

Preface and Acknowledgments

THE SEEDS for the research upon which much of this book is based were sown at a National Institute on Aging (NIA)-sponsored workshop titled "Upper Limits to Human Life Span" held at the University of California, Berkeley, in March 1987. One of the most important issues that emerged from this workshop was the paucity of information in the literature on actuarial aging (i.e., life table data) on nonhuman species: despite the thousands of life tables in the ecology and gerontology literature, the vast majority were based on a few score or a few hundred individuals. These small initial numbers thus provided virtually no information on mortality rates at older ages in any species. Immediately after this workshop James Vaupel (who had also attended it) and I agreed to explore the possibility of collaborating on a project designed to construct a large-scale life table of the Mediterranean fruit fly, a species that is reared in vast numbers at Moscamed, a medfly factory near Tapachula, Mexico. The director at that time was one of my former Ph.D. students, Pablo Liedo. A year after the idea for this large-scale life-table study was conceived we submitted a proposal to NIA as part of a larger program project (headed by James Vaupel). This program was subsequently funded, and the preliminary results were reported in a "News and Review" article in *Science* magazine (Barinaga 1992). A formal paper was published in 1992 titled "Slowing of mortality at older ages" (Carey, Liedo, Orozco, and Vaupel 1992; see also companion paper by Curtsinger et al. 1992). This set the stage for a subsequent funding cycle and a series of new research questions.

The second funding cycle of the program project began in 1994 and focused initially on concerns that were raised in "Letters to the Editor" in *Science* (Kowald and Kirkwood 1993; Nusbaum et al. 1993; Robine and Ritchie 1993; Olshansky et al. 1993; Gavrilov and Gavrilova 1991), most notably whether deceleration was due to density effects, whether the phenomenon was general and thus observed in other species, and if medflies subjected to a wide range of different environmental manipulations would also exhibit mortality deceleration at older ages. Later in this 5-year funding cycle (mid-1990s) we began to shift emphasis from life table studies involving tens or hundreds of thousands of flies in group cages to experiments involving the mortality and daily reproduction of individual flies. At that time we also began efforts at constructing a large database on the record life spans of vertebrates. The project was funded for third cycle starting in 1999 and therefore, the medfly life table project is in the 13th year of continued funding.

There are several reasons why I am hopeful that the proposed book will contribute new knowledge to the biology of aging and the biodemography of life span. First, the book reflects the overall continuity of the project from inception to present. Indeed, it is the first nonedited book on the biology of aging and longevity that focuses on a single-model system in which the experiments were designed by the same group of core scientists (i.e., myself, Vaupel, Liedo, and other key colleagues), in which the data were gathered in the same laboratory by essentially the same group of technicians (with very little turnover), and in which the results were analyzed, written up, and published quickly in uniformly high-quality journals.

Second, the overall data set on which the collective studies described in the book are based is truly unprecedented. The complete database currently consists of age- and sex-specific mortality data for over 5.6 million individuals (i.e., data quantity) in which the same types of cages, larval and adult food, physical conditions, and collection procedures were used from the beginning of the studies in 1989 to the present (i.e., data quality).

Third, the science of aging is such a rapidly moving field that knowledge of many aspects in the medfly system described in this book—including experimental designs, interpretation of results, and summaries and syntheses—may be helpful for studies using other model systems (e.g., nematode, *Drosophila*, yeast, rodents). In particular, the results presented in the book will sharpen the experimental focus and frame the thinking of researchers who use more costly vertebrate systems.

Fourth, the book will serve as an introduction to experimental demography and biodemography for a wide range of biologists not specializing in aging science (e.g., ecologists, population biologists, demographers, actuaries). There appears to be no other source of advanced concepts in life table and mortality analysis for biologists, and I am unaware of any ecology text that goes much beyond elementary life table analysis.

Fifth, the book contains several new syntheses including (i) biodemographic principles that capture the general concepts such as slowing of mortality, male-female mortality differentials, and the indeterminacy of life span; (ii) analytical models that make explicit the relationship between life history traits such as reproduction and longevity or mortality; and (iii) longevity theory that outlines a general model in social organisms describing how longevity extension coevolves with sociality. My focus at the end of the book is primarily on human longevity.

Sixth, the book contains studies that were motivated as much by the conventional *hypothesis-driven* questions (tests of specific hypotheses such as upper life-span limits) as by *discovery-driven* science, which was first characterized in the context of genome research (Aebersold et al. 2000; Idelker et al. 2001) but which I believe applies equally well to some of the research described in this book. Indeed, one of the most exciting outcomes of using

huge initial numbers in life table studies was the discovery of nuances in mortality trajectories at both young and old ages that then required hypothesis testing. It is discovery science because the research involves unknown biological and demography territory.

Much of the writing for this book was done over the past ten years in the form of refereed, coauthored publications. This series of research papers started with the 1.2 million medfly life table study (Carey et al. 1992) and ended with a paper containing a conceptual overview of life span (chapter 10) that I initially presented at the workshop "Life Span: Evolutionary, Ecological and Demographic Perspectives" held in Santorini, Greece, in May 2001. The final version of the article that became chapter 10 was not completed until early 2002 (Carey 2003). The book organization and content reflect the progression of ideas and the evolution of concepts that emerged from my thinking about the determinants of mortality, survival, and life span over these years. One of the most influential articles that shaped my thinking about the integration of longevity and mortality concepts was by the late gerontologist George Sacher (1978), "Longevity and aging in vertebrate evolution." In this paper Sacher introduced the concept of the "biology of the finitude"—a triad consisting of the biology of life span, aging, and death. In my mind this "finitude" idea provides conceptual continuity by framing life span in a functional (life history) context, aging in a mechanistic context, and death in a finality context. Thus the concept introduced in the Sacher article helped me to integrate different sections of the book—the results of studies on mortality dynamics presented in chapters 3–7 are woven into many of the general biodemographic principles presented in chapter 8, which, in turn, are used as a foundation to develop theories and concepts on longevity and life span presented in chapters 9–10. In other words, Sacher's ideas provide a bridge between the allied but different conceptual domains of mortality, longevity, and life span (I consider the "biology of death" in this book in the final chapter only briefly; however, this neglected area is ripe for development of a stand-alone research program in aging).

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Although I was lead author and writer on most of the research papers used in this book, James Vaupel (JV) and Hans Müller (HM) were the lead authors and writers of four papers from which substantial portions were used, including section 3.4 on demographic selection (JV), several subsections on modeling in chapter 5 on density effects (JV), section 6.1 on early mortality surge (HM), and section 7.2 on reproductive clock (HM).

James Vaupel has provided input at all levels and has made a difference in how I approach demography in particular and science in general. This book could not have been written had he not taken interest in the program project, recognized the potential of the medfly as a model system, and provided intellectual stimulation and camaraderie. I owe my greatest thanks to him.