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INTEGRATIVE ANALYSIS OF LONGITUDINAL STUDIES ON AGING

Collaborative Research Networks, Meta-Analysis, and Optimizing Future Studies

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Remarkable national and international efforts have produced well over 40 major longitudinal studies of individuals age 50 and older with a significant cognitive assessment component. It is widely recognized that although longitudinal information is time and effort intensive to collect, it is required to address central questions in developmental research relating to intraindividual change and variation and to population inference conditional on attrition and mortality. Given the profound investment of time, energy, and funding that these studies require, it is not uncommon for them to be multidisciplinary in nature. These existing longitudinal studies, therefore, represent an enormous wealth of information on within-person changes in a variety of domains, including cognition, health, personality, affect, lifestyle, and well-being. These studies, coupled with recent developments in statistical analysis and software for analysis of longitudinal data, provide unprecedented opportunities for describing and explaining aging-related changes and cross-process dynamics and for identifying influential factors associated with late life outcomes. Longitudinal studies permit the identification of change from a within-person baseline, thus enabling the identification of characteristics and antecedents that are potentially causally related and amenable to intervention.

As currently practiced, developmental science and theory are largely based on between-person differences, particularly in later adulthood. Given the requirements of data collection in longitudinal research, long intervals often pass until replication or cross-validation of findings. Relative to research reports from cross-sectional age-comparative studies, accumulation of knowledge from longitudinal studies has progressed very slowly. Aggravating this

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slow process are the complex varieties of measures, covariates, and statistical analyses based on the many decisions that often differ across published findings. The diversity of research interests relative to the number of longitudinal studies has also led to somewhat unique analyses, evaluation of particular models, and limited reporting of results, making comparison of findings difficult. One of the most obvious next steps in the developmental aging field is the evaluation and extension of theoretical and empirical findings in available within-person data. We must maximize what can be learned from existing data and make use of this information in the design of new studies.

The potential knowledge gains from increased collaboration and coordinated analysis of longitudinal data on aging are great. Recent major recommendations for research (Bachrach & Abeles, 2004), including executive summaries published by the National Research Council and commissioned by the National Institute on Aging/National Institutes of Health (NIH) and by the Office of Behavioral and Social Sciences Research/NIH (*The Aging Mind: Opportunities for Cognitive Research* [National Research Council, 2000, pp. 3–5]; *Preparing for an Aging World: The Case for Cross-National Research* [National Research Council, 2001a, pp. 4–7]; *New Horizons in Health: An Integrative Approach* [National Research Council, 2001b, pp. 9–13]) have highlighted the importance of such interdisciplinary, international, and collaborative research making use of longitudinal studies on aging. Butz and Torrey (2006), in *Science*, similarly highlighted the importance of longitudinal research, international replications, and advances in statistical methods to progress in the social sciences.

As we will describe in this chapter, numerous calls have been made for increased collaboration as a means to focus developmental research on within-person processes. We highlight and summarize some examples of collaborative and coordinated research, and we elaborate on some fundamental ideas for implementing strategies for maximizing our understanding of within-person aging-related changes.

We propose a collaborative system that encourages the evaluation and report of both parallel and alternative models on the same data as well as models incorporating individual- and study-level characteristics to account for disparities across studies. We believe that direct and immediate comparison and contrast of results across independent studies, based on the open availability of analysis protocol, scripts, and results, will result in the most solid accumulation of knowledge based on cross-validated evidence. This is the most powerful way to build our developmental science.

Facilitating Research on Longitudinal Studies

Reviews of Longitudinal Research

One approach to encouraging collaboration or cross-validation has been to produce a book or review that brings together work from a number of longitudinal studies. Mednick, Harway, and Finello's (1984a, 1984b) handbook of longitudinal research includes an explicit call for collaboration: "This handbook . . . is also presented to encourage scientists to consider collaborative efforts in which new questions may be put to the existing data banks" (Mednick, Harway, & Finello, 1984b, p. ix). As part of the handbook and central to this collaborative aim, extensive coding of 380 studies was incorporated into a computerized database, facilitating searches according to sample age and selection criteria as well as on antecedent and outcome variables.

Several recent reviews provide information on the number and scope of longitudinal studies on aging in existence with cognitive data. The Canadian Review of Longitudinal Studies on Aging (Health Canada, 2002) consists of a Microsoft Access database with information on 55 studies from more than 11 countries as well as a brief design description (initiation date, sample characteristics, main objective), a more detailed variable list for 51 of the studies (with a brief list for 4 studies not formally reviewed), and a short list of references for each of the studies. Of the studies reviewed, 32 collected both cognitive and objective health data, and an additional 10 contain cognitive and self-reported health. In 2006, Seematter-Bagnoud and Santos-Eggimann reviewed 70 large population-based longitudinal studies on health in individuals age 50 and over, listing them in

tabular format according to geographical region. Although these studies more often focus solely on medical issues (e.g., cancer, osteoporosis), 20 overlap with the Canadian review and almost half collected cognitive measures. Seematter-Bagnoud's and Santos-Eggimann's review also includes 9 studies from outside of North America and Europe, compared with the Canadian list, which contains only 1 (which appears in both). Both of these reviews include extensive tables with information on sampling of individuals and measures.

The National Institute on Aging and various data archive (e.g., Inter-University Consortium for Political and Social Research National Archive of Computerized Data on Aging) and Web pages on aging (e.g., AgeNet UK) are also good information sources. AgeNet's review of 55 mainly British studies was conducted in 1999. In 2006, Longview, an independent think tank promoting longitudinal research in the United Kingdom, posted a strategic review (J. Martin et al., 2006) of 92 British panel and cohort studies (many of them social and economic) commissioned by the Economic and Social Research Council. The review discusses priorities, challenges, and opportunities; summarizes the types of studies available; and includes an appendix listing characteristics of each study. One of their main projects addresses "cognitive capital" across the life span, with a recent series of seminars focusing on birth cohort studies from 1946 and 1958.

These resources are similar in format to previous major inventories of longitudinal studies that have listed studies focused on aging. The Social Science Research Council Committee on Life-Course Perspectives on Human Development published an inventory covering middle and old age (Migdal, Abeles, & Sherrod, 1981), listing mainly American (49 of 73) studies. At the request of the Social Science Research Council, Young, Savola, and Phelps (1991) of the Murray Research Center updated the inventory and combined it with parallel documentation of longitudinal studies of childhood and adolescence (Verdonik & Sherrod, 1984). The inventories provided up to several pages of summarized information on the sample, participant attrition, substantive topics, measurement instruments used, representative references, contact information, and current status of the study.

Similarly, Schneider and Edelstein (1990) and a 1995 update (more a supplement, based on its selection criteria) by Zentrum (formerly Zentralstelle) für Psychologische Information und Dokumentation der Universität Trier have focused on European behavioral and medical studies. In these inventories, approximately 30 (from eight countries, with many from Sweden) include collection of data on cognitive function in adults over 50, 6 have life span data, and many also include measures of health. Given the passage of time since publication, 15 additional studies would now include adults over age 50 if it were possible to reconnect with the participants. The information collected includes name(s) of principal investigator(s), title of study, name and address of contact person, abstract, begin and end dates of data collection, computerization of data, size and age range of sample, and relevant publications.

These relatively comprehensive inventories, however, apart from listing representative references, do not describe the scientific contributions of these studies. Published results from these studies currently are largely based on different analytic approaches, limited report of results, and outcomes and covariates that differ in measurement instrument or coding procedure. Such differences hinder direct and quantitative comparison of results across studies and limit attempts to assess generalizability.

Reviews addressing the results from longitudinal studies on aging do exist. For example, Frazier, Hooker, and Siegler (1993) summarized psychological and personality aspects of seven multidisciplinary studies and a handful of additional longitudinal and epidemiological studies, and Schaie and Hofer (2001; see also Hofer & Piccinin, 2007) reviewed current studies that emphasize psychological outcomes. It is interesting to note that both reviews present results from different research questions for each study rather than any indication of consensus, although from the available data comparisons could often be made across studies if comparable analyses were conducted. Anstey and Christensen (2000) reviewed the impact of education, activity, health, blood pressure, and Apolipoprotein E as predictors of cognitive change in older adults and found relatively consistent evidence for education on Mini-Mental

Status Examination (MMSE; Folstein, Folstein, & McHugh, 1975). It is clear, however, that beyond this screening measure it is relatively difficult to find published work that allows straightforward comparisons. Park, O'Connell, and Thomson's (2003) systematic review of cognitive decline in the general elderly population identified 5,990 abstracts, but their selection criteria reduced this number to only 19 articles describing community-based, prospective cohort studies with low attrition. Citing population, country, measure, follow-ups (length and number), and attrition differences, they presented a narrative review rather than their planned meta-analysis. It is also noteworthy that their conclusion—that cognitive decline is almost universal—stands in contrast to recent literature emphasizing individual variability in rate of change and the relative stability of cognitive function for many or most of the individuals in the samples (e.g., Rubin et al., 1998; Wilson et al., 2002).

Combining the utility of the inventory and review formats, the Cognitive and Emotional Health Project (CEHP), funded by the National Institute on Aging, the National Institute of Mental Health, and the National Institute of Neurological Disorders and Stroke has created a searchable database of 67 large-scale ($N > 500$) multidisciplinary longitudinal and epidemiological studies, 42 of which have longitudinal cognitive data on adults age 55 years and older. Queries based on a variety of study characteristics provide a list of the relevant participating studies. Links from this list led to each study's responses to dichotomous questions regarding sample characteristics and construct measurement. For this project, 26 of the studies were selected for further review of findings, and these were summarized, with a focus on risk factors for change, by Hendrie et al. (2006). It is worthwhile to note their comment that aspects of the review were limited by less than complete reporting of the often-complex results. In particular, risk factors were sometimes included as covariates, but the details regarding their impact were not described.

Reflecting on the Herculean efforts devoted to cataloguing, coding and, in the case of CEHP, reviewing such large numbers of longitudinal studies, it is worth considering the value of ensuring that the details of these products are not lost. This information and these search facilities might best be maintained and disseminated—and perhaps updated—under the aegis of a dedicated centralized repository such as a data archive.

Data Archives

Another approach to encouraging greater use of collected data has been to archive the information in a system that facilitates access. Over the past 60 years, a number of such efforts have been made to increase the accessibility of data for secondary analysis and encourage cross-disciplinary collaborations. The Roper Center is credited as the first to assemble and make available results from polls and other surveys in the 1940s. In 1960, the Zentralarchiv für empirische Sozialforschung was started in Europe (Cologne, France), and over the next few years, the Inter-University Consortium for Political and Social Research (1962) and its National Archive of Computerized Data on Aging (1978), which focuses specifically on aging and health, and the UK Data Archive (1967), were developed. The Henry A. Murray Research Archive (now part of the Harvard–MIT Data Center), a multidisciplinary archive focused on longitudinal data sets, started in 1976 and archives raw data in addition to computerized records.

Also in 1976, an umbrella organization, the Council of European Social Science Data Archives, was set up, with the main goals of cooperation in data archiving and unrestricted exchange of data. One year later, the International Federation of Data Archives/Organizations for the Social Science came into being. It is funded by membership fees and project applications, but some of the country-level archives have more often been funded by national agencies (e.g., Administration on Aging, Economic and Social Research Council, NIH), and in more recent years these agencies have increased the pressure to archive data by requiring investigators to begin the archiving process in order to obtain continued funding.

Data archives are unquestionably of value and are the most secure method for ensuring that data are not lost because of inadequate storage conditions or other problems. The maintaining and dissemination of data on such a large scale is not

feasible for individual projects, particularly once funding has ended. However, beyond the straightforward archiving of data, an investigator seeking to maximize a study's data value might also consider collaborative opportunities with external investigators. In particular, such an investigator might seek to work with others holding similar data. Although this might initially appear to go against the competitive spirit that seems to have a hold on everything, including science, it opens up the possibility of building a science based on explicit cross-validation of results. Further advantages of such a cooperative approach are distribution of the work involved, immediate examination of alternative hypotheses and statistical models, and analysis of data by the individuals most familiar with them.

Collaborative Research Networks

How successful have prior calls for cooperation been? Most of us would be hard pressed to name many of them in the social sciences. Collaborative endeavors do exist, however, and are becoming more widespread in many areas inside and outside (e.g., Wikipedia) of academe. Among the successful scientific groups are the Campbell (1999) and Cochrane (1993) collaborations, both independent, not-for-profit, international organizations relying largely on volunteer contributions to produce easily accessible, up-to-date, systematic reviews of social and health care interventions (respectively) and to stimulate high-quality research. The reviews make recommendations for future research; however, data collection and analysis are not part of the mission of these groups.

The MacArthur Foundation and the networks it sponsors are also well known for interdisciplinary work in a variety of areas, including the MacArthur Study of Successful Aging (1988–1996; Rowe & Kahn, 1997), which drew a sample from the top third, based on a set of cognitive and physical criteria, of three of the Established Populations for Epidemiologic Studies of the Elderly programs. This productive set of networks has made use of a range of approaches: collaborative development of a number of related studies (Successful Midlife Development: MIDMAC); implementation of a series of distinct studies addressing key questions (Early Experience and Brain Development, Successful Pathways through Middle Childhood); addition of measures and waves to ongoing longitudinal studies (Socioeconomic Status and Health); and parallel analyses of data from completed or ongoing longitudinal studies of development (Psychopathology and Development).

With an emphasis on aging, the AgeNet project (1997–2000) aimed to stimulate collaborative, multidisciplinary research and linkages—among academe, industry, and the National Health Service—through a database on longitudinal studies of aging and workshops on aging-related topics. AgeNet and its 1999 workshop on Longitudinal Studies of Aging were precursors of the Longview project and of current efforts for the development of a UK Birth Cohort Collaboration (Kuh & The New Dynamics of Ageing Preparatory Network, 2007). Similarly, CEHP, mentioned earlier, recommended the creation of consortia that would conduct combined analyses across studies but cautioned that this might be severely limited by study compatibility (Hendrie et al., 2006)).

Collaboration becomes a topic in a heady Nobel roundtable discussion on the future of interdisciplinary research and training (Nobel Round Table Discussions, 2006) and is also the focus of the Science of Collaboratories (Wulf, 1993), a National Science Foundation–funded project at the University of Michigan and Howard University. The Science of Collaboratories has ambitious goals of understanding the features required for successful collaborations and ultimately to have collaboration become part of the common infrastructure of science.

Some of the critical tasks in such collaborative research—and, we would argue, to advance the field in the absence of such collaboration—include harmonization of variables for maximal comparability and identification of comparable and noncomparable variables across studies. This could be a role for a data archive as well as a collaborative research network. Two examples of the work involved in harmonization are the Comparison of Longitudinal European Studies on Aging (CLESA) and the Survey of Health, Ageing and Retirement in Europe, which demonstrate the harmonization process from two extremes. CLESA investigators brought together existing measures from independent studies and

we describe, below, a variety of their solutions to the obstacles they faced. The Survey of Health, Ageing and Retirement in Europe, on the other hand, started as a multisite study, developing a central questionnaire that was then translated and pretested in all member languages. Its acronym (SHARE) aptly represents the international cooperation and the open data sharing that are central to the project.

Various collaborations have been developed with different structures and levels of linkage among investigators and data. Table 27.1 provides a sampling of some of the main collaborative models and is organized in terms of multisite studies funded as collaborations from the outset and networks of pre-existing studies.

There are clearly many benefits to collaborative endeavors related to longitudinal studies on aging, most notably the opportunity for simultaneous evaluation of longitudinal data to test, replicate, and extend prior findings on aging. Given the key issue of cross-study comparison, harmonization of variables and statistical models are critical aspects, as are the evaluation of alternative models on the same data to permit direct comparison of results across models and the determination of why results might differ. Longitudinal research by itself is challenging, and coordinating analysis across studies is more so given the diversity of study designs, samples, and variables. These challenges are not insurmountable, however, and there is great promise for new collaborations that integrate recent theoretical perspectives for within-person aging (with emphasis on both health and aging), developments in statistical analysis of within-person data, and the remarkable number of completed and ongoing longitudinal studies on aging.

Theoretical, Measurement, and Statistical Issues for Collaborative Research on Aging

In aspiring to a collaborative and accumulative developmental science, it is necessary to consider issues related to comparisons across studies. It is also worth visiting more general issues related to developmental and nonexperimental research quality. We now discuss the importance of addressing developmental questions using within-person information as well as a number of design-related and sample-related issues in quasi-experimental research.

Emphasis on Within-Person Change Related to Aging and Health

Although much previous research in cognitive aging has been performed in the context of relatively healthy aging, there is sufficient evidence in the literature to indicate that changes in cognition and health are related (e.g., Albert et al., 1995; Brady, Spiro, & Gaziano, 2005; Brady, Spiro, McGlinchey-Berroth, Milberg, & Gaziano, 2001; Haan, Shemanski, Jagust, Manolio, & Kuller, 1999; Hassing et al., 2004; Knopman et al, 2001). Theoretical explanations of cognitive aging, however, have rarely taken health into account, or they do so by attempting to exclude major diagnoses such as dementia and so assume that results are based on individuals without health problems (but see Sliwinski & Buschke, 1999). The next steps in cognitive aging and health research are to examine what happens to people as they age by emphasizing the interplay between cognition and health (e.g., Waldstein, 2000) from a multiple-process orientation.

Understanding cognitive aging requires the identification of aging-related changes due to disease processes (morbidity, comorbidity) and mortality (see chap. 16, this volume). Pathological processes (i.e., disease) may be considered distinct but not independent of nonpathological processes of aging (Busse, 1969; Fozard, Metter, & Brant, 1990; Siegler, 1989). In terms of effects on cognition, health can have both direct and indirect effects on cognitive decline. The link between health and cognition may be indirect in that consequences of disease (frailty, level of arousal) impact the level of cognitive reserve, affecting older adults more because of their lower reserve thresholds. Direct effects of health on cognition are those related to pathological changes in the integrity of the neurological, cardiovascular, and cerebrovascular systems. The challenge is to understand aging-related changes in cognition in the context of morbidity and comorbidity and in terms of population inference conditional on survival. Broader changes, such as physical disablement and mental health functioning, also are relevant.

Table 27.1 Examples of Collaborative Research Networks

Collaboration Type and Name/Acronym	*Years*	*Funding*	*Purpose and Accomplishments*
Multisite studies funded as collaborations from the outset			
Nordic Research on Aging (NORA)	1989–1995	National funding agencies and private foundations in each country (e.g., Social Insurance Institution of Finland)	Study health, functional capacity, living habits, and living conditions of 75-year-olds in Denmark, Finland, and Sweden. Summary in Viidik (2002).
Medical Research Council (MRC) Cognitive Function and Ageing Study (CFAS)	1991–	MRC	Estimate prevalence and incidence of cognitive decline and dementia, determine the natural history of dementia, and evaluate service needs. Five sites with identical design; one, established earlier, is different.
International Study of Postoperative Cognitive Dysfunction (ISPOCD)	1994–2001	European Union (EU) BIOMED-1	Investigate cognitive decline after operation and anesthesia. Identified risk factors for long-term postoperative cognitive dysfunction after 3 months: age and use of benzodiazepines before surgery.
International Collaborative of Macronutrients and Blood Pressure (INTERMAP)	1995–2005	U.S. National Heart, Lung and Blood Institute	Multinational, multicenter epidemiologic study of diet impact (especially macronutrients) on blood pressure (ages 40–59).
Cardiovascular Health Study (CHS)	1989–1999	U.S. National Heart, Lung and Blood Institute	Identify risk factors for cardiovascular disease, ages 65+. More than 400 research papers and 120 ancillary studies.
Cross-European Longitudinal Study of Aging (EXCELSA)	1998–2002	EU 5th framework program, BIOMED-2	Study of biobehavioral, psychosocial, and socioenvironmental determinants of competence across the life span.
Advanced Cognitive Training in Vital Elderly (ACTIVE)	1999–2001	U.S. National Institute on Aging	Multisite randomized controlled trial of cognitive interventions.

Collaboration Type and Name/Acronym	*Years*	*Funding*	*Purpose and Accomplishments*
Networks of previously established longitudinal studies			
Berkeley Intergenerational Studies (IGS)	~1960	Initially: Laura Spellman Rockefeller Foundation, Jean MacFarlane; Currently: proposal submitted to National Institute on Aging	Includes the Berkeley Growth Study, the Guidance Study, and the Oakland Growth Study.
Collaborative Alcohol-Related Longitudinal Project	1987–1993	National Institute on Alcohol Abuse and Alcoholism	Interdisciplinary collaborative analysis of longitudinal studies of alcohol; 14 publications.
Quebec Network for Research on Aging	1996–2008	Quebec fund for health research (Fonds de la Recherche en Santé Québec)	Support research on the aging process, from cell to society. Research sections include (among others): cognition, mental health, nutrition, successful aging. Provide infrastructure support, grants, and awards. Sponsor conferences and annual science days. Strategic initiatives include the Canadian Longitudinal Study on Aging, the Longitudinal study of Expressions of Frailty, the Quebec Longitudinal Study on Nutrition and Aging, and sustaining the PRISMA and SOLIDAGE research programs.
The AgeNet project	1997–2000	UK-MRC, BUPA, Research into Ageing, SmithKline Beecham, Westminster Health Care, Office of Science and Technology	Stimulate multidisciplinary and multisector research partnerships relevant to academia, industry, and the National Health Service that would have a beneficial outcome for the health and quality of life of older people. Created database of 55 UK studies, with Web links, ran 21 workshops, initiated e-mail discussion group.
Asia Pacific Cohort Studies Collaboration (APCSC)	1999–	New Zealand Health Research Council, Australian National Health and Medical Research Councils, Pfizer	Focus on stroke, coronary heart disease, and other common causes of death in Asia-Pacific populations. Collaborative meta-analysis. All major cohort studies with blood pressure and cause of death information invited to participate. Database contains over 650,000 participants from 44 cohort studies in mainland China, Hong Kong, Taiwan, Japan, South Korea, Singapore, Thailand, New Zealand, and Australia. It is the largest epidemiological collaboration in the Southern hemisphere and one of the world's five largest medical studies. Published/in press peer-reviewed articles: 35.

(Continued)

Table 27.1 (Continued)

Collaboration Type and Name/Acronym	*Years*	*Funding*	*Purpose and Accomplishments*
Cancer Intervention and Surveillance Modeling Network (CISNET)	2000–	National Cancer Institute (NCI)	A consortium of NCI-sponsored investigators using diverse modeling approaches on a single data set to forecast trends and determine optimal strategies. Collaborative projects on breast, colorectal, lung, and prostate cancers; 76 publications, including general methods, listed on Web site.
European Birth-Lifecourse-Studies (EURO-BLCS; a multinational epidemiological study)	2000–2003	EU 5th framework program	1) Evaluate biological, genetic, clinical, behavioral, and social risk and protective markers for cardiovascular disease over the life course; 2) Consolidate methods of data collection to improve future comparability between countries, and allow data pooling; and 3) Collect new outcome data.
Comparison of Longitudinal European Studies on Aging (CLESA)	2001–2004	EU 5th framework program	Cross-national comparison of determinants of quality of life and health services for the elderly; six countries/institutions from Europe, plus Russia and Israel. Harmonized coding for variables in common across studies. Descriptive comparison of these variables.
Center for Early Diagnosis and Therapy Research for Neurodegenerative Diseases: A Swedish Network	2004–2009	Invest in Sweden, Stiftelsen för Strategisk Forskning, Vårdal Foundation, Stiftelsen för Kunskapsoch Kompetensuteuckling; Knut och Alice Wallenbergs Stiftelse; Vinnova	Early identification and treatment of major neurodegenerative diseases of adulthood through interdisciplinary research. Sponsors twice-yearly thematic workshops to stimulate within-network collaboration.
Australian Research Council (ARC) Research Network in Ageing Well	2005–2010	ARC & National Health and Medical Research Council	Generate innovative, multidisciplinary approaches to understand aging people; relations between age groups; and economic, social, and policy contexts that shape aging experiences.
Dynamic Analyses to Optimize Ageing (DYNOPTA)	2006–2011	ARC Research Network in Ageing Well (see preceding table entry)	Combine data from 9 Australian longitudinal studies of aging to identify key factors for disease prevention and successful aging promotion.

Assuming that aging is a highly complex, dynamic, and multidimensional process, influences that affect the aging rate of multiple systems may differ across individuals, implying that there will be different patterns of biological and psychological aging. Indeed, a useful distinction can be made between *common cause* and *common outcome*, because it is entirely possible that a common cause can lead to different outcomes and that different causes can lead to common outcomes. For example, different aging-related and/or disease-related processes may influence multiple systems within an individual. Age-related environmental influences or health-related changes may be unique to each individual, although different causative "aging" influences may appear to have a common outcome in the population (e.g., Almeida & Horn, 2004; Hofer, Berg, & Era, 2003; Sliwinski, Hofer, & Hall, 2003). This heterogeneity, and increasing disease risk with age, is perhaps the main source of difficulty in differentiating aging-related changes from changes associated with disease processes. In addition, changes in health may result from a complex interaction of life span influences, including education; occupation; and behavioral, health, and genetic risk factors.

Recent work has demonstrated that some of what were once considered normative cognitive aging effects is actually attributable to non-normative processes (e.g., preclinical dementia; Sliwinski, Lipton, Buschke, & Stewart, 1996). Non-normative processes might be very important determinants of cognitive aging, especially in very old age (> 80 years), because recent longitudinal evidence has shown that cognitive loss is strongly linked to disease onset in the case of preclinical Alzheimer's disease and that cognitive function is relatively stable prior to that time (Hall, Lipton, Sliwinski, & Stewart, 2000; Rubin et al., 1998; Sliwinski et al., 2003). Haan et al. (1999) showed that cognitive decline tends to occur primarily in individuals at risk for disease (e.g., Alzheimer's disease, cardiovascular disease) and that cognition is relatively stable in individuals without such diseases. In all of these studies, disease was studied in its preclinical state—meaning that afflicted individuals were ostensibly asymptomatic during the initial study period.

By definition, a normative cause of cognitive loss occurs in most individuals as they age (e.g., Bäckman et al., 2000). However, there is compelling evidence for the operation of processes that cause cognitive loss in a restricted (but not trivial) subset of aging individuals. The development of preclinical dementia (Haan et al., 1999; Hall et al., 2000; Rubin et al., 1998; Sliwinski et al., 2003), and the progression of subclinical cardiovascular disease (Haan et al., 1999) and respiratory dysfunction (Albert et al., 1995) have all been demonstrated to substantially impact estimated rates of cognitive decline. Moreover, these processes, though increasing in prevalence and severity with age, are not strongly correlated with chronological age in cross-sectional analysis. The identification of normative changes may depend on the identification of non-normative changes.

Statistical and Inferential Issues Associated With Sampling Populations, Variables, and Time

The challenges we face in developmental and aging research are traditional ones, involving trade-offs and solutions that are less than optimal. Many of these represent barriers to progress and synthesis in the current literature. Cooperative efforts based on currently available data provide an opportunity to move beyond these limitations.

Sampling People

Generalizations to defined populations of aging individuals must be conditional on historical (birth cohort) and cultural differences. Several major longitudinal studies have obtained multiple sequential cohort samples that permit comparisons across birth cohorts, cross-sectionally and longitudinally (e.g., the Seattle Longitudinal Study). More generally, longitudinal studies on aging often differ from one another in terms of birth cohort or nationality, permitting a basis for historical and cultural comparisons. The issue of population representativeness is also critical to address (see chap. 4, this volume), but there are trade-offs here as well. It may be that we can learn a great deal about basic psychological processes even when our samples are not sufficiently representative (or are of unknown representation) of a population of aging individuals, particularly if we can demonstrate generalizability across studies differing in sampling characteristics (e.g., country, race/ethnicity).

One often-overlooked aspect of inference to defined populations relates to mortality selection. Numerous studies have demonstrated a relatively strong link among age-related outcomes, participant nonresponse, and survival. Studies limited to between-person age differences must generally ignore important population processes associated with attrition and mortality selection. Longitudinal studies with follow-up to age at death, however, permit direct inference to populations defined by both age and survival (Harel, Hofer, Hoffman, Pedersen, & Johansson, 2007; Hofer & Hoffman, 2007). The mortality selection dynamic cannot be understood by single-occasion sampling of different age groups in which selection has already occurred to different degrees and possibly for different reasons. Analyses of longitudinal data provide the opportunity to directly address attrition and mortality selection, which are essential for understanding aging-related changes in health and cognitive outcomes.

A related issue is inappropriate aggregation in the analysis of age-heterogeneous data. The analysis of within-person variability and covariation requires that higher-order levels of between-person differences and within-person change be fully accounted for (i.e., modeled) because unmodeled functions will produce spurious associations. In age-heterogeneous cross-sectional studies, associations among age-dependent processes may arise due to average population age differences and not necessarily from associations between individual "rates of change" (see Hofer, Flaherty, & Hoffman, 2006; Hofer & Sliwinski, 2001, for derivation of cross-sectional covariances from a linear change model). This is one probable reason why between-person estimates of association across age-dependent variables differ from associations based on within-person rates of change. Analysis of age-heterogeneous longitudinal studies may also show upwardly biased correlations among rates of change due to age-based periods of relatively greater change unless between-person age is included in the model (Hofer et al., 2003; Hofer, Sliwinski, & Flaherty, 2002).

Sampling Variables

It is difficult to gauge differences across studies with samples from different birth cohorts or different countries, in large part because the measurements themselves differ. Certainly, measurements used 30 or 40 years ago may not be the ones used today. However, although different studies use different variables to identify particular constructs, most studies permit comparison of constructs at the primary factor level.

A major step in comparing results across studies involves identifying comparable variables or harmonizing the data. The similarity of a measure can vary at a number of levels, and within a single nation large operational differences can be found (e.g., Weiner, Hanley, Clark, & Van Nostrand, 1990). When considering cross-cultural or cross-national data sets these differences can be magnified: Regardless of whether the same measure has been used, differences are inevitably introduced due to language, administration, and item relevance. Furthermore, sampling characteristics can be strikingly different such that results from different studies may reflect different sections of the population. A balance must be found between optimal similarity of administration, similarity of meaning, and significance of meaning—avoiding unreasonable loss of information or lack of depth. These challenges must clearly be addressed in a collaborative endeavor, but in fact they are also critical to general development of the field, because without some means for comparison, research findings lack validation. Recall the common theme in the literature reviews discussed above.

For collaborating studies, the opportunity arises to reach a consensus regarding measurement comparability before, rather than after, the research process, or at least prior to analysis. Two classic methods for harmonizing are use of national or international standards and finding a "common denominator." For example, in CLESA, commercial medication names were converted to generic names and, under supervision of qualified experts, coded according to the Anatomical Therapeutic Chemical classification system. Cause of mortality was coded according to the *International Classification of Disease—9* (World Health Organization, 1977). Addressing the issue of common information, self-reported medical conditions were included if they appeared in at least three of the six countries involved in the project (Minicuci et al., 2003).

CLESA investigator working groups made extensive use of common denominators to harmonize their variables, including the use of algorithms to create comparable variables. Cognitive and depression scores, which were based on different measures or parts of measures in the different studies, were rescored as proportion of total possible score (e.g., see Cohen, Cohen, Aiken, & West, 1999). Challenging situations inevitably arise, and a system for dealing with exceptions must be developed. In CLESA, some levels of a variable were coded as "not applicable" and presumably treated as zero or as missing in analysis (e.g., difficulty in falling asleep "sometimes" was coded "na" [not applicable] for the country that had not provided that response option). Similarly, CLESA investigators coded instrumental activities of daily living according to a single common variable based on the three items held in common across the six countries, each recoded dichotomously in terms of independence. To avoid relying solely on this very simplified coding, however, three further activity variables and a global disability item available in four of the countries were included in the database. The latter could then be used in analyses of the subset of studies with available data (Minicuci et al., 2003).

Continuing with CLESA, which should be commended for provision of excellent detail regarding the harmonization process, it is clear that there will be limits to any such process. For several sociodemographic variables such as occupation category, although a common format was established, the researchers acknowledged that the large cross-country differences reflected unavoidable cultural- and sample-related differences (Minicuci et al., 2003). Although these difficulties might be reduced in collaborations initiated prior to data collection, Nordic Research on Aging investigators have cautioned that "linguistic equivalence does not guarantee semantic equivalence" (Oden, Viidik, & Heikkinen, 2002). CLESA social network and support variables were similarly a challenge to harmonize, because of both wording and categorizing differences in the already collected data (Zunzunegui et al., 2006). As a result, only variables available in at least three countries were harmonized. It is relevant to note, however, that the process of harmonization itself provides valuable insight into study differences that must be considered when comparing results. These can also provide excellent material for follow-up hypotheses in a meta-analytic framework.

In contrast to CLESA, which relied on investigator working groups for the harmonization process, the Collaborative Alcohol-Related Longitudinal Project harmonization was carried out by a core staff and was assessed and refined by the collaborating investigators (Johnstone et al., 1991). The Asia Pacific Cohort Studies Collaboration (APCSC) relies on statistical analysis, writing, and executive committees that interact with principal collaborators in the participating studies.

For studies with ongoing data collection, investigators might agree to add variables that their studies would then hold in common. Members of the European Birth-Lifecourse-Studies project, for example, have handled cohort differences by changing questions where content is culturally dependent (e.g., those regarding types of food eaten) for future waves. Similarly, they, among others, have discussed the addition of items to strengthen their ability to address common outcomes. In the case of data and sampling differences across studies that are difficult to reconcile, new extensions to meta-analysis, which we discuss below, provide exciting possibilities for maximal use of all available data.

Sampling Time

The temporal characteristics of change and variation must be taken into account, because different sampling intervals will likely lead to different results requiring different interpretations for both within- and between-person processes (Boker & Nesselroade, 2002; M. Martin & Hofer, 2004). For example, correlations of change in two variables over time will likely be quite different for short temporal intervals (minutes, hours, days, or weeks), in contrast to change across many years, as is the case for many of the longitudinal studies on aging. Measurement interval is similarly critical for the prediction of outcome variables and for establishing evidence regarding leading versus lagging indicators (Gollob & Reichardt, 1987, 1991).

The selection of intervals between measurements is also critical for separating effects of

repeated testing (i.e., learning) from those of development/aging over longer periods of time. Estimates of longitudinal change may be attenuated due to gains occurring as a result of repeated testing, potentially persisting over long intervals (e.g., Willis & Schaie, 1994). Complicating matters is the potential for improvement to occur differentially, which could be related to ability level, age, or task difficulty and which may be due to any number of related influences, including warm-up effects; initial anxiety; and test-specific learning, such as learning content and strategies for improving performance. Differential retest gains such as these confound the identification of differential age-related changes (i.e., in older adults, retest effects may be manifest not as an increase in performance but as an attenuated decrease in performance). In most studies, retest effects are perfectly confounded with age changes and do not permit decomposition of effects at an individual level (see chap. 17, this volume; Thorvaldsson, Hofer, Berg, & Johansson, 2006). Intensive study designs, such as those involving measurement bursts with widely spaced sets of intensive measurements, are required to distinguish short-term learning gains from long-term aging-related changes (e.g., change in asymptotic performance; Sliwinski, Hofer, & Hoffman, 2006).

In addition to sampling time within individuals there are numerous ways to conceptualize and model change over time, and the choice of time process models is critical for the interpretation and understanding of change processes (Hofer & Sliwinski, 2006). Change models typically are based on age, or on time in study with chronological age included as a covariate, making level and rate of change conditional on age. Age- and time-based models are equivalent in single or narrow age cohort samples, but in age-heterogeneous samples the use of age-based models may not be appropriate without tests of the convergence of between-person age differences and within-person age changes (e.g., evaluated in the age-based model by including between-person age at Time 1 as a covariate, as in the time-in-study metric). However, time is better treated more flexibly and directly in terms of other evolving time-dependent processes, such as disease progression (e.g., time prior to or since diagnosis of dementia; Sliwinski et al., 2003; chap. 28, this volume), measured physiological changes, mortality (see chap. 17, this volume), or events such as retirement or widowhood to understand the effects of stress and psychosocial functions on cognitive outcomes. Such models provide a useful perspective for describing and explaining average change and individual variation in change relative to particular theoretical models for intraindividual change—essentially aligning individuals with common, possibly causal, processes.

Comparing Results Across Studies: Coordinated Analysis, Meta-Analysis, and Evidence Synthesis

Science typically proceeds sequentially, with replication of results often taking years to complete. A key component of collaborative approaches is the potential for immediate cross-validation of research findings. This can be achieved through parallel analysis or reanalysis of data from multiple studies.

Parallel Analysis

In addition to the use of similar measures, the implementation of parallel and of pooled analyses also facilitates comparison of results from unrelated studies. Parallel analyses providing parameter estimates based on the same statistical model (i.e., same method, covariates, control variables, etc.) can more straightforwardly be included in a meta-analytic comparison framework. Such parallel analyses can be conducted independently or can be conducted in a more centralized way by a designated group. For example, Thorvaldsson, Hofer, Skoog, and Johansson (2007) used data from the Gothenburg H-70 study to explicitly replicate terminal decline findings of Sliwinski, Stawski, Katz, Verghese, and Lipton (2006) in Bronx Aging Study data. Using the Sliwinski manuscript as a guide, they found gratifying similar results. In contrast, core staff from the Collaborative Alcohol Project conducted parallel analyses of primary data from relevant subsets of the 39 affiliated studies and combined the results using meta-analysis (Fillmore et al., 1991). Similarly, the APCSC researchers have reported pooled analyses while paying careful

attention to participant characteristic differences (e.g., age, gender) across studies.

Independent Versus Centralized Analyses

Having a data analysis core to implement the parallel analyses ensures the availability of resources for implementation of the agreed-upon models, but individual studies can also be encouraged to run their own parallel models. To reduce the impact of constraints and data loss through common denominator problems, each study can also be encouraged to conduct more extensive analyses on the core research questions, making use of more elaborated versions of the key variables and adding relevant variables that might be unique to their own project. In this way, both maximally comparable and maximally rich methods can be applied to each research question.

There are advantages to centralized as well as to distributed approaches to parallel analysis. Whereas centralized analyses facilitate careful scrutiny of sampling and measurement differences across studies, distributed analyses may better protect against capitalizing on chance and overmanipulation of data. As in many situations, a combination of both approaches may be most productive. Centralized analysis, as in the Collaborative Alcohol project, allows the clearest view of the individual study differences, because a single set or group of eyes becomes familiar with the sampling and other idiosyncrasies of each data set. This represents a strength in terms of identifying specific differences that might be due to sampling or other factors and would lead naturally into tests of hypotheses regarding the source of divergent results. It is an open question whether this can be equally well attained if everyone conducted the same exploratory data analysis and a smaller group assembled and evaluated the results. Keeping the analyses completely independent, as did Sliwinski, Stawski, et al. (2006) and Thorvaldsson et al. (2007), may, on the one hand, provide a more powerful cross-validation but may, on the other hand, be more limited in terms of testing hypotheses regarding differences if one has not first taken an interim realigning or harmonizing step.

Although the literature does not currently contain the information necessary to conduct meta-analyses of within-person questions, these methods can be used to evaluate the consistency of the findings produced in such parallel analyses. As in Fillmore's (e.g., Fillmore et al., 1988, 1991; Johnstone et al., 1991) alcohol work, and the APCSC's medical research, it would be possible to estimate average effect sizes, identify inconsistencies across studies, and evaluate the impact of specific cross-study differences (at group and individual levels) on these inconsistencies.

Meta-Analysis and Research Synthesis

The terms *meta-analysis* and *evidence synthesis* refer to approaches for combining data sets and evaluating models. Where parallel analyses of sufficiently similar variables are available, meta-analytic methods can be used to summarize findings and to identify and address variability across studies (Higgins & Thompson, 2002). Differences across studies can be due to study-level (e.g., design features or inclusion criteria) or to individual-level (e.g., education level or age) effects. Pooled raw data analyses, as opposed to pooling of summaries, are required to address questions related to individual-level effects (Stewart & Parmar, 1993).

Comparison of parameters based on models estimated on different variables, different measurement intervals, and different population and sampling characteristics presents another challenge, however. This challenge can be addressed with new methods in which well-developed meta-analytic methods are being extended to permit statistical synthesis of evidence from qualitatively different types of data. For example, various extensions of the basic meta-analysis framework have been used to combine multiple indirect sources of evidence on treatment or exposure effects in what is sometimes termed a *chain of evidence* (Ades, 2003). Bayesian hierarchical models also form the basis of methods for combining data from different types of study (Spiegelhalter, Abrams, & Myles, 2004). This is sometimes termed *generalized evidence synthesis* and requires careful consideration of the relationships between parameters across data sets (Spiegelhalter & Best, 2003). Such ideas extend naturally to the combined analysis of different longitudinal studies on aging with analysis across domains of health, cognition, and personality/affect. Analyses

gauging sensitivity to different assumptions about the relationships between parameters across data sets and the likely size and direction of any biases can also be carried out to assess robustness of inference. Bayesian graphical models provide a natural framework for combining a series of local submodels, informed by different data sources, into a coherent global analysis. This approach can be used to carry out analyses that formally combine information from multiple data sets available within a network.

Integrative Analysis of Longitudinal Studies on Aging

Any question can be approached in a variety of ways. An ongoing challenge is to make optimal use of current data resources, while acknowledging their particular strengths and limitations and integrating and synthesizing knowledge based on different designs and approaches, particularly when they are contradictory. It is time to reflect on what we know and how we have come to know it. We must learn as much as possible from existing longitudinal studies, many of which were initiated 20 to 50 years ago and are still actively collecting data. What we learn from these studies should also inform the design new studies, ideally permitting direct comparison across birth cohorts.

We have been working to develop a collaborative research infrastructure for coordinated interdisciplinary, cross-national research aimed at the integrative understanding of within-person aging-related changes in health and cognition. The Integrative Analysis of Longitudinal Studies on Aging (IALSA) project is an open research network currently comprising 25 major longitudinal studies on aging. It serves as a resource for the application of best statistical methods for inference to aging individuals and defined populations. It will encourage the exploration of cross-cultural and cross-cohort effects and direct cross-validation of research findings across independent studies. We use the term *integrative* in several ways: referring to the integration of domains of study (i.e., health, cognition, personality, well-being) that, with notable exceptions, have generally been studied in isolation of one another, as well as to the integration of information across studies and across alternative statistical models. This program of research focuses primarily on explaining aging-related changes in the context of health (i.e., morbidity, comorbidity) and health-related change. We seek explanations that integrate cross-domain information on changes in cognition, health, personality (broadly defined to include well-being), and that also consider the impact of psychosocial characteristics, and contextual factors including sociodemographic characteristics, differences across nations, life events, and stressors. These important issues require macro-level theory and integrative science featuring the analysis of empirical studies that follow individuals over critical life periods.

Studies Involved in the Integrative Analysis of Longitudinal Studies on Aging Network

IALSA membership initially represented, mainly, investigators in the area of cognition and aging with whom we were already collaborating, or at least familiar. For the most part, their studies had a major focus on cognitive aging but also included varying amounts of information on physical and mental health as well as social and demographic variables. This selection strategy admittedly differs from that of, for example, CEHP, which focused on NIH-supported studies and set size, age, and construct criteria. However, we believed that a strong collaborative network could benefit from relying to some extent on existing links.

The 25 studies currently involved in the IALSA network span eight countries and include a total sample size of approximately 70,000. They represent a mix of representative, volunteer, and special population (e.g., veterans, college students, health maintenance organization) samples. Within the network, data have been collected on individuals aged 18 (from birth in one study) to over 100, with birth cohorts ranging from 1880 to 1980 and historical periods from 1946 to the present. Between-occasion intervals range from 6 months to 17 years (the majority are 1–5 years), with between 2 and 32 (mainly 3–5) measurement occasions spanning 4 to 48 years. Education levels vary from samples in which a sizable number have only elementary level education to those reporting mainly high school and beyond. All except one include data on both men and women. Three studies have single-age samples.

Table 27.2 Characteristics of Integrative Analysis of Longitudinal Studies on Aging Network Studies

Study Title and Acronym	*Start Year*	*n (T1)*	*Age (T1)*	*Birth Cohorts*[a]	*Follow-Up (Years)*	*Intervals*	*Curr No. Occasions*	*Type Sample*
Australian Longitudinal Study of Aging (ALSA)	1992	2,087	65–103	1891–1927	11	2, 6, 3	4	Stratified sample of community-dwelling individuals and those in residential care
Bonn Longitudinal Study of Aging (BOLSA)	1965	221	62–72	1893–1903	19	Varies	8	Community volunteer sample
Caerphilly Cohort Study of Older Men (CCS)	1979	2,512	45–59	1920–1934	25	4–5	6	Electoral register plus general-practitioner lists, male only
Canberra Longitudinal Study (CLS)	1991	897	70–93	1898–1921	14	3.5	5	Community sample (electoral role), institutional care, oversampling of very old
Cardiovascular Health Study (CHS)	1989	5,888	65+	-1924	10	1	10	Noninstitutionalized Medicare-eligible sample; minorities oversampled
Einstein Aging Studies (EAS)	1980	488	70–90	1890–1910	20	1	20	Volunteer sample
Aging in Women and Men (GENDER)	1995	498	69–81	1914–1926	8	4	3	Opposite-sex twins in Sweden born between 1906 and 1925
Gerontological and Geriatric Population Studies in Göteborg, Sweden (H-70)	1971	1,000	70	1901	29	2–5	12	Representative sample of Gothenberg 70 year olds
Health and Retirement Study (HRS) and AHEAD	1992	12,600	50–60	1932–1942	14	2	7–8	National sample, minorities oversampled
Healthy Older Person Edinburgh Study (HOPE)	1990	603	70+	1900–1918	4	4	3	Medical registry
Interdisciplinary Longitudinal Study of Adult Development (ILSE)	1996	1,384	45, 65	1931, 1951	4	4	2	Former East and West Germany
Long Beach Longitudinal Study (LBLS)	1978	509	55–87	1891–1923	21	2, 14	4	Recruited from health maintenance organization

(Continued)

Table 27.2 (Continued)

Study Title and Acronym	*Start Year*	*n (T1)*	*Age (T1)*	*Birth Cohorts*[a]	*Follow-Up (Years)*	*Intervals*	*Curr No. Occasions*	*Type Sample*
Longitudinal Aging Study Amsterdam (LASA)	1991	3,107	55–85	1906–1936	9	3	4	Urban and rural municipal registries
Longitudinal Study of Cognitive Change in Normal, Healthy Old Age (LSCC)	1982 1985	2,050 2,193	49–96	1886–1936	14	1–6	4	Community volunteer sample
National Survey of Health and Development (1946 British Birth Cohort Study) (NSHD)	1946	5,362	birth	1946	60	Varies	39	Nationally representative birth cohort sample
Nordic Research on Aging Study (NORA)	1989	1,204	75	1914	5	5	2	Representative city samples
Normative Aging Study (NAS)	1963	2,280	21–81	1882–1942	42	5	13	Male veterans
Origins of Variance in the Old-Old: Octogenarian Twins (OCTO-Twin)	1990	702	80+	1900–1910	8	2	5	Swedish Twin Registry
Oregon Brain Aging Study (OBAS) and Dementia Prevention Study (DPS)	1989+ 2000	258 214	55–107 85–94	1889–1945 1906–1915	0–18 0–6.5	6 & 12 mo	1–33 (16.5) 1–13	Community volunteers
Seattle Longitudinal Study (SLS)	1956	5,000+ cumulative	22–70	1880–1980	42	7	7	Health maintenance organization
Swedish Adoption Twin Study of Aging (SATSA)	1984	1,500	40–84	1900–1944	6	3	3	Swedish Twin Registry
Swiss Interdisciplinary Longitudinal Study on the Oldest-Old (SWILSO-O)	1994 1999	340 377	80–85	1909–1919	10 5	12 or 18 months	9 5	Stratified (age/sex), initially community-dwelling in an urban and a rural setting
University of North Carolina Alumni Heart Study (UNCAHS)	(1964) 1986 1992	(7,007) 4,989 1,154	(17–25) 40–48	1942–49	(40) 20 14	1.5	- 12 7	• Students—data on file • Joined study • Spouses
Victoria Longitudinal Study (VLS)	1986 1993 2002	484 530 570	55–85 55–85 55–85	1901–1931 1908–1938 1917–1947	15 9 0	3 3 —	6 4 1	Community volunteers
Wisconsin Longitudinal Study (WLS)	1957	10,317	18	1939	48	7–17	5	Random sample high school graduates

NOTES: T1 = Time 1; Intervals = between-occasion intervals; Curr = Current.

a. Computed from reported ages and dates.

Common Outcomes and Predictors

For cross-study analysis and comparison, we consider three levels of linkage: (1) broad construct, (2) narrow construct, and (3) identical indicator. Across most studies, broad conceptual replication (e.g., comparing different measures of verbal ability across studies) is possible in almost all of the domains considered here. In many of the studies, replication on more similar variables—for example, comparing memory for different word lists across studies—is possible. On a smaller subset of studies, opportunities are available for direct comparison of identical measures. Given the generally greater strength of conceptual replications, we consider exact replication necessary mainly because it will allow a more straightforward consideration of country-level differences (although language differences will remain for some comparisons). The types of variables, organized by domain, available in the longitudinal studies on aging that are currently part of the IALSA network are shown in Table 27.3, and we provide additional detail regarding the cognitive measures in this text. This information is available in a searchable database developed for the network.

General Mental Status. The MMSE is used in 12 of the affiliated data sets and will be evaluated in cross-study analysis, with some preliminary details provided here. Because it is a screening device, this measure does not provide good specificity compared with other cognitive assessments (e.g., Royall & Chiodo, 2004). However, analysis of the MMSE in large cross-national surveys will provide important details regarding sensitivity to hypertension-related changes and relative to other cognitive and memory measures. It is also commonly used in medical and epidemiological studies that might not have other cognitive measures and so will provide a good link to this literature.

Verbal/Crystallized Knowledge. Many of the studies use at least one of the Wechsler Adult Intelligence Scales (e.g., Wechsler Adult Intelligence Scale—Revised [WAIS–R]; Wechsler, 1981) Verbal measures, with Vocabulary (seven studies), Synonyms (five studies) and Similarities (eight studies, plus two with AH4 [Heim, 1970]) the most common. In at least three studies, however, idiosyncratic or short forms (e.g., three items) of the measures were used. The National Adult Reading Test (NART; Nelson & Willison, 1991; five studies) and the Mill Hill Vocabulary Scale (Raven & Raven, 1988) are also used.

Reasoning. The WAIS Block Design subtest (in eight studies) is the most commonly used measure of reasoning. Factor-level similarities among matrices tests such as the Cattell Culture Fair Test (Cattell, 1963), the Raven Progressive Matrices (Raven, Raven, & Court, 1958), other matrices tests, and rotation tests such as Thurstone Primary Mental Abilities Spatial Orientation (Thurstone, 1948) (each available in three or fewer studies) will permit conceptual replication of general patterns. Differences between visual–spatial loaded tests and word series measures with a verbal basis can be expected, with the latter showing greater stability.

Speed. Substitution coding (e.g., WAIS Digit Symbol [six studies], Symbol–Digit [two studies], Symbol–Letter Modalities [two studies], and Alphabet Coding [two studies]) and reaction time measures dominate the speed domain.

Memory. With the great interest in age-related memory changes, this domain is well represented in virtually all studies, but with this importance to the research community comes a great variety of measures. Although many of the studies use standard measures such as the WAIS Digit Span subtests (9 studies), the Wechsler Memory Scale Logical Memory Test (Wechsler, 1945, 4 studies), or the memory items from the MMSE, virtually all of the immediate and delayed word list recall tests (12 studies) are based on different words and different numbers of stimuli and exposures. This cross-study mix of similar and different measures, however, will allow us to make best use of the strengths of both conceptual and exact replication approaches.

Attention/Working Memory. WAIS Digit Span Backward (eight studies) and Serial 7s from the MMSE are the most common measures that can be considered to measure working memory.

Table 27.3 Variable Domains by Study in the Integrative Analysis of Longitudinal Studies on Aging Network

Domain Measures	*ALSA*	*BOLSA*	*CCS*	*CLS*	*CHS*	*EAS*	*GENDER*	*H-70*	*HRS*	*HOPE*	*ILSE*	*LBLS*	*LASA*	*LSCC*	*NSHD*	*NORA*	*NAS*	*OBAS*	*OCTO-Twin*	*SATSA*	*SLS*	*SWIL SO-O*	*UNCAHS*	*VLS*	*WLS*
Biomedical and physical functioning																									
General health																									
Height	x	x	x	x	x	x	x	x	x	x	x	x	x		x	x	x	x	x	x	x	x	x	x	x
Weight	x	x	x	x	x	x	x	x	x	x	x	x	x		x	x	x	x	x	x	x	x	x	x	x
Self-rated health—																									
Overall	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Relative to age	x	x	x	x	x	x	x				x	x	x				x	x	x			x		x	x
Relative to past	x	x			x	x	x		x				x		x		x	x	x			x			x
Health conditions:																									
Self-report	x		x	x	x	x	x		x	x	x	x	x	x	x	x	x	x	x	x		x	x	x	x
Records/exam		x			x	x		x		x	x				x	x	x	x		x	x		x		
Prescribed meds	x	x	x		x	x	x	x		x	x		x	x	x	x	x	x	x	x	x	x	x	x	
Dental health	x							x		x					x	x	x		x	x		x	x		
Parents' longevity		x		x	x	x	x				x	x	x	x	x		x	x	x	x			x		
Death: Age/cause	x	x	x	x		x	x	x		x	x	x	x	x	x	x	x	x	x	x	x		x	x	
Sensory																									
Auditory acuity	x	x	x		x		x	x			x		x		x	x	x	x	x	x		x		x	x
Visual acuity	x	x		x	x	x	x	x			x		x		x	x	x	x	x	x		x		x	x
Sensory disability	x			x		x	x								x	x		x		x					x
Hand grip strength	x			x	x	x	x	x		x	x				x	x	x	x	x	x				x	
Arm flexion					x	x	x									x		x							
Knee extension						x	x									x		x							
Cardiopulmonary																									
Hypertension	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

Domain Measures	*ALSA*	*BOLSA*	*CCS*	*CLS*	*CHS*	*EAS*	*GENDER*	*H-70*	*HRS*	*HOPE*	*ILSE*	*LBLS*	*LASA*	*LSCC*	*NSHD*	*NORA*	*NAS*	*OBAS*	*OCTO-Twin*	*SATSA*	*SLS*	*SWIL SO-O*	*UNCAHS*	*VLS*	*WLS*
Heart attack	x	x	x	x	x	x	x	x		x	x	x		x	x		x	x	x	x	x		x	x	
Blood pressure	x	x	x	x	x	x	x	x		x	x	x	x		x	x	x	x	x	x	x		x	x	
Heart rate	x		x	x	x	x	x	x					x		x	x	x	x	x		x			x	
Pulmonary function		x	x	x	x	x	x	x		x			x		x	x	x	x	x	x				x	x
Blood samples	x	x	x		x	x	x	x			x		x		x	x	x	x	x	x	x				
Cholesterol	x		x		x			x							x	x	x	x		x			x		
ECG			x		x			x							x	x	x								
Neurological/ neuropsychological																									
Gait	x					x	x	x								x		x	x					x	
Balance	x					x	x	x							x	x		x	x					x	
Tapping Test						x										x		x						x	
Finger agnosia							x	x											x						
Clock Test						x		x											x	x					
Other					x													x						x	
Cerebrovascular/ dementia																									
Stroke	x	x	x	x	x	x	x	x	x	x			x	x	x		x		x	x	x		x	x	
Dementia																									
Diagnosis			x	x		x		x		x							x	x	x	x					
Questionnaires	x		x					x										x		x				x	
Genetic risk: ApoE	x			x		x		x						x				x		x	x			x	
Other systemic illness																		x							
Diabetes	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x		x		x	x	x		x	x	x
Cancer	x	x	x	x		x	x	x	x	x	x	x		x	x		x		x	x	x		x	x	x
Somatic																									
Fatigue						x	x	x								x						x			x
Pain		x		x		x	x	x	x		x		x			x	x		x	x		x	x	x	x
Health behaviors																									
Drug use	x					x		x			x	x			x			x	x			x		x	
Alcohol use	x	x	x	x	x	x	x	x	x		x	x	x	x	x	x	x	x	x	x		x	x	x	x
Tobacco use	x	x	x	x	x	x	x	x			x	x	x	x	x	x	x	x	x	x		x	x	x	x
Diet			x		x	x	x	x			x	x	x		x	x	x	x	x	x	x		x		
Exercise			x		x	x	x	x			x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

(Continued)

Table 27.3 (Continued)

Domain Measures	*ALSA*	*BOLSA*	*CCS*	*CLS*	*CHS*	*EAS*	*GENDER*	*H-70*	*HRS*	*HOPE*	*ILSE*	*LBLS*	*LASA*	*LSCC*	*NSHD*	*NORA*	*NAS*	*OBAS*	*OCTO-Twin*	*SATSA*	*SLS*	*SWIL SO-O*	*UNCAHS*	*VLS*	*WLS*
Functional capacity																									
Activities of daily living (ADL)	x		x	x		x	x	x	x	x	x		x	x	x	x		x	x	x		x			
Instrumental ADL	x			x		x	x		x	x	x		x	x	x	x	x	x	x	x					
ADL (apparatus)			x				x	x						x					x	x					
Activity level	x	x		x		x	x		x		x			x	x	x		x			x	x		x	
Hobbies			x			x	x	x			x	x		x	x	x	x	x		x		x			
Home help							x		x		x					x				x					
Cognitive functioning																									
Crystallized knowledge																									
NART	x		x	x		x				x					x										
Vocabulary	x			x		x			x			x		x			x	x						x	
Synonyms		x					x	x											x	x	x				
Comprehension	x																x								
Information		x				x					x								x	x				x	
Similarities	x	x	x	x		x			x		x			x				x		x					x
Fluid reasoning																									
Arithmetic		x							x												x				
Series												x									x			x	
Matrices		x					x	x		x			x	x		x		x	x	x					
Rotation												x					x			x	x			x	
Block Design		x				x	x	x			x	x						x	x	x					
Object Assembly		x																							
Picture Arrangement		x																							
Picture Completion		x									x							x							
General Aptitude																	x								x

Domain Measures	*ALSA*	*BOLSA*	*CCS*	*CLS*	*CHS*	*EAS*	*GENDER*	*H-70*	*HRS*	*HOPE*	*ILSE*	*LBLS*	*LASA*	*LSCC*	*NSHD*	*NORA*	*NAS*	*OBAS*	*OCTO-Twin*	*SATSA*	*SLS*	*SWIL SO-O*	*UNCAHS*	*VLS*	*WLS*
Speed																									
Substitution coding	x	x		x	x	x					x		x	x		x		x	x	x				x	
Number copy task						x																		x	
Figure identification							x	x											x	x					
Identical pictures																	x				x			x	
Number comparison						x						x									x			x	
Finding A/I/O														x	x						x	x			
Reaction time		x	x	x		x										x								x	
Memory																									
Digit Span		x				x		x			x					x	x	x	x	x					
Free recall						x	x	x	x		x	x	x	x	x		x	x			x			x	
Delayed						x	x	x	x		x	x		x	x		x	x			x				
Recognition	x		x	x			x	x				x						x	x	x				x	
Prose recall			x			x		x		x		x				x		x	x					x	
Cued recall						x																		x	
MIR Memory Test								x											x						
Incidental memory	x		x						x					x											
Coin Test								x											x						
Mental Status Exams																									
Mini-Mental	x		x	x	x		x	x	x	x			x				x	x	x	x				x	
Blessed						x												x		x					

(Continued)

Table 27.3 (Continued)

Domain Measures	*ALSA*	*BOLSA*	*CCS*	*CLS*	*CHS*	*EAS*	*GENDER*	*H-70*	*HRS*	*HOPE*	*ILSE*	*LBLS*	*LASA*	*LSCC*	*NSHD*	*NORA*	*NAS*	*OBAS*	*OCTO-Twin*	*SATSA*	*SLS*	*SWIL SO-O*	*UNCAHS*	*VLS*	*WLS*
Attention																									
Serial 7s	x			x		x	x	x	x											x					
Backward Span		x	x			x		x			x					x	x		x						
Other			x			x																		x	
Word fluency																									
Category				x		x								x	x		x	x				x		x	
FAS	x		x			x						x				x		x			x				
Boston Naming	x					x											x	x							
Self-rated cognition																									
Cognition					x		x	x		x								x				x			
Memory				x		x	x	x	x			x			x		x		x	x		x	x		
Metamemory	x								x		x		x			x								x	
Psychosocial and demographic																									
Personality																									
Eysenck				x			x	x						x	x		x		x	x					x
NEO				x							x	x								x	x		x	x	x
Type A behavior			x														x			x					
Behavioral rigidity		x																			x				
Self-esteem	x	x	x							x			x	x									x	x	
Other			x				x						x			x	x						x		

Domain Measures	ALSA	BOLSA	CCS	CLS	CHS	EAS	GENDER	H-70	HRS	HOPE	ILSE	LBLS	LASA	LSCC	NSHD	NORA	NAS	OBAS	OCTO-Twin	SATSA	SLS	SWIL SO-O	UNCAHS	VLS	WLS
Interpersonal functioning																									
Social networks	x	x		x	x	x	x	x		x	x	x	x	x	x	x	x		x		x	x	x		x
Network history						x	x	x									x		x				x		
Support/help	x		x	x	x	x	x	x			x		x		x	x	x		x	x		x	x	x	
Loneliness						x	x	x					x			x			x			x			
Personal control																									
General	x			x			x	x			x		x	x					x	x		x			
Health	x						x												x						
Memory/cognitive														x				x						x	
Mastery																	x								x
Life satisfaction/ mental health																									
Mood/depression	x	x	x	x	x	x	x	x	x		x	x	x	x	x	x	x	x	x	x		x	x	x	x
Life satisfaction		x	x	x			x								x	x	x		x	x	x	x	x		
Morale	x										x		x				x							x	
Self-rated emotional health							x		x				x				x								
Quality of life	x				x																				
Stress/life events																									
Life events	x				x						x		x	x	x		x			x		x	x		
Anxiety/agitation			x	x			x				x		x		x		x			x			x		x
Perceived stress		x					x				x		x	x		x	x						x		
Illness/handicap related to job							x		x						x										
Demographics																									
Education	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Occupation	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Socioeconomic status	x	x	x	x		x	x	x	x	x	x		x	x	x		x	x	x	x	x	x		x	x
Family income	x	x			x	x	x	x	x		x	x	x		x	x	x	x	x			x	x		x
Marital status	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Living arrangement	x	x		x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x		x	x
Employment history									x						x			x		x			x	x	x

NOTE: Study acronyms are presented in Table 27.2.

Word Fluency. This domain, which does not fit clearly into either verbal ability or memory, is measured mainly by category (seven studies, some using different categories) and first letter (FAS) word fluency (three studies). Category word fluency has also been used as a measure of executive function.

Coordinated Research Process

The coordinated research process begins with a project proposal that delineates the problem, briefly cites relevant research, and details a preliminary protocol for analysis and structure of results.

1. The searchable database is used to identify studies with targeted variables and characteristics that permit implementation of the analysis. Investigators on these studies are alerted to the proposal and collaborate on developing the protocol in terms of available variables (coding differences) and plans for analysis.
2. Preliminary analyses begin by finalizing a protocol for harmonizing variables and development of statistical analysis by the leading project.
3. Parallel analyses will then be performed independently by each group of researchers (or in some cases by the Statistics Core or a single research team) and reported in common format.
4. Results will be combined in tables and figures to identify differences and to permit the discussion of alternative models and follow-up analyses, including pooled, meta-analysis, and evidence synthesis.
5. The process is completed by submission for publication of each study's findings and a summary paper describing the cross-study comparison of results.

Exemplar Analysis

Seven members of the IALSA network have contributed to initial analyses addressing the within-person changes in MMSE with age (Piccinin et al., 2006). Remarkable similarity was found in the rate of change in scores of the MMSE. On average, at age 80 years (85 for the Gothenburg "H-70" study), individuals scored between 25 and 27 on the MMSE and, assuming a linear trend, declined about 0.3 points per year. Consistent with this, older individuals tended to score lower initially (0.1–0.2 point per year) and decline at a faster rate (0.01–0.08 more decline per year). Marked country and birth cohort differences in educational attainment range from an average of 6 or less years in the 1900 birth cohorts in Sweden to 12 in the more recent U.S. birth cohorts. Focusing on studies with similarly coded education, more highly educated participants have higher initial scores (0.2 to 0.4 point) and show less decline (0.02–0.09). Figures 27.1 and 27.2 show expected trajectories for men and women, respectively, of several representative ages (e.g., 75, 80, 85), for the studies with similarly coded education, based on the parameter estimates from the independent analyses.

The IALSA network takes a coordinated and collaborative approach to the integrative understanding of aging, with particular focus on changes in health, cognition, and personality. This approach permits the identification and reconciliation of differences found across studies in terms of measurement; sampling; and demographic, social, and health indicators. The collaboration is broad, with extensive multidisciplinary expertise and interdisciplinary interests. The diversity of perspectives is maintained in the decision-making process and analysis protocol development, ensuring generalizability of results and evaluation of result sensitivity to decisions regarding harmonization of measurements, statistical analysis, and choice of theoretical models. The findings from this program of research will provide a basis for prevention and intervention efforts and inform health policy by identifying premorbid and subsequent changes associated with morbidity and comorbidity as well as the sociodemographic and psychosocial moderators of these changes.

Optimizing Future Research on Cognitive Aging

What are the possible outcomes of the collaborative research described and proposed here? In addition to the clear potential to make confident strides in knowledge about the aging of cognitive capabilities, the collaborative nature of the

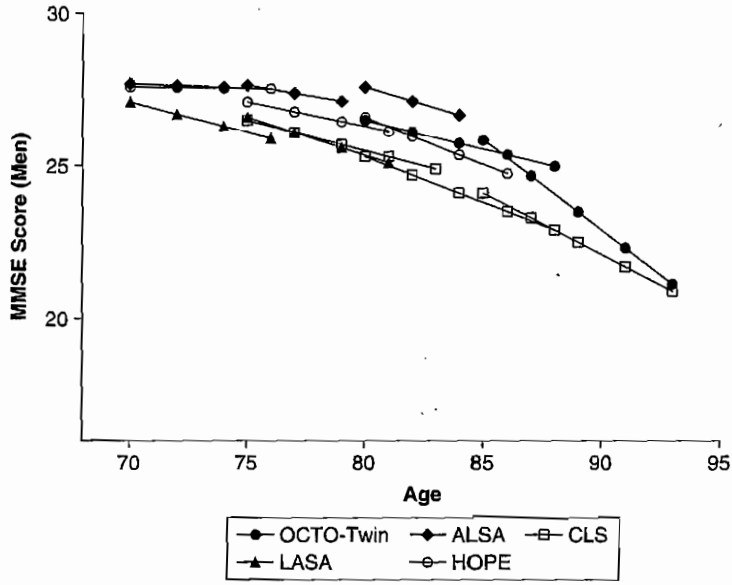

Figure 27.1 Predicted Mini-Mental State Examination (MMSE) Scores for Men From the OCTO-Twin, LASA, CLS, ALSA, and HOPE Longitudinal Studies

NOTE: Study acronyms are presented in Table 27.2.

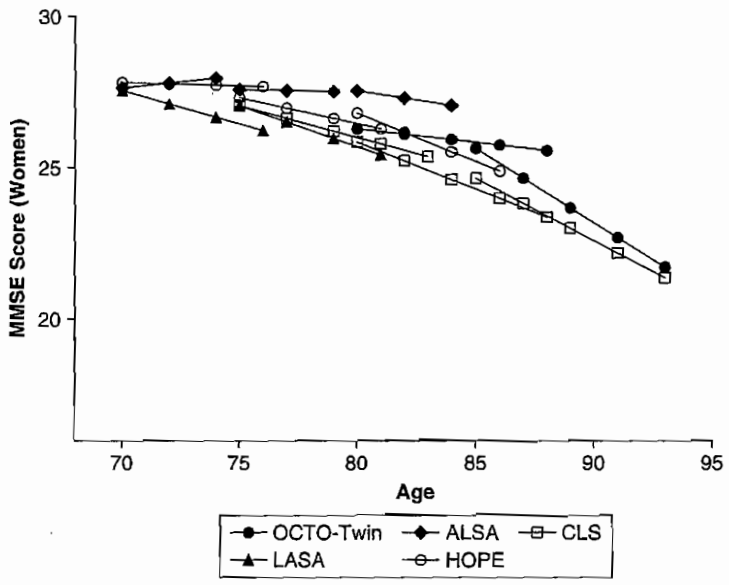

Figure 27.2 Predicted Mini-Mental State Examination (MMSE) Scores for Women From the OCTO-Twin, LASA, CLS, ALSA, and HOPE Longitudinal Studies

NOTE: Study acronyms are presented in Table 27.2.

work may facilitate the future application of what is learned—in terms of both substantive and methodological advances. Focused communications among investigators from different countries will increase the likelihood of the development of sensitive measures of within-person changes, optimally designed for translatability across languages and cultures. In addition, careful scrutiny of the variety of measurement intervals and sampling characteristics may lead to principled design recommendations for future longitudinal studies. The interdisciplinary nature of the work will contribute to the development of concrete and more elaborated public health recommendations.

Among the strengths of the proposed network model is the focus on progress of the field rather than individual careers, acceleration of the accumulative research process, and greater ability to study rare events. The benefits of coordinated, collaborative models for the analysis of existing longitudinal studies are many, and include the following:

1. Accelerated generation of knowledge from within-person studies on aging
2. Immediate replication and cross-validation of central hypotheses for development of theories of aging-related changes from a within-person perspective
3. Implementation of advanced statistical models across major studies
4. Training of individuals for state-of-the-art statistical modeling of longitudinal data
5. Opportunities for generalized evidence synthesis making optimal use of available study data and joining studies in ways that will advance knowledge further than possible in any particular study
6. Optimized comparison of measurements and of results from particular studies through harmonization of variables
7. Identification of measures for use in the next assessments or future studies to permit better comparative analysis
8. Cross-national comparison stratified by socioeconomic status, education, and health services

The major challenge in such endeavors remains the balancing of collaborative and competitive forces. Although language, cultural, demographic, design, and measurement differences across studies might also be seen as challenges, these exist in the current literature regardless and so can hardly be seen as a challenge to collaboration, only to cumulative science and understanding. Collaboration is in fact the most powerful tool with which to address the challenge of understanding aging from a within-person perspective.

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