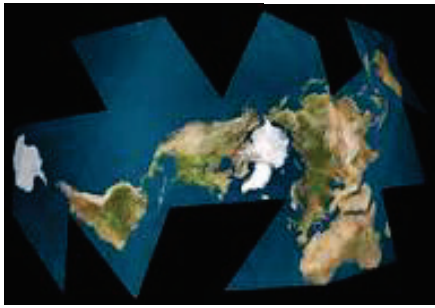

Integrative Analysis of Longitudinal Studies on Aging

A Coordinated Analysis Approach for the Replication of Longitudinal Research

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The Integrative Analysis of Longitudinal Studies of Aging (IALSA) research network is supported by a grant from the National Institutes of Health: 1R01AG026453.

University of Victoria

Authors claim **"Most Published Research Findings are False"**

Ioannidis (2005); Young, Ioannidis, Al-Ubaydli (2008), www.PloSmedicine.org

- Dramatic or important results are more likely to turn out to be false
  - Less dramatic results unpublished or in less prestigious journals
- Why?
  - Competition for "original" contributions: Highly selected studies are overvalued and unrepresentative of true outcomes
  - Bias towards publishing positive results
  - Artificial scarcity; Best journals publish best (i.e., most dramatic) research; excuse for rejection
- Solution: Provide basis for evaluating replicability
  - Publish all research that meets quality threshold (internet)

Need for Replication

(e.g., Hendrick, 1990; Park, 2004; Rosenbaum, 2001)

- Replication is essential for a cumulative and innovative science
  - "The fact that a theory has passed one test provides no evidence at all that it will pass a repetition of a test" (Miller,1980)
  - "The results in a single study are important primarily as one contribution to a mosaic of study effects" (APA Task Force on Statistical Inference, 1999)
  - "…a confirmation, if it is to be worth anything in its own right, must be done in an elegant new way or in a manner that will noticeably advance the state of the art" (Collins, 1992)
  - "Successful replication provides the basis for further and deeper explanatory studies and theory" (Lindsay & Ehrenberg, 1993)

Replication of Observational Research

- Experimental Research
  - Random assignment to groups
  - Explicit experimental protocol/control

- Observational Research
  - Group membership not randomly assigned
  - Unknown combinations of influences

Replication in Longitudinal Research

- Replication of research based on observational longitudinal data necessary to protect against uncritical acceptance of empirical results.
  - Complex data structures and statistical models
  - Extant scientific evidence used to structure, justify and extend research.
- Research findings and conclusions often vary across independent studies addressing the same topic.
  - No one study can control for all extraneous influences
  - Due to unique study characteristics (e.g., sampling, measures, design)
  - Noncomparable results based on different statistical analyses/models
- Between-study variability points to the need for skepticism regarding a single instance of a result and to the importance of multiple replications in the evaluation of scientific findings.

Outline

- Types of replication and analysis strategies
- Longitudinal studies of aging: Potential for replication research
- Coordinated analysis approach

Types of Replication

(Lykken, 1968; Hendrick, 1990; Lindsay & Ehrenberg, 1993)

- Literal (Exact, Close)
  - Exact duplication of sampling procedure, conditions, measurement, and analysis methods
- Operational (Partial)
  - Duplication of sampling and experimental procedures (i.e., minimal essential conditions)
  - Measurement and analysis methods congruent
- Constructive (Conceptual, Differentiated)
  - Evaluation of empirical “fact”due to conceptual factors and not study particulars; broad test of validity

Nature of Replications (Hendrick, 1990)

- Aspects of the total research situation that must be considered
  - Subject characteristics
    - Age, sex, education, SES,
  - Specific research histories of subjects
    - Previous test exposure
  - Historical (socio-cultural) context
    - Birth cohort, culture, education systems
  - General physical setting of the research
    - Group vs individual testing
  - Control agent
  - Specific task variables
    - Measures (language, sensitivity, text size, mode of presentation)
  - Primary information focus
    - Instruction set for performing tasks (timed; speed/accuracy)
  - Modes of data reduction and presentation

Analysis strategies for evaluating replicability/generalizability of results

- **Sequential replication**: Evaluation of a published result on an independent set of data.
- **Meta-analysis**: Combines standardized effects from a set of published findings in order to estimate the general effect and to understand why studies differ in their results (i.e., meta-regression).
- **Coordinated replication**: Coordinated analysis of individual data sets in ways that maximize comparison across studies, permitting optimal meta-analysis of results.
- **Data Pooling**: Methods for combining individual-level data sets within a single analysis (i.e., individual patient meta-analysis, mega-analysis) permitting evaluation of both study-level and individual-level effects.
- **Generalized evidence synthesis**: Methods for combining data from multiple sources and analyzing models that cannot be evaluated in any single source of data.

Current limitations for meta-analysis of longitudinal observational studies

- Paucity of published information on particular research questions
- Complexity of longitudinal designs and analysis
- Differences across longitudinal studies impede pooled data analysis, operational replication, and meta-analysis.
  - Differences in design, sampling (e.g., birth cohort, culture), and measures.
  - The complexity and range of statistical analyses used and limited reporting of results make comparison and replication of published findings difficult.
  - Summarizing regression slopes is challenging because of different measures (metrics) for X and Y and differences in statistical models (e.g., predictor sets) (Becker & Wu, 2007)

IALSA

Integrative Analysis of Longitudinal Studies on Aging (IALSA)

A collaborative research network for cross-validating and extending results from longitudinal data

NIH/NIA R01AG026453

University of Victoria

IALSA: Integrative Analysis of Longitudinal Studies on Aging

- The IALSA network is currently comprised of over 25 longitudinal studies on aging, spanning eight countries.
  - Mix of population representative, volunteer, and special population samples, aged from birth to 100 years (focus 50+), with birth cohorts ranging from 1880 to 1980, assessed during historical periods from 1946 to the present. Between-occasion intervals range from 6 months to 17 years (the majority 1-5 years), with up to 32 (typically 3-5) measurement occasions spanning 4 to 48 years of within-person assessment.

- Primary goal: To facilitate new longitudinal research in ways that permit direct comparison of findings and cumulative knowledge from a within-person perspective
  - Direct involvement of PIs and research teams

Affiliated Longitudinal Studies on Aging

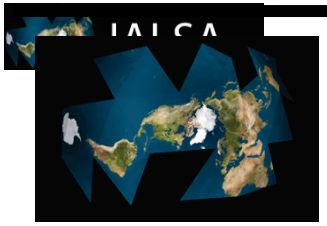
- **Australia**: Australian Longitudinal Study of Aging (ALSA); Canberra Longitudinal Study (CLS)
- **Canada**: Victoria Longitudinal Study of Aging (VLS)
- **Germany**: Bonn Longitudinal Study of Aging (BOLSA); Interdisciplinary Longitudinal Study of Adult Development (ILSE)
- **Netherlands**: Longitudinal Aging Study Amsterdam (LASA)
- **Sweden**: Aging in Women and Men (GENDER); Gerontological and Geriatric Population Studies in Göteborg, Sweden (H-70); Nordic Research on Aging (NORA); Origins of Variance in the Old-Old: Octogenarian Twins (OCTO-Twin); Swedish Adoption / Twin Study of Aging (SATSA)
- **Switzerland**: Swiss Interdisciplinary Longitudinal Study on the Oldest Old (SWILSO-O)
- **United Kingdom**: Caerphilly Cohort Study of Older Men (CSS); Healthy Older People in Edinburgh (HOPE); Longitudinal Study of Cognitive Change in Normal, Healthy Old Age (LSCC)
- **United States**: Cardiovascular Health Study (CHS); Einstein Aging Study (EAS); Health and Retirement Study (HRS/ADAMS); Long Beach Longitudinal Study (LBLS); Midlife in the United States (MIDUS II); Normative Aging Study (NAS); Oregon Brain Aging Study (OBAS); Seattle Longitudinal Study (SLS); University of North Carolina Alumni Health Study (UNCAHS); Wisconsin Longitudinal Study (WLS)

IALSA Approach

- Evaluate evidence and refine theory from within-person change perspective
  - Integrate health, psychosocial and demographic factors in models of aging-related changes in cognitive and functional outcomes, personality, and emotional well-being.
- Evaluate result sensitivity to measurement and analysis/modeling decisions
  - Evaluate and report alternative models on same data
- Accumulate knowledge from replicated evidence
  - Open, direct and immediate comparison and contrast of results across independent studies
  - Availability of analysis protocol, scripts, and results

Harmonization

- Goal: Obtain comparable answers to key questions
- Levels of Harmonization
  - Research Questions
  - Statistical Models
  - Measurements
- Harmonization permits synthesis of results
  - Account of how other variables/processes, country and other sampling differences, initial representativeness, attrition, historical period, age range sampled, etc. relate to differences across studies.



Coordinated Analysis

- Interactive development of research protocol
  - Aim: Maximize data value from each study while making results as comparable as possible
- Evaluation of alternative models
- Complete reporting of results permits direct comparison across studies and variations in models
  - Analysis scripts and extended results available on IALSA site
  - Direct and interactive evaluation of complex hypotheses across longitudinal studies on aging
  - Emphasis on cross-culture, cross-study comparisons
- Communication: Publication models
  - Joint authorship of single paper
  - Series of independent reports, submitted together or independently
    - Possible introduction and consensus paper
    - e.g., analysis of two studies using common statistical approach

navigation

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- Australian Longitudinal Study of Aging (ALSA)
- Canberra Longitudinal Study (CLS)
- The Gerontological and Geriatric Population Studies in Göteborg, Sweden (H-70)
- Healthy Older Person Edinburgh (HOPE)
- Longitudinal Aging Study Amsterdam (LASA)
- Normative Aging Study (NAS)
- Origins of Variance in the Oldest-Old

MMSE: Age, Sex, and Education Effects

Up one level

This cross-study analysis features the MMSE in a descriptive comparison of between-person (BP) and within-person (WP) age differences and the effects of sex and education.

Analysis of MMSE scores

This analysis will feature the MMSE in a descriptive comparison of between-person (BP) and within-person (WP) age differences. We might expect that such differences can result from population selection/mortality differences, one of the key methodological issues we aim to address in the proposal. These results will be primarily descriptive and will demonstrate the ability for cross-national collaboration and pooled data analysis.

Combined Study Results and Figures

This folder contains tabled results and figures showing overall results.

Relevant Papers

Example Scripts (SAS, SPSS, Mplus)

Scripts for analysis of longitudinal change in MMSE scores.

Australian Longitudinal Study of Aging (ALSA)

Canberra Longitudinal Study (CLS)

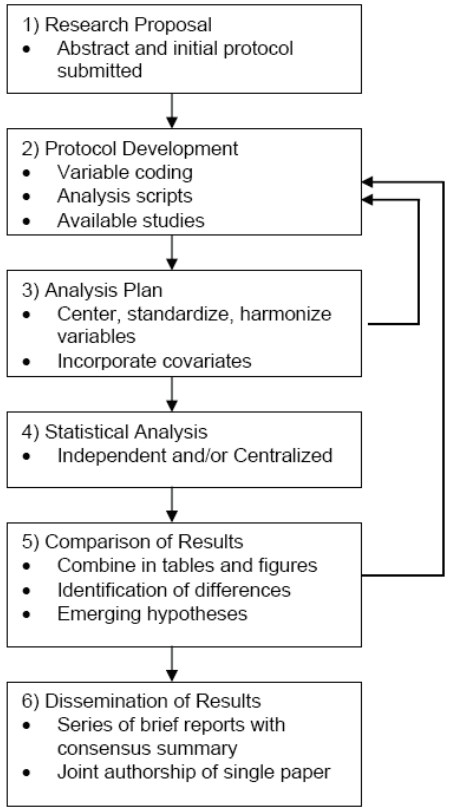
The Gerontological and Geriatric Population Studies in Göteborg, Sweden (H-70)

Healthy Older Person Edinburgh (HOPE)

Longitudinal Aging Study Amsterdam (LASA)

Normative Aging Study (NAS)

Origins of Variance in the Oldest-Old (OCTO-Twin)



news

Second Revised R01 application submitted
March 01, 2006

Two analysis projects are active
June 27, 2005

What is the logo?
April 05, 2005

More...

« May 2006 »

Su	Mo	Tu	We	Th	Fr	Sa
	1	2	3	4	5	6
7	8	9	10	11	12	13
14	15	16	17	18	19	20
21	22	23	24	25	26	27
28	29	30	31			

Data Comparability: Searchable Database

Longitudinal Studies on Aging

View Summary | Add/Edit a Study | Add/Edit a Measure

Studies with Common Measures/Domains:

(1) - Biomedical and Physical Functioning - Cerebrovascular / Dementia - Dementia Diagnosis
(2) - Psychosocial and Demographic - Demographics - Education
(3) - Cardiovascular / Pulmonary - (Any)
(4) - Speed - (Any)
(5) - Memory - (Any)
(6) - Stress / Life Events - (Any)

4 Studies Matching 6 Measures/Domains:	(1)	(2)	(3)	(4)	(5)	(6)
CLS	x	x	x	x	x	x
NAS	x	x	x	x	x	x
CCS	x	x	x	x	x	x
SATSA	x	x	x	x	x	x
10 Studies Matching 5 Measures/Domains:	(1)	(2)	(3)	(4)	(5)	(6)
ALSA		x	x	x	x	x
BOLSA		x	x	x	x	x
EAS	x	x	x	x	x	
GENDER		x	x	x	x	x
H-70	x	x	x	x	x	
ILSE		x	x	x	x	x
LASA		x	x	x	x	x
LSCC		x	x	x	x	x
NORA		x	x	x	x	x
OCTO-Twin	x	x	x	x	x	
6 Studies Matching 4 Measures/Domains:	(1)	(2)	(3)	(4)	(5)	(6)
HOPE	x	x	x		x	
LBLS		x	x	x	x	
SLS		x	x	x	x	
SWILSO-O		x	x	x		x
VLS		x	x	x	x	
HRS		x	x		x	x
1 Study Matching 3 Measures/Domains:	(1)	(2)	(3)	(4)	(5)	(6)
WLS		x	x			x
0 Studies Matching 2 Measures/Domains:	(1)	(2)	(3)	(4)	(5)	(6)
0 Studies Matching 1 Measure/Domain:	(1)	(2)	(3)	(4)	(5)	(6)

Return to Select Different Measures/Domains

Data Availability by Domain

- Cognition
  - Memory, speed (20), Gf, Gc (19), attention (15), MMSE (14)
- Health
  - CVD (25), BMI (24), SRHealth, diabetes (23), death (22), BP (21), stroke (18), functional (16), blood (15), dementia dx (8)
- Personality
  - Neuroticism, Extraversion (13), Openness (7)

NIH Specific Aims (AG026453)

- SA 2: To document general patterns of population average and individual variation in change in cognitive capabilities across major longitudinal studies on aging.

- SA 3: To evaluate the commonality and specificity of cognitive changes with age, including tests of psychological theories of speed and working memory, from a within-person change perspective.
  - Evaluate interdependence between processing speed and other cognitive abilities based on within-person (WP) models of correlated and coupled change. Replication and extension of Sliwinski & Buschke (1999) and Zimprich & Martin (2002).

Philosophy of the Approach

Psychological Methods
2009, Vol. 14, No. 2, 150–164

1082-989X/09/$12.00 DOI: 10.1037/a0015566

Integrative Data Analysis Through Coordination of Measurement and Analysis Protocol Across Independent Longitudinal Studies

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Replication of research findings across independent longitudinal studies is essential for a cumulative and innovative developmental science. Meta-analysis of longitudinal studies is often limited by the amount of published information on particular research questions, the complexity of longitudinal designs and the sophistication of analyses, and practical limits on full reporting of results. In many cases, cross-study differences in sample composition and measurements impede or lessen the utility of pooled data analysis. A collaborative, coordinated analysis approach can provide a broad foundation for cumulating scientific knowledge by facilitating efficient analysis of multiple studies in ways that maximize comparability of results and permit evaluation of study differences. The goal of such an approach is to maximize opportunities for replication and extension of findings across longitudinal studies through open access to analysis scripts and output for published results, permitting modification, evaluation, and extension of alternative statistical models and application to additional data sets. Drawing on the cognitive aging literature as an example, the authors articulate some of the challenges of meta-analytic and pooled-data approaches and introduce a coordinated analysis approach as an important avenue for maximizing the comparability, replication, and extension of results from longitudinal studies.

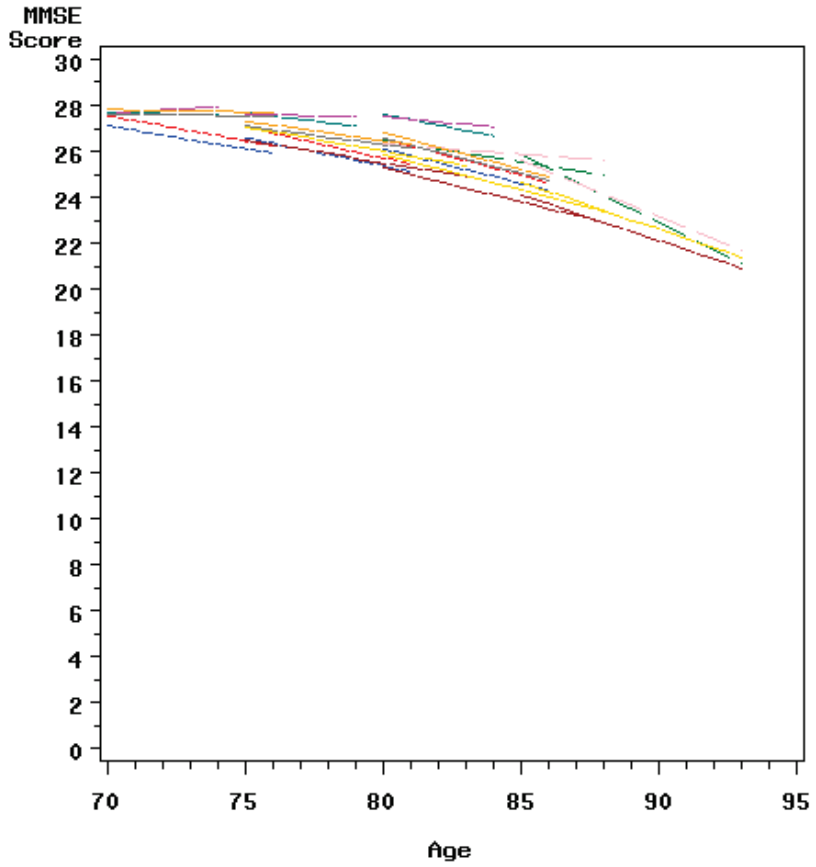
Keywords: longitudinal, integrative data analysis, meta-analysis, data pooling, longitudinal studies

Simultaneous replication of same measure

Predicted MMSE scores for hypothetical individuals based on age, sex, and education.

Study (male, female):

ALSA (teal, magenta),
LASA (blue, red),
OCTO-Twin (pink, green),
CLS (brown, gold),
HOPE (grey, orange).



Sequential replication of similar measures

J Neurol (2008) 255:1486–1494
DOI 10.1007/s00415-008-0942-3

ORIGINAL COMMUNICATION

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Development of classification models for early identification of persons at risk for persistent cognitive decline

Received: 27 July 2007
Received in revised form: 12 March 2008
Accepted: 16 March 2008
Published online: 14 July 2008

Abstract *Objective* To develop two classification models for use in primary care to aid early identification of persons at risk for persistent cognitive decline. *Methods* Data were used from the Longitudinal Aging Study Amsterdam

dition to the first set, predictors requiring additional measurement (e.g. markers determined in blood) were included in the analyses. Age was again the strongest predictor of persistent cognitive decline. In persons > 75 years, having a low to-

Simultaneous Replication with Different Measures

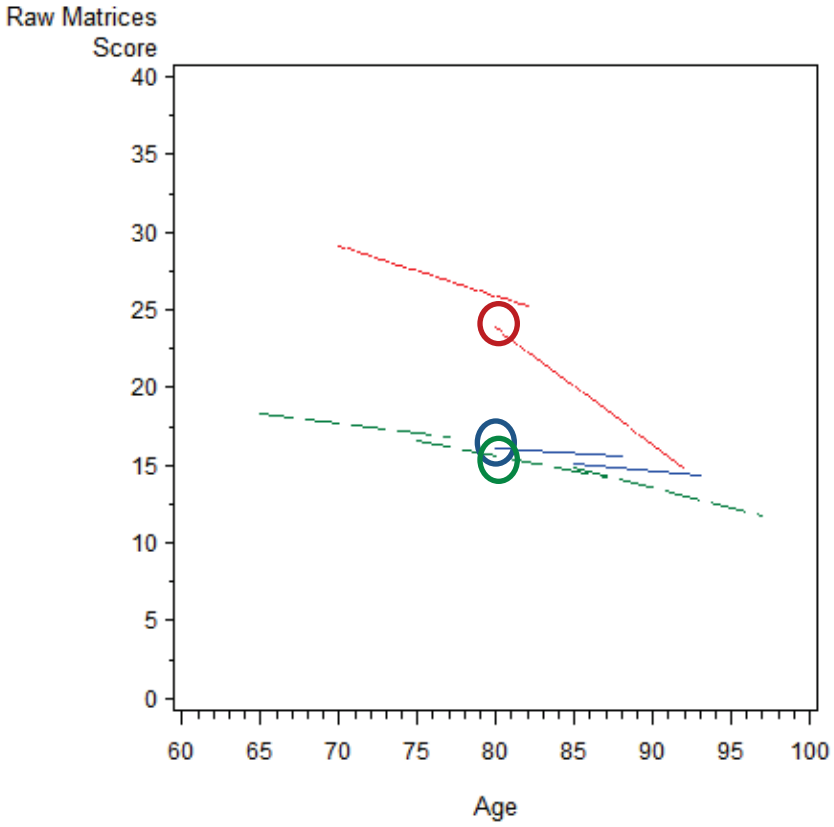
- Pre-standardization using relative age and education differences
  - Between-Person Mean and SD for relative age and education group in common across studies at T1
  - Individuals aged 80-85 with 6-10 years education for each sample.

Statistical Model

- Growth curve
- Time-based, linear, centered at T1
- Covariates:
  - baseline age - centered at 80
  - sex - centered at male
  - education - centered at 7
- Findings:
  - All covariates predicted level
  - Only baseline age predicted slope

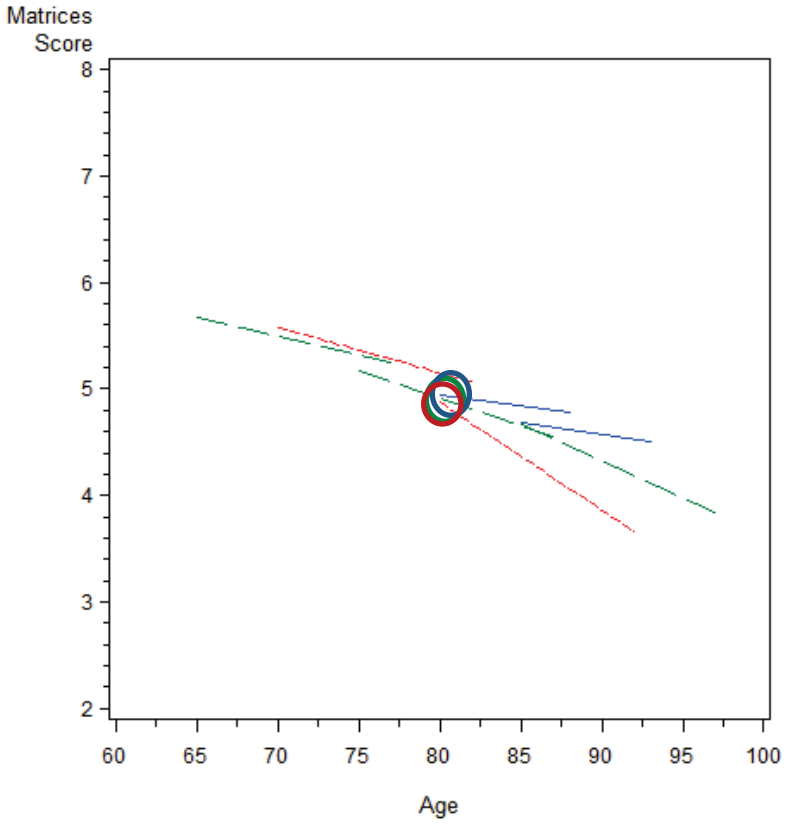
Model-predicted Trajectories: Matrices

Raw Score



HOPE
LASA
OCTO

Relative Age & Education Standardized



Multi-Study Projects

- Analysis of rare events and G-E interactions
  - e.g., ApoE

Alleles	CLS	LASA	OBAS	SATSA	LSCC	CHS	CCS(Caps)	EAS	TOTAL
22	2	10	0	3	2	24	9	6	**56**
23	63	162	18	60	108	453	179	81	**1124**
24	10	37	1	20	15	89	40	22	**234**
33	389	863	60	265	447	1985	795	391	**5195**
34	127	290	17	117	174	674	313	116	**1828**
44	10	44	3	13	12	46	30	9	**167**
	601	1405	99	478	758	3271	1366	625	**8603**

Identification of Risk Factors for Accelerated Cognitive Decline

- Initial focus on BP-WP patterns of change across cognitive outcomes, comparability across studies
  - Age, Sex, Education
- Basis for evaluation of risk factors
  - SES: Education, Occupation, Income
  - Smoking, Alcohol, BMI
    - Add to recent systematic reviews of Alcohol, Smoking, & BMI for risk of dementia and cognitive decline
  - Intellectual and Social Engagement
- Emphasis on links between health and cognition
  - Comprehensive analysis of health pathways underlying cognitive change
  - Evaluation of risk factors in health context

Typical Developmental Science

- Idiosyncratic analyses and evaluation of particular models
  - Measures, covariates, and statistical analysis often differ across published findings
- Limited reporting of results make comparison of findings difficult
- Long interval between replication/validation, thus slow accumulation of knowledge
- Theory and most evidence based largely on cross-sectional between-person differences, particularly in older age samples

Optimal Developmental Science

- Harmonization of variables for maximal comparability and identification of noncomparable variables
- Knowledge of result sensitivity to measurement and analysis/modeling decisions
  - Evaluation and report of alternative models on same data
  - Immediate follow-up of alternative hypotheses and accounting for disparities by individual and study-level characteristics
- Open, direct and immediate comparison and contrast of results across independent studies
  - Exact vs. conceptual replication depends on comparable variables and sampling characteristics
- Evaluation and extension of theoretical and empirical findings in available “within-person” data
- Accumulation of knowledge based on cross-validated evidence
  - Open availability of analysis protocol, scripts, and results

IALSA as a Collaborative Method

- "Collaboration is a group problem-solving process that requires the creative integration of needs and joint ownership of decisions. It involves working in teams, coalitions, alliances, partnerships, and networks. It involves trust and consensus building. It allows different leadership styles to contribute simultaneously. The goal of collaboration is not to solve problems through compromise but to achieve synergies that lead to innovative solutions" *APA President Dr. Carol Goodheart, April 2010 Monitor on Psychology.*

Friday Harbor Workshop

- Influence of activities on cognitive decline:
  - Intellectual
  - Physical
  - Social
- Four studies:
  - Long Beach Longitudinal Study
  - Octo-Twin Study
  - Seattle Longitudinal Study
  - Victoria Longitudinal Study
- Methods:
  - Growth curve and related longitudinal models

Workgroups

- Familiarization with data, workgroup
- Within-group discussion of method/approach
- Cross-group discussion: measures & methods
- Implementation
- Revision, alternate models, etc.
- Determine publication structure