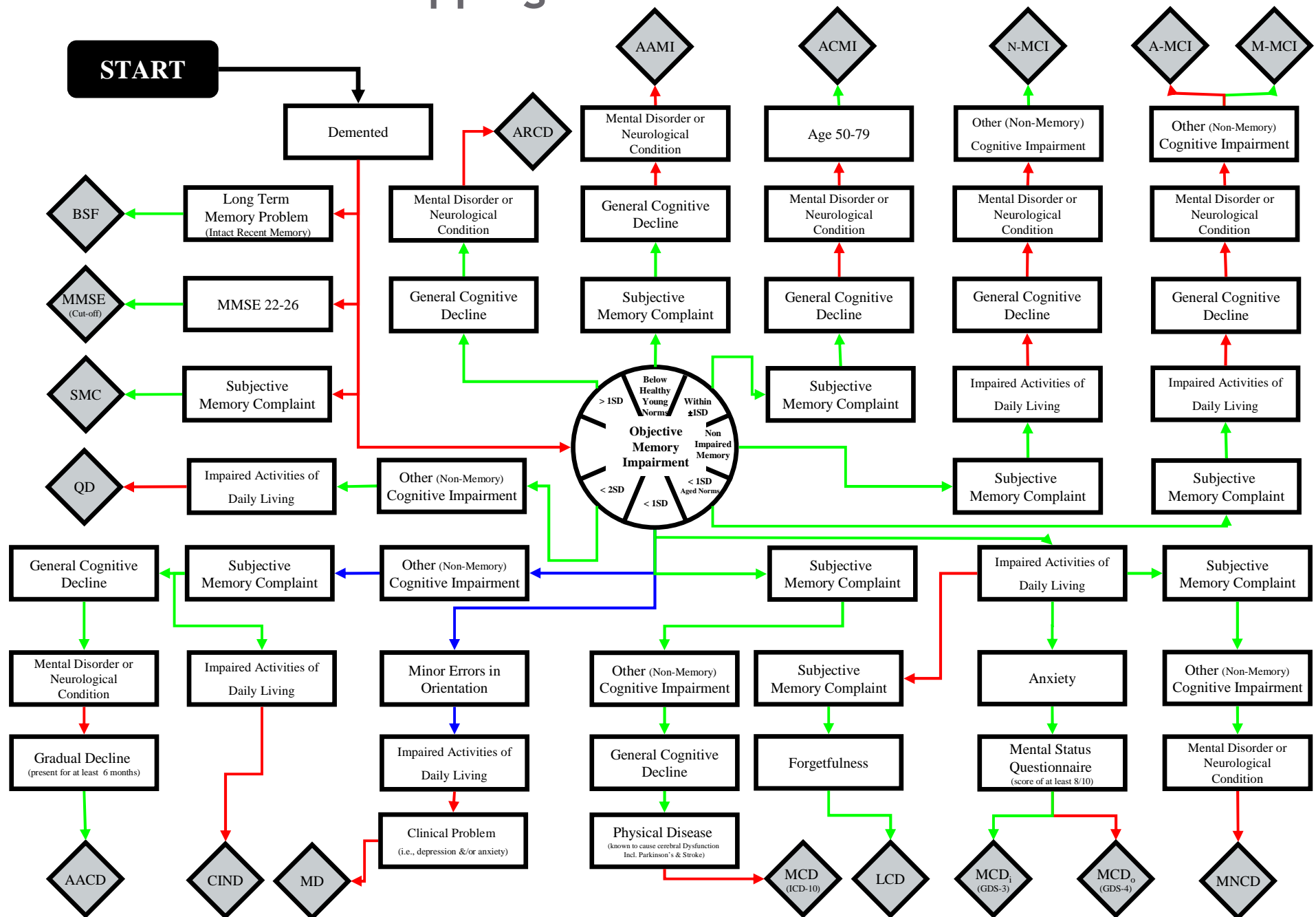
- Various definitions proposed, but no consensus criteria
- Differences in focus and diagnostic criteria
- Definitions can be broadly divided into four groups

System	Description
<b>(1) Classifications Associated With Age Related Cognitive Change</b>	
ACMI	Age Consistent Memory Impairment
ARCD	Age Related Cognitive Decline
<b>(2) Category System</b>	
MMSE Grouping	Mini Mental State Examination Cut-offs [3 Groups]
SMC	Subjective Memory Complaint
<b>(3) Classifications Associated With Pathological Decline</b>	
MNCD	Mild Neurocognitive Disorder
CIND	Cognitive Impairment No Dementia
BSF	Benign Senescent Forgetfulness
AAMI	Age Associated Memory Impairment
LCD	Limited Cognitive Disturbance
QD	Questionable Dementia
AACD	Age Associated Cognitive Decline
MCD	Mild Cognitive Disorder [ICD-10]
<b>(4) Mayo Clinic Criteria</b>	
N-MCI	Non-Amnesic Mild Cognitive Impairment
A-MCI	Amnesic Mild Cognitive Impairment
M-MCI	Multiple Mild Cognitive Impairment

**Search Strategy:** 1950-January 2006

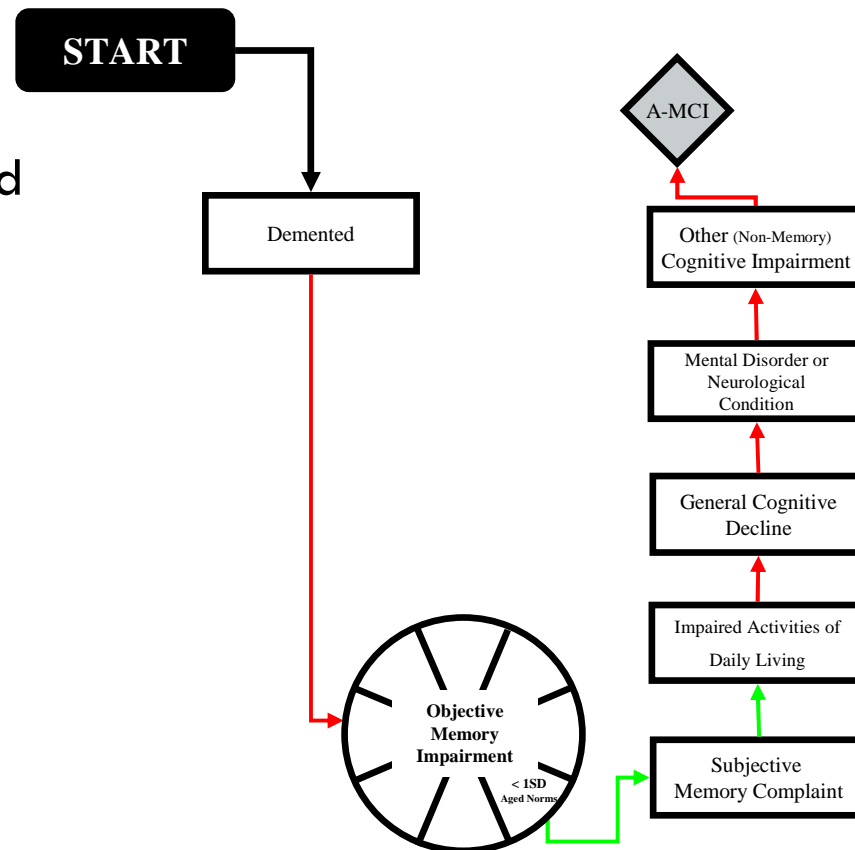
# Framework For Mapping MCI

REFERENCE: Matthews, F. E. et al. Operationalisation of Mild Cognitive Impairment: A Graphical Approach. PLoS Medicine 4, e304 doi:10.1371/journal.pmed.0040304



# Mayo Criteria: Amnestic MCI [A-MCI]

1. Absence of dementia
2. Reduced memory test performance (1 SD below aged corrected norms)
3. Memory complaint (self or informant)
4. No impairment in activities of daily living (ADL)
5. No impairment in general cognitive functioning
6. No medical or neurological condition
7. No impairment in non-memory test performance



# Problems with MCI Criteria



- The multiple definitions MCI can be constructed from a collection of 16 different symptoms
- Definitions vary in content and amount of detail:
  1. Domain of impairment
  2. Operationalisation of each criterion
  3. Exclusion criteria
  4. Acceptable restriction on activities of daily living
- Which criteria?
  - ▣ Selection will depend on which best predicts dementia in the target population (for example, clinical vs. population-based screening)

# The Medical Research Council Cognitive Function and Ageing Study (CFAS)

- Large-scale multi-centre multidisciplinary multi-phased longitudinal study of ageing in the UK
  - 13,004 individuals aged 65+
  - Baseline interview beginning in 1991
  - Five identical centres (6<sup>th</sup> site in Liverpool – different methodology)
  - Rural and urban sites
  - 10 years follow-up completed
  - Biological Resource Program
  
- Core data resources include: sociodemographic, health, genetics, cognitive function, psychiatric symptomatology and disability



Figure. Sites in Britain

# Classifying the Population

- When applied MCI criteria classify individuals into one of three groups:
  1. **Not impaired (NCI)** - Performs within normal limits on all criteria
  2. **MCI** - Satisfies **ALL** MCI criteria for necessary for a case diagnosis
  3. **Other Cognitive Impairment no Dementia (OCIND)** - Are not demented, are not normal but fail to fulfil one or more MCI criteria

# Prevalence and Mean Age for Different Classification Criteria

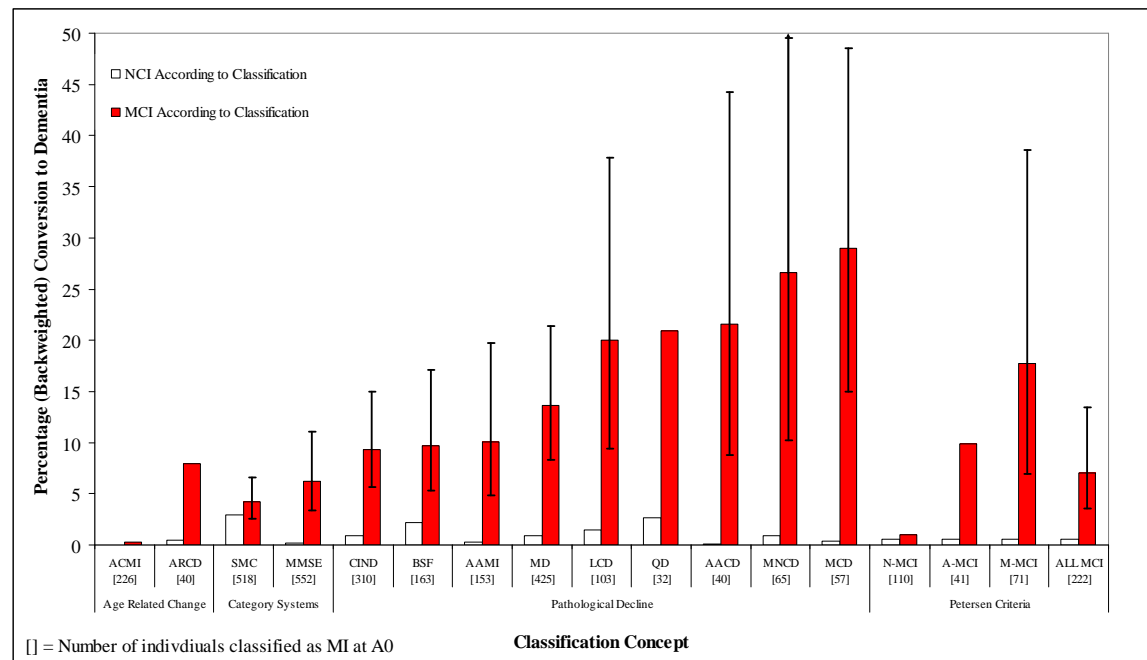
System	N (/2,053)	% (95% CI)	Age (95% CI)
SMC	1035	42.0 (39.3-44.8)	75.0 (74.4-75.5)
MMSE	869	35.2 (32.6-37.9)	74.8 (74.2-75.3)
MD	499	16.7 (14.8-18.7)	76.0 (75.1-76.8)
CIND	449	16.2 (14.4-18.3)	76.5 (75.6-77.4)
ACMI	202	12.7 (10.8-14.9)	71.9 (71.2-72.6)
BSF	299	8.2 (7.0-9.5)	76.5 (75.2-77.7)
N-MCI	109	5.3 (4.2-6.8)	73.4 (72.0-74.8)
LCD	145	4.9 (3.9-6.1)	77.8 (76.1-79.5)
M-MCI	70	2.6 (1.8-3.5)	72.8 (71.4-74.3)
A-MCI	43	2.5 (1.7-3.6)	75.3 (72.9-77.8)
AAMI	28	2.0 (1.3-3.3)	73.6 (71.4-75.8)
MCD10	97	1.8 (1.4-2.2)	80.5 (78.9-82.1)
ARCD	61	1.8 (1.3-2.6)	77.6 (75.3-79.9)
MNCD	74	1.4 (1.0-1.8)	85.1 (83.3-87.0)
AACD	65	1.4 (1.0-1.9)	81.1 (78.8-83.4)
QD	45	0.7 (0.5-1.0)	78.0 (75.6-80.4)
MCDi	10	0.3 (0.1-0.7)	74.4 (70.8-77.9)
MCD <sub>o</sub>	5	0.1 (0.0-0.2)	75.6 (66.3-84.9)

- Prevalence of MCI is highly variable:
  - Non-pathological Impairment: Range: 1.4-1.8%
  - Pathological Impairment: Range: 0.1-42%
- Concordance across classifications is poor (*range: 0-24%*)

**Key:**

AACD	Age Associated Cognitive Decline	MCD <sub>o</sub>	Moderate Cognitive Decline (GDS4)
AAMI	Age Associated Memory Impairment	MCD10	Mild Cognitive Disorder
ACMI	Age Consistent Memory Impairment	A-MCI	Mild Cognitive Impairment (Amnesic)
ARCD	Age Related Cognitive Decline	M-MCI	Mild Cognitive Impairment (Multiple)
BSF	Benign Senescent Forgetfulness	MD	Minimal Dementia
CIND	Cognitive Impairment No Dementia	MNCD	Mild Neurocognitive Disorder
LCD	Limited Cognitive Disturbance	SMC	Self-Reported Memory Complaint
MCDi	Mild Cognitive Decline (GDS3)	QD	Questionable dementia

# Rates of Progression in CFAS

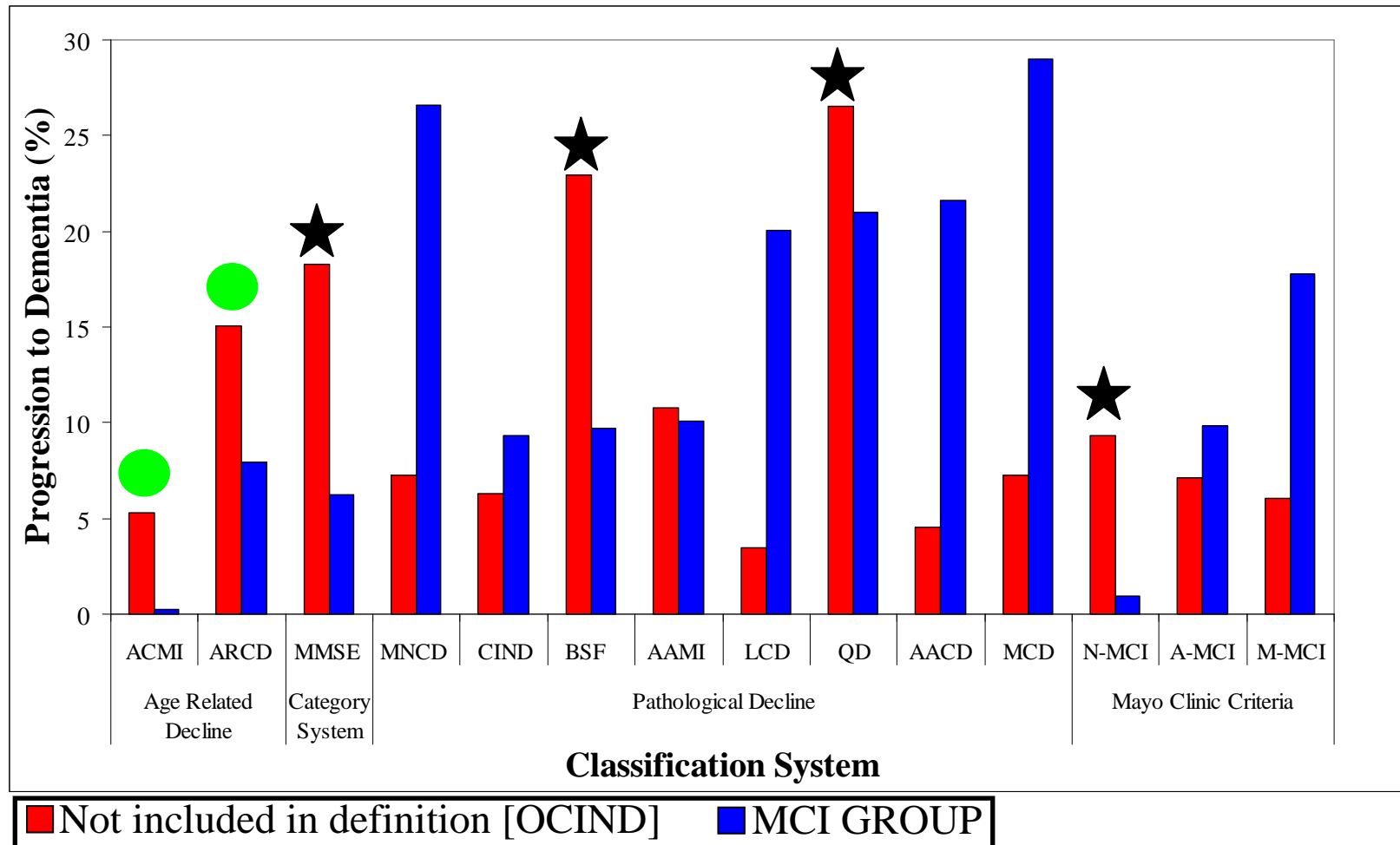


**Figure.** Two-year risk of dementia across the different criteria for MCI

- Progression to dementia at two years was variable across all groups
  - NCI range: 0.0 - 2.4%
  - Cognitive Impairment
    - Non-pathological Impairment Range: 0.3 - 4.0%
    - Pathological Impairment Range: 2.6-30.6%
  - OCIND range: 3.7 - 30.0%
- Inaccurate case selection when using MCI

# Progression to Dementia

## MCI vs. OCIND



- For the OCIND groups progression for some definitions was higher relative to their respective MCI groups

# Two-year Outcomes From MCI

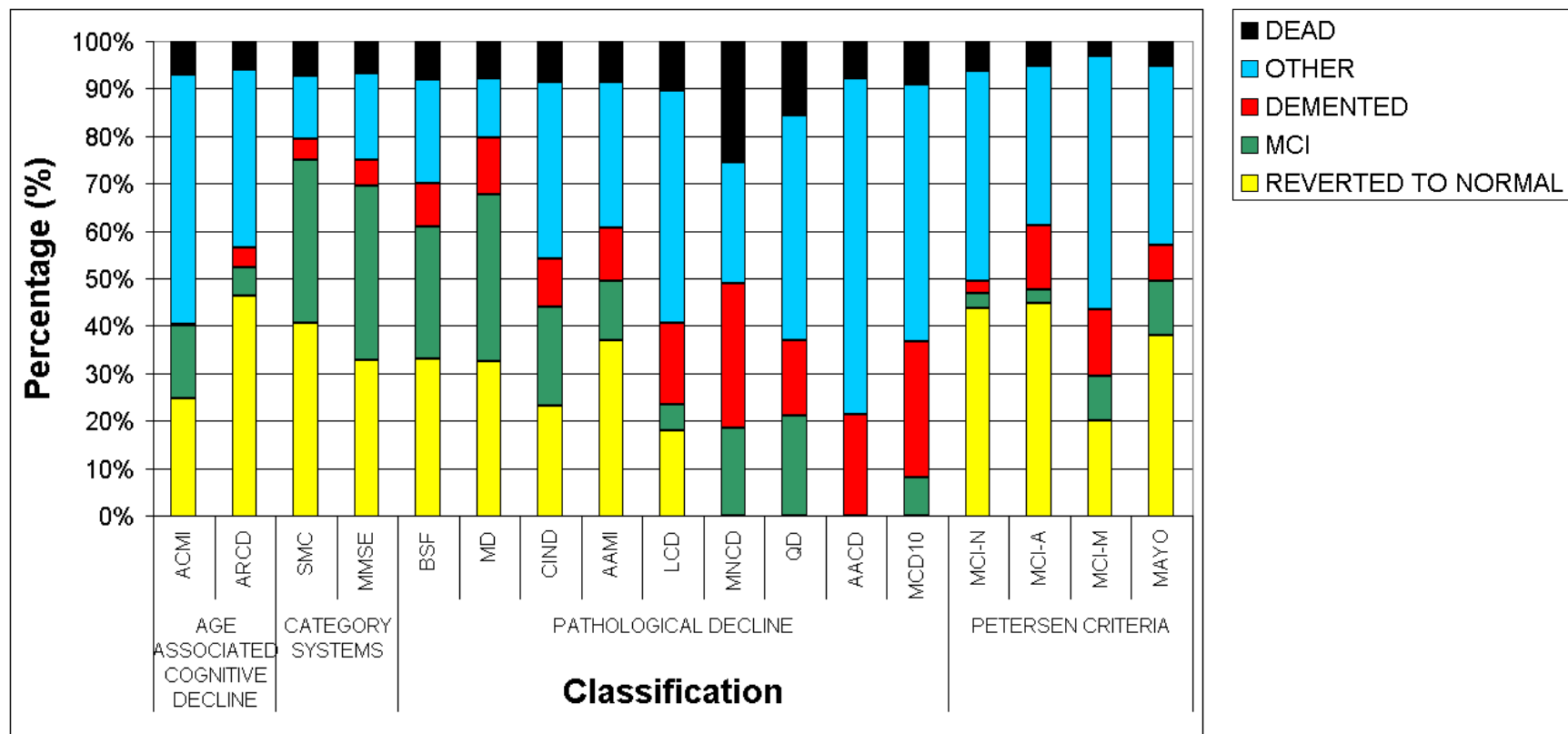


Figure. Two-year outcomes across the different criteria for MCI

- The dominant outcome from MCI at two years was **NOT DEMENTIA** but an impairment which was not classifiable (OTHER) or reversion to normality (NCI)

# Outcomes From MCI

## Clinic vs. Population-Based Samples

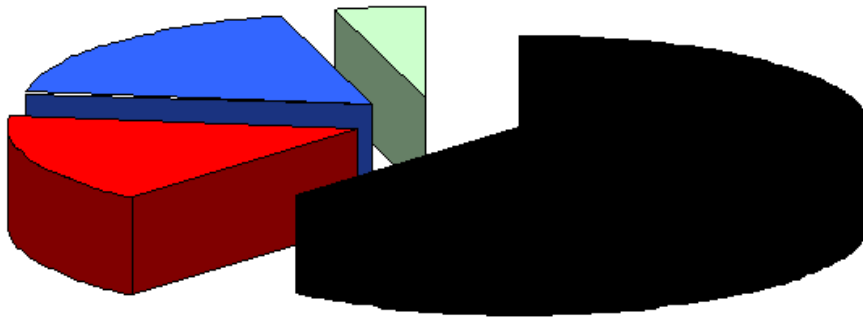
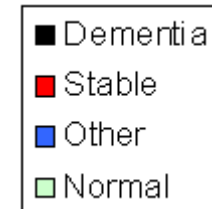


Figure. Clinic Based Outcome

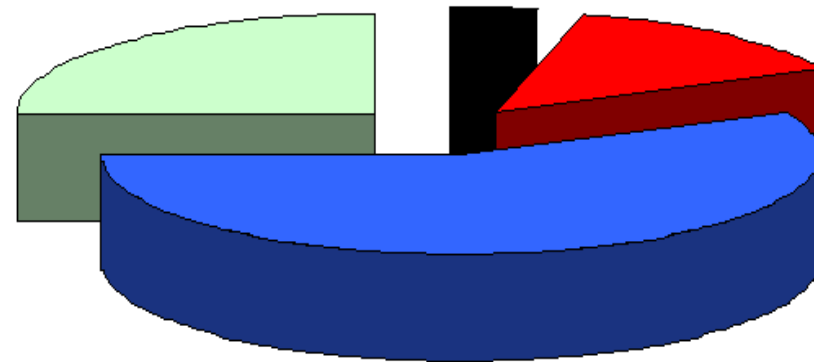


Figure. Population Based Outcome

- Clinical criteria for MCI do not appear to transfer well to the population
- Higher dementia progression in the clinic (clinical judgement?)
- Variable outcome across **BOTH** clinic and population based samples

# Discussion & Conclusions



- The definition of MCI is still currently debated
- No one consensus set of criteria exists that reduces the many heterogeneous systems to a single system
- An individual maybe considered normal in one instance, yet in another impaired
- Most classifications were found to be not sufficiently useful for prediction of dementia
- **CONCLUSION** Early identification of those at risk of progressing to dementia is a major challenge for current concepts of MCI

# Acknowledgements

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***[www.cfas.ac.uk](http://www.cfas.ac.uk)***