

# **Patient Reported Outcome Measures of Visual Functioning**

Robert W. Massof, PhD

Professor of Ophthalmology and Neuroscience

*Lions Vision Research & Rehabilitation Center*

*Wilmer Eye Institute*

*Johns Hopkins University School of Medicine*

# Outline of Presentation

- Overview of how to model outcome measurements from rating scale responses (start with more familiar patient self-report)
- Modeling different effects of intervention
  - Modeling effects of interventions that change the person trait
  - Modeling effects that change item difficulty
  - Modeling effects that change the respondent's response criteria

# Rating scale questionnaires produce conjoint observations

## VF-14

- Patient-reported functional ability questionnaires consist of a set of items, each of which describes an activity.
  - The person responds with an ordered category.
  - The items serve as the standard references against which we will compare each person.
- Read small print such as labels on medicine bottles, a telephone book, or food labels
  - Read ordinary newsprint
  - Read large-print book, or large-print newspaper, or numbers on a telephone
  - Recognize people when they are close to you
  - See steps, stairs, or curbs
  - Read traffic signs, street signs, or store signs
  - Do fine handwork like sewing, knitting, crocheting, or carpentry
  - Write checks or fill out forms
  - Play games such as bingo, dominos, card games, or mah-jongg
  - Take part in sports like bowling, handball, tennis, or golf
  - Cook
  - Watch TV
  - Drive During the daytime
  - Drive at night

No difficulty  
Some difficulty  
Moderate difficulty

Extreme difficulty  
Unable to do  
Not applicable

# Measuring functional ability

- Functional ability is a latent variable (trait of the person)
- Each person has some level of functional ability called the “person measure”:  $P_n$  for person  $n$
- Each activity requires some level of functional ability to be performed with ease called the “item measure”:  $I_j$  for item  $j$
- Functional reserve = difference between person’s functional ability and ability required by the activity:  $R_{nj} = P_n - I_j$
- Perceived difficulty of performing the activity is expected to depend on functional reserve
- To respond with difficulty rating “x”, functional reserve must fall in the interval for x:  $C_x < R_{nj} < C_{x+1}$  where  $C_x$  is the criterion functional reserve for responding with rating category x

# But $P_n$ , $I_j$ , $C_x$ are fixed variables

- Deterministic measurements
  - Functional ability is a fixed property of the person  $P_n$
  - Required functional ability is a fixed property of the item  $I_j$
  - The response threshold,  $C_x$ , is a fixed property of the interval  $x$
- In the real world these variables are inferred from the observations and there is uncertainty about the inferred values



Item 5	Score
Obs 1	1
Obs 2	0
Obs 3	0
Obs 4	0

Item 5 score = 1

Items  $I_j$



Categories  $C_x$



# Assumptions of measurement theory

- $P_n$  is a fixed trait of person  $n$
- $I_{nj}$  is person  $n$ 's estimate of required functional ability of item  $j$
- $I_j$  is the expected required functional ability of item  $j$  (average value of  $I_{nj}$  across people in the target population):

$$I_j = \sum_{n=1}^N \frac{I_{nj}}{N}$$

- $e_{nj}$  is a random between person and item variable:

$$e_{nj} = I_{nj} - I_j$$

# Assumptions of measurement theory

- $C_{nx}$  is person  $n$ 's response criterion for using rating category  $x$
- $C_x$  is the expected response criterion for response category  $x$  (average value of  $C_{nx}$  across people)
- $e_{nx}$  is a random between person and category variable  $e_{nx} = C_{nx} - C_x$



# Assumptions of measurement theory

- Person  $n$  uses difficulty ratings to estimate the magnitude of his own functional reserve for item  $j$

$$R_{nj} = P_n - I_j - e_{nj}$$

- To respond with rating category  $x$ , functional reserve must be greater than the threshold for  $x$  and less than the threshold for  $x+1$

$$C_x + e_{nx} < P_n - I_j - e_{nj} < C_{x+1} + e_{nx+1}$$

- Item Response Theory (IRT) models assume that the response thresholds are fixed, i.e.,

$$e_{nx} = 0$$

# Assumptions of measurement theory

- To respond with rating category  $x$ , functional reserve must be greater than the threshold for  $x$  and less than the threshold for  $x+1$

$$C_x + e_{nx} < P_n - I_j - e_{nj} < C_{x+1} + e_{nx+1}$$

- Define a new random term

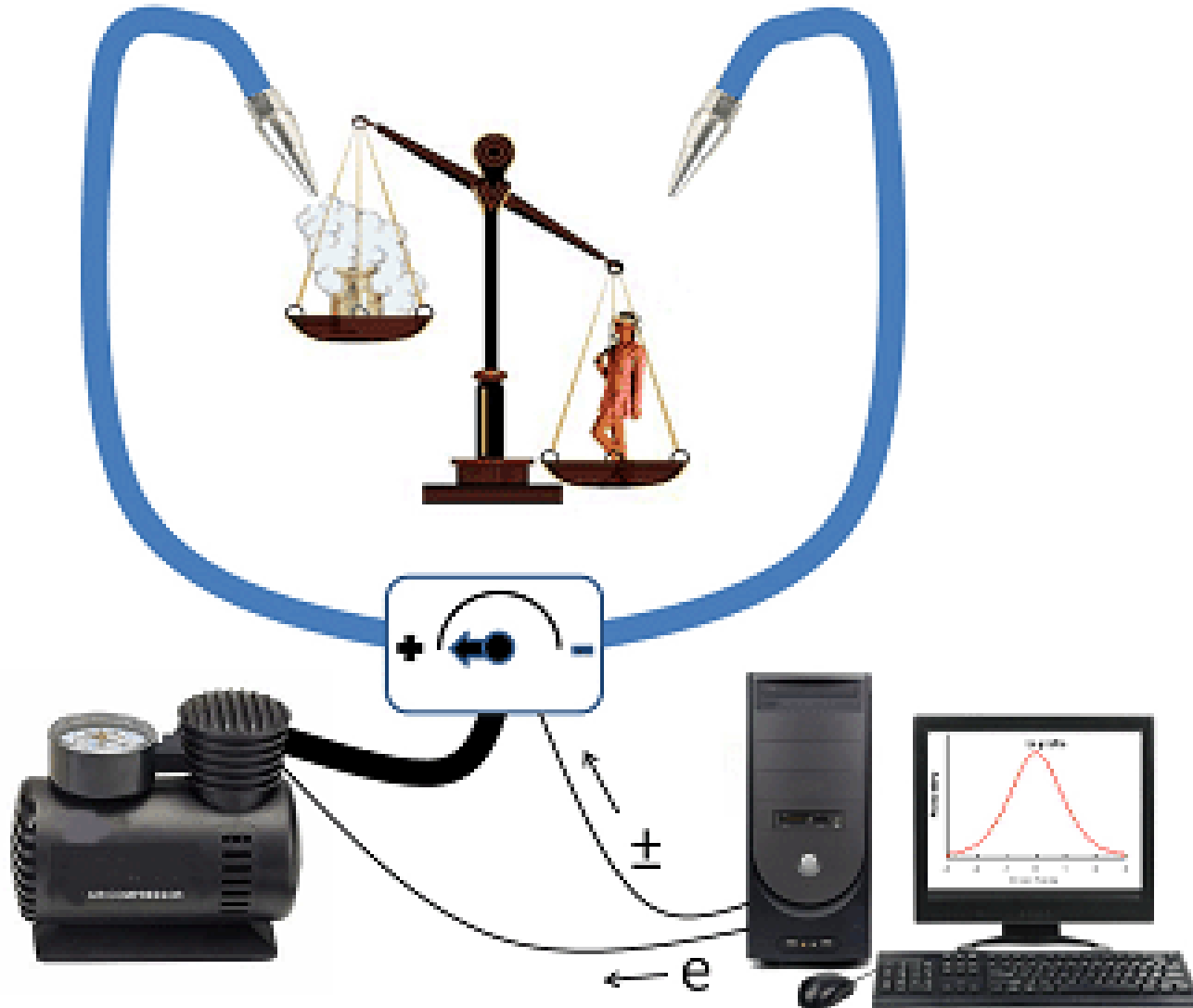
$$e_{njx} = e_{nj} + e_{nx}$$

- Therefore, the simplified measurement theory is

$$C_x + e_{njx} < P_n - I_j < C_{x+1} + e_{njx+1}$$

- Rasch theory assumes statistical independence of  $e_{njx}$

# Addition of randomly generated error



# Rating scale questionnaires produce conjoint observations

## VF-14

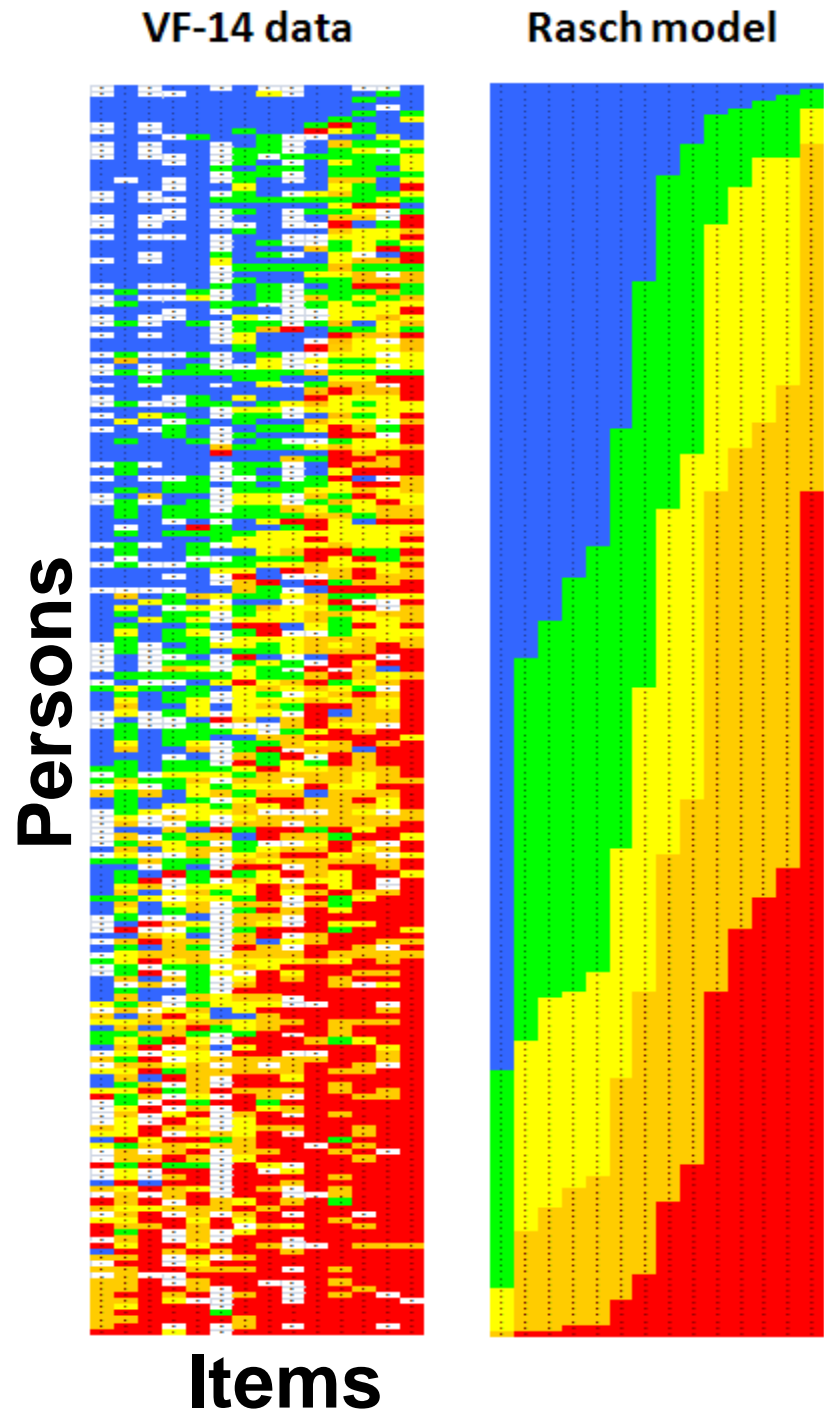
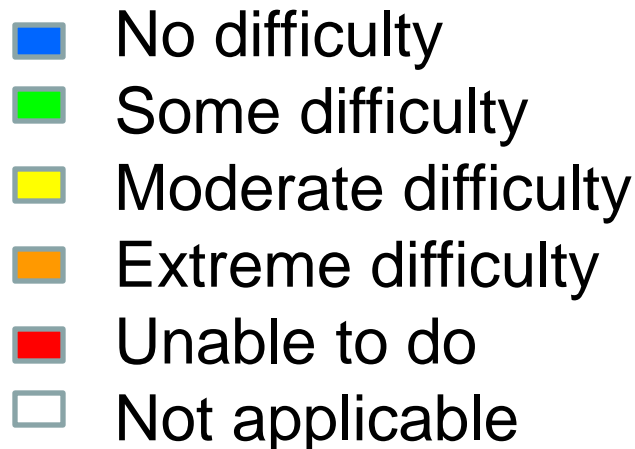
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# Maximum Likelihood Estimation of Fixed Variables

- P for each person
- I for each item
- C for each threshold



# Validity

## (Accuracy of assumptions)

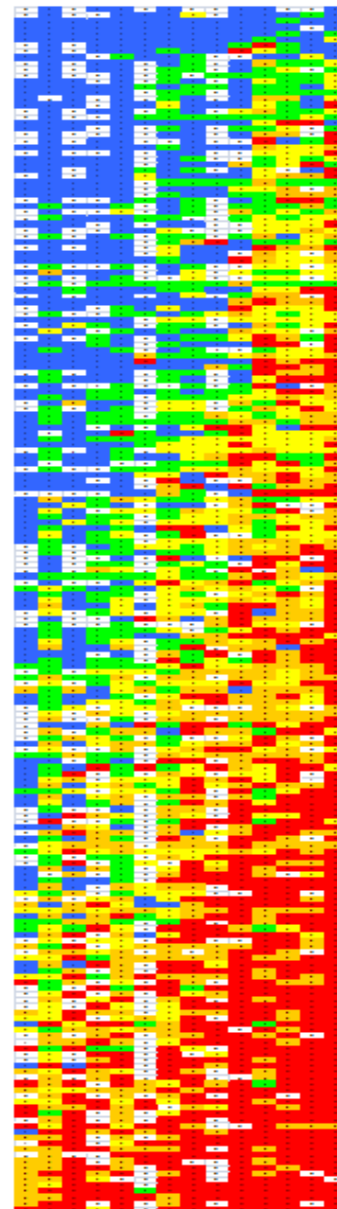
Mean square fit statistic for each person (tests assumption that all stochastic variance can be attributed to a single source, viz.,  $e_{nj|x}$ )

Mean square residual for each person

Model's predicted variance for each person

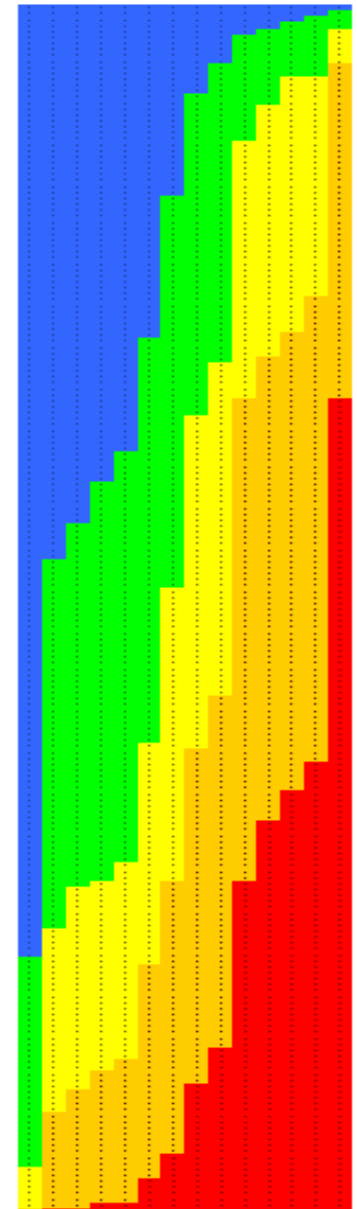
$$\frac{\sum_{j=1}^J (x_{nj} - E\{x | P_n, I_j\})^2}{\sum_{j=1}^J E\{x^2 | P_n, I_j\} - E\{x | P_n, I_j\}^2} = \frac{\chi^2}{df}$$

VF-14 data



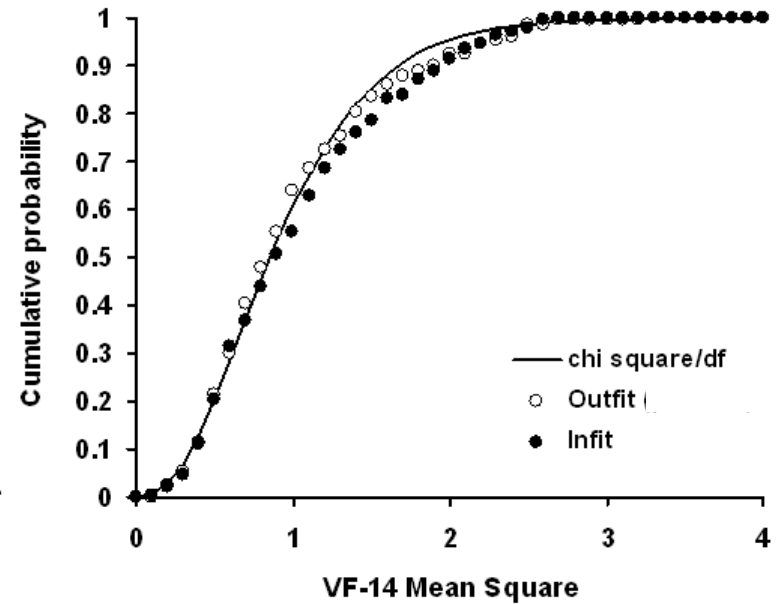
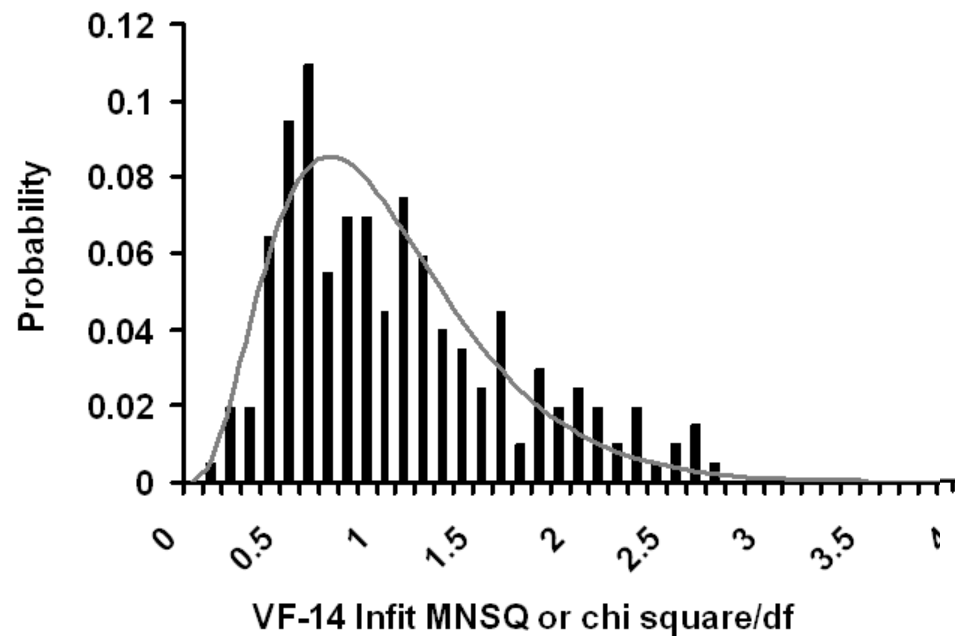
$x_n$

Rasch model



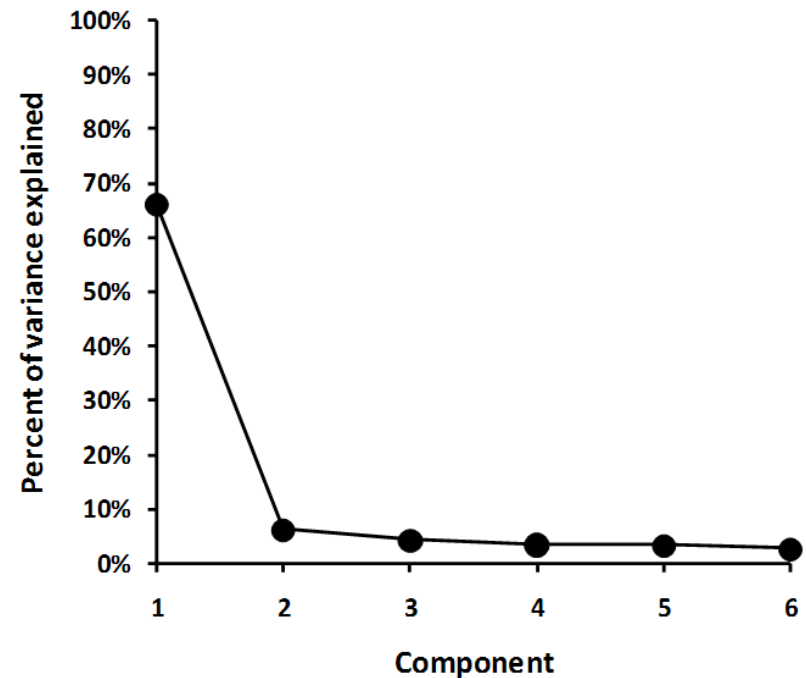
$E\{x | P_n, I_j\}$

# Testing validity of measure of visual ability in low vision patients with VF-14



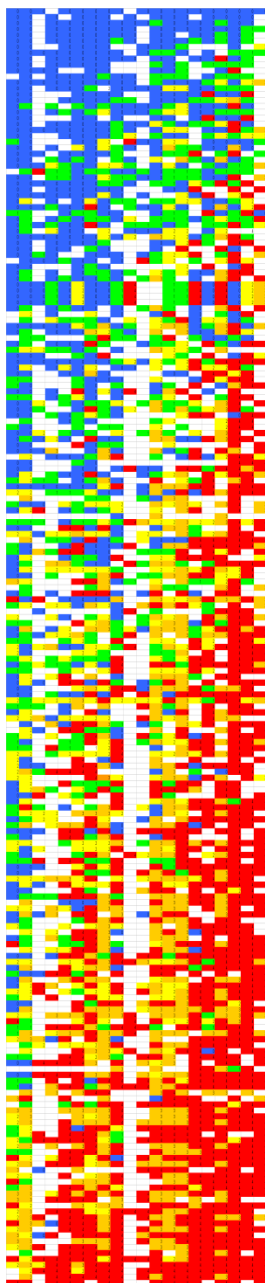
# Principal components analysis of residuals

- Person measure is first principal component (explains 67% of variance)
- Remaining variance is random noise ( $e_{njx}$ ), which is expected by the model

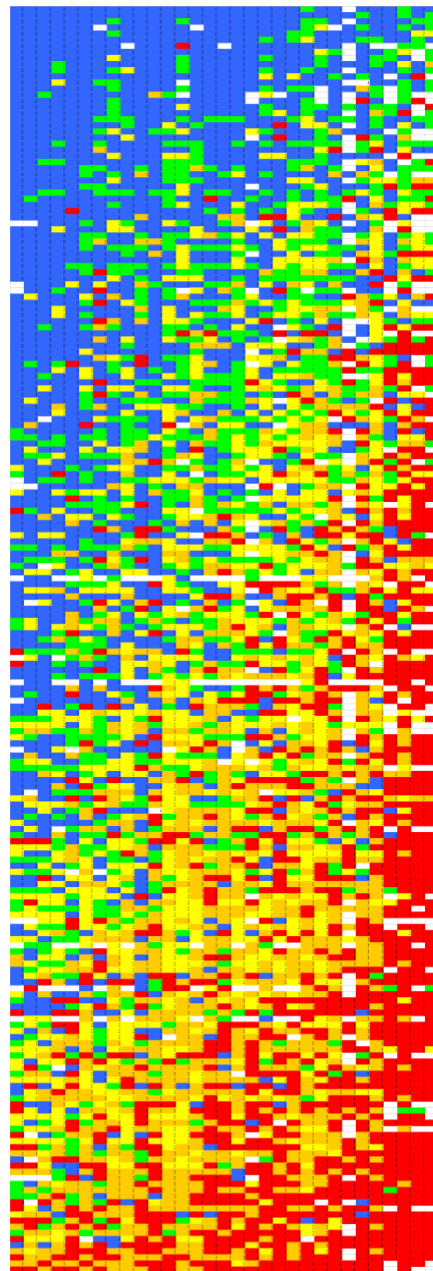




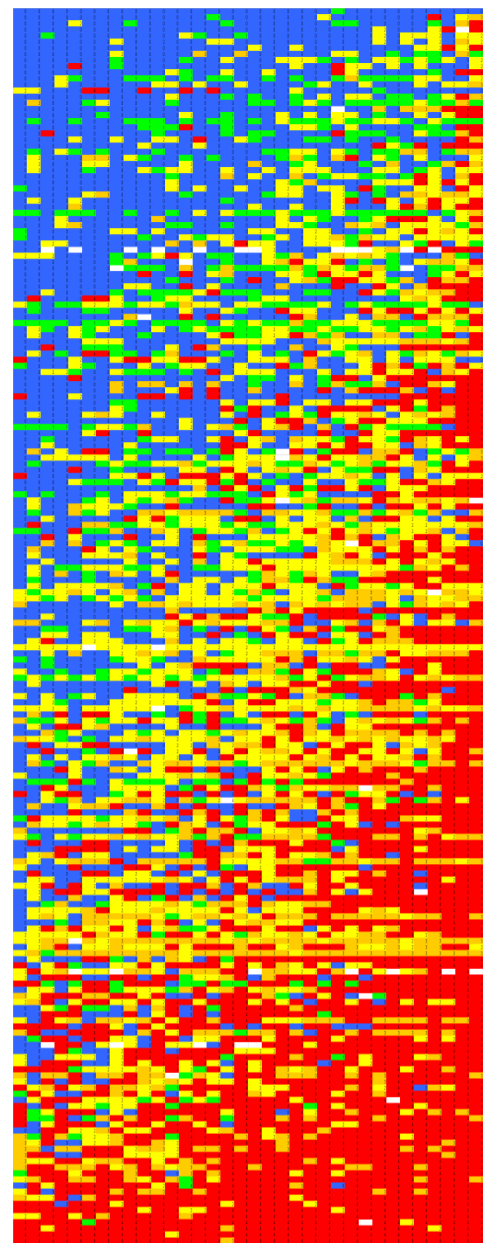
**ADVS**



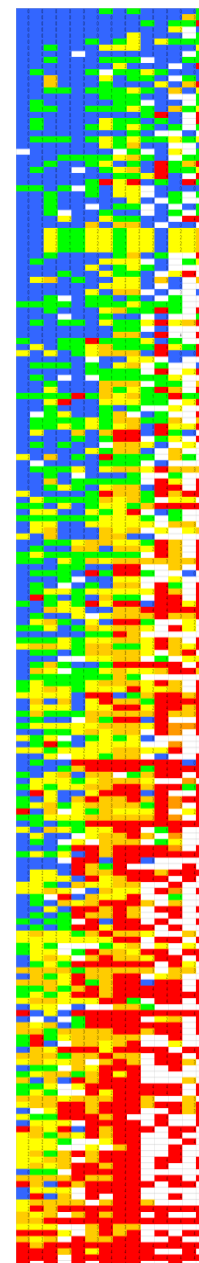
**NEI VFQ**

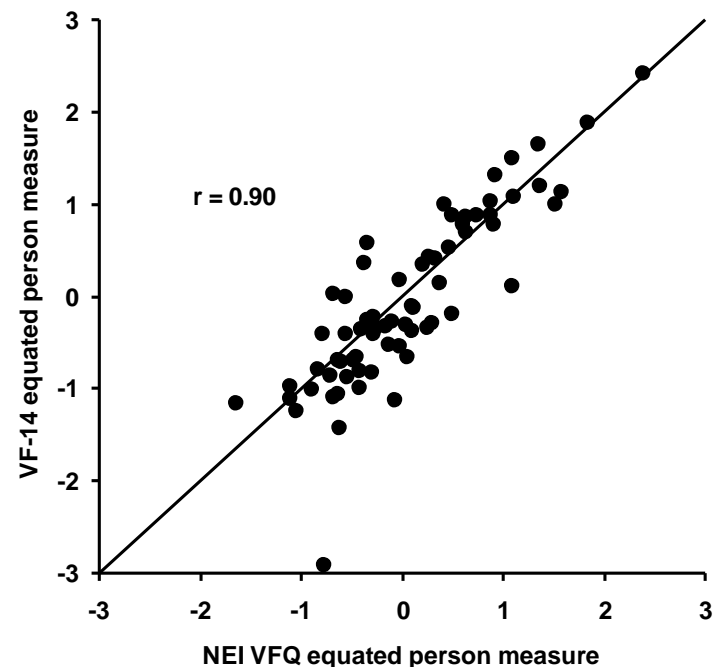
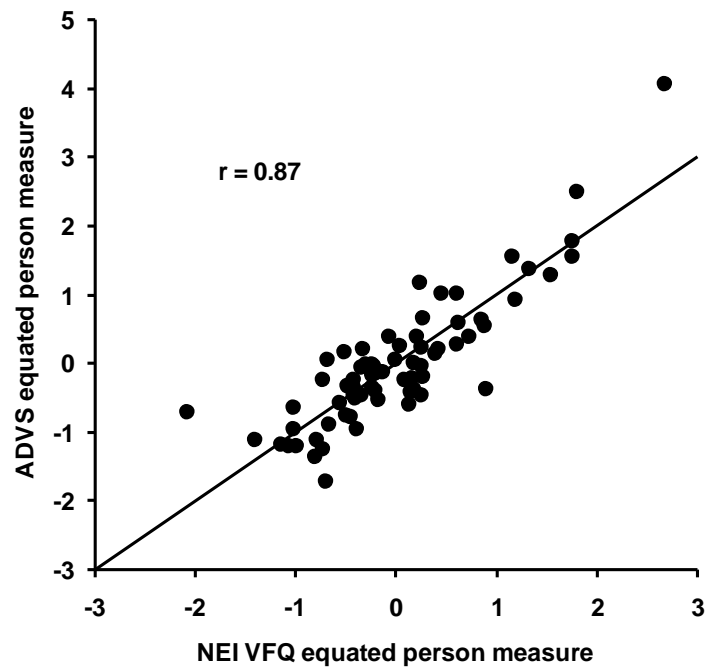
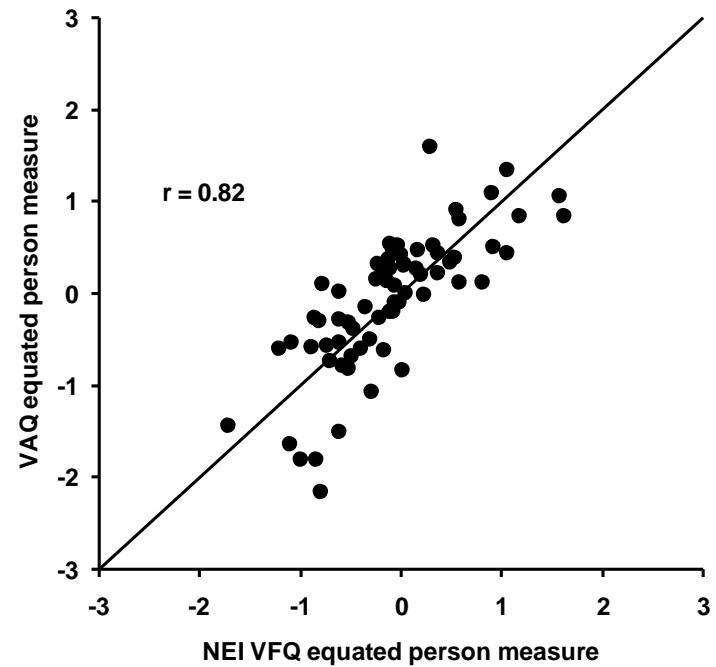
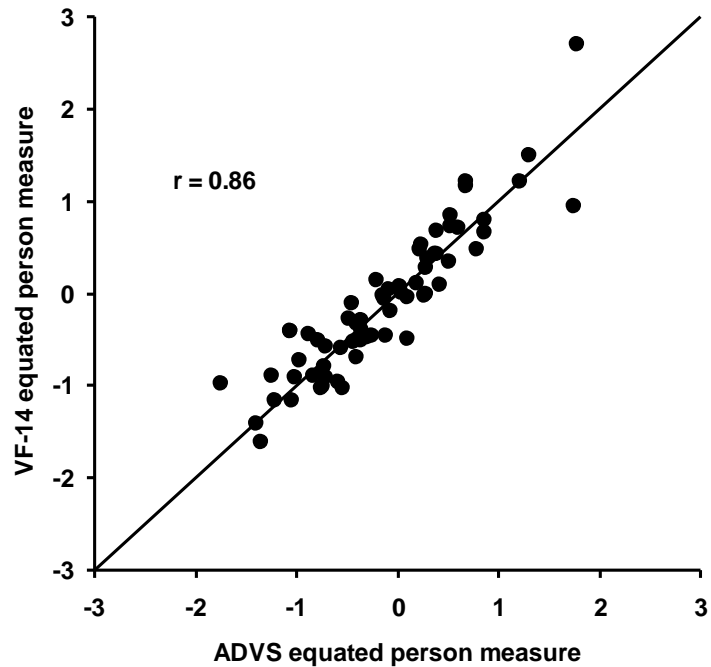


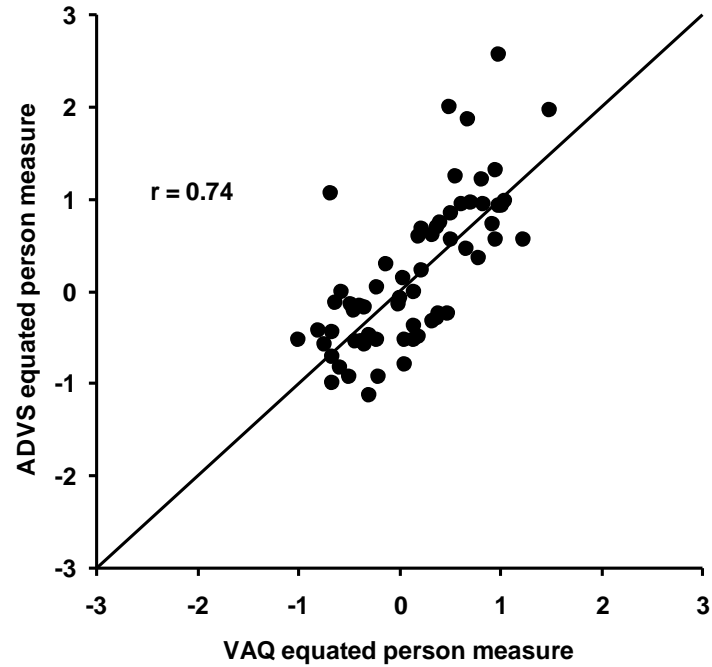
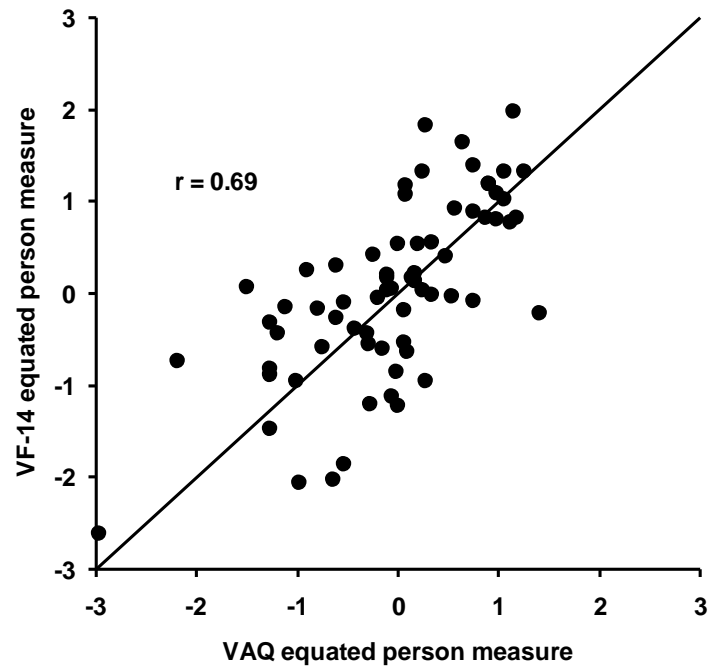
**VAQ**



**VF-14**







# Possible effects of intervention

- Change the person measure:

$$P_n(t) = P_n(t_0) + \Delta P_n$$

$$\Delta P_n = P_n(t) - P_n(t_0)$$

- Change the item measure:

$$I_{nj}(t) = I_j(t_0) + \Delta I_{nj}$$

$$\Delta I_{nj} = I_{nj}(t) - I_j(t_0)$$

- Change in the person's response bias:

$$C_{nx}(t) = C_x(t_0) + B_n$$

$$B_n \cong \sum_{x=1}^m \frac{\Delta C_x}{m}$$

# Change in functional reserve

$$C_x(t_0) + e_{njx} < P_n(t_0) - I_j(t_0) < C_{x+1}(t_0) + e_{njx+1}$$

$$C_x(t_0) + e_{njx} < R_{nj}(t_0) < C_{x+1}(t_0) + e_{njx+1}$$

$$C_x(t_0) + e_{njx} + B_n < R_{nj}(t_0) + \Delta P_n - \Delta I_{nj} < C_{x+1}(t_0) + e_{njx+1} + B_n$$

$$C_x(t_0) + e_{njx} < R_{nj}(t_0) + \Delta P_n - \Delta I_{nj} - B_n < C_{x+1}(t_0) + e_{njx+1}$$

$$C_x(t_0) + e_{njx} < R_{nj}(t_0) + \Delta R_{nj} < C_{x+1}(t_0) + e_{njx+1}$$

$$\Delta R_{nj} = \Delta P_n - \Delta I_{nj} - B_n$$

# Single outcome measure

Average change in functional reserve

$$\Delta R_{nj} = \Delta P_n - \Delta I_{nj} - B_n$$

$$\overline{\Delta R_n} = \sum_{j=1}^J \frac{\Delta R_{nj}}{J} = \sum_{j=1}^J \frac{\Delta P_n - \Delta I_{nj} - B_n}{J}$$

$$\overline{\Delta R_n} = \Delta P_n - B_n - \overline{\Delta I_n}$$

$$\overline{\Delta I_n} = \sum_{j=1}^J \frac{\Delta I_{nj}}{J}$$

Anchor item measures and response category thresholds to baseline values

$$\overline{\Delta R_n} = \Delta P_n - B_n - \overline{\Delta I_n}$$

$$\Delta P_n = \overline{\Delta R_n} + B_n + \overline{\Delta I_n}$$

$$I_{nj}(t) \equiv I_j(t_0) \because \overline{\Delta I_n} \equiv 0$$

$$C_x(t) \equiv C_x(t_0) \because B_n \equiv 0$$

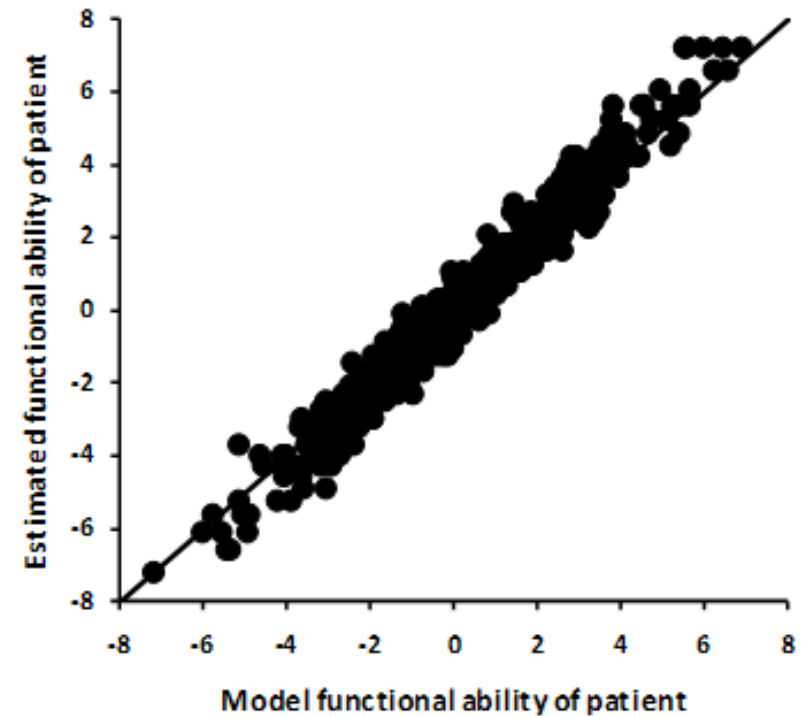
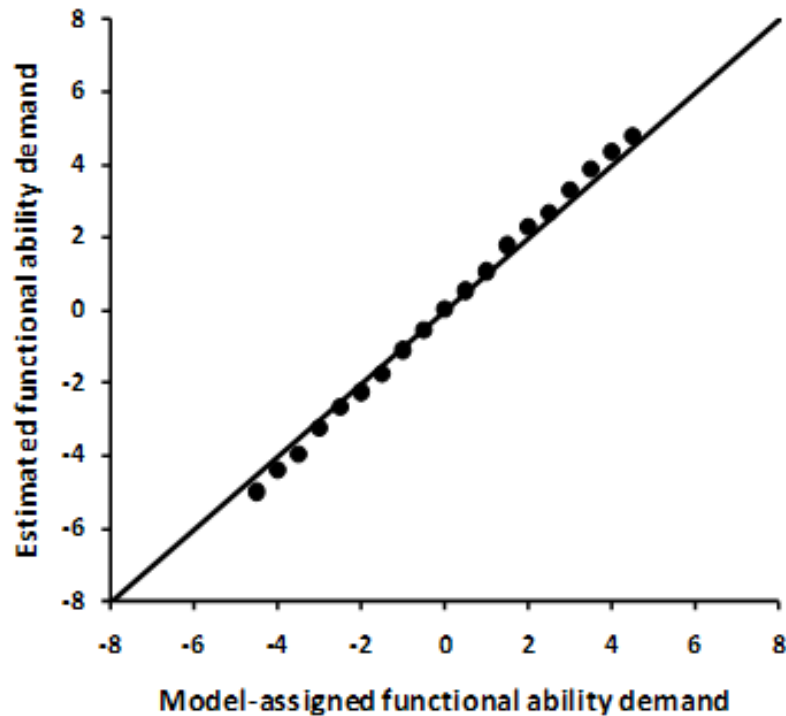
$$\Delta P_n = \overline{\Delta R_n}$$

# Simulation

- 500 persons, 19 items, 4 response categories
- $P_n(t_0)$  is normally distributed with mean = 0 logit and sd = 2.5 logit
- $I_j(t_0)$  ranges from -4.5 to 4.5 logits in 0.5 logit steps
- $C_1(t_0) = -2; C_2(t_0) = 0; C_3 = 2$
- $e_{njx}$  is normally distributed,  $\sim N(0, \pi/\sqrt{3})$ , with a constant diagonal covariance matrix
- $C_x(t_0) + e_{njx} < P_n(t_0) - I_j(t_0) < C_{x+1}(t_0) + e_{njx+1}$

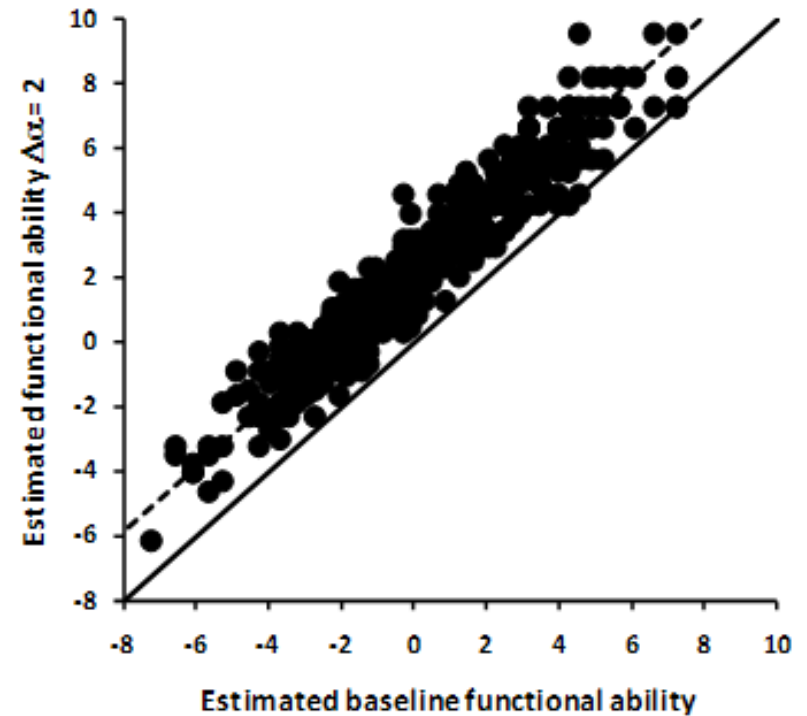
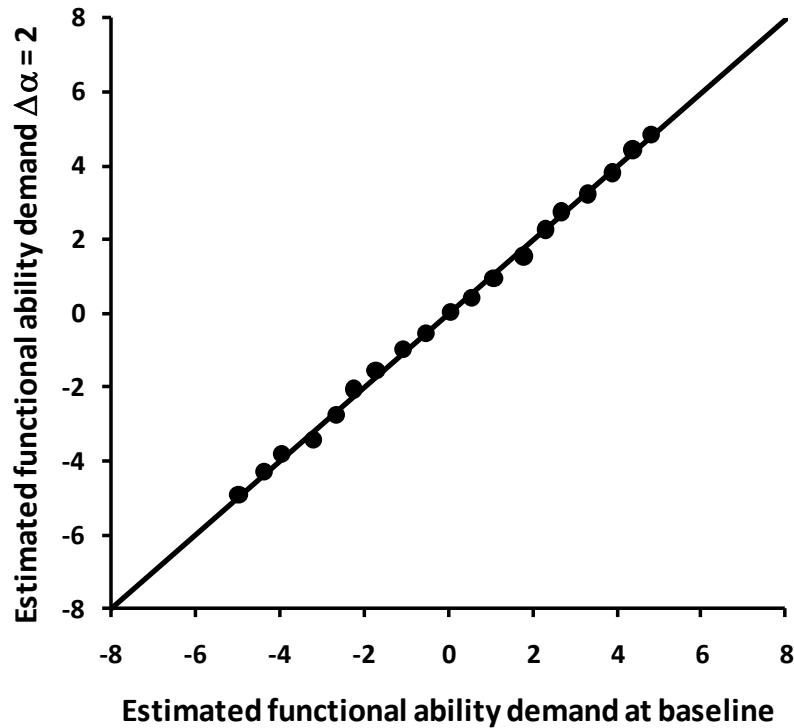


# Simulation of baseline responses



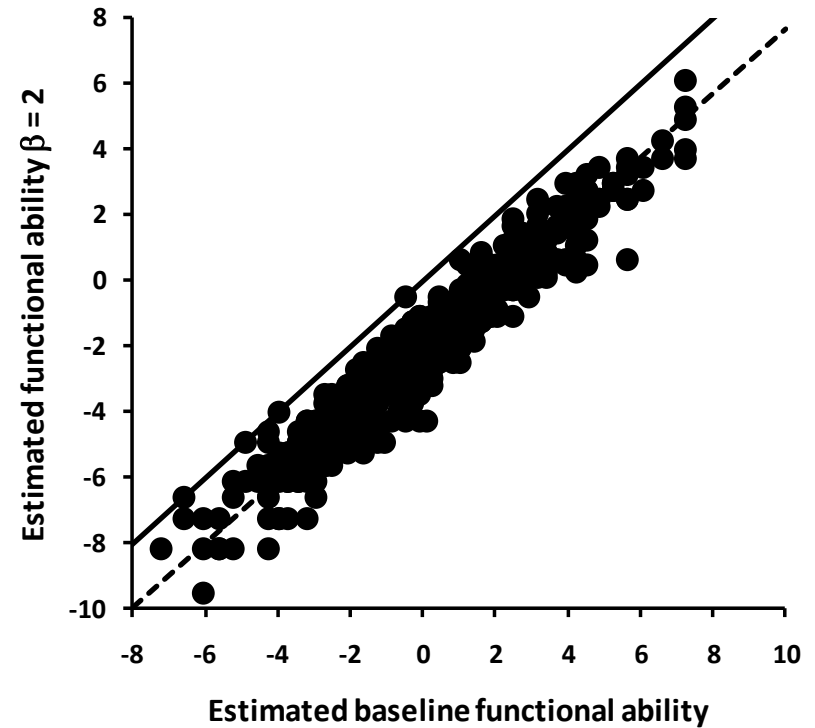
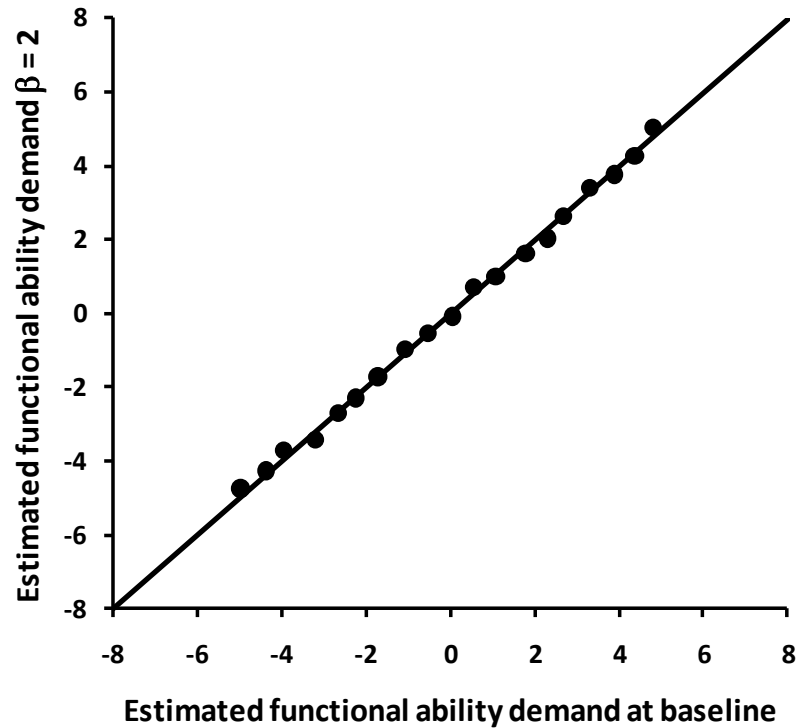
$$C_x(t_0) + e_{njx} < P_n(t_0) - I_j(t_0) < C_{x+1}(t_0) + e_{njx+1}$$

# Simulation $\Delta P_n = 2$



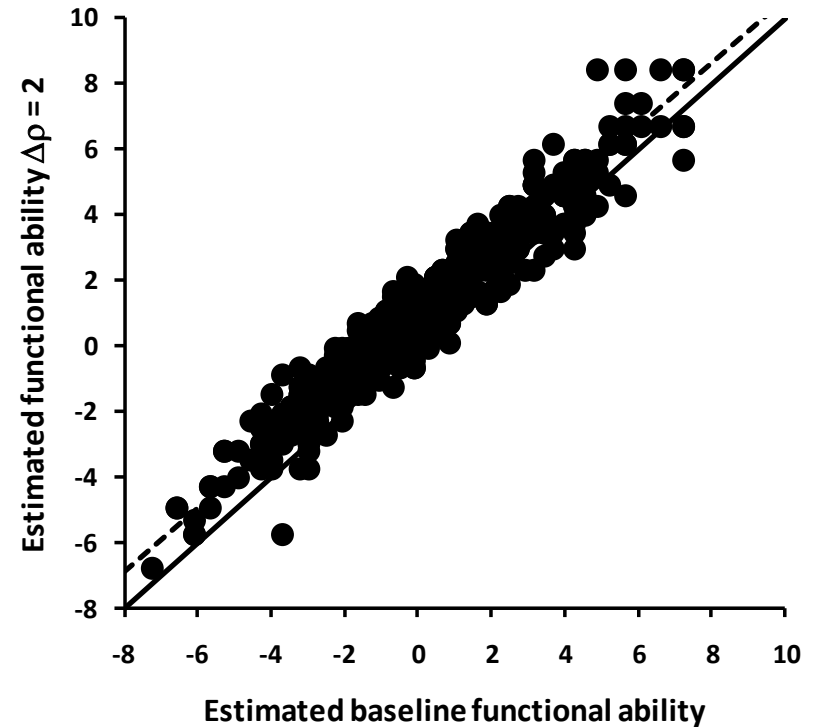
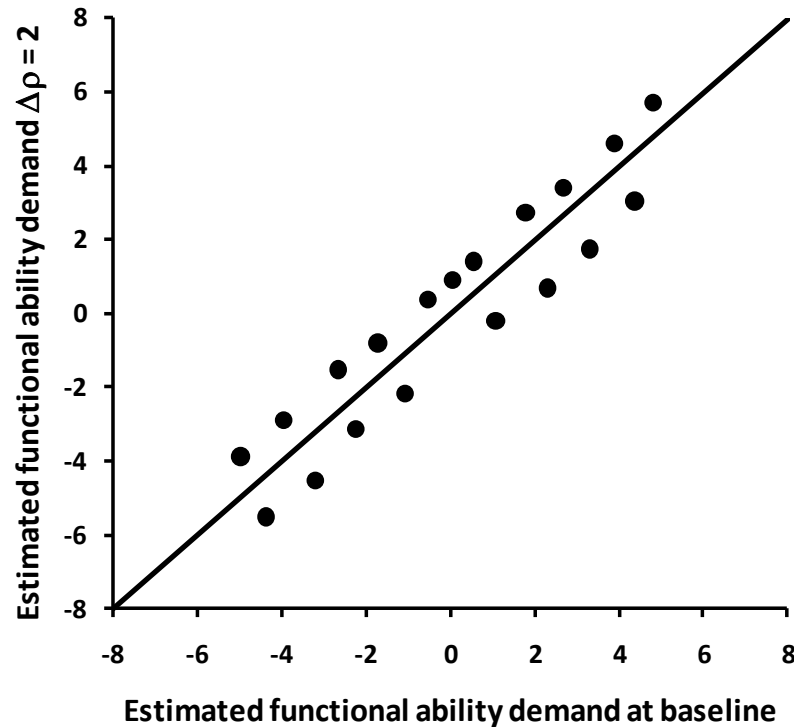
$$C_x(t_0) + e_{njx} < P_n(t_0) + \Delta P_n - I_j(t_0) < C_{x+1}(t_0) + e_{njx+1}$$

# Simulation $B_n = 2$



$$C_x(t_0) + e_{njx} + B_n < P_n(t_0) - I_j(t_0) < C_{x+1}(t_0) + e_{njx+1} + B_n$$

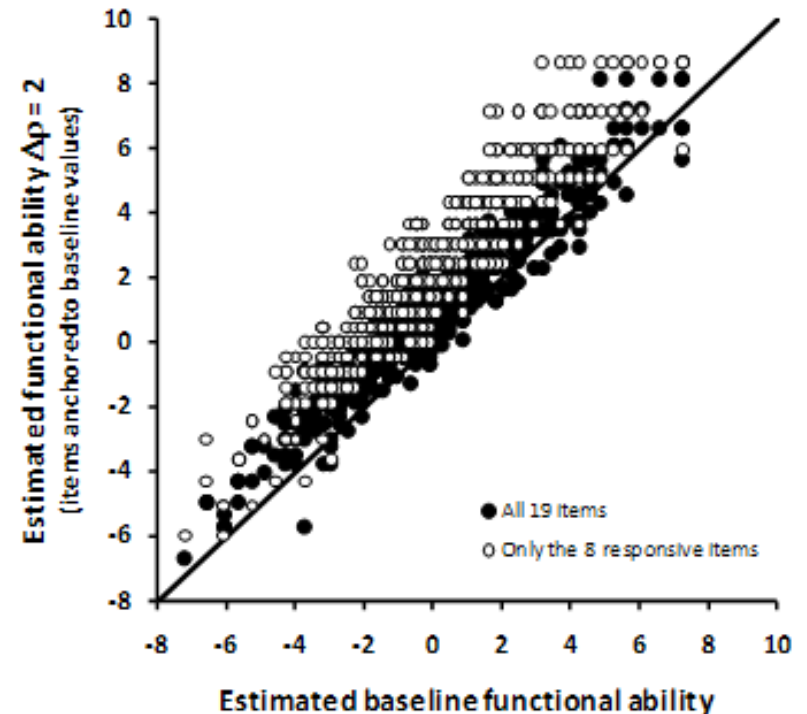
Simulation  $\Delta I_j = -2$  for 8 items  
and  $\Delta I_j = 0$  for 11 items



$$C_x(t_0) + e_{njx} < P_n(t_0) - I_j(t_0) - \Delta I_{nj} < C_{x+1}(t_0) + e_{njx+1}$$

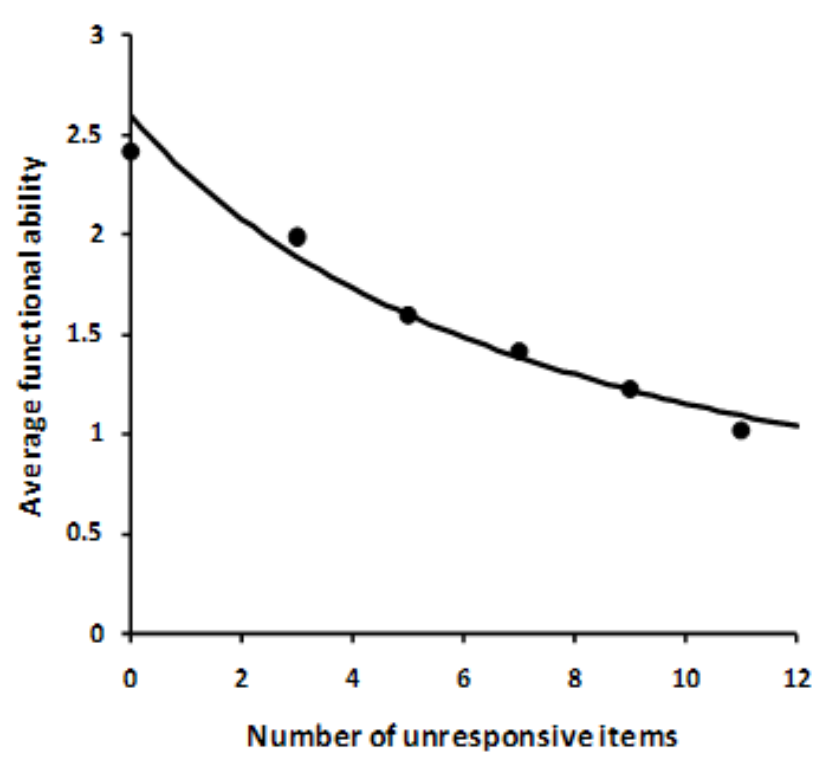
# Simulation $\Delta I_j = -2$ for 8 items and $\Delta I_j = 0$ for 11 items

- Rasch analysis performed with item measures and category thresholds anchored to baseline values
- Filled circles: simulated responses to all 19 items included in analysis
- Open circles: only the 8 responsive items



$$C_x(t_0) + e_{njx} < P_n(t_0) - I_j(t_0) - \Delta I_{nj} < C_{x+1}(t_0) + e_{njx+1}$$

# Unresponsive items dilute effect of intervention



$$\overline{\Delta I}_n = \sum_{j=1}^J \frac{\Delta I_{nj}}{J} = \sum_{k=1}^K \frac{\Delta I_{nk}}{U + K} \quad \text{where} \quad U + K = J$$

$$\Delta I_j = \sum_{n=1}^N \frac{\Delta I_{nj}}{N}$$

$$\Delta R_{nj} = \Delta P_n - \Delta I_j$$

- Removing a cataract  $\rightarrow \Delta P_n$
- Providing a magnifier  $\rightarrow \Delta I_j$
- $\Delta I_j \neq 0$  indicates intervention-specific differential item functioning (DIF)
- Usually DIF is considered bad, in this case DIF is an indicator of a positive outcome

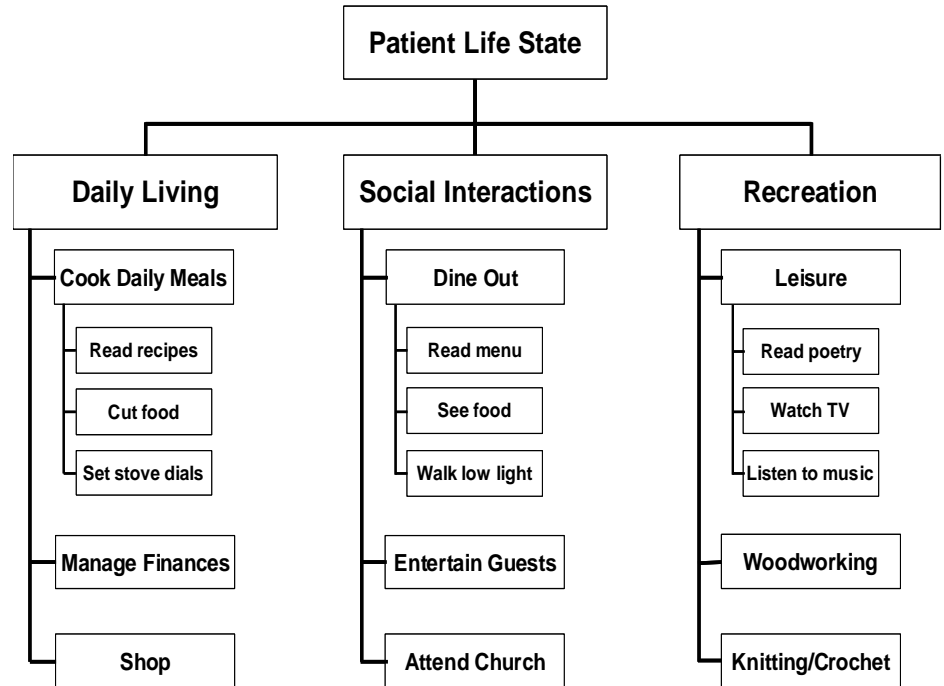




# Supplemental Slides

# Activity Inventory (AI)

- AI is an adaptively administered rating scale questionnaire
- Design and administration guided by the Activity Breakdown Structure
- 50 standard activity goals which commonly are reported within the low vision population
- 460 tasks nested under the 50 goals
- Rasch analysis is used to estimate the inherent difficulty of each goal and task and visual ability for each person



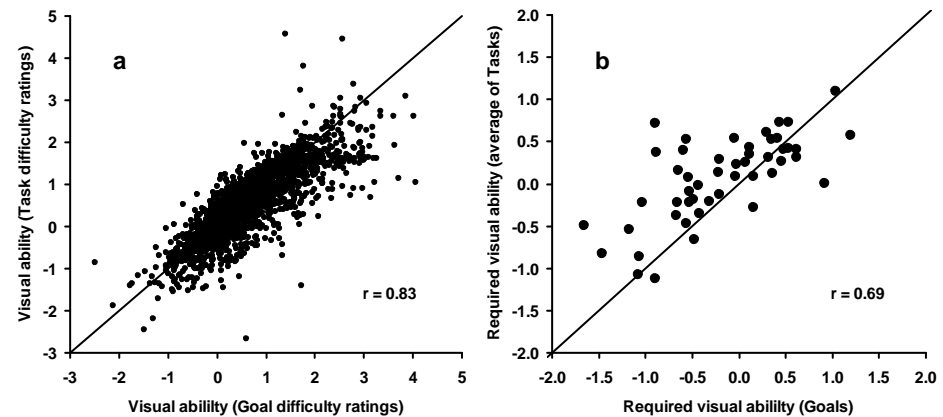
Schematic of the Activity Breakdown Structure (ABS). The patient's life state is broken down into daily living, social interactions and recreation objectives. Each objective is broken down into the goals of activities (e.g., cook daily meals, manage finances, and shop under daily living). Each goal is broken down into subsidiary tasks that must be performed to achieve the goal (or may be deemed not applicable). Examples of tasks are read menu, see food, and walk in low light under the dine-out goal.

# Adaptive administration of the AI

- Patient rates the importance of each goal
- Patient rates the difficulty of goals that exceed a criterion level of importance
- Patient rates the difficulty of tasks under goals that exceed a criterion level of difficulty, or responds that the task is not applicable (tagged as missing data)

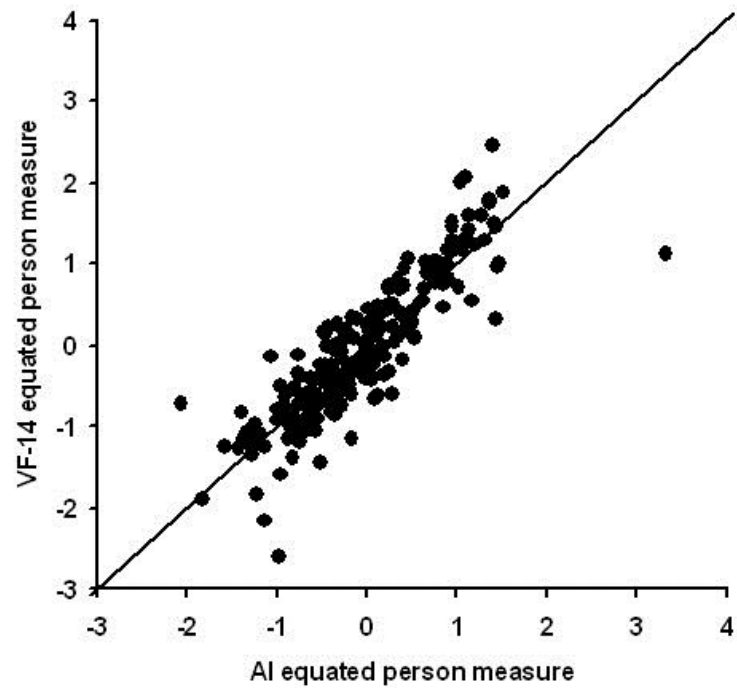
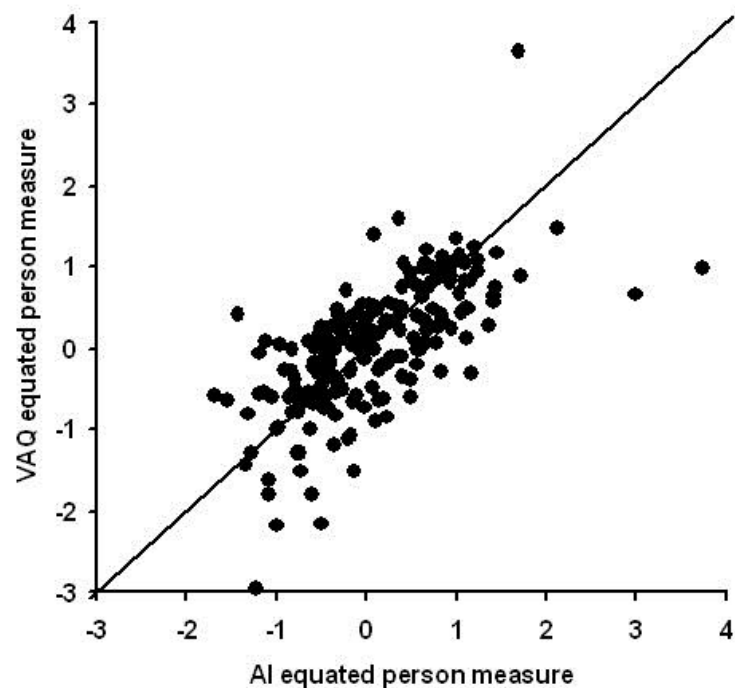
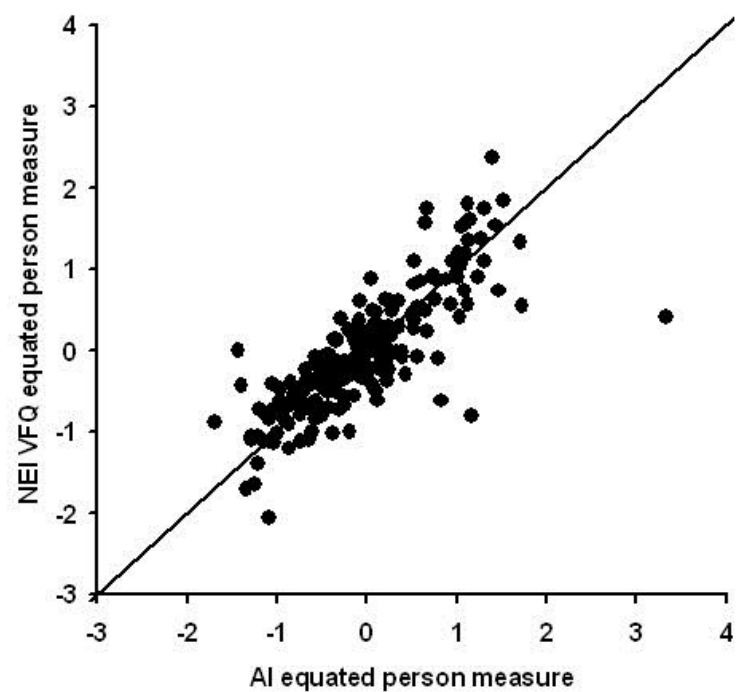
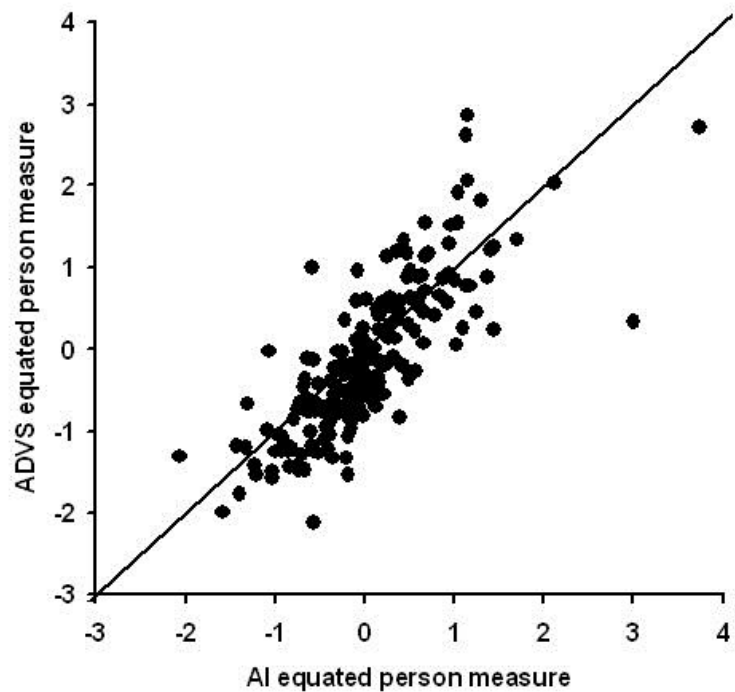
# Activity Breakdown Structure (ABS)

- Baseline person measures estimated from difficulty ratings of tasks agree with baseline person measures estimated from difficulty ratings of goals
- The goal item measure is well approximated by the average item measure of subsidiary tasks



a) Visual ability person measures estimated by Rasch analysis from task difficulty ratings in the AI vs visual ability person measures estimated from AI goal difficulty ratings. Solid line – identity line. Pearson correlation is 0.83.

b) Average of required visual ability across tasks that serve the same goal in the AI vs required visual ability of the goal. Each point represents a different goal. Solid line – identity line. Pearson correlation is 0.69.

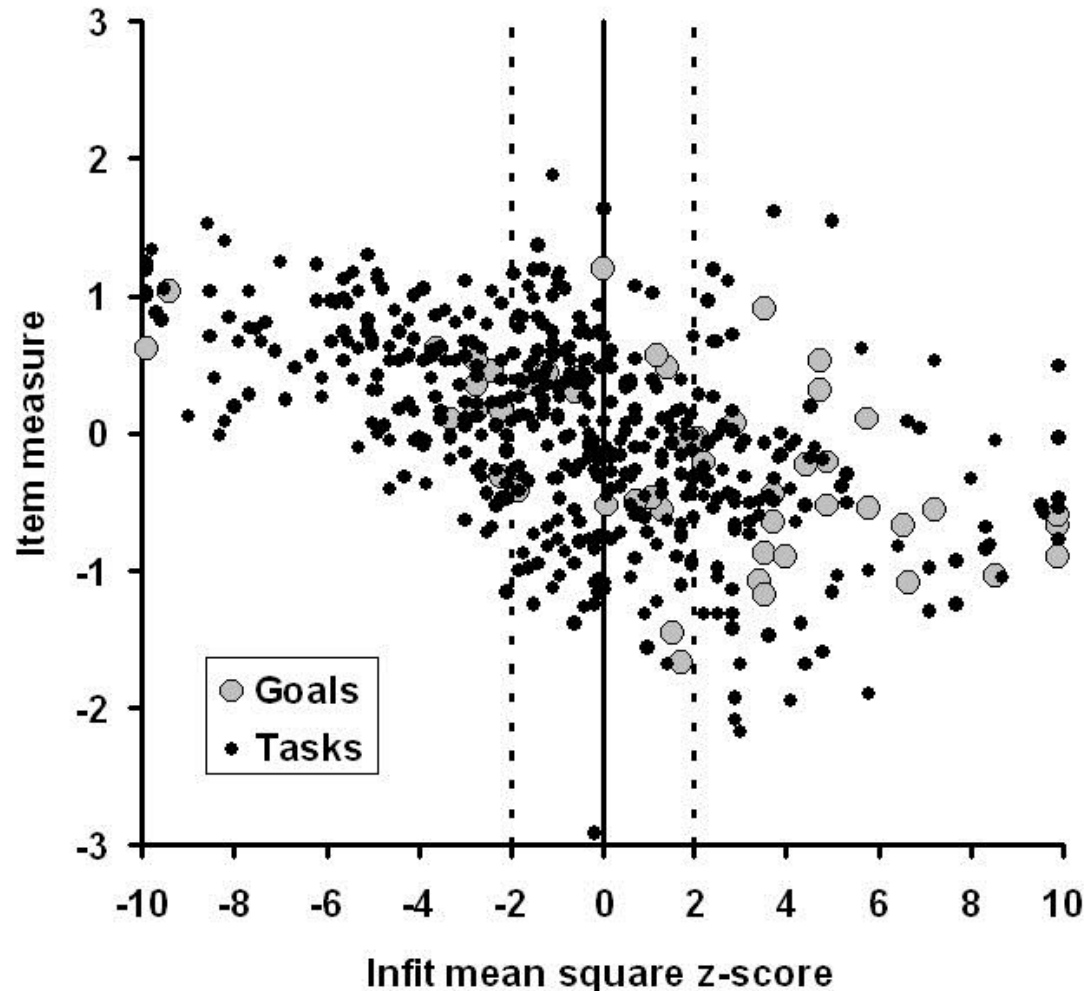


# Calibrated item bank

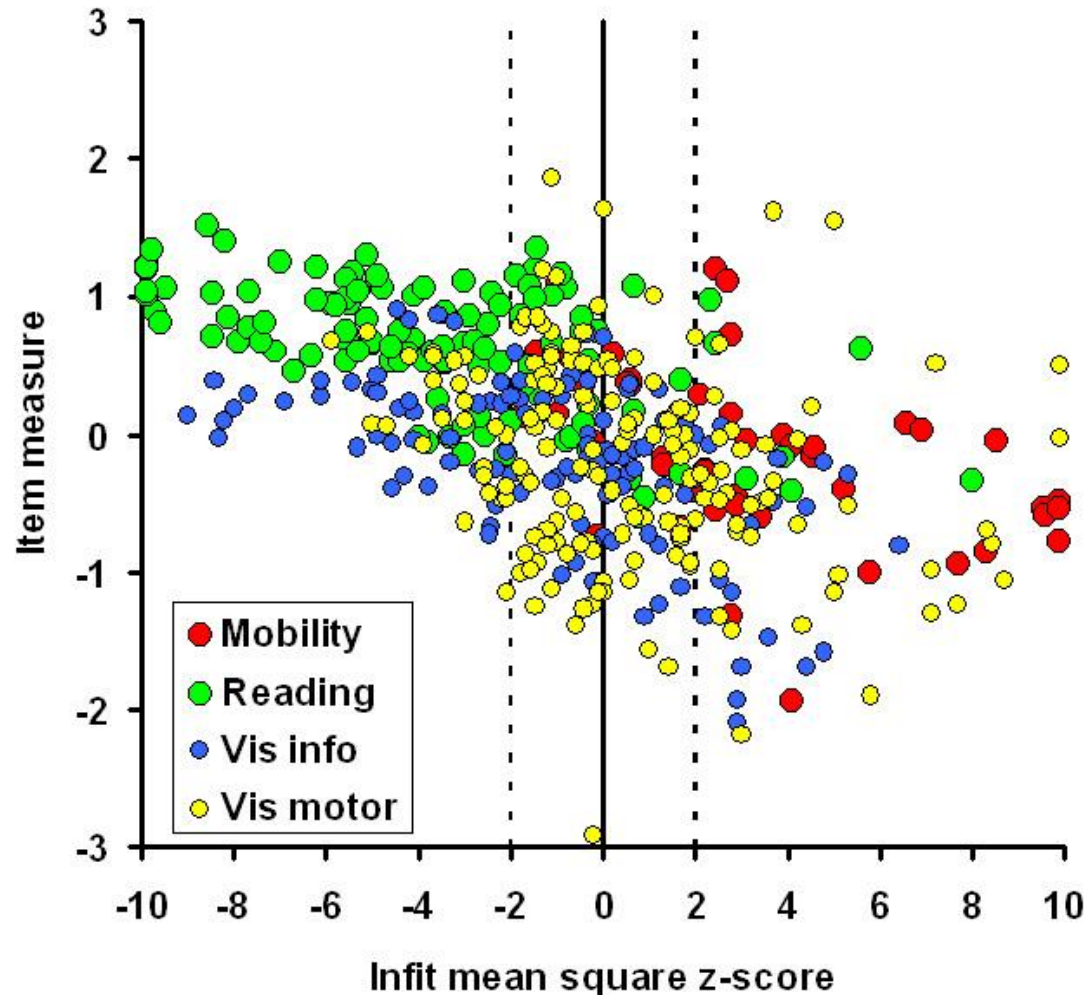
- AI difficulty ratings were obtained from 3200 low vision patients
- Item measures were estimated for each of the 50 AI goals and 460 AI tasks to create a calibrated item bank
- Visual ability can be estimated for each patient from their difficulty ratings of items they identify to be important to them and have some level of difficulty

Goldstein JE, Chun MW, Fletcher DC, Deremeik JT, Massof RW, LVRN Study Group. Visual ability of patients seeking outpatient low vision services in the United States. JAMA Ophthalmol 2014; doi:10.1001/jamaophthalmol.2014.1747 (Epub before print)

# Mean square fit statistic transformed to z-score (standard normal deviate)



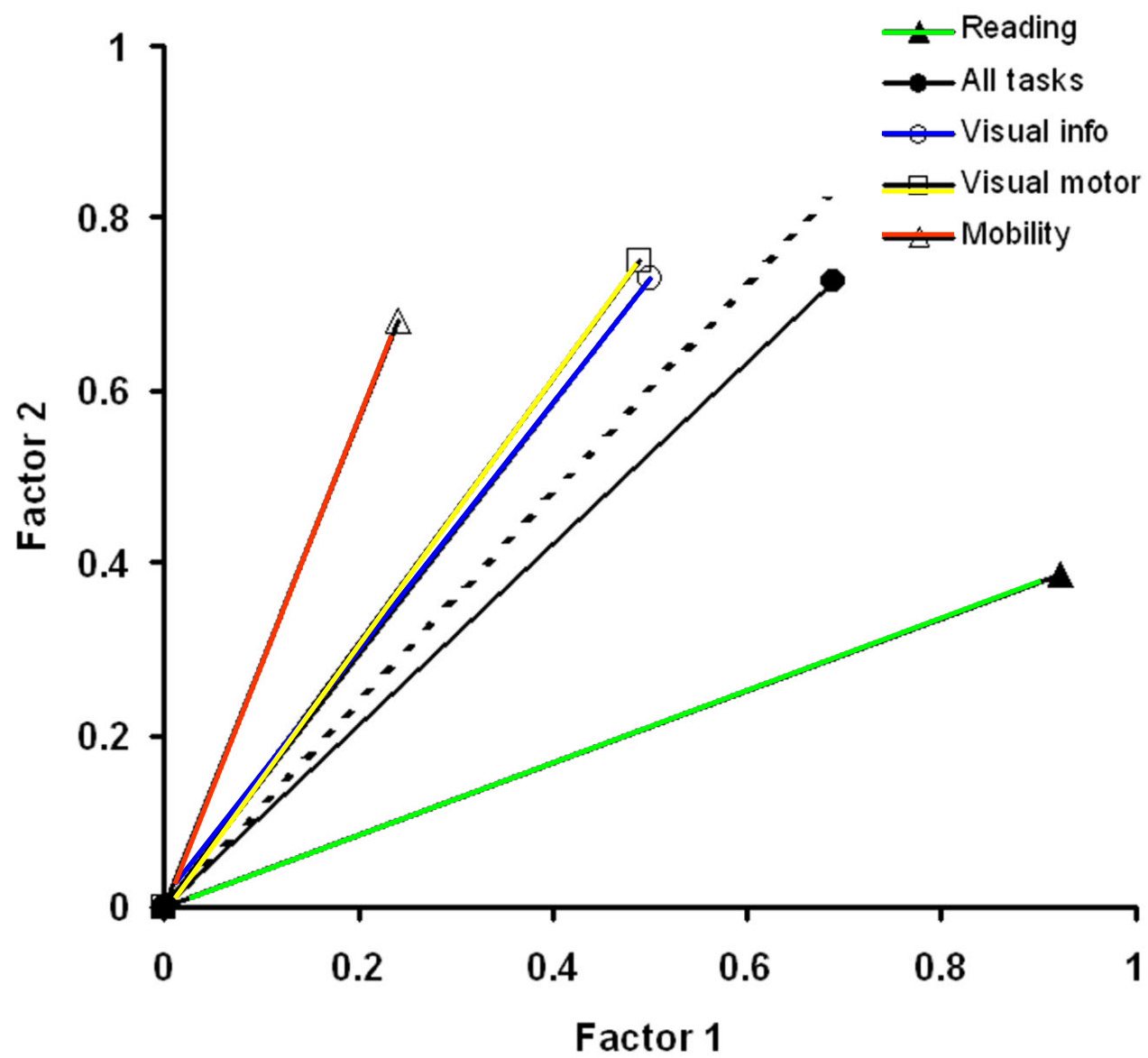
# Mean square fit statistic transformed to z-score (standard normal deviate)

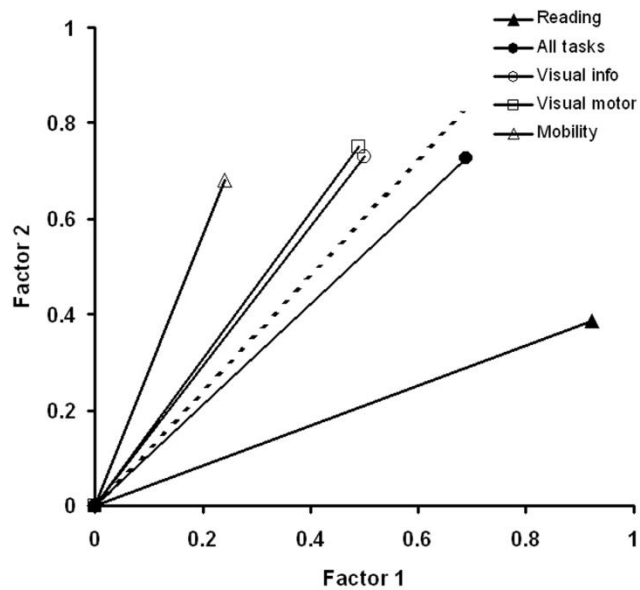
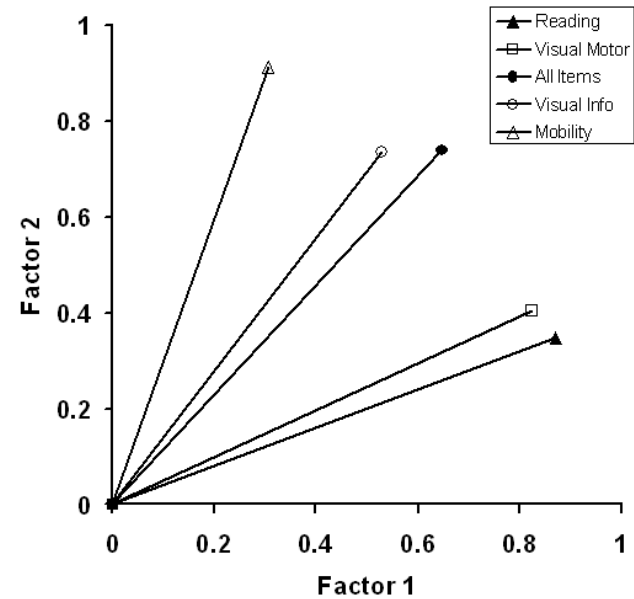
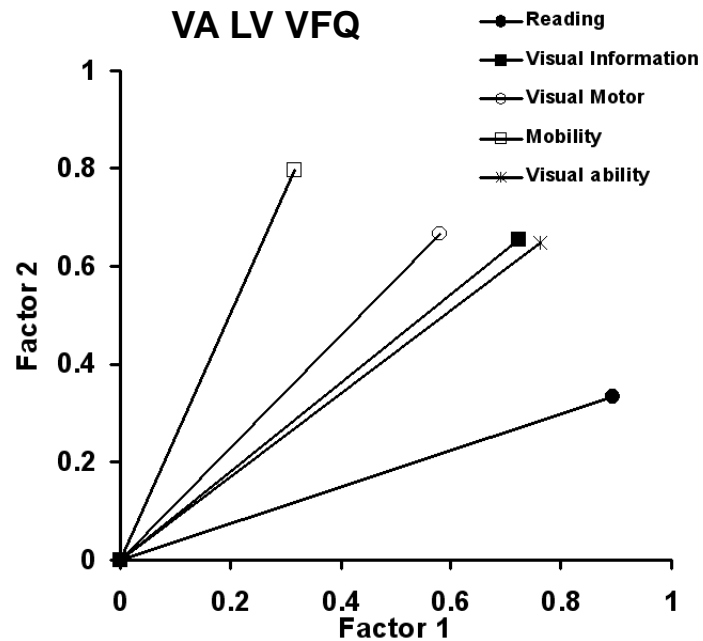
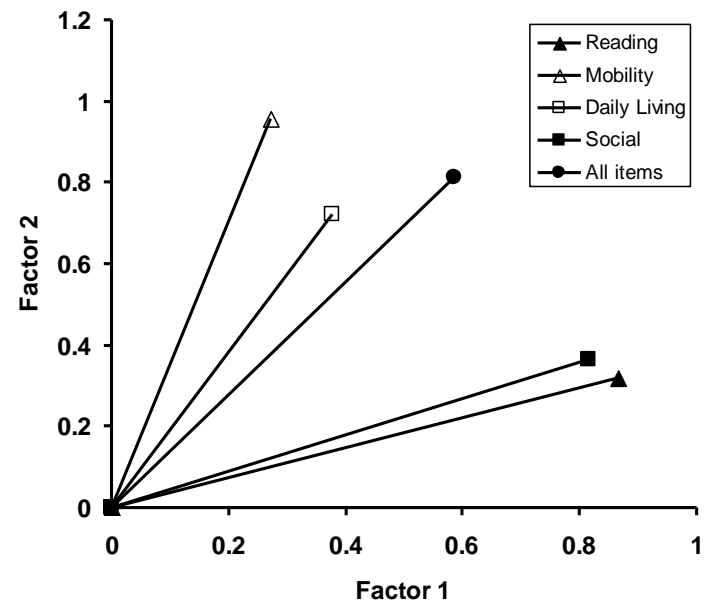




# Analysis of AI functional subscales

- Anchor the task item measures
- Estimate person measures from
  1. Responses to all types of tasks
  2. Responses to only reading tasks
  3. Responses to only mobility tasks
  4. Responses to only visual information tasks
  5. Responses to only visual motor tasks
- Perform exploratory factor analysis to determine the number of independent dimensions that are necessary and sufficient to explain the observed variance and the correlation matrix



**AI****ADVS/NEI VFQ/VAQ/VF-14****VA LV VFQ****Chinese LVQOL**

# Two visual ability factors

(Visual ability is a composite variable)

