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Editorial

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Abstract
Human aging is characterized by large differences between and within older adults. Numerous factors are known to contribute to these differences, including genetic and immunological, somatic and medical, cognitive and behavioral, psychosocial and experiential, as well as socioeconomic and geospatial conditions. Continuing and expanding the scientific objectives of the Berlin Aging Study, the Berlin Aging Study II (BASE-II) seeks to comprehensively describe phenomena associated with aging and old age and to better understand the multiple different underlying factors and their interactions. To this end, BASE-II was established as a multiinstitutional project combining and integrating interdisciplinary perspectives ranging from molecular genetics and immunology, geriatric medicine and psychology, to sociology and economics. In this Special Issue, we have compiled seven empirical analyses that feature examples of interdisciplinary insights that BASE-II provides by linking data across multiple levels of analyses at which human functioning and development occur in old age. Here, we provide an overview of the study, note commonalities between BASE-II and earlier studies, and highlight some of its unique qualities.

The Berlin Aging Study II – An Overview

Heterogeneity in virtually each and every aspect of life is one of the hallmarks of aging [1, 2]. Some people do reach old and very old age in good physical health, remain cognitively fit and socially integrated, and live autonomous and satisfying lives. In contrast, other older adults are confronted with severe health decrements and functional limitations, experience considerable losses in cognitive functioning, live socially and emotionally isolated lives, and are faced with elevated mortality hazards. Many different distinct constellations lying between these two extremes are characteristic of the lives of older adults [3, 4]. A myriad of factors is known to contribute to these individual differences, including genetic and immunological, somatic and medical, cognitive and behavioral, psychosocial and experiential, as well as socioeconomic and geospatial variables. Following in the footsteps of the seminal Berlin Aging Study launched in the early 1990s

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(BASE) [5], the Berlin Aging Study II (BASE-II) was initiated in 2010 to comprehensively describe phenomena associated with age and aging and to better understand the multiple underlying factors and their interactions. BASE-II was established as a multi-institutional project combining and integrating multidisciplinary perspectives ranging from molecular genetics and immunology, geriatric medicine and psychology, to sociology and economics. In this Special Issue, we have compiled seven empirical articles that feature examples of interdisciplinary insights that BASE-II provides by linking data across multiple levels of analyses at which human functioning and development occur in old age. In this editorial, we provide an overview of the study and its design, participants, variables, and assessment procedures. In doing so, we note commonalities between BASE-II and earlier studies and highlight some of its unique qualities.

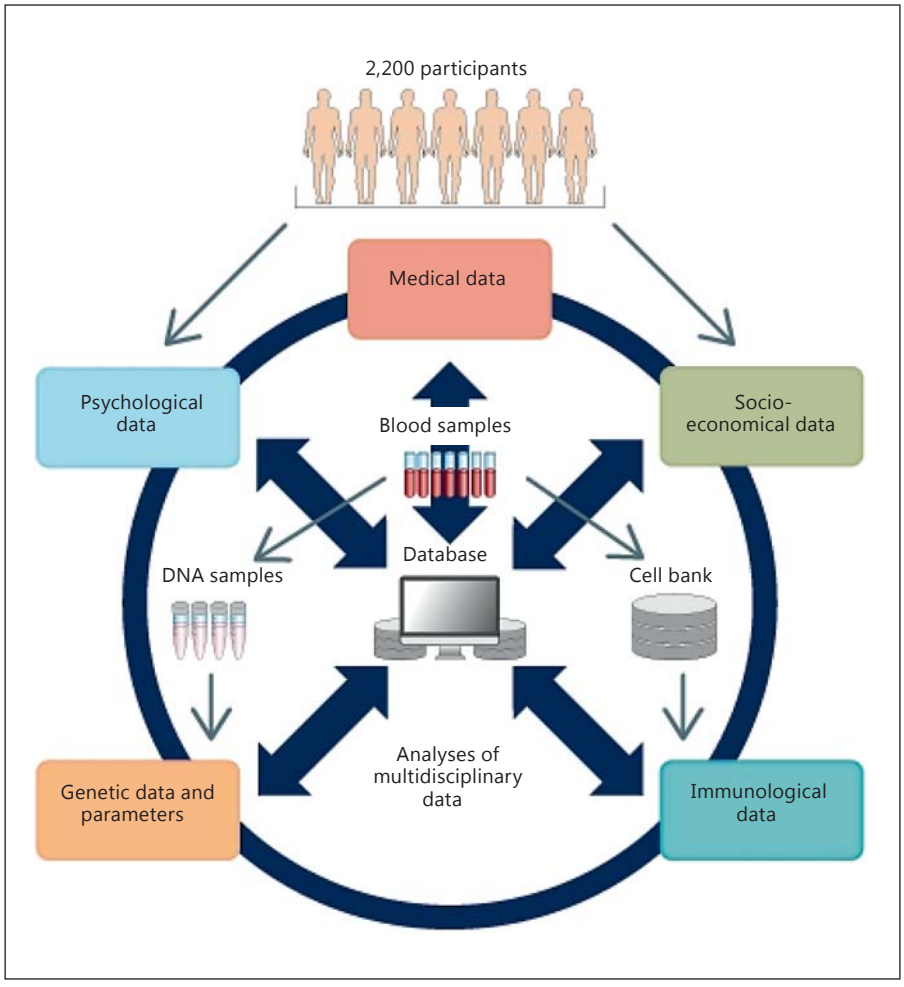
The Berlin Aging Study II

BASE-II differs from the first Berlin Aging Study in three fundamental aspects [see also 6]. First, the core sample of BASE-II is markedly larger than that of BASE (n = 2,200 vs. n = 516) and also includes younger adults in their 20s and early 30s who serve as a reference population and control group for the older adults. In the empirical articles compiled here, four reports make use of this feature [7–10]. A second unique feature is that BASE-II focuses on relatively young seniors, with the large majority of the 1,600 older adults being in their 60s and early 70s. In contrast, the youngest participants in the earlier BASE were 70 years old, and the average age of the sample was 85 years. Our focus on individuals at the very beginning of the Third Age [11] aimed at establishing a comprehensive baseline assessment when people are still in relatively good health, thereby allowing us to detect (in longitudinal extensions of the study) early forms and antecedents of disease and pathology and to track how these develop and accumulate with advancing age.

A third distinct characteristic feature of BASE-II is the new, extended, and/or refined assessment of major constructs of interest, including a much improved genetic analysis (e.g., genome-wide association study with some 450,000 measured and several million imputed single nucleotide polymorphisms), immunological biomarkers (e.g., establishing an immune risk profile of more late-differentiated CD8+ T-cells together with fewer B-cells and seropositivity for cytomegalovirus), physical health (e.g., metabolic syndrome, frailty), cognitive abilities (e.g., decision making, reading abilities, episodic memory), the expectations people have towards their own aging (e.g., subjective health horizons), and the social and physical environments (e.g., geo-coding of people's living area). As a consequence, BASE-II allows for an examination of key questions that could not be addressed with the earlier BASE and makes use of contemporary assessment tools and of those that help push assessment developments further.

While many other studies involve larger samples, one of the particular strengths of BASE-II (in line with BASE) is its depth and comprehensiveness. In particular, participants went through a 2-day medical assessment with information being gathered about physical capacity, vision, hearing, the cardiovascular system, the musculoskeletal system, and also information about nutrition, among other constructs. Blood samples were then collected, DNA extracted and genome-wide genetic screening performed, relative leukocyte telomere length assessed, and about 100 laboratory parameters determined. Peripheral blood mononuclear cells were isolated, cryopreserved, and used for analyses of immune parameters. Serum and plasma were separately stored and used for virological and serological analyses. Additionally, lymphoblastoid cell lines were established from a subsample of more than 450 participants. In the context of our interest in disease development, our medical assessment included known and putative risk factors for diseases and geriatric syndromes, including a comprehensive serum lipid profile and body composition measured by dual X-ray absorptiometry. The psychological assessment comprised cognitive and psychosocial domains. In the cognitive domain, participants worked, on two separate days, on a computer-supported battery of cognitive tests that provides a multi-indicator representation of several cognitive abilities including episodic memory, working memory, perceptual speed, reading ability, and decision making. In the psychosocial domain, participants were given an equally comprehensive collection of self-report measures targeting various aspects of self-related functioning and psychosocial development, including well-being, social activities, and social integration.

In the context of these unique qualities of BASE-II, we deliberately selected several sets of measures that had already been used in closely related studies. For example, we repeatedly implemented measures collected as part of the nationwide German Socio-Economic Panel study (SOEP) [12] on socioeconomic background, lifestyle, personality, and living conditions. The direct comparability to SOEP and in part to other studies in Germany (e.g., the so-called



Color version available online

Fig. 1. A schematic representation of the multidisciplinary assessment in the BASE-II.

National Cohort) allows a direct quantification (and correction) of sample selectivity using nationally representative samples as reference [see 13, 14]. In a similar vein, we included medical, cognitive, and psychosocial measures that had been used in BASE. This design strategy places us in a position to compare, for example, key aspects of functioning between same-aged participants from the later-born cohorts of BASE-II (tested in 2012–2014) with earlier-born cohorts of BASE (tested in 1990–1993). Figure 1 provides a schematic representation of the multidisciplinary assessment in the BASE-II.

The Special Issue

Our collection of articles is aimed at showing how genetic analyses, physiological and immunological data, participant-reported and physician-observed medical diagnoses, performance-based cognitive tests, and self-reports can be productively used and combined to help us better understand the factors acting as antecedents, correlates, or consequences of age-related differences. Towards this overarching end, Lill et al. [8] make use of genetic data and link these with key phenotypes in the physical health domain. They provide independent validation of previously reported genetic association signals for the body mass index and bone mineral density and emphasize the advantage of combining effects of multiple genetic markers into one analysis using a weighted genetic profile score approach.

Goldeck et al. [9] assess immunological parameters and extend earlier reports stating that the distribution of late-stage differentiated T lymphocytes is associated with age in people infected with cytomegalovirus (CMV), but is not associated with age in uninfected people. Specifically, the authors go beyond this by showing that the dis-

tribution of another main type of lymphocyte, the B cells (antibody-producing cells), is associated only with CMV, but not with age. These results have implications for the identification of confounding factors in immune monitoring and may provide mechanistic insights into the way in which CMV relates to immunity and the low-level inflammatory state termed 'inflammaging'.

Meyer et al. [7] combine genomic DNA analyses and medical data to examine how relative leukocyte telomere length is related to hematological parameters and anemia. In contrast to reports from other studies, results from BASE-II suggest that the length of the chromosome ends plays only a marginal role for hematopoietic parameters among community-dwelling older adults.

Eckstein et al. [15] use several layers of data obtained in the medical assessment battery to link metabolic syndrome and its constituent elements to bone mineral density. Analyses revealed evidence for differential associations by gender and anatomical sites. For example, among women, the known association of higher body weight with more bone mineral density was corroborated. In contrast, however, increased waist circumference, a marker of central obesity, was associated with less bone mineral density in both men with and without Metabolic Syndrome. This apparent paradoxical finding evidently shows that gender and regional fat distribution need to be taken into account when interpreting the effects on bone mineral density.

Düzel et al. [16] use data obtained as part of the psychological assessment battery and link these with cognitive test performance and objective physical health parameters from the medical assessments. In particular, they validate a new instrument that assesses distinct dimensions of individuals' self-reported future time horizons to engage in physically and socially active lifestyles. Two of these dimensions show differential associations with performance on a memory test and with metabolic status, pointing to new opportunities for identifying and enhancing mechanisms that contribute to active aging.

Hülür et al. [17] focus on data collected in the psychosocial questionnaires in BASE-II and link these with parallel assessments obtained 20 years earlier in BASE. Comparing case-matched controls from BASE and BASE-II reveals that 75-year-olds nowadays feel less lonely and less dependent on external circumstances than 75-years-olds in the early 1990s. This report provides a compelling illustration of the plasticity of aging outcomes [see also 18].

Finally, Eibich et al. [10] analyze data obtained in the socioeconomic part of the study and link these with detailed geo-referenced information on neighborhood characteristics, as obtained from administrative sources such as the Berlin Police. Using the almost exact street address of the participants, the authors link residential characteristics such as crime and distance to amenities with individual-level BASE-II data on health and well-being. Exploiting the age-heterogeneous design of BASE-II, results revealed evidence for age-differential associations. For example, they find that links of neighborhood social capital to health and well-being are particularly strong among older residents.

Taken together, the articles compiled in this Special Issue showcase the multidisciplinary breadth of BASE-II and highlight that several sets of key insights could only be gained through the systemic collaboration across disciplines that only a study like BASE-II allows. For instance, the thorough and multi-perspective investigation of commonalities and differences between birth cohorts in psychosocial measures [17, 18] was possible because the disciplinary angle of the psychologists on the team was enriched by intense collaboration with other units. Taking into account medical data such as participant-reported and physician-observed medical diagnoses allowed controlling for individual and cohort differences in the number of physical diseases. In a similar vein, collaborating with the socioeconomics unit allowed (a) computing education indices that were normed to the different cohorts in BASE and BASE-II and (b) providing quantification of sample selection in both studies using a nationally representative sample (SOEP) as the reference. Finally, working together with the cognitive aging experts allowed controlling for cohort differences in performance on a fluid intelligence measure.

The noted heterogeneity of aging outcomes is also illustrated nicely in several of the figures included in this Special Issue. For example, figures 1 and 2 in Goldeck et al. [9] show that over and above mean-level differences between the groups examined, individuals profoundly differ from one another in B-cell differentiation and transitional B-cells. This was the case both across CMV groups and within CMV groups, suggesting that differences related to CMV (and to birth cohort in Hülür et al. [17]) represent only one of many contributing factors to individual differences in late-life immunological parameters (and psychosocial functioning).

In conclusion, the present series of articles demonstrates that the multidisciplinary measurement protocol of the BASE-II fulfills its intended purpose: to identify key factors that contribute to functional heterogeneity in old age. At the same time, this protocol also offers an excellent baseline for future longitudinal observations on the BASE-II study participants. These observations will pro-

vide a more dynamic and increasingly mechanistic account of individual differences in aging, and inform evidence-based, individualized attempts at prevention and amelioration of decline [19].

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BASE-II has implemented a transparent and sustainable procedure that allows external scientists to use BASE-II data for their analyses. Potentially interested scientists apply directly to the Steering Committee, which reviews and decides about the request.

References

1 Dannefer D: Cumulative advantage/disadvantage and the life course: cross-fertilizing age and social science theory. J Gerontol B Psychol Sci Soc Sci 2003;58:S327–S337.

2 Baltes PB, Lindenberger U, Staudinger UM: Life span theory in developmental psychology; in Lerner RM, Damon W (eds): Handbook of Child Psychology, ed 6. Vol. 1: Theoretical Models of Human Development. Hoboken, Wiley, 2006, pp 569–664.

3 Smith J, Baltes MM: The role of gender in very old age: profiles of functioning and everyday life patterns. Psychol Aging 1998;13:676–695.

4 Smith J, Baltes PB: Profiles of psychological functioning in the old and oldest old. Psychol Aging 1997;12:458–472.

5 Baltes PB, Mayer KU (eds): The Berlin Aging Study: Aging from 70 to 100. New York, Cambridge University Press, 1999.

6 Bertram L, Böckenhoff A, Demuth I, Düzel S, Eckardt R, Li S, Lindenberger Ulman, Pawelec G, Siedler T, Wagner GG, Steinhagen-Thiessen E: Cohort profile: The Berlin Aging Study II (BASE-II). Int J Epidemiol 2014;43:703–712.

7 Meyer A, Salewsky B, Buchmann N, Steinhagen-Thiessen E, Demuth I: Relative leukocyte telomere length, hematological parameters and anemia – data from the Berlin Aging Study II (BASE-II). Gerontology 2016;62:330–336.

8 Lill CM, Liu T, Norman K, Meyer A, Steinhagen-Thiessen E, Demuth I, Bertram L: Genetic burden analyses of phenotypes relevant to aging in the Berlin Aging Study II (BASE-II). Gerontology 2016;62:316–322.

9 Goldeck D, Oettinger L, Janssen N, Demuth I, Steinhagen-Thiessen E, Pawelec G: Cytomegalovirus infection minimally affects the frequencies of B-cell phenotypes in peripheral blood of younger and older adults. Gerontology 2016;62:323–329.

10 Eibich P, Krekel C, Demuth I, Wagner GG: Associations between neighbourhood characteristics, well-being and health vary over the life course. Gerontology 2016;62:362–370.

11 Baltes PB, Smith J: New frontiers in the future of aging: from successful aging of the young old to the dilemmas of the fourth age. Gerontology 2003;49:123–135.

12 Headey B, Muffels R, Wagner GG: Long-running German panel survey shows that personal and economic choices, not just genes, matter for happiness. Proc Natl Acad Sci USA 2010;107:17922–17926.

13 Wagner GG, Frick JR, Schupp J: The German Socio-Economic Panel Study (SOEP): scope, evolution and enhancements. Schmollers Jahrbuch 2007;127:139–169.

14 Saßenroth D, Kroh M, Wagner GG: Selectivity Processes in and Weights for the Berlin Aging Study II (BASE-II). SOEPpapers on Multidisciplinary Panel Data Research. Berlin, German Socio-Economic Panel (SOEP), DIW, 2013 (608). www.diw.de/documents/publikationen/73/diw_01.c.432989.de/diw_sp0608.pdf.

15 Eckstein N, Buchmann N, Demuth I, Steinhagen-Thiessen E, Nikolov J, Spira D, Eckardt R, Norman K: Association between metabolic syndrome and bone mineral density – data from the Berlin Aging Study II (BASE-II). Gerontology 2016;62:337–344.

16 Düzel S, Voelkle MC, Düzel E, Gerstorf D, Drewelies J, Steinhagen-Thiessen E, Demuth I, Lindenberger U: The Subjective Health Horizon Questionnaire (SHH-Q): assessing future time perspectives for facets of an active lifestyle. Gerontology 2016;62:345–353.

17 Hülür G, Drewelies J, Eibich P, Düzel S, Demuth I, Ghisletta P, Steinhagen-Thiessen E, Wagner GG, Lindenberger U, Gerstorf D: Cohort differences in psychosocial function over 20 years: current older adults feel less lonely and less dependent on external circumstances. Gerontology 2016;62:354–361.

18 Gerstorf D, Hülür G, Drewelies J, Eibich P, Düzel S, Demuth I, Ghisletta P, Steinhagen-Thiessen E, Wagner GG, Lindenberger U: Secular changes in late-life cognition and well-being: towards a long bright future with a short brisk ending? Psychol Aging 2015;30:301–310.

19 Lindenberger U: Human cognitive aging: corriger la fortune? Science 2014;346:572–578.