The MATRICS Consensus Cognitive Battery

Keith H. Nuechterlein, Ph.D.

UCLA

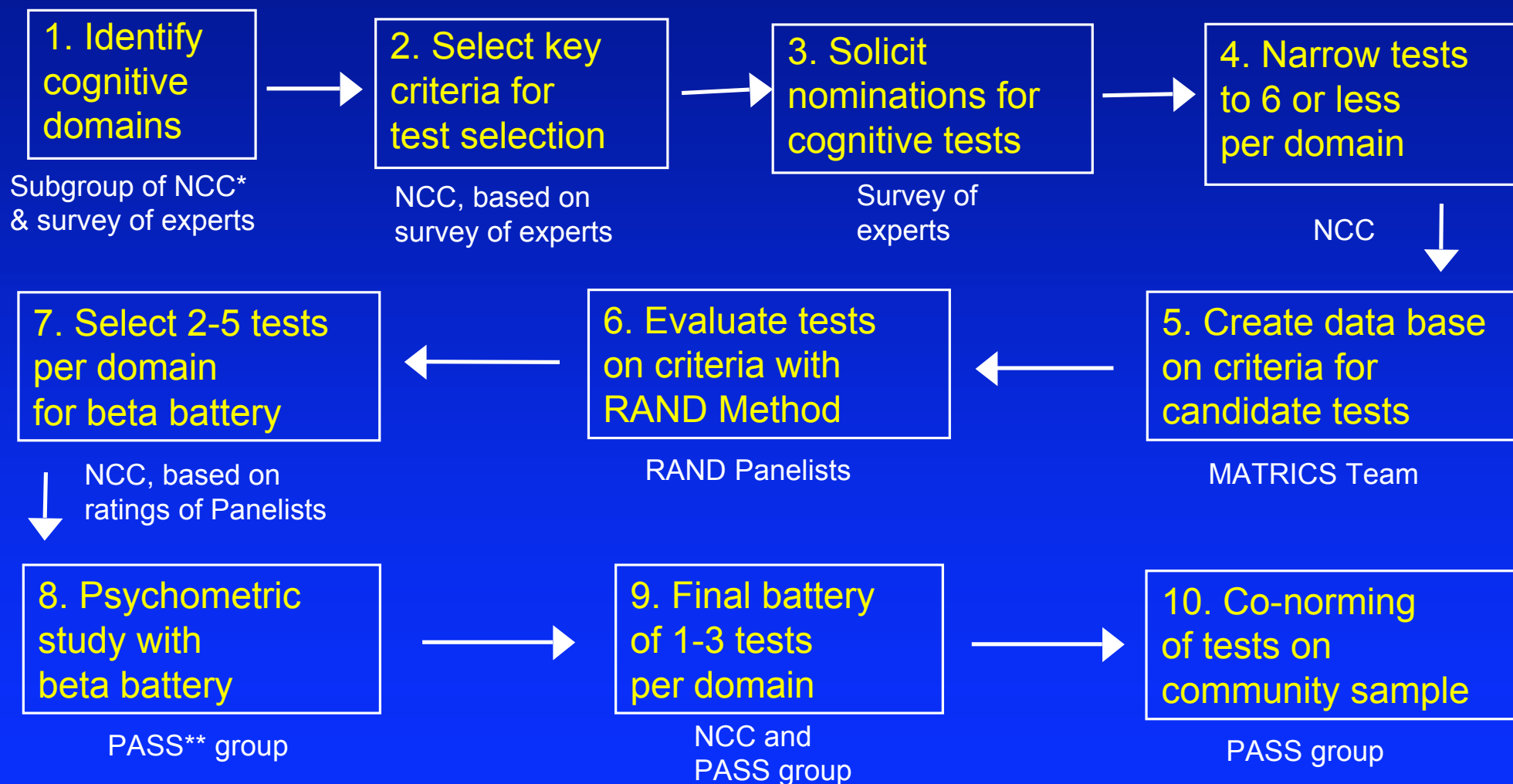Co-Chair, MATRICS Neurocognition Committee

Goals of NIMH-MATRICS Initiative:

- Create a standardized cognitive battery for use in clinical trials that represents a consensus among experts.
- Define optimal experimental designs.
- Facilitate path to FDA approval.
- Attract large pharmaceutical companies to focus efforts on this important clinical target.

Neurocognition Committee for MATRICS-NIMH Consensus Cognitive Battery for Clinical Trials in Schizophrenia

- Keith Nuechterlein (UCLA) - Co-Chair
- Michael Green (UCLA) - Co-Chair
- Deanna Barch (Washington University)
- Jonathan Cohen (Princeton University)
- Susan Essock (Mt. Sinai School of Medicine)
- Wayne Fenton (NIMH)
- Fred Frese (Summit County Recovery Project)
- Jim Gold (Maryland Psychiatric Research Center)
- Terry Goldberg (NIMH)
- Robert Heaton (UCSD)
- Richard Keefe (Duke University)
- Helena Kraemer (Stanford University)
- Daniel Weinberger (NIMH)
- Steve Zalcman (NIMH)

Steps to MATRICS Consensus Cognitive Battery

1. Identify cognitive domains

Subgroup of NCC* & survey of experts

→

2. Select key criteria for test selection

NCC, based on survey of experts

→

3. Solicit nominations for cognitive tests

Survey of experts

→

4. Narrow tests to 6 or less per domain

NCC

↓

7. Select 2-5 tests per domain for beta battery

NCC, based on ratings of Panelists

←

6. Evaluate tests on criteria with RAND Method

RAND Panelists

←

5. Create data base on criteria for candidate tests

MATRICS Team

↓

8. Psychometric study with beta battery

PASS** group

→

9. Final battery of 1-3 tests per domain

NCC and PASS group

→

10. Co-norming of tests on community sample

PASS group

*NCC: MATRICS Neurocognition Committee
**PASS: MATRICS Psychometric and Standardization Study

MATRICS

Process of Delineating Separable Cognitive Factors in Schizophrenia
(Nuechterlein, Barch, Gold, Goldberg, Green, and Heaton, 2004)

- **Emphasis on a few dimensions that are independent or only weakly intercorrelated**
- **Emphasis on replicable dimensions**
- **Initial guidance from research on separable neuropsychological factors in normal samples (e.g., WAIS-III and WMS-III)**
- **Examination of 13 factor analytic studies of cognitive measures in schizophrenia**
- **Consideration of probable pharmacological sensitivity**

MATRICS

Separable Cognitive Domains in Schizophrenia

- **Speed of Processing**
- **Attention/Vigilance**
- **Working Memory**
- **Verbal Learning and Memory**

- **Visual Learning and Memory**
- **Reasoning and Problem Solving**
- **Social Cognition**

Nuechterlein, Barch, Gold, Goldberg, Green, & Heaton (2004), *Schizophrenia Research.*

MATRICS

Essential Criteria for Consensus Cognitive Battery for Clinical Trials in Schizophrenia

Battery:

- **Inclusion of the seven cognitive domains**

- **Valid assessment of cognition at the level of all individual major cognitive domains**

Individual Tests:

- **High test-retest reliability**

- **High utility as a repeated measure**

- **Demonstrated relationship to functional outcome**

- **Demonstrated tolerability and practicality**

  Green, Nuechterlein, et al. (2004), Biological Psychiatry.

Evaluation of Over 90 Nominated Neurocognitive Tests

1) The Neurocognition Committee discussed over 90 nominated tests and chose the most promising 36 tests for formal ratings by a separate RAND Panel of experts (April – July, 2003).

2) The RAND Panel rated these 36 tests on each of the selection criteria (September, 2003).

3) The Neurocognition Committee selected the 20 most promising tests for direct comparison in a psychometric study (2004).

MATRICS

The MATRICS Psychometric and Standardization Study (PASS)

PHASE 1:

To collect psychometric data for beta version of battery -- provide basis for selection of final consensus battery

To assess validity of proxy measures of functional outcome & interview-based assessments of cognition

- 176 schizophrenia patients at baseline; 167 at 4 weeks

PHASE 2:

To provide co-norms for the final MATRICS battery so that results can be standardized relative to a community sample and composite scores can be derived

- 300 adults ascertained through survey sampling from general community, stratified by age, education, and gender

MATRICS

The MATRICS Psychometric and Standardization Study (PASS)

5 - Site Study:

- **UCLA / Los Angeles VA (M. Green/K. Nuechterlein)**
- **Duke University (R. Keefe)**
- **Harvard University (L. Seidman/R. Mesholam)**
- **Maryland Psychiatric Research Center (J. Gold)**
- **University of Kansas (L. Baade)**

Selection of Final MATRICS Consensus Cognitive Battery

MATRICS Neurocognition Committee:

- All with conflict of interest recused themselves for that domain
- Committee evaluated data for each criterion
- Used blind votes to rank candidate tests
- Selected the highest rank test(s)
- Final battery takes 64 minutes of testing time

MATRICS Consensus Cognitive Battery
Listed at www.matrics.ucla.edu

Speed of Processing
- Category Fluency
- BACS Symbol Coding
- Trial Making A

Attention / Vigilance
- Continuous Performance Test
  - Identical Pairs version

Working Memory
- Letter-Number Span
- WMS-III Spatial Span

Verbal Learning
- Hopkins Verbal Learning Test-R

Visual Learning
- Brief Visuospatial Memory Test-R

Reasoning and Problem Solving
- NAB Mazes

Social Cognition
- MSCEIT Managing Emotions

Recommendations from the NIMH to the FDA re: MATRICS Consensus Cognitive Battery

- The MATRICS Consensus Cognitive Battery should be used as the standard battery for all clinical trials of potential cognition-enhancing agents for schizophrenia.
- The battery should always be administered in its entirety in clinical trials (64 minutes).
- An overall cognitive composite score consisting of equal weighting of the 7 domain scores is the primary cognitive endpoint for agents believed to enhance cognition broadly.
- Alternatively, a small subset of domains may be combined as the primary cognitive endpoint for agents believed to enhance cognition selectively (e.g., the learning and memory domains).

MATRICS

Availability of MATRICS Consensus Cognitive Battery

- The tests are being consolidated into a unified and convenient testing battery.

- The battery will include a computer program that generates standardized scores for each domain and the overall composite score.

- We anticipate that this testing kit will be available by the end of 2005.

- Orders for the battery will be placed through The Psychological Corporation or Multi-Health Systems, or possibly also through Psychological Assessment Resources, Inc.

MATRICS

Kit for MATRICS Consensus Cognitive Battery

1) Manual for the MATRICS Battery
2) CPT-IP Program Disk
3) Scoring Program Disk
4) BACS Symbol Coding Scoring Template
5) BVMT-R Recall Stimulus Booklet
6) WMS-III Spatial Span Board
7) 25 MATRICS Battery Administrator's Forms
8) 25 MATRICS Battery Respondent's Booklets
9) 25 HVLT Test Booklets
10) 25 NAB Mazes Record Forms

MATRICS

Steps in Translation of MATRICS Consensus Cognitive Battery

- Identify languages into which component tests are already translated
- Identify primary languages into which battery should be translated
- Agreements with test owners
- Translation and back-translation
- Possible co-norming in new languages

MATRICS

Computerizing the MATRICS Consensus Cognitive Battery: Pros

- Once successfully computerized, the standardized administration of the tests would be somewhat easier to achieve.

- Less training of the test administrator would be needed for some tests in the battery.

- If a fully computerized scoring system could be successfully developed, scoring would be faster.

MATRICS

Computerizing the MATRICS Consensus Cognitive Battery: Cons

- The optimal psychometric properties that led to test selection would need to be fully duplicated.
- Some tests (e.g., BVMT-R) would be difficult to computerize in a wholly comparable way.
- The resulting battery would not necessarily be much easier to use than the original battery, as tests were chosen for ease of use in present form.
- Reactions to computerized tests in developing countries might not be comparable to those in high-tech countries.
- Copyrighted tests would need to be computerized by their owners or through formal arrangements with the owners.

MATRICS

Summary of Status of the MATRICS Consensus Cognitive Battery

- A 10-test battery that takes 64 minutes of testing time has been finalized.
- Tests were selected for ease of use and ease of scoring.
- A consolidated testing kit, with a complete Manual, will be available in the next few months.
- Ordering of the full battery kit and associated test booklets will be convenient through major psychological test publishing companies.
- Survey being completed now to estimate needed supplies.

MATRICS

Reorder Packet for
MATRICS Consensus Cognitive Battery

1. **25 MATRICS Battery Administrator's Forms --Instructions for administering Category Fluency, Trail Making Part A, BACS Symbol Coding, CPT-IP, Letter-Number Span, WMS-III Spatial Span, BVMT-R, NAB Mazes, MSCEIT Managing Emotions**

2. **25 MATRICS Battery Respondent's Booklets –**
    a) **Trail Making Part A**
    b) **BACS Symbol Coding**
    c) **BVMT-R Response Pages**
    d) **MSCEIT Item Booklet-Managing Emotions**

3. **25 HVLT Test Booklets**

4. **25 NAB Mazes Record Forms**

MATRICS