Mild Cognitive Impairment: Definition, Diagnosis, Treatment

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Objectives

• Become familiar with:
  - Types of MCI
  - Diagnostic criteria
  - Associated Language and cognitive changes
  - Assessment
  - Treatment (effectiveness of cognitive stimulation)
MCI Defined

*Transitional zone* between normal cognition and dementia. However, not all individuals with MCI develop dementia. **50% will not**

MCI affects approximately 20% of the population over the age of 70 years.

Petersen, 2003
Mayo Clinic, 2009
**Amnestic** Single Domain
**Amnestic** Multiple Domain

**Non-amnestic** Single Domain
**Non-amnestic** Multiple Domain

**Possible Etiologies**
- Degenerative
- Vascular
- Metabolic
- Traumatic
- Psychiatric
MCI - AD

- AD is the most common etiology.
  - Memory impairment is the usual manifestation
  - Exceptions:
    - Primary Progressive Aphasia
    - Posterior Cortical Atrophy
PPA and PCA

• PPA
  - Progressive decline in language is early hallmark symptom
  - Memory deficits appear later

• Posterior Cortical Atrophy
  - Progressive selective decline in complex visual processing
  - Pathology extensive in back of brain
  - Tends to occur at a younger age
CURRENT DIAGNOSTIC ALGORITHM FOR DIAGNOSING AND SUBTYPEING MCI

Cognitive complaint
Not normal for age
Not demented
Cognitive decline
Essentially normal functional activities

MCI
Memory impaired?
Yes
Amnesiac MCI
Memory impairment only?
Yes
Amnesiac MCI
Single Domain
No
Amnesiac MCI
Multiple Domain

No
Non-Amnesiac MCI
Single non-memory cognitive domain impaired?
Yes
Non-Amnesiac MCI
Single Domain
No
Non-Amnesiac MCI
Multiple Domain

© CNS Spectrums
Frequency of MCI Subtypes

• Single domain amnestic MCI is rare.
• Most individuals display deficits in multiple domains (Saunders & Summers, 2010).
• Executive dysfunction is frequently reported (Brandt et al., 2009).
• Evidence indicates that degree of executive dysfunction is predictive of progression to dementia (Albert et al., 2007; Belanger & Belleville, 2009).
NIH-ADRDA new criteria for MCI-AD (McKhann et al 2011)

- Concern regarding change in cognition compared to prior level.
- Impairment in one or more cognitive domains.
- Preservation of independence in functional abilities.
- Not demented.
NIH-ADRDA recommendations included Biomarker criteria

- Reflect
  - disease-related patho-physiological processes
  - Molecular pathology/ accumulation of signature proteins
  - Structural changes - loss of hippocampal volume, reduction in glucose metabolism
  - Biochemical events such as inflammation.
MCI and the trajectory of Alzheimer’s Disease

Karen Bell (2008), Columbia University
Relationship between healthy aging, MCI, and AD
Brains of individuals with MCI - AD

- Pathological changes in medial temporal lobe.
- Degree of temporal lobe atrophy on MRI is associated with conversion to dementia.
Disease typically begins in hippocampal complex

Pretangles – Accumulation of amyloid beta - NFTs

Beta amyloid plaques

Normal neuron

Neurofibrillary tangles

Disease typically begins in hippocampal complex

Pretangles – Accumulation of amyloid beta - NFTs
3-D surface renderings show regions of gray matter loss in groups of patients with amnestic MCI compared to AD.
Notice the relatively restricted pattern of loss in the anteromedial temporal lobes in MCI compared with more widespread loss in temporo-parietal association cortex in AD.
1993: Clinically Normal

1997: Diagnosed with MCI

2001: Diagnosed with AD

2004: Severe atrophy

Serial MRI sections showing progressive hippocampal atrophy
Explosion

- In number of Americans with AD and related dementia
  - 50% of people 75+ have dementia
  - 5.4 million in 2012
  - By 2050, 16 million!

Alzheimer’s Association, 2012
Cost is Staggering

200 billion now
1 trillion in 2050
6th leading killer
If an intervention could delay onset by 5 years ... 

There would be a 57% reduction in the number of AD patients. And a reduction in Medicare costs by 230 billion!

(Sperling et al., 2011)
Risk Factors

• Age
• Apoe carrier status
• Diabetes
• Hypertension
• Depression
• Increased cholesterol
• High alcohol consumption
• Lack of exercise
Protective Factors

- Absence of APOE 4 variant
- Lifetime of exercise
- One alcohol drink
- Nonsmoking
- Controlled cardiovascular risks
- Social stimulation
- Youth
- Healthy diet
Frequency of MCI conversion to dementia

10 to 15% per year

12 to 20% by 30 months

Approximately 48% thereafter
Nidhi Mahendra, PhD
Cognitive-Linguistic changes

Cognitive-Linguistic Deficits
Language Impairments

A powerful predictor of late-life cognitive function
The Nun Study (1991-2002)

Snowdon et al., JAMA, 1996
Kemper et al., Psychology & Aging. 2001, 16 (2): 227-239

- Longitudinal study of 678 Catholic Sisters
- Members of the School Sisters of Notre Dame
- All born before 1917
Linguistic measures in the Nun Study

• **Idea Density**
The average number of ideas expressed per 10 words.

• **Grammatical complexity**
Rated on a 0 to 7 point scale
Early signs of late life AD symptomatology

Low idea density

Less grammatical complexity

I enter'd upon the execution of this plan for self-examination, and continu'd it with occasional intermissions for some time. I was surpris'd to find myself so much fuller of faults than I had imagined; but I had the satisfaction of seeing them diminish. To avoid the trouble of renewing now and then my little book, which, by scraping out the marks on the paper of old faults to make room for new ones in a new course, became full of holes, I transferr'd my tables and precepts to the ivory leaves of a memorandum book, on which the lines were drawn with red ink, that made a durable stain, and on those lines I mark'd my faults with a black-lead pencil, which marks I could easily wipe out with a wet sponge. After a while I went thro' one course only in a year, and afterward only one in several years, till at length I omitted them entirely, being employ'd in voyages and business abroad, with a multiplicity of affairs that interfered; but I always carried my little book with me.

My scheme of ORDER gave me the most trouble; and I found that, tho' it might be practicable where a man's
Nuns with low idea density scores were **30 times more likely** to perform poorly on the MMSE, than those with more complex writings.

More dramatically, neurofibrillar tangles appeared in **90% of nuns** who had low linguistic ability in early life.
Following the Nun Study

Investigations of language in individuals with MCI continue

2002: Chapman and colleagues reported impairment in:
- Processing discourse
- Deriving story gist

Garrard, Maloney, Hodges, and Patterson evaluated lexical diversity of three novels written at different life stages:

- Structure and grammar of her last novel relatively unchanged

- Vocabulary more restricted and simplified

- Smallest number of unique word types

Brain. 128(2), 250-260.
Deficits in episodic memory and category fluency present in 8/10 patients by end of Year 1.

Naming deficits more unstable and variable (assessed using the naming task from the Cambridge semantic test battery).

Impairment of semantic memory, visuo-spatial and attentional abilities eventually developed, but not in a definitive sequence.

Hodges et al. (2006). Dementia and Geriatric Cognitive Disorders. 21, 380-391.
Harris, Kiran, Marquardt, & Fleming reported subtle changes in the discourse of 10 adults with MCI compared to 30 healthy young and 22 HOA.

- **Trip to New York discourse**
- **Variety of discourse analyses conducted**

Individuals with MCI provided:
- **less thematic information**
- **more irrelevant comments**
- **greater verbosity**

**Follow-up**
- **MCI = significantly fewer words and core elements than control groups though average length of T-unit did not differ.**

Harris et al., 2008. Aphasiology, 22(7-8), 813-825.
2008: Review of Language Performance in AD and MCI (Taler & Philips)

- Performance on verbal tasks – An important diagnostic criterion for MCI
  - 60-second category fluency (not letter fluency)
  - Verb fluency more impaired than noun fluency

- Persons with amnestic, multiple domain-MCI or non-amnestic, multiple domain MCI are more likely to progress to AD.
- Authors affirmed the clinical utility of assessing narrative discourse.

2009

- Oulahaj, Wilcock, Smith, and de Jager reported results of a 20 year study
- 241 participants
- CAMCOG
- Language expression was a stronger predictor of duration to conversion than either “learning” or memory.

*Neurology, 73(18), 1436-1442.*
Lifelong bilingualism is associated with a delay in the onset of AD.

Authors aimed to determine if this delay in symptom onset for bilinguals would be seen in onset of symptoms of aMCI.

Effect of bilingualism examined on the age of diagnosis in persons with single- or multiple-domain aMCI who were administered a battery of neuropsychological tests and questionnaires about their language and social background.

2012: Ossher, Bialystok, Craik, Murphy, & Troyer

- **Results**
  - Interaction between aMCI type and language history.
  - Only persons diagnosed with single-domain aMCI demonstrated a later age of diagnosis for bilinguals than monolinguals.
  - Preliminary evidence in support of the early protective advantage of bilingualism and that this may be specific to single-domain aMCI.

Longitudinal study of cognitive-linguistic impairments in MCI

WORK IN PROGRESS
Case 1: BH
Age: 84, Yrs Ed: 18, Former lawyer

- **Initial referral:** Episodes of verbal agitation in response to forgetting
- **No ADL Impairment:** Did not self-report memory problems*, staff reported increased forgetting
- **Medical history:** HTN, Hyperlipidemia, PVD, Hx of Knee Replacement
- **MMSE Year 1:** Score **28/30**
  - Passed a reading comprehension screen (scored 5/5)
MMSE Year 2: Score 26/30. Reading comprehension screen: 2/5

Additional Testing: Using the Dementia Rating Scales-2 and diagnosed as multiple domain MCI given 19th-28th percentile scores in 2 domains.
Case 2: TL
Age 81, Yrs Ed: 12, Former bus driver

- **Initial referral:** Embarrassed by recent memory lapses, failed recent driving test for license renewal
- **No ADL Impairment:** In independent living setting
- **Medical history:** HTN, Asthma
- **MMSE Year 1:** Score **27/30.** DRS-2: Non-impaired range of scores across domains
- **Arizona Battery for Communication Disorders of Dementia:** Total ABCD score was 2 standard deviations below the mean of HOA.
Case 2/Year 2: TL

- **MMSE Year 2:** Score 26/30
- **DRS-2:** No change in total raw score; slightly worse performance on Similarities subtest.
- **ABCD Year 2:** Total ABCD score plummeted a little and now fell within Mean + 2 SD of scores for Mild AD group
- **Year 3 Update:** TL was diagnosed with vascular dementia
Summary: Early language changes

Language expression
Comprehension
Category naming
Defining
Quality of written discourse
Verbal memory
CHERYL TOMOEDA, MS
Role of SLP

Education
Identification
Treatment
ASHA’s Position

• SLPs play a primary role in “screening, assessment, diagnosis, treatment, and research of cognitive-communication disorders associated with dementia” (ASHA, 2005)

• Further, “screening is recommended for all persons, regardless of age, who have a condition that increases their risk for cognitive-communicative problems”. (ASHA, 2005)
Benefits of early ID

- Access to clinical trials
- Can plan for future
- Avoidance of medications that worsen cognitive function
- Access support services
- Make lifestyle changes
Identification

SLPs are uniquely qualified to detect subtle early changes in language and cognitive functions.
But...

- What constitutes “impairment”
- Some go with decline of 1.5 SD
- Others use less
- Workgroup on diagnosis of MCI due to AD (Albert et al., 2011) – individuals with MCI typically score 1 to 1.5 SD below age- and education-matched peers on cognitive tests
Testing for MCI

• Diagnosis of MCI cannot be made on the basis of the results of a single neuropsychological or cognitive-communicative test alone.
• Requires evidence of intrapersonal change (Albert et al., 2001)
• Look for pattern of performance across tests and across time.
Evidence suggests

Testing:
Language
Memory
Mental Status
Language

Verbal Fluency Tests Popular
Quick, easy to score

Two types:
Letter
(FAS)
Semantic category
(Animals, transportation)

SS with MCI worse on both
Category fluency more sensitive

(Taler & Phillips, 2008; Clark et al. 2009)
## MCI/AD performance on Category Fluency

<table>
<thead>
<tr>
<th>Category</th>
<th>Group</th>
<th>Count (Mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABCD</td>
<td>Young Adults</td>
<td>13 (3.2)</td>
</tr>
<tr>
<td></td>
<td>Older Adults</td>
<td>11 (3.4)</td>
</tr>
<tr>
<td></td>
<td>Mild AD</td>
<td>7 (3.5)</td>
</tr>
<tr>
<td></td>
<td>Mod AD</td>
<td>3 (2.9)</td>
</tr>
<tr>
<td></td>
<td>Clark et al. 2009</td>
<td>“Transportation”</td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Clark et al. 2009</td>
<td>“Animals”</td>
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<tr>
<td></td>
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<td></td>
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<tr>
<td></td>
<td>Clark et al. 2009</td>
<td>“Supermarket”</td>
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</tbody>
</table>
- Sensitivity to MCI improves if paired with a story-retelling test in an immediate and delayed condition.
- Story-retelling is particularly sensitive to the episodic memory impairment typical of early AD.
Mental Status

Mini-Mental State Examination - MMSE

Orientation 11 Items
General Knowledge 15 Minutes
Memory 30 Best
Communication 24 and below – Dementia
Copying 25-26 QUESTIONABLE

Mild Cognitive Impairment
Mild Dementia
Moderate Dementia
Severe Dementia

97%
99%
100%
30%
50%
100%
Accuracy of MCI Screen
Accuracy of MMSE
Montreal Cognitive Assessment
MoCA

10 MINUTES
30 BEST
SCORE
26 AND ABOVE IS NORMAL

Attention
Concentration
Executive function
Memory
Language
Visuoconstructual skills
Conceptual thinking
Calculation
Orientation

Nasreddine et al., 2005
www.mocatest.org
# MOCA Scores

<table>
<thead>
<tr>
<th></th>
<th>Normal Controls (NC)</th>
<th>Mild Cognitive Impairment (MCI)</th>
<th>Alzheimer’s Disease (AD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects</td>
<td>90</td>
<td>94</td>
<td>93</td>
</tr>
<tr>
<td>MoCA average score</td>
<td>27.4</td>
<td>22.1</td>
<td>16.2</td>
</tr>
<tr>
<td>MoCA standard deviation</td>
<td>2.2</td>
<td>3.1</td>
<td>4.8</td>
</tr>
<tr>
<td>MoCA score range</td>
<td>25.2 – 29.6</td>
<td>19.0 – 25.2</td>
<td>21.0 – 11.4</td>
</tr>
<tr>
<td>Suggested cut-off score</td>
<td>≥26</td>
<td>&lt;26</td>
<td>&lt;26ψ</td>
</tr>
</tbody>
</table>

ψ Although the average MoCA score for the AD group is much lower than the MCI group, there is overlap between them. The suggested MoCA cut-off score is thus the same for both. The distinction between AD and MCI is mostly dependent on the presence of associated functional impairment and not on a specific score on the MoCA test.
Repeatable Battery for the Assessment of Neuropsychological Status

RBANS

30 MINUTES
2 forms

story memory
line orientation
digit span
coding
figure copying
figure recall
picture naming
semantic fluency
list recall & recognition

Randolph et al., 1998
### RBANS: MCI & Elderly Controls

(Duff, Hobson, Beglinger, & O’Bryant, 2010)

<table>
<thead>
<tr>
<th>RBANS Indexes</th>
<th>MCI</th>
<th>Cognitively Intact</th>
<th>F-value, p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Scale Score</strong>*</td>
<td>92.4 (9.1)</td>
<td>101.5 (10.2)</td>
<td>24.9, &lt;.001</td>
</tr>
<tr>
<td><strong>Immediate Memory</strong>*</td>
<td>97.9 (10.8)</td>
<td>107.1 (12.8)</td>
<td>16.9, &lt;.001</td>
</tr>
<tr>
<td><strong>Visuospatial Constructional</strong></td>
<td>98.3 (12.4)</td>
<td>101.7 (10.9)</td>
<td>4.0, .05</td>
</tr>
<tr>
<td><strong>Language</strong>*</td>
<td>91.2 (9.0)</td>
<td>95.5 (8.8)</td>
<td>8.0, .005</td>
</tr>
<tr>
<td><strong>Attention</strong></td>
<td>100.4 (11.6)</td>
<td>103.1 (14.2)</td>
<td>1.5, 2.3</td>
</tr>
<tr>
<td><strong>Delayed Memory</strong>*</td>
<td>92.4 (9.5)</td>
<td>101.4 (9.2)</td>
<td>22.4, &lt;.001</td>
</tr>
</tbody>
</table>
Pilot data

Suggest sensitivity of certain subtests of the Arizona Battery for Communication Disorders of Dementia (Bayles & Tomoeda, 1993):

• Story-retelling immediate and delayed
• Generative naming
• Defining
• Repetition
• Mental status
• Word learning
## Arizona Battery for Communication Disorders of Dementia (ABCD)

<table>
<thead>
<tr>
<th>Task</th>
<th>Mild AD</th>
<th>Normal Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Story Retelling - Immediate</td>
<td>14.0 (2.8)</td>
<td>17.3 (4.1)</td>
</tr>
<tr>
<td>Story Retelling – Delayed</td>
<td>1.0 (2.6)</td>
<td>12.4 (4.5)</td>
</tr>
<tr>
<td>Generative Naming (category)</td>
<td>7.1 (3.5)</td>
<td>11.4 (3.4)</td>
</tr>
<tr>
<td>Concept Definition</td>
<td>41.2 (11.3)</td>
<td>56.6 (5.0)</td>
</tr>
<tr>
<td>Repetition</td>
<td>59.2 (11.5)</td>
<td>67.9 (7.0)</td>
</tr>
<tr>
<td>Mental Status</td>
<td>9.9 (2.6)</td>
<td>12.8 (0.6)</td>
</tr>
<tr>
<td>Word Learning – Total Recall</td>
<td>7.7 (3.9)</td>
<td>15.1 (1.2)</td>
</tr>
</tbody>
</table>
Screen

- Individuals 55 and older
- Health fairs
- Clinics
- Hospital in-patients
- Reside in housing designed for elders
- Spouses of elders with communication problems
Questionnaire

• Ask about risk factors
  – Diabetes
  – High cholesterol
  – Smoking
  – Depression (change in mood)
  – Amount of exercise
  – Amount of alcohol consumption
  – Amount of social participation
Consider these opportunities

- Visits for hearing tests
- Residents of nursing and rehabilitation centers
- Spouses of individuals getting therapy
- Cardiovascular or bone density screenings
- When admitted to hospitals
Hospitalized elders (Bickel et al., 2006)

N = 794 non-demented pts. 65-85 years

Prevalence of MCI = 36%
61% 3.5 months later
Bedside screenings

Measures to consider:

• Verbal Fluency (Category)
• MoCA
• ABCD Story Retelling (Immediate and Delayed Recall)
Kim McCullough, PhD
Treatment of MCI

Intervention the KEY to Prevention?
Reports of the benefits of cognitive intervention for both Healthy Older Adults and individuals with MCI have given affected individuals hope.
Cognitive Intervention Defined
(Belleville. 2008)

Cognitive Training
• Teaching theoretically based strategies & skills to optimize cognition
• Standardized fashion
• Individual or Small group

Cognitive Stimulation
• Focus on increase of general cognitive and social skills in a non-specific format
• Discussions, leisure activities
• Small groups
Systematic literature review addressed the efficacy of 15 cognitive intervention programs on individuals with amnestic MCI.

Significant improvements were reported:

- On 44% of memory measures
- 12% of other measures of cognition
- On 49% QoL, mood and subjective reports of memory
Meta-analysis: Li et al., 2011

• 17 MCI cognitive intervention studies included

Key points:

• Improvement in overall cognition & self-ratings
  – Small improvements in episodic and semantic memory, EF, attention, processing speed
  – Moderate improvements in Language (2 studies)
Meta-analysis: Li et al., 2011

- Computer-based intervention and structured teaching intervention both good for cognitive training
Healthy Older Adults: The ACTIVE Trial (2006)

- N=2832 volunteers
- MMSE 27.3 (23-30)
- Intervention: Cognitive Training
  - 10 one hour sessions
  - 4 session “Booster training” at 11mths & 35mths
  - 3 intervention groups: Memory, Reasoning or Speech of Processing

Healthy Older Adults: The ACTIVE Trial (2006)

- **Memory Training**
  - Mnemonic strategies (organization, visualization, association) for remembering verbal material

- **Reasoning Training**
  - Strategies for finding patterns in letter or word series
  - Identifying the next item in a series

- **Speed of Processing Training**
  - Visual search and divided attention (computer based)
Healthy Older Adults: The ACTIVE Trial (2006)

- Cognitive Training resulted in less functional decline compared to a control group.
- Improved (trained) Cognitive Abilities remained 5 years after intervention.

MCI Adults: Episodic Memory (Belleville et al., 2006)

- N = 28 MCI, 17 HOA
- Treatment & Control groups
- MMSE 28.94 – MCI, 29.0 for HOA
- Intervention: Cognitive Training
  - 8 wkly 2 hour sessions plus homework
  - Small group of 4-5
MC I: Episodic Memory

(Belleville et al., 2006)

• Components:
• **Session 1**
  – Education about aging, cognition, & program
• **Sessions 2-3**
  – Computer Assisted Attention training:
• **Sessions 4-8**
  – Memory Strategies/Techniques
  – Face-name association, PQ RST, method of loci, verbal organization
MCI: Episodic Memory  
(Belleville et al., 2006)

Results

- Treatment groups (MCI & HOA) improved on objective measures; control groups (MCI & HOA) did not improve
- MCI can improve memory performance (delayed word recall and face-name memory) and increased self-reported memory functioning in daily life
Evidence of Brain Plasticity in MCI (Belleville et al., 2011)

- fMRI used to measure effect of training on brain activation in HOA & MCI
- N=15 MCI, 15 HOA
- 2 pre-training scans, 1 post-training scan
  - Verbal encoding and retrieval
- Intervention: Belleville et al., 2006
  - 6 weeks, 2 hour sessions, 12 hours total
Evidence of Brain Plasticity in MCI (Belleville et al., 2011)

- **MCI Results**
  - Training resulted in large network of increased brain activation
    - **Encoding**
      - (R) inferior parietal lobe & frontal gyrus
    - **Procedural Memory**
      - Right cerebellum and left BG
    - **Retrieval**
      - Left parietal and prefrontal cortex & superior temporal gyrus bilaterally
Evidence of Brain Plasticity in MCI (Belleville et al., 2011)

- Brain areas activated correlated with the “content” of the intervention.
- Memory training resulted in significant neural changes that are measurable with brain imaging.
Memory Intervention: Goal-Oriented Rehab (Londos et al., 2008)

- N = 15 MCI
- Memory strategy group training program-
  - learned problem-solving to overcome memory problems and mind-mapping strategies
- 2 days/week for 8 weeks
- Results: improvements in cognitive processing speed, occupational performance, and QoL domains
Memory Intervention: Mnemonic Strategy Training (Hampstead et al., 2012)

- N = 18 aMCI and 16 HOA
- **Intervention:** Taught to use a three-step process for object location based on a salient feature close to the object
- 5 sessions within 2 weeks
- **Results:** MCI Mnemonic strategies group showed increased activity within the left hippocampal body for both trained and untrained stimuli
Cognitive Intervention: Computer-Based Training (Barnes et al., 2009)

- N = 47 MCI
- 100 minutes/day, 5 days/week for 6 weeks
- Designed to improve processing speed and accuracy through several tasks that adaptively changed difficulty.
- **Results:** Computer-based training is feasible. Verbal learning and memory favored the intervention.
Intervention: Final Thoughts

• More research
  – Larger sample sizes, randomized controlled designs
• Intervention Format
• Outcome measures
• Generalization
• Functional impact
• Long-term efficacy
References


References

References