Practical issues in the assessment of Cognition

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Disclosure

Consulting, Grants, Speakers Bureau

- Addex, Abbot, AstraZeneca, BMS, Credit Suisse First Boston, Eli Lilly, Enkam, Fidelity Life Sciences, GSK, Janssen, Johnson and Johnson
- Lundbeck, Morgan Stanley, Nomura, Novartis, Organon, Parexel, Quinitles, Sanofi, Solvay, Targacept, Pfizer, Wyeth

Shareholder :

- Cogtest Inc
- Cognition Group Inc
- Psychmed Inc
- Sovereign Health plc

What type of compound and what type of tests

- Broad Spectrum Antipsychotic
- Specific Cognitive Enhancer
- Add on?
- Types of tests, batteries and platforms
- Pharmacosensitivity

PIVOTAL MEASURES

- Which are the key domains?

- Significant difference from placebo in
  - One domain
  - Several domains
  - Neurocognitive Global Score

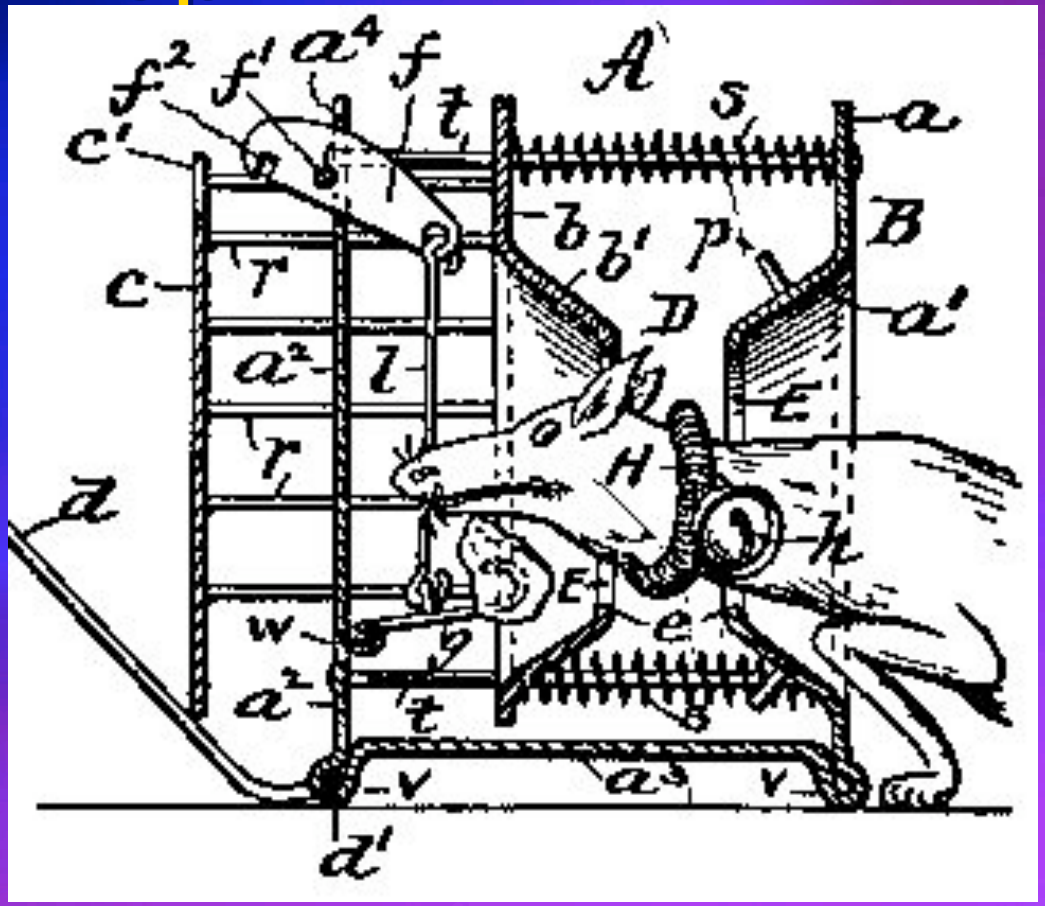
Do all Domains follow a similar course?

Figure 2. Age Effect on Composite Scores

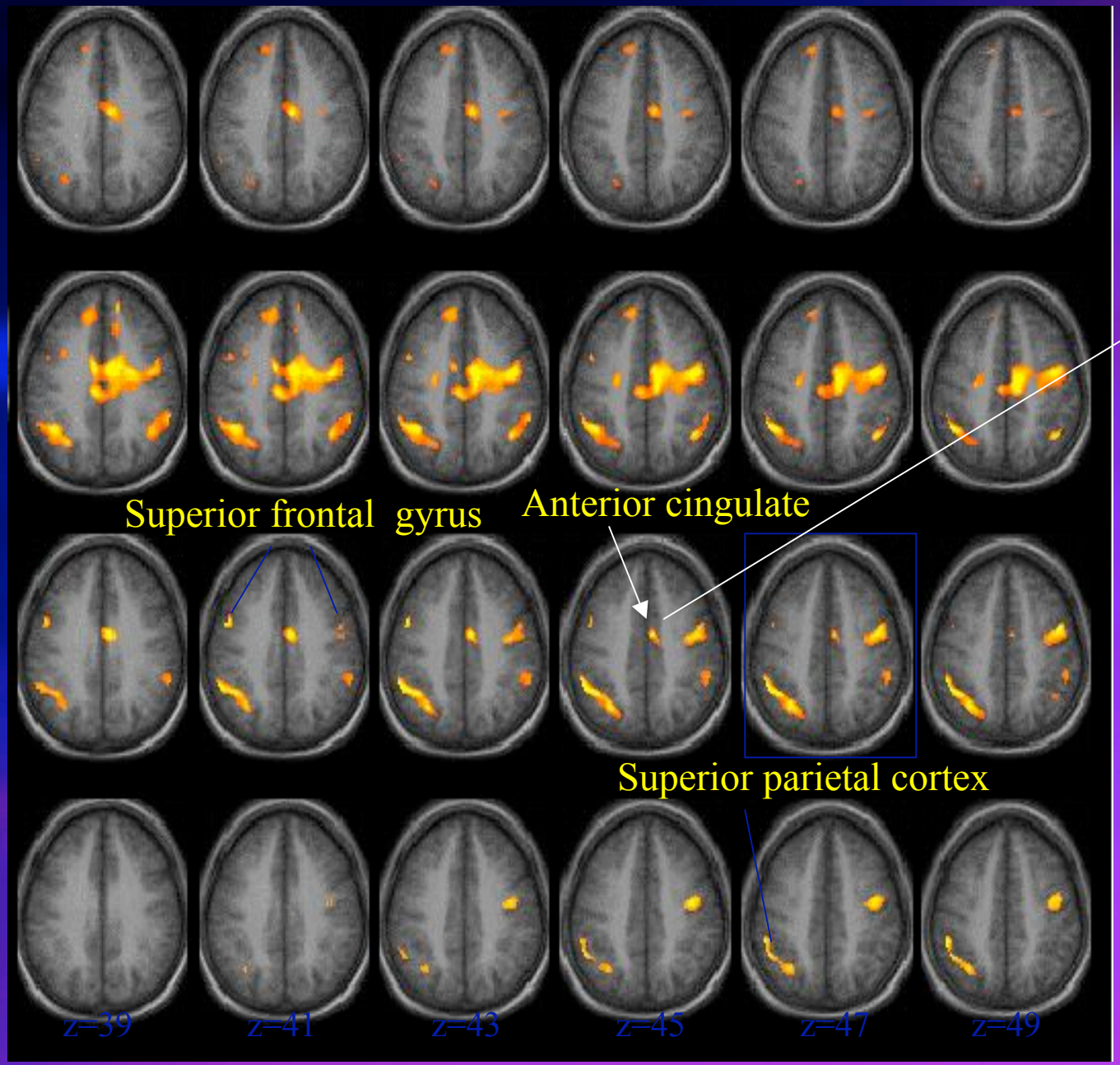
Can We Build a Better Mouse Trap?

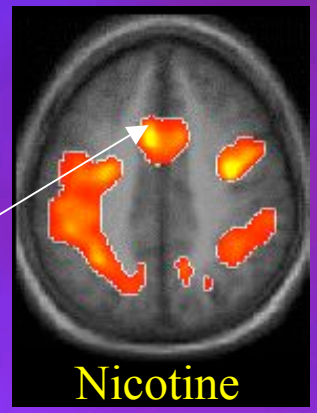
DEVICE EMPLOYED FOR EXTERMINATING RATS, MICE, AND OTHER ANIMALS

Patent No. 883,611
Issued: March 31, 1908



Kumari et al, Effects of subcutaneous nicotine …Neuroimage 2003





Superior parietal cortex

International studies

- Language translations and validations
- International Project management
- Vendor Capabilities
- Training Issues

International Studies

español

汉语

日本語

italiano

ελληνικά

हिन्दी

français

cérebro

deutsch

한국

русско

Pros and Cons of Conventional “paper and pencil” cognitive testing in clinical trials

- Administrators might be familiar with widely used paper and pencil tests
- More familiar, usually more track-record
- Less vulnerable to “crashes”
- Less technical oversight needed
- Can’t do some tests (e.g., CPT), so must have computer anyway
- Precision of stimulus presentation may be limited
- Precision of response collection limited by manual recording and “stop-watch reaction time”
- Examiner training can be more intensive
- Audit trail may lack sufficient detail for objective quality monitoring

Computerized tests

- **Test presentation quality**
  - All stimuli can be presented for precisely the declared amount of time
  - Necessary for some tests (e.g., CPT)
- **Increased reliability**
  - Instructions completely standardized
  - Stimulus delivery completely controlled
  - Every response recorded with *millisecond* accuracy - more objective
- **Facilitates monitoring, data cleaning**
  - complete datasets uploaded automatically to central monitoring site
  - 100% verification, automatic cleaning
  - Complete scoring of datasets is virtually instantaneous
  - Download reports with complete tabulations of scores, referenced by age, sex, and education
  - Automatic computation of all summary indices and factor scores, along with between-test and between-factor discrepancy statistics
- **Decreased training time, staffing costs**
  - More precise stimulation and response
  - Full audit trail, automated scoring, monitoring, and cleaning possible
  - Better standardization across sites, easier training

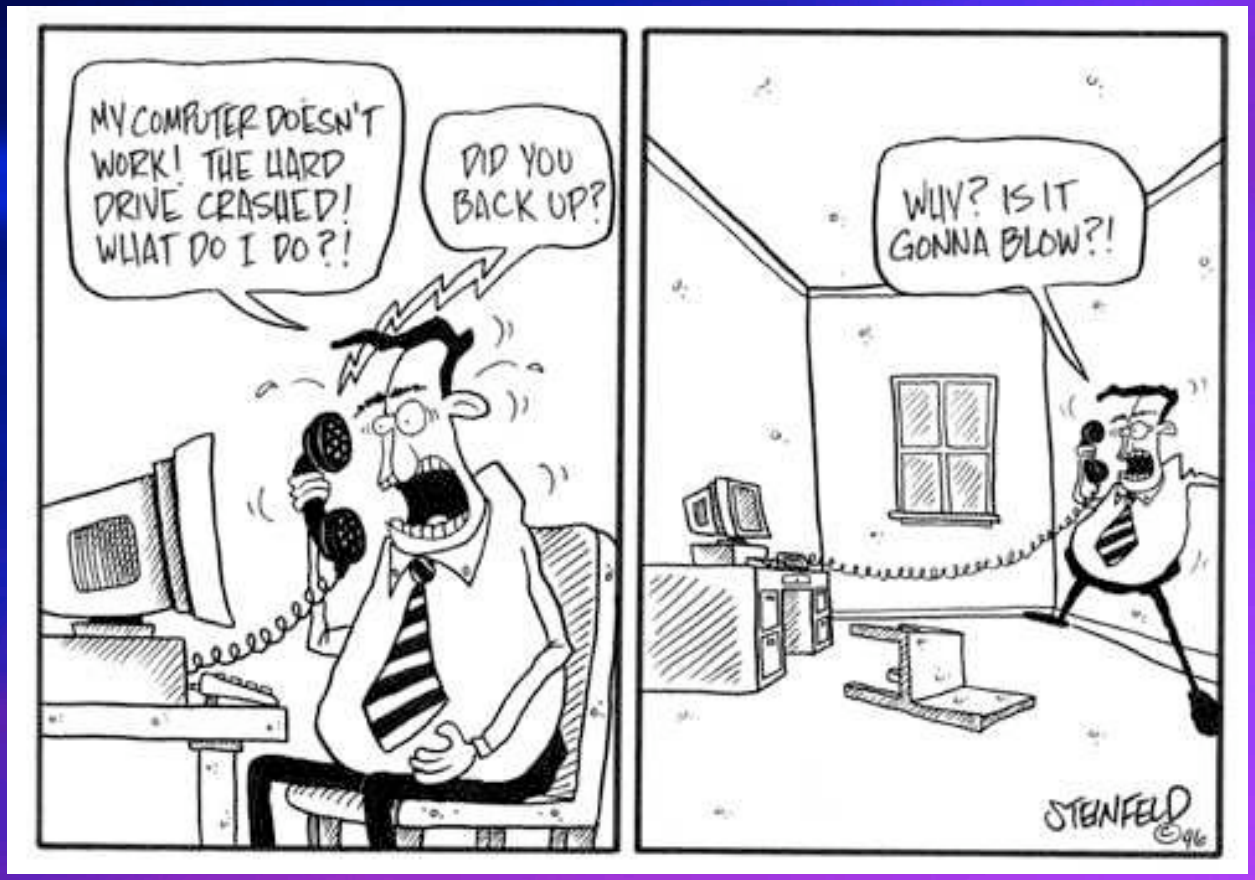
Technical Advantages of computerization

- Minimal technical competency needed to install and maintain testing stations
- Multiple alternate forms for repeated-measures exams
- *Dynamic Titration Strategies* - tests automatically adjust difficulty level, branch to relevant items
  - minimizes total testing time for valid assessment
  - terminates testing rationally if assessment results might be invalid
  - decreases costs for subjects who might otherwise undergo costly procedures without yielding useful data

Efficiency Important in Cognitive Assessment for Clinical Trials

- Construct measurement: 10% increase in reliability may yield 30% decrease in total testing duration
- Minimization of random error (from measure itself, administration errors, scoring errors, patient refusal)

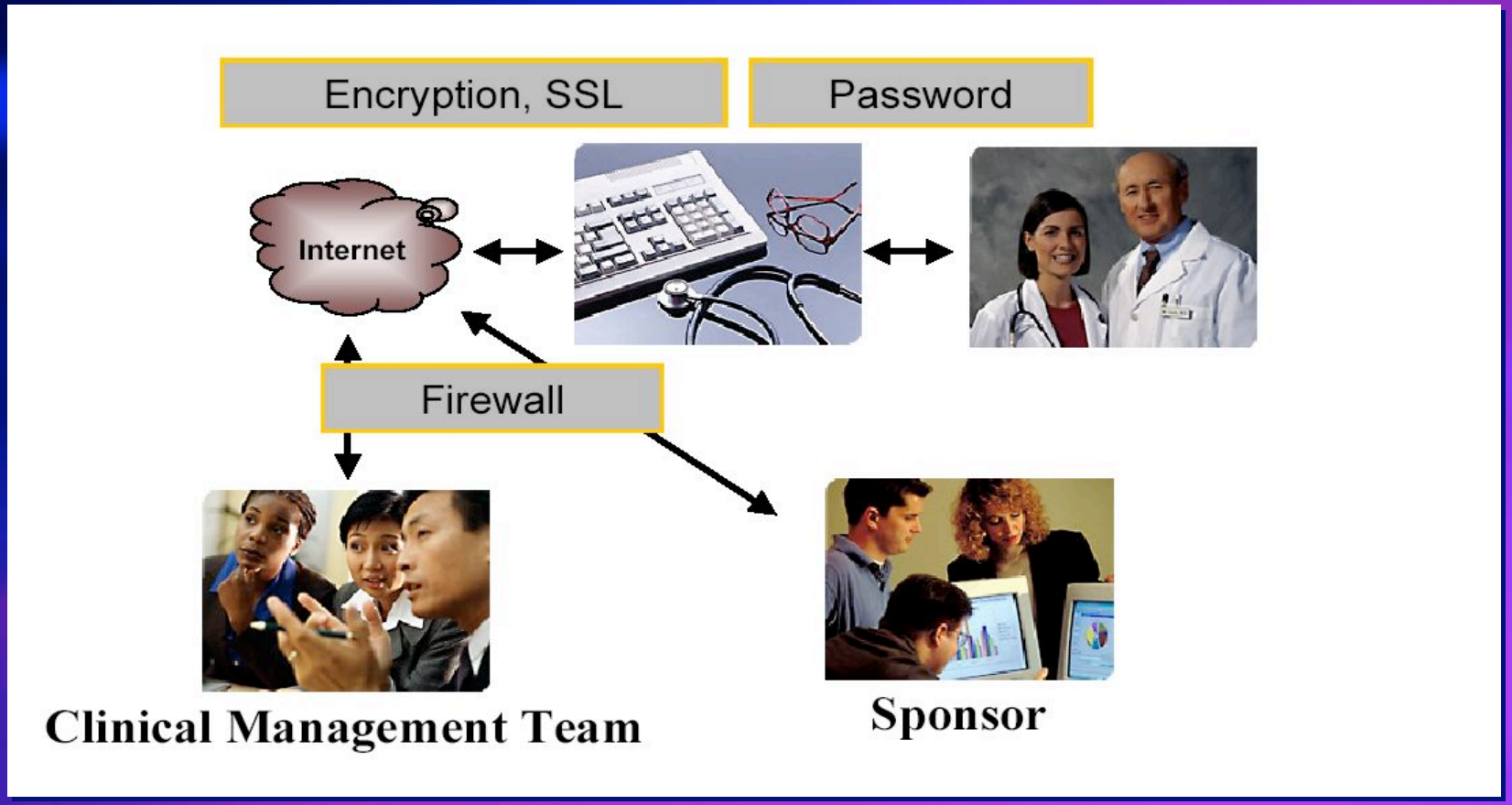
Disadvantages of Computerization



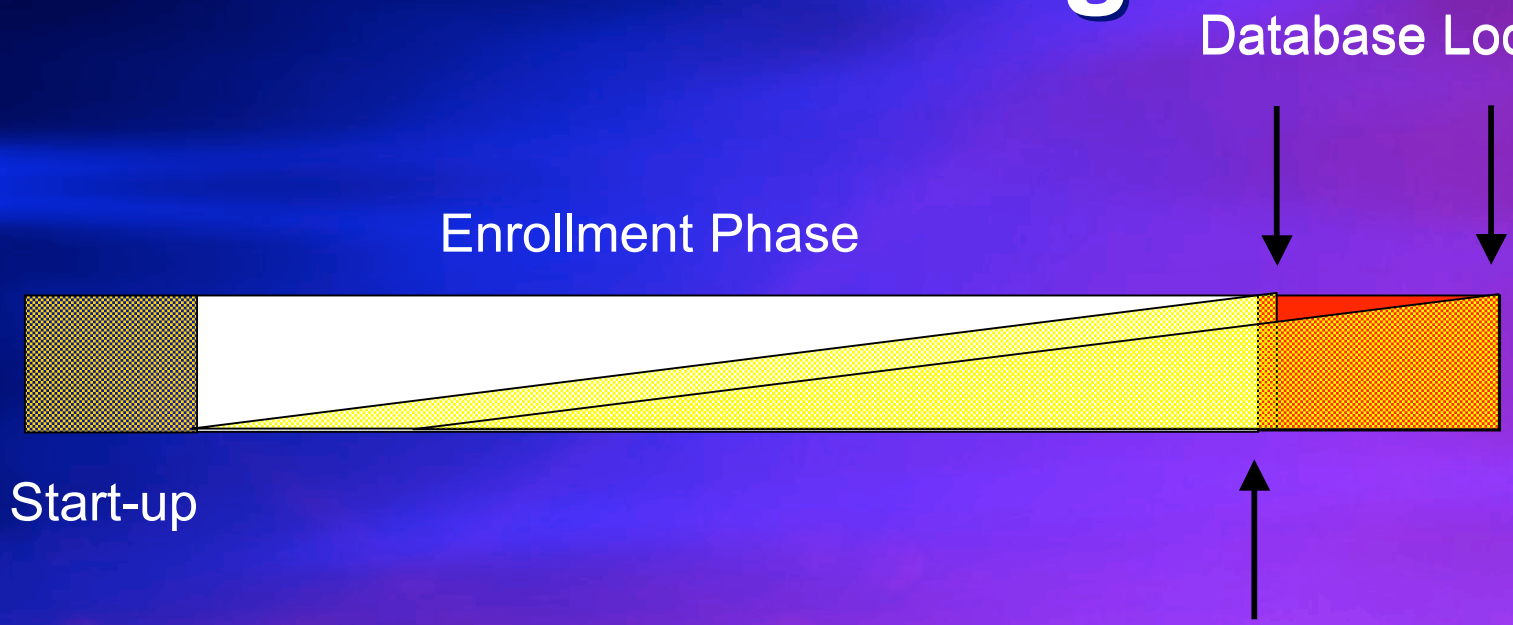
Disadvantages of Computerization

- Validation
- What happens when the human interaction factor is reduced?
  - Is it reduced?
- Can computerized testing catch decrements in motivation as well as face-to-face testing?
  - Standardization and Effort Testing
- What happens when the tester or patient has trouble with computerization?
  - Is there a 24/7 helpdesk with a toll free number?
- Are technical problems more likely with computerized testing?
  - Advantages Vs Disadvantages
  - Similar to moving to EDC for clinical trials

SECURITY


Encryption, SSL
Password
Internet
Firewall
Clinical Management Team
Sponsor

Data Cleaning



The Psychometric Bottom Line

- Increase reliability of construct definition (more tests, or longer tests; data reduction)
- Increase test-retest stability (more reliable tests, multiple baseline sessions to “wring out” exposure effects, or more efficient pre-test practice)
- Decrease patient fatigue and refusal rate (various clinical factors, shorter or easier tests?)
- Decrease administration errors, scoring errors, data entry errors, or if using a computer, computer software and data transmission glitches

Training Issues

- Inter-rater reliability
- Intra-rater reliability
- Providing training for new raters
  - Online pre certification
  - ‘On demand’ training for new raters and new sites so that training is consistent