

**THE FEASIBILITY OF PREDICTING LONGEVITY  
IN THE ELDERLY:  
CONCEPTUAL AND EMPIRICAL ASPECTS**



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*Mogelijkheden en beperkingen van het voorspellen  
van de overlevingsduur bij bejaarden:  
conceptuele en empirische aspecten*

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## INTRODUCTION

Longevity has long been a central theme in research on aging. The question of whether and how human life might be prolonged has intrigued men through the ages (Lehr 1982). In ancient Greece and Rome, philosophers like Hippocrates, Plato and Cicero already commented upon how to bring about “rejuvenation” and attain old age in good physical and mental health. However, in those days average life expectancy from birth may have been as low as 20 years. Since the last century, the interest in prolongation of life of those happy few who were able to live past midlife has made way for an interest in prevention of premature death for everybody. A century of improving hygiene, nutrition, public and personal health (together with declining fertility) has created what has been referred to as the “demographic revolution” (Butler 1980). Longevity has become a democratic good. Average longevity, or life expectancy, is considered a primary indicator of the health status of a population.

In recent years, motivated by the awareness that the rapidly increasing number of older persons in the population may cause an equally rapidly increasing burden on the health care system if the age-specific incidence of disease does not change, there is a growing emphasis on the quality of the increased life span (Manton 1982). Concepts such as “active life span” or “disability-free life expectancy” are being investigated. Longevity research today, then, is as much motivated by a concern for public health as by a search for an extension of healthy and productive life.

### *A typology of longevity studies*

The number of studies published on determinants of longevity has increased considerably since the 1960's, when data sets became available in which subjects were observed on multiple aspects — including physical, mental and social characteristics — subsequent to which their vital status and causes of death were ascertained. These — essentially longitudinal — longevity studies provide prospec-

tive information on factors associated with survival time in a living population, as opposed to — essentially cross-sectional — mortality studies which provide information on (demographic) factors correlated with mortality among those who have died. Since our interest lies in factors prospectively associated with longevity — or, conversely, with premature death — of living individuals, mortality studies will not be considered here.

Longevity studies are, thus, based on data sets which allow the researcher to relate baseline characteristics to follow-up mortality data. Roughly, these studies can be divided into three categories:

1. basically descriptive studies attempting to determine which characteristics are associated with longevity, in order to learn about the aging process;
2. basically descriptive studies attempting to identify groups at risk of premature death;
3. hypotheses-testing studies focussing on a particular characteristic and determining its relative risk of premature death.

Note that these categories have a temporal sequence: many of the early longevity studies can be found in the first category, while studies belonging to the second and third categories tend to be of a later date. It must be added that the approaches describing each of these categories are not mutually exclusive, in the sense that one study can be characterized by one approach only. Rather, within the context of one study, more than one approach can be followed to study different research questions. However, judging by initial objectives and published findings, each study tends to have a predominant focus in one category.

Below, examples are given of studies in each category (cf. Deeg 1989). References cited are of studies dealing with the prediction of longevity based on multiple factors only.

Studies in the first category are concerned with basic-scientific questions. They are aimed at detecting factors associated with aging, where aging is conceived as a phenomenon not necessarily related to chronological age, and characterized by (physical) declines ultimately leading to death. It is recognized that aging is a process in time, but that it is not “time lived so far” but rather “time yet to be lived” that is thought crucial to this process. The samples on which these studies are based are usually not representative of the general population but consist of volunteers who are willing to undergo the large number of physical and psychological tests included in these studies. This category, typically, includes some of the pioneer longitudinal studies of aging initiated in the 1950’s and 1960’s: the study of Aging Twins (Jarvik & Blum 1971), the Baltimore Longitudinal Study of Aging (Tobin 1981), the Bonn Longitudinal Study of Aging (Lehr et al. 1987), the Duke Longitudinal Study of Aging I (Palmore 1970, 1974, 1982), the Hamburg study (Riegel et al. 1967), the National Institute of Mental Health study (Libow 1974), and the Normative Aging Study (Bell et al. 1972).

The second category is practice oriented and aimed at identifying groups at risk. Longevity is considered an appropriate indicator of the absence of morbidity or other health related problems. Factors negatively associated with longevity help to define groups in need of increased medical, and perhaps social, attention. Studies in this subcategory are usually based on representative samples and include measurements that do not put an excessive burden on the subjects. Some of these studies were initiated in the pioneer years of longitudinal aging research: the Alameda County study (Kaplan et al. 1987), and the Dutch Longitudinal Study among the Elderly (Deeg et al. 1985). Later examples include: the Established Populations for the Epidemiologic Study of the Elderly (Cornoni-Huntley et al. 1986), the Gisborne study (Campbell et al. 1985), the Koganei study (Koyano et al. 1986), the Massachusetts Health Care Panel Study (Katz et al. 1983), the Melton Mowbray study (Jagger & Clarke 1988), and the Older Americans Resources and Services study (Blazer 1982). Some studies in this subcategory combine a locally or nationally representative sample with information from extensive physical and/or psychological tests: the Evans County study (Schoenbach et al. 1986), the Glostrup study (Agner 1983), the Göteborg 70-year-old study (Svanborg 1988), the Jerusalem study (Abramson et al. 1982), the St. Louis study (Botwinick et al. 1978), the National Health and Nutrition Examination Survey I Epidemiologic Follow-up Study (Madans et al. 1986), the Tampere study (Heinämäki et al. 1986), and the Tecumseh Community Health Study (House et al. 1982).

Although studies in the first and second categories typically consider all-cause mortality, attempts to understand the factors found to be associated with longevity lean on explanations in terms of specific causes of death. Therefore, a link exists with studies of the etiology of diseases, which may not be population based but rather utilize clinical samples.

The third category of studies may consider other outcomes in addition to longevity, such as hospitalization, admission to a long-term care facility, or the incidence of disability. The association of the characteristic of interest with the outcome is evaluated while controlling for a number of factors judged to be potential confounders of the association studied. The samples used in this type of study are not necessarily representative or population based. The link with etiological studies is very close. Examples of studies based on locally representative samples are: the Dunedin study (Van Oyen et al. 1989), the Framingham Heart Study (Harris et al. 1988), the Kyriat Ono study (Kaplan et al. 1988), and the Manitoba Longitudinal Study of Aging (Mossey & Shapiro 1982). Studies of longevity in this category based on selective samples are: the Harvard Alumni study (Paffenbarger et al. 1984), the New Haven Forced Relocation study (Zuckerman et al. 1984), and the Whitehall study (Ebi-Kryston 1988).

How do the findings of these three categories of studies contribute to our knowledge concerning predictors of longevity? Furthermore, what is the predictive ability of predictors ascertained?

In studies in the third category, the most conventional expression of the magnitude of the associations tested is currently in terms of relative risks or odds ratios. Less often the associations are evaluated in terms of population attributable risk (Rose 1981). Relative risks and odds ratios are individualized measures and do not give an impression of the relative importance of the factors reported to predict longevity in terms of impact on population level. In studies in the first and second categories, associations are usually analyzed by means of statistical techniques based on correlations of baseline characteristics with mortality or survival time. The multiple regression techniques often employed yield a global measure of the total predictive ability of the predictors found: the variance explained. In those cases where this statistic is reported, it appears to be of a rather disappointing magnitude. Only rarely does it rise above the level of 30%, implying that at least 70% of all variance in longevity remains unexplained. This fact is largely ignored. On the contrary, predictors of longevity, reported in terms of risk ratios or odds ratios, are often presented as great steps forward in the pursuit of health and well-being.

The large margin of uncertainty resulting from the considerable amount of unexplained variance, however, has practical consequences. Possible effects of intervention on society are likely to be overestimated. It might be questioned whether identification of groups at risk and application of preventive measures intended to lower particular health risks are of significant benefit to society, even if the relative risk of the indicator of these health risks is significant in a statistical sense.

### *This dissertation's theme*

The present dissertation is a report of a search process to find out if the level of variance explained typically reported in longevity studies can be increased. Two premises form the rationale of this endeavor:

1. the methods used in most studies of longevity may be improved upon;
2. the data used to predict longevity in most studies may not be the most appropriate with regard to the target population: those persons indicated as "elderly".

In the course of this search process, several new concepts and empirical approaches will prove to be useful. If the search process has a positive outcome, it will offer guidelines to investigators planning longevity studies in the near future. If its outcome turns out to be negative, the lack of predictive ability of longevity

studies may be a basic fact which can no longer be ignored and which has consequences for our thinking about and interpretation of predictors of longevity.

This dissertation, in other words, deals with the feasibility of predicting longevity in the elderly, from a concern with both the scientific value and the practical applicability of findings. In terms of the typology described above, the research constituting the search process follows the approach of the second category: basically descriptive studies that attempt to identify groups at risk.

### *The Dutch Longitudinal Study among the Elderly (DLSE)*

The impetus to the present research process came from the opportunity to study longevity in the elderly based on a representative sample with information on physical, mental, and social characteristics: the Dutch Longitudinal Study among the Elderly (DLSE). This study of a national probability sample of persons aged 65 and over was conducted by Dr. R.J. van Zonneveld when he was with the Organization for Applied Scientific Research, TNO (Van Zonneveld 1961). Initial examinations took place from 1955 to 1957 on 3149 subjects who were randomly selected from the practices of 374 family physicians who had volunteered to collaborate in the study by examining 10 persons each. Purposes of the study were to describe the health status of Dutch elderly and possibly related social and psychological factors, and to bring to the attention of the physicians the particular health problems of their elderly patients. In 1960, it was decided to conduct an identical follow-up study. From then on until 1975, six such studies were carried out on traceable, surviving subjects. In 1983, vital status and causes of death were ascertained of 84% of the initial sample. Of those 2645 subjects whose vital status was determined, 28 were still alive (ages: 92 years and over). Longevity across this 28-year follow-up period was related to all available baseline information. This effort yielded a variance explained of 20% (Deeg et al. 1985).

This result was considered rather disappointing, especially because the longevity study possessed several characteristics that warranted the expectation of a reasonable predictive ability. These characteristics — which might be considered to be minimal conditions of a longevity study in the first category defined above — are:

1. an approximately representative sample;
2. a broad scope of information collected, especially with regard to physical health;
3. a duration of follow-up sufficiently long to have information on the date of death (c.q. exact survival time or longevity) of a majority of subjects;

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4. a measure of survival time that not only enables comparison of all subjects with respect to survival time independent of age and sex, but also makes full use of information concerning survival time;
5. a statistical method of analysis that allows for non-linear relationships of the independent variables with survival time.

However, the low percent of variance explained may also be attributed to shortcomings of the DLSE longevity study. Characteristics of this study that might have affected the results in a negative sense are:

1. the inter-observer variability is probably large;
2. the information included in the study was not selected to predict longevity;
3. the information was recorded in a rather compressed way as compared to the present state of the art, resulting in loss of information.

In order to separate methodologic, data-dependent from essential, data-independent causes of poor predictive ability, opportunities were sought to apply the method used to predict longevity in DLSE to data from other studies, and to compare the results as to nature and predictive ability of the predictors found. Differences across studies in information available, sampling frame, sample selectivity, historic period, and cultural background would have to be taken into account. Should the results be similar to the DLSE outcome, these differences would underline the essential limitations of attempts to predict longevity in the elderly. Should, on the other hand, the results provide evidence that improvement of predictive ability is possible, careful evaluation of the differences across studies would be warranted in order to identify those study characteristics which played an essential role in improving the predictive ability.

### *The Study of Disability in a Home for the Elderly (SDHE)*

Many of the pioneer studies of predictors of longevity in the elderly were based on so-called "captive" populations: residents of nursing homes or other long-term care facilities, and geriatric patients. These studies basically belong to the second category described above. Results from these studies and results from studies based on non-institutionalized samples are commonly cited without due reference to the population on which they were based. An interesting question is whether results from both types of studies are comparable; in other words, to what extent do results based on institutionalized populations correspond to those based on non-institutionalized populations? A proper answer to this question can be given only if the same method is used to predict longevity.

The opportunity to study longevity in residents of a home for the elderly using the same method as in the DLSE longevity study presented itself in the Study of Disability in a Home for the Elderly (SDHE, Van Loveren et al. 1988). In this study,



all residents of a large residential home for the elderly in the eastern part of the Netherlands were assessed by staff members at three-month intervals over four and a half years. The assessments included ratings of physical, mental and social functioning. Two hundred and ninety-eight residents were followed from baseline (June 1981) through January 1986 when their vital status and, in case of death, date of death was ascertained. At that time, 40% of these residents had died.

### *The First National Health and Nutrition Examination Survey (NHANES I)*

The purpose of this dissertation would not have been fully answered without the application of the method used in the DLSE longevity study to another sample representative of a total population, preferably without most of the shortcomings of DLSE listed above. The opportunity to study longevity in a suitable sample presented itself in the First National Health and Nutrition Examination Survey (NHANES I) and its Continued Follow-up Study of the Elderly, based on a national probability sample of the civilian, non-institutionalized population of the coterminous United States (Madans 1986). Data were collected on 23,808 persons in the ages 1-74 years. For our purposes of comparison, it sufficed to study White persons aged 65-74 at the baseline examination in 1971-1975. Of 3137 of these persons (98.7% of the initial sample) vital status and, in case of death, date of death were ascertained in 1986.

The information in NHANES I was collected more recently, and therefore more uniformly and according to a more advanced state of the art than in DLSE. The drawback is that the follow-up period was not so long as to provide exact dates of death on virtually all NHANES I participants. Still, one half of all 65-74 year old sample members had died — a proportion that might be considered large enough for applying the measure of survival time used in DLSE. For the current purpose, the NHANES I data suffer another limitation. Because NHANES I was not specifically designed to study the health status of the elderly, the study design omitted assessment of cognitive and physical functioning, both widely considered essential indicators of health in later life. However, the wealth of detailed clinical and biological information collected should be potentially relevant to longevity.

### *The predictive ability of change*

The basic design of the longevity studies alluded to so far deals with observation at one point in time in relation to subsequent survival time. It may well be that rate

of change of a characteristic has a greater predictive ability for longevity than the level of the characteristic at a rather arbitrary point in time. This issue is only beginning to be addressed in gerontologic literature. In this dissertation, it is examined using data from the first three cycles of DLSE and subsequent survival time.

One further modification of design might improve or complement the prediction of longevity. All studies discussed so far are prospective: survival time subsequent to observation is ascertained. Such a study design, however, provides no information about how characteristics change as individuals approach death. In other words, nothing can be inferred concerning *trajectories* that in the end lead to death. These trajectories may represent either gradual or precipitous change — a distinction that in gerontologic literature has been termed *terminal decline* versus *terminal drop*. Knowledge of this terminal change is useful from the point of view of geriatric practice: it may lead to improved case management, placement decisions, and therefore improved quality of life. In addition, knowledge of these trajectories is desirable from a scientific-methodologic point of view: it allows addressing the issue of whether the characteristics showing decline prior to death are the same as those having long-term predictive ability in the prospective design.

The study of terminal change requires retrospective data derived from a prospective, longitudinal design. Since it is of interest to distinguish between gradual and precipitous, i.e. linear and curvilinear change, a minimum of three observations prior to death are needed which are close enough together for relevant change to be detected. The data collected in the SDHE provide the opportunity to study terminal change in those residents having died during the 4½ years of observation, and therefore to compare predictors of mortality from both prospective and retrospective designs.

### *Research agenda*

In summary, this dissertation addresses various approaches to the prediction of longevity in the elderly. Some of the approaches are focussed on the choice and definition of predictors, others on the analytic method used to predict longevity. The issues addressed can be stated as follows:

1. What is an optimal operational definition of longevity in a long-term follow-up study of the elderly?
2. Which predictors of longevity can be identified consistently across different studies?
3. What can be concluded regarding total predictive ability across studies of different design?

4. Do predictors of longevity based on studies of institutionalized populations correspond to predictors based on studies of non-institutionalized populations?
5. Does inclusion of (rates of) change in characteristics improve the prediction of longevity as compared to levels of characteristics?
6. Are factors showing changes just prior to death the same as those which are found to be predictive of longevity in the longer run?
7. Which characteristics of the aging process account for the observation that longevity studies attain a predictive ability of far less than 100%?

### *A guide to reading this book*

Part II of this book presents empirical material pertinent to the issues formulated above. First, in chapter II.1 an operational definition of longevity is presented that is considered optimal in long-term follow-up studies of elderly samples which are heterogeneous as to age and sex, and that allows comparison of results across studies of samples of different age and sex distribution. This measure of survival is called the realized probability of dying (RPD). Statistical analyses to evaluate predictors of longevity in the subsequent chapters will utilize the RPD.

Chapter II.2 describes the results of the longevity study in DLSE. As already briefly noted, the total variance explained in this study was just 20%. One of the possible causes of this deficient predictive ability, the interdependence of predictors indicating medical and psychosocial conditions, is examined in detail. The possibility that a statistical model incorporating change in predictors might improve predictive ability, is examined in chapter II.3. In the specific case of cognitive function, it is examined in chapter II.4 whether consideration of rate of change is to be preferred above level of function with regard to predictive ability. In this chapter, results of statistical analysis using the RPD are compared to results based on statistical methods frequently used in literature, i.e. a comparison of five-year survival rates and the statistical analysis of failure time data using Cox proportional hazards models.

Data from the NHANES I Continued Follow-up of the Elderly are evaluated in chapter II.5, using the approach of chapter II.2. Since the NHANES I design involved data collection in such a way that more detailed information was collected in representative subsamples, prediction of longevity is compared across subsamples.

Prediction of longevity of residents in a home for the elderly is attempted in chapter II.6, based on data from SDHE. Special consideration is given to the particular selectivity of this population as compared to the total Dutch elderly

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population. In chapter II.7, finally, terminal change is evaluated in those residents deceased during the 4½ year study period.

Discussion of the findings in part II is pursued in part III. Answers to the questions listed in the research agenda above are suggested, and consequences for both the empirical study of determinants of longevity and the practical application of the evidence from the current studies are described.

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II

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EMPIRICAL STUDIES  
OF PREDICTORS  
OF LONGEVITY





## II.1

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# A MEASURE OF SURVIVAL TIME FOR LONG-TERM FOLLOW-UP STUDIES OF THE ELDERLY

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## Abstract

Studies of determinants of longevity in the elderly by means of a follow-up study are usually based on samples with a wide age range and some selectivity. This poses the problem of constructing a measure of longevity that:

1. will make subjects in the sample comparable regarding survival time, independent of their age and sex;
2. is suitable for long-term follow-up studies;
3. can be used to check the absence or presence of selectivity of the sample with regard to longevity;
4. improves the comparability of studies with different designs and sampling schemes;
5. can take the mortality development over time into account.

An individual measure of survival time is presented that satisfies these requirements: the Realized Probability of Dying (RPD). Its construction is described. The RPD is derived from population life tables based on age, year of birth, and sex. For each subject, the relative position on the survival curve within the birth cohort is determined.

In an illustration, the RPD is applied to data from a 28-year follow-up study of the elderly in the Netherlands. A comparison is made with other survival measures commonly used in this type of studies. It is concluded that the RPD is a powerful and valid measure of longevity in elderly subjects, and that it can be useful in the study of determinants of longevity.

*Keywords:*

Longevity / Life expectancy / Epidemiologic methods / Longitudinal studies / Demography / Aged

## Introduction

Although longevity belongs to the oldest interests of epidemiology, research reports on determinants of longevity has been sparse until quite recently [1]. An important reason for the late start of longevity research is the rarity of adequate data, that allow reliable generalizations. For this type of research, data are needed for individuals who are followed until death, or until a substantive proportion of their cohort has died. The retrieval of such data requires specific organizational provisions.

This paper deals with a central methodological aspect of longevity research: the establishment of a measure of longevity which allows pooling across demographic strata (birth cohort, sex) having different survival curves. As we are dealing with follow-up studies, the measure we are looking for will be a measure of survival or survival time.<sup>1</sup>

The measure should allow comparisons between studies based on different samples. One way to compare samples as to survival time is by way of their survival curves. To provide a sample survival curve, there should be sufficient and sufficiently specific information available.

The simplest and often employed survival measure compares the characteristics of decedents to those of survivors after some period of follow-up. The ratio of decedents/survivors (or, similarly, the percentage of decedents) is a satisfactory measure after an arbitrary follow-up period as long as the study sample is random or non-selective, consists of one birth cohort, and is followed from the same age onward. In this case, the percentage of survivors corresponds to the point on the survival curve of this specific cohort, defined by the follow-up time. However, such a study design is rarely feasible nor often desirable. This survival measure will fall short when there is a substantial age range in the study sample. Here, employing the ratio of decedents/survivors at the end of a follow-up period of fixed duration amounts to considering several age- or cohort-specific survival curves at once. This will not convey information about the shape of each birth cohort's survival curve, and may cause the inference of determinants of longevity to be inaccurate.

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1 Across different studies, longevity is operationalized as survival as well as survival time. We distinguish between the two such, that *survival* pertains to the number of survivors versus number of decedents at the end of the follow-up period, while *survival time* pertains to the actual number of years (months, days) lived by the subjects during the period of observation. Strictly speaking, longevity is synonymous with length of life, with the implication that the particular life referred to is long. Studies of longevity in the elderly, however, for practical reasons measure length of life from a certain (older) age onward and do not consider total length of life or life span. Similarly, the probabilistic concept of life expectancy can be calculated from birth as well as from older ages onward.

Moreover, the existence of a certain age selectivity in the sample will affect the survival measure in a way that is hard to appreciate.

Also, it may be of interest to make inferences with respect to a larger trajectory than one time point of a survival curve. It makes more sense to know for an individual whether he or she will stay alive during a relatively short or a relatively long period or during a period that agrees with the average life expectancy, than to know whether he or she has or has not lived out the follow-up period the researcher was able to observe. This can only be achieved when information concerning the actual survival time of individuals is used.

In addition, a comparison of numbers of decedents and survivors gives rise to relevant determinants of survival, only if the follow-up period is relatively short. In cases where the follow-up period increases well beyond the average life expectancy of the sample, differences between decedents and survivors on initial characteristics are likely to diminish (“ceiling effect”): by this time, also a considerable number of originally healthy subjects will have died.

Recently, determinants of longevity are often studied by means of Cox models for the statistical analysis of survival times (proportional hazards model [2]). With this method, information on the full survival curve is taken into account — i.e. across the period of observation. However, in order to control for initial age, the data still to some extent will have to be collapsed over birth cohorts. Models controlling for age do not provide explicit information on the contribution of each age stratum to the survival measure as well as to the determinants inferred. Again, this problem is aggravated when the sample is somewhat age-selective. And again, Cox’ models are sensitive to the “ceiling effect”. The parameter of interest, the relative hazard associated with a particular risk factor, is essentially estimated as the average of the relative risks for many very short time intervals over the total length of the follow-up period. A large relative risk in the early part of the follow-up period will thus be diluted by the virtual absence of an elevated risk in the part of the follow-up period that extends beyond the average life expectancy of the sample.

Both of the above mentioned approaches fall short in a more conceptual way. Longevity can be considered as an individual characteristic, indicating length of life or age at death. Therefore, it would be best studied as an individual characteristic which is related to other individual characteristics. However, both the ratio of decedents/survivors and the relative hazard in Cox models are aggregate statistical measures, resulting from pooling sample subjects.

In the following section, we propose a measure of survival time that characterizes each individual and assigns him or her a rank order in the sample according to survival time, relative to birth cohort and sex. With this measure, the results will not be confounded by the age and sex composition of the sample, and strengthened

rather than weakened by a long follow-up period. Furthermore, the measure serves to check the representativeness of the sample regarding survival time.

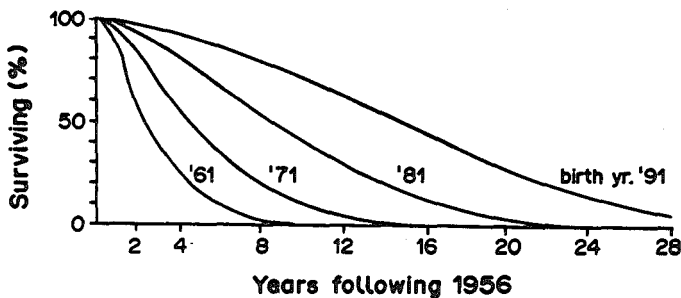
### The Realized Probability of Dying

The realized probability of dying (RPD) indicates for each individual the probability of death at a specific time relative to the survival curve of that part of his or her cohort that is still alive in the year of initial examination. It is an individual measure of survival time, calculated according to year of birth, year of initial examination and sex, and based on population life tables. In other words, the RPD reflects how soon a subject has died in comparison with his or her peers in the total population of the same sex and age at initial examination.

For example (Figure 1), a man born in 1891, aged 65 at initial examination (1956) and deceased after 21 years (1977) has a realized probability of dying of 0.3, because out of that part of his birth cohort that was still alive in 1956, 30% was still alive in 1977. For a man born in 1861 and aged 95 in 1956, the RPD would be 0.3 when he would have lived 4 years following initial examination. Thus, given that they are alive in 1956, the remaining longevity of both men, however different in age and absolute survival time, rank the same.

In the following calculation of the realized probability of dying, it is assumed that times at birth, examination and death are expressed in calendar years. Thus, the time unit in the data under study need not be smaller than a year. For each year of birth and for each sex, the probability of being alive in each calendar year following initial examination is calculated. The product of the yearly probabilities

Figure 1. Survival curves of birth cohorts 1861 through 1891, alive in 1956, Dutch males.



## II.1 Survival time in the elderly

of survival on population level is calculated until the moment of death.<sup>2</sup> The probability of surviving  $n$  years up to and including death becomes:

$$\text{RPD} = \prod_{i=1}^n (1 - d_i^{(b,s)})$$

where:

$i$  = the sequence number of the calendar year following initial examination

$d_i$  = the probability of death according to the life table in year  $i$

$b$  = the year of birth

$s$  = the sex.

Ideally, the calculation of this survival measure makes use of cohort life tables, covering the mortality of the sample cohort during the study period. This is of special importance when studying older age (80 years and over), as in this group mortality has strongly declined during the last decades (cf. Table 1 for the Netherlands). Because such cohort life tables are not readily available, second best is to make use of period life tables, which are based on cross-sectional mortality data, and cover the consecutive years following initial examination.

Generally, life tables provide probabilities of death according to age instead of year of birth. Probabilities of death ( $d_i$ ) are given for the period of one year immediately following the birthday. In order to make these of use for the present calculations, the assumption has been made that, on the average, the elderly subjects are examined on their birthdays. Now, (1) can be reformulated as: the probability of surviving  $n$  life years. In other words, it is the probability of realizing each age,  $n$  years higher than age at initial examination and conditional on age at initial examination. Further assuming that within the calendar year of initial examination the average of all birth dates is halfway the year, (1) runs from the middle of the calendar year of initial examination. At initial examination, its value is 1.

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2 As the calculation of the RPD is based on *survival* probabilities, the name realized probability of *dying* seems less appropriate than, for instance, realized probability of *survival* (RPS). However, the value of the RPD is determined by the time of death or, alternatively, the age realized at death. The term "realized probability of survival" does not sufficiently convey that it deals with a specific kind of survival, namely survival until death. Calling the measure "RPD" instead of "RPS" has, furthermore, the practical advantage that it has a large value when the probability of dying shortly after baseline is large, and a small value when the probability of dying is small.

**Table 1. Remaining life expectancy of the Dutch population at ages 65 and 80 by sex: change since 1880.<sup>1)</sup>**

	age 65		age 80	
	males	females	males	females
1880-1889	11.1	11.7	4.7	4.9
1931-1940	12.8	13.3	5.2	5.5
1956-1960	14.1	15.4	5.8	6.2
1961-1965	14.0	16.0	6.0	6.6
1966-1970	13.7	16.4	6.2	6.8
1971-1975	13.6	16.9	6.2	7.1
1976-1980	13.8	18.0	6.4	7.8

<sup>1)</sup> Taken from: Compendium Gezondheidsstatistiek Nederland 1974, Central Bureau of Statistics, p. 234, and Sterfetafels voor Nederland over de Perioden 1971-1975 en 1976-1980, Central Bureau of Statistics.

For (very) high ages, the probability of surviving one year is considerably smaller than for younger ages, which implies that it affects the eventual realized probability of dying relatively strongly. Moreover, at high ages there is a rather large variation in the probability of survival because of the small numbers of cohort survivors and the fluctuation over calendar years. Therefore, it is desirable to make an exact calculation of the last factor in the RPD. For details, the reader is referred to the appendix.

Thus, a measure of survival time is obtained that compares for each individual, according to year of birth and sex, his or her survival time with the survival time of the appropriate cohort. It introduces a rank order among all sample subjects that simultaneously adjusts for the effects on survival time of birth cohort, sex, and survival to the age at initial examination.<sup>3</sup>

For individuals who are known to be alive at the follow-up date, the calculation of the RPD is modified in a straightforward fashion. The survival times of these individuals can be considered as censored observations: the study is broken off before the endpoint under study (i.e. death) is reached. As is customary in the

3 For the actual calculations, a spreadsheet in Symphony was prepared, an example of which is available upon request to: M. Wolz, National Institute on Aging, Epidemiology, Demography and Biometry Program, Federal Building, Room 618, Bethesda, MD 20892, USA.

actuarial calculation method for survival time with censoring, the RPD for these living individuals is estimated by multiplying the probability of the age realized in the censoring year by one half. This multiplication factor of 0.5 is the expected value of the realized probability of dying in the population alive at any moment, and subsequently in those persons alive at the follow-up date. For example, a man born in 1891 and examined in 1956 at 65 years of age reaches at follow-up in 1983 the age of 92 with probability 0.08 (Figure 1); his imputed RPD will be 0.04, implying that he is expected to die when only 4% of his cohort is still alive. Note that this method accommodates follow-up periods of unequal lengths.

When the calculation of the RPD for all individuals in the sample is completed, the RPD can directly serve to check the representativeness of the sample regarding survival time. Representativeness is reached, if the distribution of the survival time of the study sample follows that of the population. This is equivalent to requiring that the RPD is uniformly distributed on the interval (0,1).

Uniformity of the distribution of the RPD yields near normality of its logit. Therefore, the logit of the RPD can be used as the dependent variable in regression models ascertaining predictors of longevity.

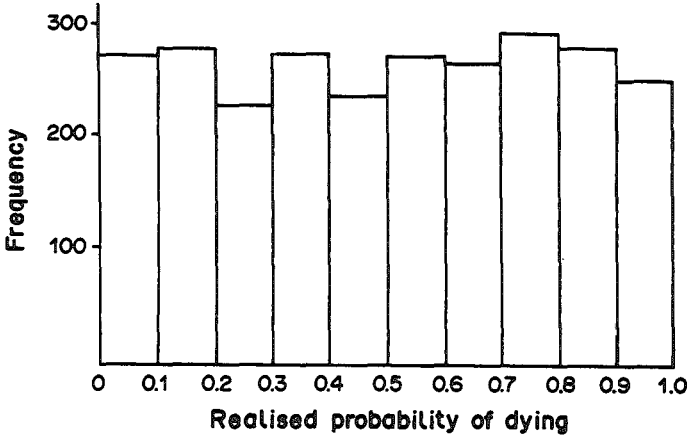
### **Illustration**

To exemplify the use of the realized probability of dying and the kind of study for which its use is to be preferred above other techniques, it will now be applied to the Dutch Longitudinal Study among the Elderly. This is a study with a follow-up of 28 years in which observations were made on the health status and mental and social characteristics of a nation-wide probability sample of 3149 persons aged 65 and over. The sample was stratified according to age (65-69, 70-74, 75-79, 80+) and sex. The age of the study sample at initial examination varied over a range of 35 years (from 65 to 99). The elderly subjects were randomly selected from the practices of 374 family physicians who had agreed to collaborate in the study by examining 10 patients each. The study was initiated by Dr. R.J. van Zonneveld with the Organisation for Applied Scientific Research (TNO), The Netherlands [3]. Initial examinations took place during 1955-1957 until it was judged that sufficient subjects were examined for statistical evaluation of the results. The sample was followed longitudinally with 1983 as the most recent follow-up year. At that time, 84% of the original sample could be traced, the tracing being more successful in the older age strata (77% traced in the youngest through 89% in the oldest stratum). Of the persons traced, 2617 had died with known date of death, while 28 persons were known to be alive. These 2645 persons form the present study sample.

For four male birth cohorts in the Dutch population, survival curves from 1956 onward (year 0 through year 28) are shown in Figure 1. From these curves, the



Figure 2. Dutch Longitudinal Study among the Elderly. Histogram of the distribution of the Realized Probability of Dying, total sample (N=2645).



RPD of a sample individual can be determined along the y-axis, given his survival time (along the x-axis).

To check the representativeness of the study sample for survival time, the RPD is averaged over the total sample. This average turns out to be 0.501. The standard deviation is 0.289, exactly the standard deviation of the uniform distribution on the

Table 2. Dutch Longitudinal Study among the Elderly. Mean realized probability of dying by sex and by age at baseline.<sup>1)</sup>

		mean	S.D.	N
men		.490	.290	1359
women		.513	.287	1286
age at baseline	65-69	.522	.300	541
	70-74	.507	.290	665
	75-79	.487	.289	674
	80-84	.511	.284	490
	85-89	.466	.269	211
	90+	.466	.266	64

<sup>1)</sup> Although the original sample was stratified into four age classes (65-69, 70-74, 75-79, 80+), six age classes are presented in this table for better evaluation of trends.

**Table 3. Dutch Longitudinal Study among the Elderly. Realized probability of dying by age at baseline for each sex.<sup>1)</sup>**

		mean	S.D.	N
<i>men</i>				
age at baseline	65-69	.538	.298	266
	70-74	.482	.297	347
	75-79	.466	.288	352
	80-84	.504	.281	258
	85-89	.440	.263	112
	90+	.482	.268	24
<i>women</i>				
age at baseline	65-69	.506	.301	275
	70-74	.533	.280	318
	75-79	.510	.288	320
	80-84	.518	.286	232
	85-89	.494	.275	99
	90+	.456	.268	40

<sup>1)</sup> cf. note to Table 2

interval (0,1). To examine the distribution further, the RPD is divided into 10 classes of equal width and the frequency in each class is plotted (Figure 2). The RPD does turn out to be uniformly distributed ( $\chi^2_9 = 11.1, p = 0.26$ ). Thus, the study sample may be considered representative of the population regarding survival time.

In the pursuit of further results, it is of importance to know whether this representativeness is maintained for sex and age cohorts separately. In other words, whether any differential selectivity within strata of the sample exists. From Table 2, a small tendency appears that women in the study group die a little earlier and men die a little later than expected from the population ( $F = 4.4, p = 0.04$ ).

The differences in average RPD between 5-year age cohorts are not significant either. However, a trend can be seen: the older elderly studied have a smaller RPD than the younger elderly studied ( $F_{\text{linearity}} = 4.8, p = 0.03$ ). This trend differs slightly for men and women (Table 3). While the trend for men declines consistently from young to old ( $F_{\text{linearity}} = 5.1, p = 0.02$ ), for the women such a clear trend cannot be inferred ( $F_{\text{linearity}} = 0.7, p = 0.40$ ). The only agreement with the

trend for the men is the small value of the RPD for women in the oldest group, equivalent to a relatively long survival time.

The noted trend is confirmed by the significantly positive correlation coefficient of RPD with year of birth in the total sample (0.061,  $p = 0.001$ ). This finding suggests a certain age selection in the study sample, which may be caused partly by the differential tracing success, partly by the initial recruitment of the sample. These causes may be understood as follows. Although the general practitioners did not exert influence on the selection of the sample of elderly subjects they were to examine, some general practitioners may have had a certain preference to first examine the more healthy older-elderly as well as the less healthy younger elderly. For the former, the examination would be less of a burden, while with the latter a regular contact already existed. A number of physicians were not able to examine all ten elderly in their sample before the closing date of the study, September 1957.

To explore a possible bias as described, correlation coefficients are calculated between age at baseline, objective health (i.e. health as rated by the general practitioner), frequency of doctor's visits and year of examination. Table 4a shows the coefficients for the total sample, while Table 4b shows the coefficients for those

**Table 4. Dutch Longitudinal Study among the Elderly. Correlation coefficients possibly related to sample selectivity.**

*a. All examinees (N = 2645).*

	age at baseline	objective health	freq. doctor's visits	year of examination
age at baseline	1			
objective health	0.19*	1		
freq. doctor's visits	0.04*	0.35*	1	
year of examination	0.07*	0.02	0.04*	1

*b. Subjects examined by g.p.'s who examined 8 subjects from their sample or less (N = 703).*

	age at baseline	objective health	freq. doctor's visits	year of examination
age at baseline	1			
objective health	0.10*	1		
freq. doctor's visits	-0.05	0.35*	1	
year of examination	-0.03*	-0.05	0.01	1

\* significant ( $p < 0.05$ )

## *II.1 Survival time in the elderly*

subjects who were examined by general practitioners who failed to examine two or more of the 10 subjects sampled from their practice. The correlation coefficients of age with objective health and of objective health with frequency of doctor's visits reflects the obvious: older elderly are less healthy and have more frequent medical treatments than younger elderly. Objective health in Table 4b shows a lesser correlation with age at baseline than in the total sample (0.10 versus 0.19). This indicates that these younger elderly are slightly less healthy and these older elderly are slightly healthier than those in the total sample. In order to understand the (significant) correlation between year of examination and frequency of doctor's visit in Table 4a, the sampling procedure has to be described in some detail. Sampling took place within each separate general practice, which was rather time consuming. Consequently, for several practices the sample was only drawn in the course of 1957. The general practitioners whose practices were sampled later, had less time to examine all elderly sampled than the general practitioners whose practices were sampled earlier. The significant correlation coefficient of 0.04 between year of examination and frequency of doctor's visit supports the hypothesis that the general practitioners who started later, were more likely to examine elderly subjects with whom they were more frequently in touch. (When the younger subjects, ages 74 and younger, are analyzed separately, this correlation coefficient rises to 0.10, indicating that this relationship particularly holds for the younger elderly. Note also the absence of the expected positive correlation between age and frequency of doctor's visits in Table 4b.) In addition, as noted earlier, the tracing of sample members up to 1983 was less successful in the younger age strata. A key role in the tracing effort was played by the examining physicians, who are likely to have had more information on the whereabouts of those subjects whom they saw more frequently. These findings further explain the observed differential selectivity in the age strata.

In summary, the total sample studied is representative of the relevant part of the population on the aspect of survival time from initial examination onward. Nevertheless, a trend in the realized probability of dying across age cohorts is apparent, declining from young to old. The survival trends over age cohorts of men and women agree to a reasonable extent.

Elsewhere [4] predictors of longevity are described, ascertained from multiple regression models with the logit of the RPD as the dependent variable. Because of the above noted relationship between age at baseline, or equivalently year of birth, and RPD, year of birth is joined as an independent variable in the regression equation.

This illustration shows how utilization of the RPD in a straightforward way reveals an unexpected age bias in the study sample that in subsequent analyses can be controlled for. With e.g. Cox' models for the analysis of survival time data, such bias would not have been revealed, because it rank orders the sample subjects in

terms of the observed survival times within the sample. The RPD, by contrast, is based on external data pertaining to the entire population to which results are intended to be generalized.

## Discussion

The operationalization of longevity is approached in various ways across follow-up studies among the elderly. The majority of studies take the approach of a direct comparison of deaths and survivors at the end of the follow-up period (e.g. [5-9]) or of a comparison of proportions of deaths (relative risks: [10,11]). Other studies approach longevity by incorporating survival time. In several of these studies, the calculation of the survival measure is based on the sample mortality in successive periods [12-18]. This approach is also (implicitly) taken in studies using the Cox proportional hazards model for the statistical analysis of failure time data (e.g. [19,20]). Again, other studies seek to compare sample mortality to population mortality during or at the end of the follow-up period [21-25].

All of the above approaches to the operationalization of longevity are based on aggregate mortality data. However, as the concept of longevity refers to an individual's length of life, a preferable approach would be to define longevity as an individual characteristic. Of this individual characteristic, then, correlates can be ascertained from individual characteristics determined in sample subjects at initial examination. Thus, rather than ranking groups of individuals, it seems more natural and accurate to rank all individuals in the sample. And, rather than basing ranks on observed mortality, it seems preferable to base ranks on realized life lengths or survival times.

A survival measure that combines relatedness to the concept of individual longevity with comparability to population survival — like the realized probability of dying described in this article — is introduced by Palmore [26] as the “longevity quotient” (LQ), defined as:

$$LQ = \frac{n + e(\text{follow-up})}{e(\text{initial examination})}$$

where:  $n$  = number of years survived after initial examination

$e(t)$  = life expectancy at time  $t$ , with  $e(\text{follow-up}) = 0$

when the follow-up period exceeds  $n$ .

This measure utilizes population life expectancy data for two purposes: to relate the survival time of the sample individuals to that of the population based on year of birth and sex (denominator), and to estimate the remaining survival time of those individuals still alive at the end of the study (numerator). The longevity quotient allows comparison between individuals of different ages, because it is standardized for remaining life expectancy at first examination, based on population data according to year of birth and sex.

Up to this respect, the longevity quotient and the realized probability of dying are similar. There are several differences however, that become especially apparent in studies of the elderly.

First, for the LQ, the remaining life expectancy is usually based on the probabilities of death of the older birth cohorts of a cross-section of the population in the year of initial examination. Changes in the probabilities of death reflecting the development of mortality after this year are not considered. On the other hand, in the calculation of the RPD any possible changes in the probabilities of death over the successive years are taken into account. This is especially important in the period under consideration, in which the probabilities of death of elderly persons (c.q. their remaining life expectancies) are subject to relatively large declines (cf. Table 1). As a consequence, because the life expectancy in the denominator is underestimated, the LQ for older cohorts increases too steeply. This causes differences between survival times of older subjects to be overemphasized as compared to those of younger subjects.

While this difference between LQ and RPD may be overcome by calculating the remaining life expectancy for the LQ based on the probabilities of death in the successive years constituting the follow-up period, the second difference is more fundamental. This difference pertains to the shape of the curve representing the trend of the survival measure over time. In the case of the LQ, this curve is linear: for each cohort and sex, the increment in survival time is always one year divided by the same denominator. The RPD, by contrast, is S-shaped (cf. Fig. 1). This is especially true for older cohorts. Even so, for the Netherlands, for the cohort aged 65 in 1956 a full S-shape is apparent within the follow-up period of 28 years. In the near-horizontal parts of the curve, then, the sensitivity to differences in survival time is small. Thus, persons surviving a very short or a very long time exert less influence on the results. By contrast, the LQ assigns equal weight to extreme and average survival times, which will cause the persons with extreme survival times to exert more influence on the results. When, for instance, the follow-up time is relatively short compared to the life span of the sample, this will mean that the relatively short lived persons determine most of the study outcome. The researcher can choose to compensate for this by an appropriate transformation.

A third difference between LQ and RPD concerns the treatment of censored observations. While for the LQ the survival time after the last follow-up date is estimated by the life expectancy at the age at last follow-up, necessarily based on cross-sectional probabilities of death at last follow-up, for the RPD it is estimated by the value corresponding to the median survival time of the population alive at any moment in time. The latter approach is preferable, because of its independence of follow-up time. As long as the mortality rates are decreasing over time, the survival time of censored persons estimated with the LQ will be lower than the survival time that would be observed when the sample has died off

completely. This amounts to a reduction of the sensitivity of the LQ in the ranges corresponding with relatively long survival times. This is especially true for those cohorts in which the mortality rates decrease most rapidly — which at present are the older cohorts. Depending on the number of censored observations, this lesser sensitivity of the LQ will be “compensated” by its overemphasis on extreme survival times as discussed in the previous paragraph.

In conclusion, RPD and LQ, being similar in concept, are also similar in operationalization — provided that the LQ is calculated more elaborately than has been the case until now. However, as some laboriousness seems inevitable, the RPD involves a slightly more straightforward and accurate procedure.

A last remark concerns the close relation between the choice of the survival measure and the statistical method to ascertain predictors of longevity. In order to enable an evaluation of predictors in terms of their relative importance, multivariate methods of analysis are required. However, the majority of longevity studies until recently do not employ such methods. This may be due for a large part to the choice of survival measure. With a dichotomous survival measure (for instance, dead versus alive), a multivariate statistical analysis is confined to discriminant analysis with usually the requirement of continuity of discriminating variables, or logistic regression analysis, which technique has been accessible only fairly recently.

When the survival measure is based on sample mortality in successive intervals of the follow-up period (e.g. the survival time in years), Cox models for the statistical analysis of survival times may be used. At least in some well-known standard computer packages however, the number of variables to be involved in these models is restricted. With a continuous survival measure (e.g. the proportion of observed and expected deaths, the survival time itself, the LQ or the RPD), older and more well-known statistical techniques can be applied, like analysis of variance or multiple regression analysis. Considering the multiplicity of factors related to longevity, and the importance of retaining as much information in the survival measure itself as possible, thus embarking upon a continuous measure of survival time, these last techniques provide better models in which to ascertain predictors of longevity.

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## Appendix

It is assumed that the researcher knows only the calendar year of death of the sample subjects. The last factor in the RPD, then, depends on the time of death in the  $n$ th life year within the calendar year of death. Because the probability of surviving this year is equivalent to a survival function exponential in time to death  $t$ :

$$P(T > t) = S(t) = \exp[-H(t)],$$

the last factor in the RPD depends exponentially on  $t$ , while the unit of  $t$  remains one year. Suppose within this one year the distribution of the time to death  $t$  can be expressed as a function of a "hazard"  $a$  as follows [2]:

$$P(T < t) = 1 - S(t) = 1 - \exp(-at).$$

The hazard  $a$  is equivalent to the age- and sex-specific mortality rate, which is assumed to be constant in the year considered. When  $a$  is small,<sup>4</sup> it follows by Taylor-expansion that:

$$P(T < t) = at.$$

---

<sup>4</sup> In high ages,  $a$  is not "small". Monte Carlo experiments showed, however, that even for  $a = 0.5$  the average time until death is of the same magnitude as for smaller  $a$  (approximately 0.3)

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The calculation follows either of two possibilities:

#### a. death in the calendar year of intake.

The average time until death, given initial examination on time  $s$ , is

$$E(u|s) = \frac{1-s}{2}$$

in which  $u = t - s$ .

Persons examined early in the year have a higher chance of dying in this year than persons examined late in the year. So for all persons dying in this year, the average time until death is

$$E \frac{\int_0^1 a(1-s)E(u|s)ds}{\int_0^1 a(1-s)ds} = 1/3.$$

Thus, death takes place on the average 1/3 year after initial examination. The realized probability of dying is:

$$RPD = (1 - d_1^{(b,s)})^{1/3}.$$

#### b. death in a later calendar year.

We assume the subject has lived through the first part of the  $(n-1)$ th life year (probability:  $(1 - d_{n-1})/2$ ). There are two possibilities to be considered:

- (1) death before birthday (life year  $(n-1)$ ),
- (2) death after birthday (life year  $n$ ).

(1) The average time until death, given death before birthday on  $s$ , is:

$$E(t|s) = \frac{s}{2}.$$

Now, the later in the year the birthday takes place, the higher are the chances of dying before the birthday:

$$t_{(1)} = \frac{\int_0^1 s \cdot 1/2s ds}{\int_0^1 s ds} = 1/3.$$

As the average birthday is assumed to take place halfway the calendar year,  $t_{(1)}$  applies to the second half of the  $(n-1)$ th life year, and the contribution to the RPD becomes:

$$((1 - d_{n-1}^{(b,s)})^{1/2})^{1/3}$$

(2) The average time until death following birthday on  $s$ , given death after birthday, is (analogously to a.):

$$t_{(2)} = \frac{\int_0^1 a(1-s) \cdot 1/2(1-s)ds}{\int_0^1 a(1-s)ds} = 1/3.$$

Applying  $t_{(2)}$  to the first half of the  $n$ th life year, the contribution to the RPD becomes:

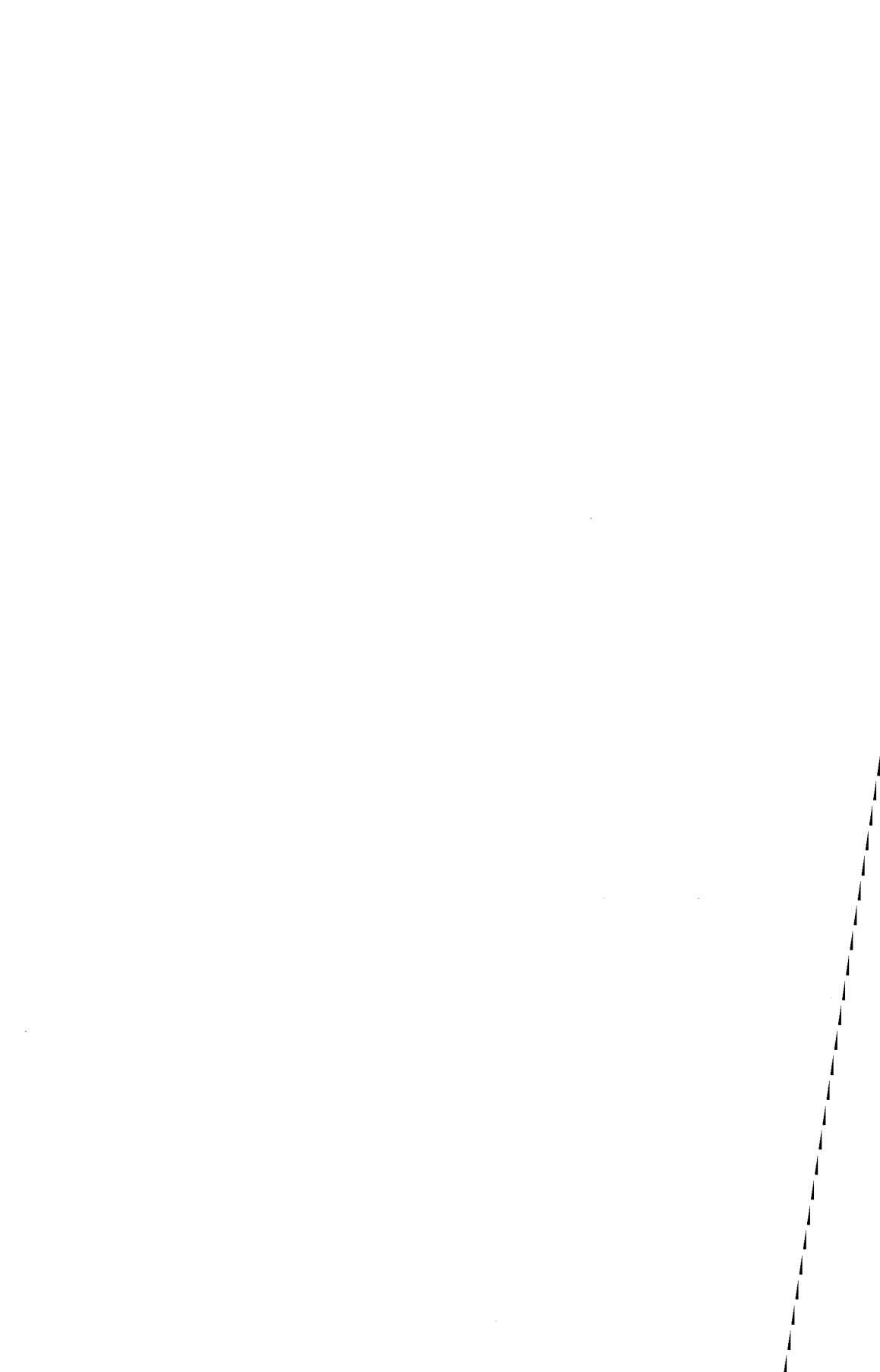
$$((1 - d_{n-1}^{(b,s)})^{1/2} \cdot (1 - d_n^{(b,s)})^{1/2})^{1/3}.$$

The contribution of both (1) and (2) to the RPD is:

$$(1 - d_{n-1}^{(b,s)})^{1/3} \cdot (1 - d_n^{(b,s)})^{1/6}.$$

The full realized probability of dying in the  $n$ th calendar year following the initial examination becomes:

$$\text{RPD} = (1 - d_1^{(b,s)})(1 - d_{n-2}^{(b,s)})(1 - d_{n-1}^{(b,s)})(1 - d_n^{(b,s)})^{1/6}.$$



## II.2

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# MEDICAL AND SOCIAL PREDICTORS OF LONGEVITY IN THE ELDERLY: TOTAL PREDICTIVE VALUE AND INTERDEPENDENCE

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## Abstract

In the Dutch Longitudinal Study among the Elderly, a probability sample of 3149 persons from the population of the Netherlands, initial ages 65-99 years, was followed from 1955-1957 for 28 years. Vital status was determined in 1983 for 84% of the original sample. Multivariate regression models were used to predict the Realized Probability of Dying (RPD), a measure of longevity based on actual survival time, sex and age at baseline. Predictor variables included physical, mental and social indicators of health status. The total variance explained was 20.2%. Objective health (rated by the examining physician) showed the strongest relationship with the RPD. Upon removing objective health from the model, 19.5% of the variance remained explained. Separate analyses were performed for (1) bio-medical, physical and mental examination variables, (2) disability and health care use variables, and (3) social and psychological variables; in each case the variance explained was over 11%, demonstrating considerable interdependence among predictors. Across different regression models, bio-medical and disability variables proved to be the most stable predictors of longevity.

### *Key words*

aged / longevity / physical health / health behavior / psycho-social health / predictive ability

## Introduction

Over the past years, the number of studies reporting factors related to longevity in the elderly has greatly increased. An extensive review up until 1982 is published by Lehr [1]. Numerous studies have followed, most of them focusing on a certain factor or group of factors. However, the question of how well these factors explain longevity has hardly been addressed. In 1978 Botwinick et al. [2], following Riegel et al. [3], suggested that in the elderly in contrast to younger persons no accurate prediction of survival is possible. While both Botwinick and Riegel mainly dealt with prediction of longevity from cognitive performance, the same question about accuracy may be asked concerning other frequently reported predictors of longevity in the elderly.

The issue of accuracy implies in the first place predictive ability, or variance explained. In most studies, the amount of variance explained in longevity is not encouraging. Second, the issue of accuracy involves uniqueness of a reported predictor. Does a factor reported to be related to longevity contribute a direct effect on longevity that no other factor contributes, or does it just indicate the effect of other, associated factors that work through the factor considered? Empirical survey studies can help to determine the independent effect of a predictor, but cannot provide an ultimately satisfactory answer to the issue of whether the effect of a factor is direct or indirect. However, within the framework of an empirical survey it is possible to investigate to what extent various predictors of longevity are interchangeable and how they are interdependent.

The type of empirical survey ideally suited to the study of the issues of predictive value and interdependence of correlates of longevity in the elderly combines the following characteristics. First, the sample should be sufficiently large and non-selective, such that the results are optimally comparable to results of other studies dealing with correlates of longevity. Second, the sample subjects should be followed up until death, such that exact survival information can be obtained, optimizing the predictive ability of factors related to longevity. Third, the baseline data should cover a wide range of physical and non-physical aspects of health, such that predictors of longevity can be optimally studied in terms of their relative importance.

This study draws on data that essentially have the qualifications of a large sample size, a satisfactory representativeness, a follow-up period sufficiently long for 99% of the sample to have died, and the availability of physical as well as mental and social baseline data. Sampling, design and organization are described in detail in order to allow evaluation of their potential impact on the study's results.

## Material

As has been described in more detail elsewhere [4], the Dutch Longitudinal Study among the Elderly is based on a national probability sample of 3149 persons aged 65 and over, stratified according to sex and age (65-69, 70-74, 75-79, 80-99 years) such that strata of approximately equal size were obtained. Initial examinations took place from 1955 to 1957, until it was judged that the number of subjects examined was sufficient for statistical evaluation of the results.

The elderly subjects were randomly selected from the practices of 374 family physicians who had volunteered to collaborate in the study by examining 10 patients each. The collaborating physicians, 9% of all Dutch family physicians at the time, responded to a recruiting advertisement in two weekly journals for health professionals. From lists of all persons over 65 belonging to their practice, a probability sample was drawn within each practice [4].

By mail and in regional meetings the physicians were instructed how to use the questionnaire and how to carry out the physical examination. In this way, inter-observer variability was expected to be reduced. However, no procedures were devised to assess inter-observer variability. One examination took 2-3 hours, which — so as to minimize the burden on both elderly subject and physician — could be spread out over 2 or 3 sessions.

Of the subjects sampled, 2% had already died when approached for examination and 2.5% refused to take part in the examination. Another 2% could not be reached for reasons of a change in residence, a change in physician, etc. As a consequence of the method of recruiting subjects through family physicians, those elderly residing in nursing homes and hospitals were not covered by the study when they were no longer the responsibility of a family physician. Their percentage is estimated to be 3%.

The representativeness of the final sample was checked according to province, income, religion and marital status and proved to be satisfactory [4]. The bias with respect to health status and longevity which might be introduced by the method of subject selection is discussed with the presentation of results below.

In 1960, it was decided to carry out an identical follow-up study. From then on until 1975, six such studies were carried out on the traceable, surviving subjects. Several results of this longitudinal study are reported elsewhere [5,6]. In 1983, vital status and causes of death were ascertained of 84% of the sample. The 16% lost-to-follow-up can be attributed to factors unrelated to health status of the subjects, like physicians giving up their practice or withdrawing their participation in the study. When an elderly subject changed residence, the new physician was not always found willing to continue the examination. These factors were compounded by an imperfect administration. Of the 2645 persons traced in 1983, 2617



had died with known date of death, while 28 were known to be alive. These 2645 persons constitute the current study sample.

The examination consisted of a questionnaire to be filled out by the physician, covering nine fields with a total of 204 variables. For convenience, they are grouped into three summarizing categories (Table 1): the physical and mental variables are referred to as *symptoms* {I}, the health related variables are referred to as *indicators* {II}, and the social and psychological variables are referred to as *co-factors* {III}.

**Table 1. Nine fields representing aspects of health status covered by the questionnaire.**

group name	field
{I} Symptoms	{1} medical history
	{2} anthropometric and biomedical data
	{3} physical examination data
	{4} memory test
{II} Indicators	{5} activities of daily living (ADL), recreational activity, work ("activity")
	{6} health care use
{III} Co-factors	{7} socio-demographic data
	{8} family history
	{9} use of leisure time, adaptation, attitude toward aging ("psycho-social data")

This broad range of variables was in agreement with the initial objective to describe the health status of the elderly and social and psychological factors related to it [4]. Two variables which assess overall health status were included: *objective health* (the physician's rating of the subject's health) in field {3}, and two indicators of *subjective health* (the subject's answers to the questions: "Do you feel healthy?" and "How is your present health?") in fields {1} and {9} respectively.

## Method

The study sample is characterized by a large age range (in excess of three decades) and a long follow-up period at the end of which only 1% of subjects was still alive. The long follow-up period implies that using mortality-at-follow-up as an operational definition of longevity does not differentiate among the 99% of decedents. An operational definition based on survival time is therefore preferable. Since expected survival time decreases with increasing age, the age composition of the sample confounds the relationship between baseline characteristics and longevity. The same confounding results from the sex composition of the sample, since women have a greater life expectancy than men. The relationship between baseline characteristics and longevity should therefore be studied while controlling for age and sex. A further concern is that sample selectivity for reasons other than the age and sex composition may confound the relationship studied. To check the extent of such selectivity, the survival time in the sample should be compared to that in the general population.

To meet these concerns, the concept of longevity is expressed as the Realized Probability of Dying (RPD), a function of survival time, sex and age at baseline [7]. The RPD compares each individual subject's survival time with the survival time of those peers in the total population who have the same age and sex and who were still alive at the baseline examination. Possible values of the Realized Probability of Dying are between 0 and 1. The value of an individual's RPD is 0.7, if at the time of his or her death 70% of his or her cohort is still alive. These values introduce a rank order among all sample subjects corresponding to age and sex controlled survival time.

If the RPD is uniformly distributed on the interval (0,1), the survival distribution of the sample represents that of the total population. For the sample used in our study, the RPD is indeed uniformly distributed. Therefore, the logit of the RPD (LRPD) is approximately normally distributed with mean 0. The LRPD is used as the dependent variable in regression analysis, the main analytical method in this study.

The data analysis is carried out in two steps:

1. selection of a set of independent variables for further analysis;
2. multivariate evaluation of the association of these variables with the LRPD.

In step 1, within each of the nine fields, the main predictors of the LRPD are calculated by forward stepwise regression analysis. Those variables with more than two categories are recoded such that the categories obtain a rank order according to a monotonically increasing or decreasing expected impact on longevity. To provide for possible non-linear relationships, both the linear and the quadratic term of each independent variable with more than two categories is included. Only

variables adding significantly ( $p < 0.05$ ) to the variance explained in each field are retained for analysis step 2.

Missing values in the physical variables and indicators occur in less than 1% of the cases (exception: blood sedimentation rate in 11% of the cases), and in the memory test and psycho-social data in 1-9% of the cases. Questions related to the latter variables were asked at the end of the questionnaire. A number of physicians did not administer this part of the examination for lack of time. In order to retain a maximum number of cases in the multivariate models, the mean is substituted for missing values.

The resulting list of predictors is modified in four ways. First, variables which do not have a significant univariate association with the LRPD are removed. Second, the two variables indicating subjective health are summed to one variable and grouped with {9}. Third, in the fields {3} and {9} up to four variables are added based on their strong univariate associations with the LRPD. Fourth, in fields {4} and {5} some variables are added that represent different aspects of memory test and ADL, according to factor analysis and insights of the investigators. The resulting list of 43 variables is shown in Table 2, together with their directionality and the sign of their association with the RPD.

In step 2 of the data analysis, all variables selected are entered as independent variables in forward stepwise regression analysis with the LRPD as the dependent variable. Those independent variables adding significantly to the variance explained are reported as independent predictors. For an understanding of the relative importance of the significant predictors, both their zero-order correlations with the LRPD and their standardized regression coefficients are reported. In order to examine possible overlap, the three groups of independent variables (symptoms, indicators, and co-factors) are evaluated separately by comparing the variances explained by each group of variables with the variance explained by all variables. In three regression models, each including all variables from one group, those variables having significant regression coefficients are ascertained. The same three models are used in further analyses, in which the stability of the regression coefficients in one group is examined after variables of the two other groups have been added in a forward stepwise fashion. These analyses yield information with respect to the interdependence of predictor variables from different groups.

## Results

The total variance explained in the LRPD is 20.2% (Table 3). It is apparent that physical, mental and behavioral indicators of health as well as social and psychological characteristics have some independent effect on longevity. The main predictor of longevity turns out to be objective health. By itself, it explains 9,5%

**Table 2. Predictors of longevity in the elderly. Results of first selection within nine fields and univariate association with longevity.**

variable	directionality	association with LRPD
<b>{I} Symptoms</b>		
<b>{1} medical history</b>		
present heart complaints	none — severe	+
<b>{2} anthropometric and bio-medical data</b>		
sitting height	as given	-
erythrocyte sedimentation rate	as given	+
<b>{3} physical examination</b>		
objective health	good — poor	+
abnormalities of breasts	none — severe	+
abnormalities of heart and major blood vessels at percussion	none — severe	+
systolic murmur	none — clear	+
dyspnea	none — w/o exertion	+
<b>{4} memory test</b>		
personal orientation	poor — good	-
time orientation	poor — good	-
general orientation	poor — good	-
logical memory	poor — good	-
auditive and visual memory	poor — good	-
total memory test score	poor — good	-
<b>{II} Indicators</b>		
<b>{5} activity</b>		
cooking disability	none — needs help	+
shopping disability	none — needs help	+
money handling disability	none — needs help	+
instrumental disability	none — severe	+
ADL disability	none — severe	+
total disability through leg or arm complaints	none — severe	+
total disability through shortness of breath or heart complaints	none — severe	+
total disability through general weakness	none — severe	+
recreational activity	passive — active	-
continued working	no — vigorous	-

(table 2 — continued)

variable	directionality	association with LRPD
<i>{6} health care use</i>		
time since last medical treatment	short — long	-
regular medical treatment	no — yes	+
health care use for cardiovascular and kidney disease	none — frequent	+
health care use for cancer	none — frequent	+
drug use	none — more than one	+
<i>{III} Co-factors</i>		
<i>{7} socio-demographic data</i>		
present income	low — high	-
evaluation of present income in comparison to age 60	low — high	-
year of birth	as given	
living arrangement	indep. — dependent	+
<i>{8} family history</i>		
mother alive	yes — no	-
age at death of mother	as given	-
health status of spouse	good — poor	-
<i>{9} psycho-social data</i>		
subjective health	good — poor	+
evaluation of living arrangement with children	positive — negative	+
contact with children	none — good	-
self-perceived health decline	no — yes	+
perceived value of present life	negative — positive	-
self-perceived problems related to aging	yes — no	-
evaluation of present society in comparison with before	better — worse	+

of the variance in the LRPD. Interestingly, subjective health is not selected in the multivariate model that includes objective health. Further predictors are the symptoms: dyspnea, erythrocyte sedimentation rate, abnormalities of heart and large blood vessels, systolic murmur, and total memory test score. Some of these symptoms are related to heart disease, others are not associated with one specific disease. In addition, several indicators of health contribute to the prediction of longevity: instrumental disability, continued working, regular medical treatment,

health care use for cancer, and health care use for cardiovascular and kidney disease. Although their independent predictive ability is slightly less, several co-factors are also predictive of longevity: evaluation of present income in comparison to age 60, self-perceived problems related to aging, perceived value of present life, and mother alive. The direction of the effect of these predictors is generally in accordance with expectation: the worse the condition (greater dyspnea, poorer achievement on memory test, more health care use, etc.) the higher the LRPD or the shorter the longevity.

There are two exceptions. First, the year of birth shows an unexpected, independent positive association with the LRPD: the younger the subject, the more likely he or she is to die relatively early. Since the calculation of the LRPD is based on year of birth, such a relationship should not exist if the sample were fully representative of the population as to survival time. However, as has been noted elsewhere [7], the sample is likely to have a slight overrepresentation of less-than-average healthy elderly among the younger, and a slight overrepresentation of more-than-average healthy elderly among the older subjects. The latter overrepresentation is partly a consequence of the sampling method noted above: because all subjects belonged to the practices of family physicians, and not all nursing homes were covered by family physicians, elderly living in nursing homes may be underrepresented in the sample. This bias will be more noticeable in the oldest age groups. Also, the selection noted may be due to a certain preference among the examining physicians to first examine the more healthy old-elderly (for them the examination would be less of a burden) as well as the less healthy young-elderly (with them, a regular contact existed already). One-third of the physicians were not able to examine all 10 elderly in their sample before the closing date of the study (September 1957) [7].

A second unexpected relation in Table 3 is shown by the variable *mother alive*: a still living mother appears to have an inverse relation with the elderly child's longevity. More detailed analyses focusing on those whose mother is still alive at baseline, reveal that a chance combination of other factors indicating poor health is present in the majority of these subjects. This chance combination is likely to overshadow a possible association due to a positive heredity effect.

The predominance of the role of objective health in the prediction of longevity is further investigated by comparing the above results to the results from a regression model without this variable. Now, still 19.5% instead of 20.2% of the variance is explained, while in addition to the variables of the earlier model, subjective health enters into the regression equation. Thus, the objective health rating by the physician does not contain much more information than is already contained in the other variables selected for multivariate analysis. Indeed, 50.9% of the variance of objective health is explained by subjective health on the one hand and many of the symptoms and indicators listed in Table 3 on the other hand.

**Table 3. Independent predictors of longevity (LRPD<sup>¶</sup>) from stepwise, multiple regression analysis on the 43 variables from table 2, including and excluding objective health (OH): zero-order correlations (r), standardized regression coefficients (beta), and total variance explained. Only variables with significant ( $p < 0.05$ ) beta are listed.**

variable <sup>†</sup>	r	including OH beta	excluding OH beta
<b>{I} Symptoms</b>			
objective health (q)	0.31	0.11	—
dyspnea (l)	0.25	0.11	0.12
sedimentation rate (l)	0.16	0.08	0.09
abnormalities heart (l)	0.17	0.06	0.07
systolic murmur (q)	0.14	0.04	0.04
total memory test score (l)	-0.15	-0.28	-0.32
(q)	-0.13	0.17	0.20
<b>{II} Indicators</b>			
instrumental disability (l)	0.23	0.07	0.09
continued working (l)	-0.15	-0.24	-0.25
(q)	-0.13	0.20	0.20
regular medical treatment	0.23	0.07	0.07
health care use cancer (l)	0.09	0.06	0.06
health care use CVD (l)	0.18	0.04	0.04
<b>{III} Co-factors</b>			
evaluation of income (q)	-0.08	-0.05	-0.05
subjective health (l)	0.25	—	0.05
perceived problems aging (l)	-0.16	-0.07	-0.07
value present life (q)	-0.10	-0.05	-0.05
mother alive	-0.06	-0.05	-0.05
year of birth (q)	0.06	0.23	0.23
total variance explained:		20.2% (including OH)	19.5% (excluding OH)

<sup>¶</sup> Logit of the realized probability of dying.

<sup>†</sup> The letter in brackets following the variable name indicates whether the linear (l) or the quadratic (q) term of the variable is entered into the regression equation. When both linear and quadratic terms are entered, the two corresponding zero-order correlation and regression coefficients are given.

II.2 Predictive value and interdependence

**Table 4. Predictive value of symptoms {I} before and after entering indicators and co-factors {II and III} into the regression equation<sup>¶</sup>: standardized regression coefficients (betas) and variance explained.**

variable	beta-before		beta-after	
	linear	quadratic	linear	quadratic
<b>{I} Symptoms</b>				
present heart complaints	0.04	0.08*	n.s.	n.s.
sitting height	0.13	-0.08	n.s.	n.s.
sedimentation rate	0.10*	0.01	0.09	n.s.
abnormalities breasts	-0.15	0.20	n.s.	n.s.
abnormalities heart	0.15	-0.07	0.07	n.s.
systolic murmur	0.03	0.02	0.05	n.s.
dyspnea	-0.00	0.15	n.s.	0.12
personal orientation	-0.08	0.01	-0.05	n.s.
time orientation	-0.06	0.00	n.s.	n.s.
general orientation	-0.00	0.01	n.s.	n.s.
logical memory	0.01	-0.01	n.s.	n.s.
auditive & visual memory	-0.07	0.06	n.s.	n.s.
total memory test score	-0.06	0.04	-0.10	n.s.
<b>{II} Indicators</b>				
instrumental disability	—	—	0.09	n.s.
continued working	—	—	-0.26	0.21
regular medical treatment	—	—	0.07	
health care use cancer	—	—	0.05	n.s.
health care use CVD	—	—	0.04	n.s.
<b>{III} Co-factors</b>				
evaluation of income	—	—	n.s.	-0.05
self-perceived health decline	—	—	0.27	-0.22
perceived problems aging	—	—	-0.07	n.s.
value present life	—	—	n.s.	-0.05
mother alive	—	—	-0.05	
year of birth	—	—	0.24	n.s.

variance explained: 11.7% (before) 19.8% (after)

<sup>¶</sup> All symptoms {I} are entered into the regression equation, yielding beta's-before for both linear and quadratic terms. Next, indicators {II} and co-factors {III} are added in a stepwise fashion, provided the beta-after of their linear or quadratic term is significant ( $p < 0.05$ ). In this stage, linear and quadratic terms of symptoms {I} are allowed to drop out if their beta-after is not significant. Variables of {II} and {III} with beta-after of neither linear nor quadratic term significant are not listed.

\* Significant ( $p < 0.05$ ).



**Table 5. Predictive value of indicators {II} before and after entering symptoms and co-factors {I and III} into the regression equation<sup>†</sup>: standardized regression coefficients (betas) and variance explained.**

variable	beta-before		beta-after	
	linear	quadratic	linear	quadratic
<b>{II} Indicators</b>				
cooking disability	-0.04	0.03	n.s.	n.s.
shopping disability	0.01	-0.03	n.s.	n.s.
money handling disability	0.01	0.01	n.s.	n.s.
instrumental disability	0.13†	-0.00	0.09	n.s.
ADL disability	0.00	0.12	n.s.	n.s.
total disability through leg or arm	-0.14	0.07	n.s.	n.s.
total disability through heart	0.07	-0.06	n.s.	n.s.
total disability through weakness	0.00	-0.01	n.s.	n.s.
recreational activity	-0.08	0.06	n.s.	n.s.
continued working	-0.25*	0.20*	-0.25	0.21
time since last medical treatment	-0.07	0.01	n.s.	n.s.
regular medical treatment	0.08*		0.05	
health care use cancer	0.21	-0.05	0.06	n.s.
health care use CVD	0.07	0.01	n.s.	n.s.
drug use	0.01	0.01	n.s.	n.s.
<b>{I} Symptoms</b>				
dyspnea	—	—	0.11	n.s.
sedimentation rate	—	—	0.08	n.s.
abnormalities heart	—	—	0.07	n.s.
systolic murmur	—	—	n.s.	0.04
total memory test score	—	—	-0.29	0.17
<b>{III} Co-factors</b>				
evaluation of income	—	—	n.s.	-0.05
self-perceived health decline	—	—	0.27	-0.22
perceived problems aging	—	—	-0.06	n.s.
value present life	—	—	n.s.	-0.05
mother alive	—	—	-0.05	
year of birth	—	—	0.24	n.s.
variance explained: 11.5% (before) 19.9% (after)				

<sup>†</sup> All indicators {II} are entered into the regression equation, yielding beta's-before for both linear and quadratic terms. Next, symptoms {I} and co-factors {III} are added in a stepwise fashion, provided the beta-after of their linear or quadratic term is significant ( $p < 0.05$ ). In this stage, linear and quadratic terms of indicators {II} are allowed to drop out if their beta-after is not significant. Variables of {I} and {III} with beta-after of neither linear nor quadratic term significant are not listed.

\* Significant ( $p < 0.05$ ). † Borderline significant ( $0.05 < p < 0.10$ ).

## *II.2 Predictive value and interdependence*

Co-factors other than subjective health do not show independent relationships with objective health.

Independence and stability of symptoms, indicators and co-factors in predicting longevity are further evaluated in three regression models. These analyses are performed without the variable objective health. In each regression model, all variables of one group are forced into the regression equation (top half Tables 4, 5 and 6). It turns out that the variance explained by each of the three groups of variables hardly differs in magnitude: symptoms, indicators and co-factors explain 11.7%, 11.5% and 11.2% of the variance respectively. Furthermore, each set of variables can be seen to explain more than half of the total variance explained (= 19.5%). This indicates both an independent contribution and a considerable interchangeability among the three sets with regard to the prediction of longevity.

A closer look at the symptoms (top half Table 4), reveals that present heart complaints and blood sedimentation rate have a significant, independent contribution to the prediction of the LRPD when indicators and co-factors are left out of the model. When indicators and co-factors are added to the regression equation in a forward, stepwise manner while the variables that were forced into the equation are allowed to drop out (bottom half Table 4), the results should approach Table 3. Indeed, the symptom present heart complaints drops from the equation, while the symptoms that were predictive in Table 3 become significant. However, personal orientation, an aspect of the memory test, also becomes significant, while of the total memory test score the quadratic term drops from the model. Newly included is the co-factor self-perceived health decline, which, apparently, substitutes for subjective health (zero-order correlation between both predictor variables: 0.56).

From the indicator variables alone (top half Table 5), continued working and regular medical treatment contribute significantly and independently to the prediction of the LRPD, while instrumental disability does so with marginal significance. After adding symptoms and co-factors (bottom half Table 5), again the result should approach Table 3. This appears true, except that health care use for cardiovascular and kidney disease is not included in the model, while self-perceived health decline, again, is entered into the model.

The significant, independent predictors among the co-factors alone (top half Table 6) are year of birth, self-perceived health decline, mother alive and age at death of mother. Value of present life contributes with marginal significance. When symptoms and indicators are added to the regression equation (bottom half Table 6), the same predictors are selected as in Table 3, except health care use for cardiovascular and kidney disease. In addition to self-perceived health decline, age at death of mother stays in the regression equation, although this is not an independent predictor in Table 3.

**Table 6. Predictive value of co-factors {III} before and after entering symptoms and indicators {I and II} into the regression equation<sup>†</sup>: standardized regression coefficients (betas) and variance explained.**

variable	beta-before		beta-after	
	linear	quadratic	linear	quadratic
<b>{III} Co-factors</b>				
present income	-0.10	0.07	n.s.	n.s.
evaluation of income	0.08	-0.12	n.s.	-0.05
year of birth	0.12*	0.01	0.24	n.s.
living arrangement	0.00	0.06	n.s.	n.s.
mother alive	-0.07*		-0.06	
age at death of mother	0.39*	-0.41*	0.31	-0.32
health status of spouse	-0.17	0.12	n.s.	n.s.
evaluation living with	-0.14	0.12	n.s.	n.s.
contact with children	0.10	-0.13	n.s.	n.s.
subjective health	0.13	0.02	n.s.	n.s.
self-perceived health decline	0.46*	-0.39*	0.30	-0.25
value of present life	0.03	-0.10†	n.s.	-0.05
perceived problems aging	-0.14	0.05	-0.07	n.s.
evaluation of present society	0.32	-0.29	n.s.	n.s.
<b>{I} Symptoms</b>				
dyspnea	—	—	n.s.	0.12
sedimentation rate	—	—	0.08	n.s.
abnormalities heart	—	—	0.07	n.s.
systolic murmur	—	—	n.s.	0.05
total memory test score	—	—	-0.32	0.20
<b>{II} Indicators</b>				
instrumental disability	—	—	0.09	n.s.
continued working	—	—	-0.25	0.20
regular medical treatment	—	—	0.09	
health care use cancer	—	—	0.06	n.s.

variance explained: 11.2% (before) 20.1% (after)

<sup>†</sup> All co-factors {III} are entered into the regression equation, yielding beta's-before for both linear and quadratic terms. Next, symptoms {I} and indicators {II} are added in a stepwise fashion, provided the beta-after of their linear or quadratic term is significant ( $p < 0.05$ ). In this stage, linear and quadratic terms of co-factors {III} are allowed to drop out if their beta-after is not significant. Variables of {I} and {II} with beta-after of neither linear nor quadratic term significant are not listed.

\* Significant ( $p < 0.05$ ). † Borderline significant ( $0.05 < p < 0.10$ ).

In summary, in spite of the rather low percentage of total variance explained, a considerable interchangeability of symptoms, indicators and co-factors regarding predictive value for longevity can be noted. Neither of the three groups of predictors has more explanatory power than any other group. Of the symptoms, the bio-medical variable in Table 3 turns out to be the most stable predictor. Physical examination, medical history and memory test variables show some dependence on the particular regression model used (*context dependence*). Of the indicators, those predictors pertaining to activity/disability in Table 3 are stable, but health care use shows some context dependence. The co-factors also show context dependence: subjective health and self-perceived health decline interchange, and age of mother at death is included only when it is forced into the model in the first regression step. Nevertheless, those co-factors that are predictors in Table 3 are found in each of the three final regression equations.

## Discussion

In this report, physical, mental as well as social variables were shown to be related to longevity in the elderly after 28 years of follow-up. Each individual's longevity was operationally defined as a percentile of the survival distribution of the population according to sex and age at baseline. An attempt was made to ascertain the independent contribution of each of three groups of variables to the prediction of longevity, namely symptoms of illness, indicators of health and social and psychological co-factors.

The total amount of variance explained by predictors from these three groups was 20.2%. This amount is comparable to findings in other studies among elderly [2,8-14]. Nonetheless, it may be questioned what has been the increase in knowledge about longevity and its predictors, when almost 80% of variance remains unexplained. From a methodological point of view, this result is not satisfactory, since design and method of this study combine several qualifications that warrant the expectation of valid results with a maximum of variance explained: a large and non-selective sample, a long follow-up time, information on physical as well as non-physical aspects of health to be evaluated with multivariate methods, and an operational definition of longevity ensuring the maximum use of information available.

A first issue to be considered in connection with the rather small amount of variance explained is whether the information available at baseline is pertinent to the prediction of longevity. As stated earlier, the original objective of the baseline study was to describe the health status of the elderly in a broad sense. The decision to use these data to predict longevity is of a much later date. Conditions and impairments leading to disability are not necessarily related to mortality [15,16].

For example, whereas cancer may not have a great impact on disability, it ranks among the most frequent causes of death. In contrast, whereas locomotive disorders such as arthritis, and sensory impairments are clearly disabling, they are not found among common causes of death. This study's baseline information included extensive data on the latter conditions and only indirect data on cancer.

Furthermore, for practical reasons information based on relatively intrusive examinations or time-consuming interviews was not collected, such as more extensive blood analyses, electrocardiograms, nutritional information, and social network characteristics. Other studies have provided evidence of the predictive ability of such information for longevity [14,17-22].

Some further loss in variance explained may have occurred due to choices in organization, design, and analysis. First, many observers were involved in the data collection. Although no assessment is available of inter-observer variation, there is reason to assume that it is non-negligible. The "noise" that is thus introduced, is likely to decrease the variance explained.

Second, a non-negligible amount of missing values occurred in some mental and social variables (1-9%, compared to less than 1% on the physical variables). The method followed in dealing with these — mean substitution — does retain the largest possible number of subjects for analysis, but reduces the variance of the variables and thus their predictive power.

Third, improvement may be possible on the ordering of the categories of the variables. Since these were originally designed for a cross-sectional, descriptive study, recoding of the categories was needed such that they were ordered according to expected association with survival time. Because in many instances knowledge of the relative effects of specific categories was lacking, the order decided upon may not always have resulted in a linear or quadratic relationship with longevity. By consequence, loss in variance explained may have occurred.

Fourth, the RPD refers to an external standard of mortality (i.e. population mortality). In comparison, a measure of survival which refers to the internal mortality of the sample only, may produce larger predicted effects. Such a measure, however, does not have the advantages associated with the RPD of detecting the presence of a mortality bias in the sample, and of achieving a "natural" ordering between the sample subjects — i.e. according to the deviation of their actual mortality from the population mortality.

In comparison to some other studies of predictors of longevity, this study will inevitably produce a lower variance explained for two further reasons. First, the very important predictors of longevity: age and sex, are already taken into account before explanation, such that they will basically not contribute to the variance explained. Second, it is common experience that the smaller the sample studied, the larger is the variance explained. In this sense, ironically, a large-sample study

is at a disadvantage when the predictive value is evaluated by the percent variance explained.

Apart from the magnitude of the predicted effect, some comments on the content of the predictors are in order. The main predictor of longevity is found to be objective health: the overall health rating by the examining physician. In comparable studies in which a physician's rating is obtained, it emerged as a primary predictor as well [2,10,11,13,14,23]. Similarly, the predictive ability of dyspnea has been confirmed in other studies [24-26]. Considering the continuing first place of heart disease as a cause of death in later life [27], it is not surprising that symptoms of heart disease are found to predict longevity in the present study. Interestingly, variables derived from the physical examination override the predictive ability of blood pressure, an often cited predictor of longevity [25,28-30]. Possibly, the latter is more sensitive to inter-observer variability than physical examination variables. Alternatively, elevated blood pressure can only be noted after the underlying process of atherosclerosis has advanced to a considerable degree. Indeed, obliterations of coronary and peripheral vessels have been found to have a greater zero-order correlation coefficient with longevity than hypertension [27].

Intellectual functioning, including memory function, has already been recognized as a predictor of longevity in early studies [31-36] as well as more recently [37,38]. Activities of daily living and other types of activity are increasingly recognized as predictors of overall health and longevity [39-42]. The present study confirms their importance in a multivariate model. The same is true for health care use [43,44].

Several studies have provided evidence of the independent predictive ability of subjective health [11,45-47]. However, these studies differ from the present study in that either no objective information on health was available, or that was controlled for objective health variables. These choices in design hamper comparison with the present study, in which the role of objective health clearly overrides that of subjective health. However, in the present study other subjective variables are found to correlate independently with longevity. These can be characterized as indicating satisfaction with various aspects of life, in particular with health [48].

Three groups of predictors, summarized as symptoms, indicators and co-factors, each turn out to explain 11-12% of the variance. Upon comparing this percentage to the 20.2% of total variance explained, it is apparent that considerable interdependence among groups of predictors exists. Bio-medical and activity variables prove to be the most stable longevity predictors. While it is not surprising that a laboratory test should best indicate a life-threatening condition, this result is more notable with regard to activity. Instrumental disability and the inability to continue working reflect not only poor health, but also loss of independence. Such loss affects the quality of life, which may be crucial to a person's resilience.

Health care use, physical examination, medical history, family history and psycho-social variables show a lesser stability. With respect to health care use, it might be argued optimistically that, in case an association with longevity might exist, it should be a positive one instead of the negative association reported here. Has not health care improved the longevity of the elderly? As it is, even in a multivariate model, the variables related to health care use apparently capture diseases which are not fully covered by other study variables. The context dependence of the other less stable variables may have a different explanation. It is less clear what is measured by self-reports like those constituting medical history and psycho-social variables, and even by physician reports, than by bio-medical assessment. By consequence, the unique contribution of physician- and self-reports to the prediction of longevity is likely to depend on the information incorporated in other variables in the model. The emergence of age of mother at death as the only independent predictor from the family history variables indicating heredity suggests that the effect of heredity, although representing an independent mechanism [49-51], is largely overshadowed by the more immediate effects of physical, mental and social mechanisms acting in the present.

The very interdependence of health and other variables in the attempt to predict longevity is often heard as an argument in favor of the establishment of gerontology as a separate discipline [52,53]. To shed more light on this interdependence, questions may be put forward such as: Does physical decline precede mental and social deterioration eventually leading to death, or is physical decline initiated by mental or social deterioration? Can patterns be detected revealing one group of elderly as susceptible to one kind of deterioration and another group to another kind? For this type of questions, studies should be undertaken based on longitudinal data and focusing on what retrospectively appeared to be the last phase of life [54].

Finally, among all possible trajectories leading to death, one less positivist possibility should be considered. Perhaps every attempt to predict longevity in the elderly is deemed to fall short. Indeed, because of the short remaining life expectancy of elderly persons, relatively small differences in survival time are to be explained. Also, death may result from — to young persons — meaningless disorders, of which the time of occurrence and the specific appearance are largely due to chance. For an individual, then, a sufficient basis to predict his or her remaining duration of life may not seem feasible. For health care planning purposes, however, findings like those reported here may serve to indicate which health aspects are likely to give the most reliable information regarding longevity of older population groups. This study provides evidence that indicators of activity are well-suited to provide such information.

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## II.3

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# CHANGE AND STABILITY IN HEALTH INDICATORS PREDICTING LONGEVITY IN THE ELDERLY

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## Abstract

A method is presented for an empirical evaluation of the association of changes in characteristics over time and longevity. Essentially, regression analyses are performed with, as dependent variable, the realised probability of dying, an operational definition of longevity based on survival time, year of birth and sex. The independent variables include physical, mental and social characteristics recorded at two cycles five years apart in a longitudinal study. At baseline, the study subjects constituted a probability sample of elderly persons in the Netherlands. The total follow-up time was 28 years.

Two types of predictors of longevity are distinguished: 1. those taking their predictive value from a decline in the predictor variable that occurred recently; 2. those taking their predictive value from a longer lasting, more or less stable level reflecting a poor health condition. Objective health status, physical disability and activity are found to be in the former category. Systolic blood pressure, memory test score, inguinal hernia and satisfaction with present life are characteristics found to be in the latter category of predictors.

## Introduction

One frequently studied aspect of *development* in the last phase of life is mortality or — more positively phrased — longevity. In this phase, like in other phases of life, a developmental process is going on (*aging*), that so far has not been empirically related to longevity in its various aspects. In the vast majority of studies of longevity, characteristics at one point in time are related to vital status as ascertained after a certain passage of time. In order to relate aging-as-a-process to longevity, longitudinal data are needed that represent change in all characteristics of interest. Moreover, the data should pertain to a sufficiently large number of subjects in order to make reliable statistical inference. Appropriate methods to make this type of inference are only recently being developed.

The authors are fortunate to have access to a longitudinal data-set on a large number of elderly persons, the first cycle of which dates back to the mid-1950's. At the time of the last cycle almost all participants had died. This enables us to address the two substantial questions referred to above. The first is: "What characteristics differentiate shorter from longer living elderly?" Having data available from more than one point in time, we are able to compare characteristics predictive of longevity at successive points in time. The second, more specifically process-oriented question is: "What changes in characteristics over time will affect longevity?" We hypothesise that a fuller understanding of longevity is obtained when changes in characteristics are related to longevity, as compared to when only outcomes at one point in time are considered. After addressing the two substantial questions listed, we will have a closer look at the justifiability of this hypothesis. We will present a method that involves a treatment of not only the independent variables (the characteristics of interest), but also the dependent variable (longevity).

## Material

In 1955 through 1957, a probability sample of 3149 persons was examined in the first cycle. The sample was distributed over the Netherlands and sex- and age-stratified, such that 65-69, 70-74, 75-79, 80-99 year old age groups contained an equal number of men and women. The study was initiated by dr. R.J. van Zonneveld with the Netherlands Organisation for Applied Scientific Research (TNO). The elderly subjects were examined by their own practitioner; a total of 374 general practitioners cooperated. For each of the examinees, they recorded outcomes of over 200 items covering 9 "fields":

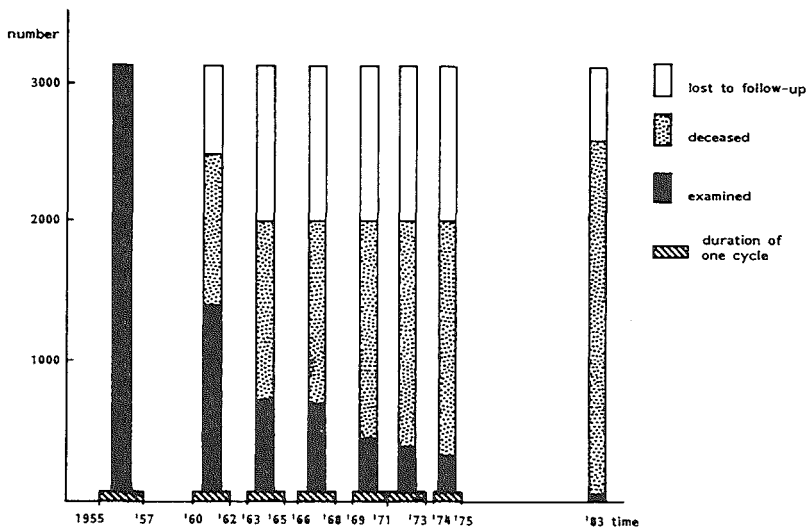
- (1) socio-demographic data
- (2) family history

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- (3) health care use
- (4) medical history
- (5) activities of daily living, recreational activity, work
- (6) anthropometric and bio-medical data
- (7) physical examination
- (8) psycho-social data (use of leisure time, adaptation, attitude to aging)
- (9) memory test scores.

This broad range of variables is in agreement with the initial study objective to describe the health status and related psycho-social factors of a cross-section of the elderly (Van Zonneveld 1961). Two variables which assess overall health status are included: in (7) *objective health* (the physician's rating of the subject's health) and in (4) is contained *subjective health* (the subject's rating of his or her own health).

Figure 1 Study participation over time



From 1960-62 through 1974-75, there were six follow-up cycles, in which traceable elderly subjects were reexamined when their general practitioners were willing to continue cooperation (which was done by the majority of general practitioners). In 1983, data on the vital status of 84% of the subjects could be obtained. In Figure 1, the numbers of participating subjects and subjects lost to follow-up over time are depicted. There is a considerable decline in the number of subjects examined, roughly parallel to the increase of number of subjects



deceased. The majority (70%) of the subjects not traced were lost to follow-up immediately after the baseline cycle. This reflects the fact that the study originally was not intended to be longitudinal. In a comparison of the baseline data of those not traced and those examined at the second cycle, the two groups did not differ significantly regarding the main health variables (Beek & Van Zonneveld 1976).

In this paper, analyses are restricted to the first and second cycles only. As there is a period of five years between these cycles, the subjects examined in the second cycle were 70 years of age and over. Therefore, for the comparison of first and second cycle results, the first cycle subjects are restricted to those 70 years and over as well. Thus, age will not confound this comparison (Botwinick, 1984, ch. 20). The numbers of subjects studied, then, are 2104 and 604 in the first and second cycles, respectively. As all subjects examined at cycle two were also examined at cycle one, there are 604 subjects available for the assessment of change in relation to longevity.

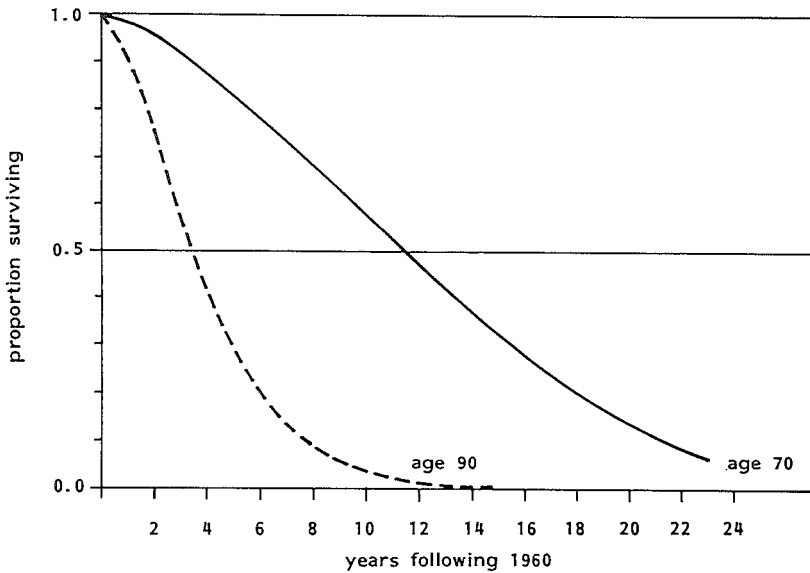
## Method

The concept of longevity is expressed as the realised probability of dying, a function of survival time. This function is designed to make the survival times of sample subjects of different ages and sexes comparable. The problem of comparison is illustrated by the following example. A man of age 65 years at baseline examination who lives five more years until death, lives a relatively short time compared to his life expectancy; on the other hand, a man of 99 years at baseline who lives five more years, lives a relatively long time. The same problem of comparison is present when the survival times of men and women are to be compared, because the life expectancy of men is shorter than that of women.

The realised probability of dying reflects how young or how old a subject has died in comparison with the total population of the same sex and age at baseline. Thus, it compares each individual subject's survival time with the survival curve of that part of his or her cohort that is still alive at the time of the baseline examination. The survival curves are based on the population mortality rates in the successive years following baseline through 1983 (Deeg et al. 1989).

Figure 2 depicts, as an illustration, two survival curves: one of all Dutch men aged 70 years in 1956 and one of all Dutch men aged 90 years in 1956. It can be derived that a male subject aged 70 in 1956 (the year of his baseline examination) who dies in 1967 (11 years after baseline) has a realised probability of dying of approximately 0.5, or 50%, because out of that part of his birthcohort that was still alive in 1956, 50% was still alive in 1967. For a person aged 90 at the same year of baseline examination, the realised probability of dying would be 0.5, when he would have lived approximately four years following baseline.

Figure 2 Survival curves for males aged 70 and 90 in 1960



Thus, the realised probability of dying takes values between 0 and 1. If it is larger than 0.5, the subject has survived a relatively short time; if it is smaller than 0.5, the subject has lived a relatively long time. The realised probability of dying of subjects examined in the second cycle is based on the survival curves of the birth cohorts still alive in 1960-62 and aged 70 and over, thus reflecting the relative survival time from the second cycle onward. The realised probabilities of dying at cycle one and cycle two will be referred to as  $RPD_1$  and  $RPD_2$  respectively.

For those subjects still alive at the end of the study (1983), viz. 28 and 10 subjects out of all examinees at first and second cycle respectively, a value of the realised probability of dying is imputed.  $RPD_1$  and  $RPD_2$  for these subjects are estimated by multiplying the probability of reaching their age in 1983 by one half. For instance, a woman born in 1890 and first examined in 1956, i.e. at 66 years of age, reaches the age of 93 (in 1983) with probability 0.22; her imputed  $RPD_1$  will be 0.11, implying that it is expected that she will die when only 11% of her cohort is still alive. This approach is derived from the actuarial method.

The logit of the RPD is then taken as the dependent variable in regression analysis. As the realised probability of dying itself is uniformly distributed in the samples at both first and second cycle, its logit is approximately normally distributed with mean 0.

The independent variables in the regression analyses are recoded versions of the originally recorded characteristics. They are recoded such that they can be

considered ordinal variables with categories ordered according to increasing or decreasing expectation of survival. (For a detailed description of the scales is referred to Deeg et al. 1985.) In order not to miss curvilinear relationships, regression models with linear as well as quadratic terms are applied.

The data analysis is then carried out in three steps, indicated in Table 1. In the first, variables predictive of survival time are selected by both univariate and forward, stepwise, multivariate regression analyses within each of the nine fields listed above, for each time of measurement. Thus, the risk of collinearity is reduced in the multivariate analyses of the second and third step, in which all fields are combined. At cycle one, the selection of predictor variables is based on RPD<sub>1</sub>, while at cycle two, it is based on RPD<sub>2</sub> as the dependent variable.

**Table 1. Diagram summarising the three analysis steps.**

	step one	step two	step three
cycle	one and two separately	one and two separately	one and two combined
sample	<i>cycle one:</i> age 70+ (N=2104) <i>cycle two:</i> all (N=604)	<i>cycle one:</i> age 70+ (N=2104) <i>cycle two:</i> all (N=604)	<i>cycle two:</i> all (N=604)
dependent variable	RPD <sub>1</sub> and RPD <sub>2</sub> separately	RPD <sub>1</sub> and RPD <sub>2</sub> separately	RPD <sub>2</sub>
independent variables	all recorded (9 fields separately)	selections made from 9 fields combined for cycles one and two separately	selections made from 9 fields combined for cycles one and two separately
regression model	univariate and fieldwise forward stepwise multivariate forward stepwise	multivariate forward stepwise multivariate, cycle	<i>part one:</i> one variables simultaneously <i>part two:</i> additionally, cycle two variables forward stepwise

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The second analysis step should provide the answer to the first substantial question addressed in this paper: “Which characteristics independently differentiate shorter from longer living elderly?” In this step, independent predictors are obtained by forward stepwise regression analysis of the variables selected in the first step at one point in time, until a variable added no longer yields a significant increase in the variance explained. The variables retained in the regression equation can be considered independent predictors of survival time.

The third analysis step is carried out to provide an answer to the key question of this paper: “What changes in characteristics over time will affect longevity?” For this step, the analysis concentrates on those 604 subjects who are examined at both first and second cycle. The dependent variable is RPD<sub>2</sub>. The independent variables comprise all variables selected from both cycles at step one. In order to restrict the amount of variables in the regression analysis, only linear and no quadratic terms are considered in this analysis step. The cycle one variables are entered first in the regression equation, after which the same variables, now as measured at cycle two, are entered in a forward stepwise manner until there is no longer a significant increase in the variance explained. In other words, after forcing the cycle one variables into the regression equation, cycle two variables will be entered only if they contribute significantly beyond the cycle one variables, all of which are retained in the equation. Thus, conditional upon predictors of the first cycle, predictors of survival time from the second cycle are ascertained.

This analysis yields several pieces of information. First, it identifies those factors that at cycle two, independent of baseline level, best predict survival time for those subjects surviving at least five years after baseline. Irrespective of the baseline level of these predictors, it is the change in level that provides the predictive value. The second piece of information is derived from the first cycle factors that appeared as independent predictors in the first stage of the regression analysis, and stayed in the regression equation after the second cycle variables were admitted. Their initial levels did not change (or the distribution of these factors remained the same over time), but these stable levels are independently predictive of survival time. The first type of predictors may be interpreted as short term predictors, the second type as long term predictors of survival time.

## Results

Table 2 presents the results from the first analysis step. For both cycle one and cycle two, the variables selected from each of the nine fields are listed, as well as their zero-order correlation coefficients with the realised probability of dying. From the first cycle, the number of variables selected is 35, while this number is 33 from the second cycle (dependent variable RPD<sub>1</sub> and RPD<sub>2</sub>, respectively). The

**Table 2. Variables selected based on univariate association and chapterwise multivariate association with realised probability of dying: zero-order correlation coefficients for ages 70 and over at cycles one and two.**

chapter	variable	cycle one (N=2104) correlation coefficient	cycle two (N=604) correlation coefficient
<i>(1) socio-demographic data</i>			
	year of birth	.04	.01
	sex	—	.08
	present income	-.05	—
	income compared to age 60	-.06	—
	living arrangements	.08	.08
<i>(2) family data</i>			
	health status spouse during life	-.04	—
	age of spouse at death	—	-.12
<i>(3) health care use</i>			
	regular doctor's visit	.22	.25
	time since last medical treatment	-.21	—
	hospital admission since age 60	—	.16
	health care use cardiovascular disease	.16	—
	health care use cancer	.08	.12
	drug use	.15	—
	non-prescribed drug use	—	.09
<i>(4) medical history</i>			
	subjective health	.25	.26
	heart complaints	.19	—
	inguinal hernia	—	.10
	asthma	—	.09
	diabetes	—	.09
<i>(5) activities of daily living</i>			
	instrumental disability	.24	.26
	physical disability	.24	.30
	disability due to leg and arm complaints	.08	—
	disability due to dispnea and heart disease	.17	—
	disability due to overall weakness	.13	.24
	recreational activity	-.09	-.19
	continued (motor) bicycling	—	-.16
	continued working	-.15	—

Table 2 (continued)

<i>(6) anthropometric and bio-medical data</i>		
sitting height	-.02	—
body mass index	—	-.06
blood sedimentation rate	.17	.20
pulse frequency	—	.11
systolic blood pressure	—	.08
breathing frequency	—	.14
<i>(7) physical examination</i>		
objective health	.32	.31
breast abnormalities	.04	—
abnormalities heart and large blood vessels	.17	—
systolic murmur	.15	—
dyspnea	.25	.20
albuminuria	—	.21
<i>(8) psycho-social data</i>		
frequency social visits	-.11	-.11
loneliness	.10	.07
relationship spouse	-.07	.13
contact children	-.06	—
perceived health decline	.21	.19
evaluation (physical) aging	-.16	-.15
value present life	-.12	-.16
attitude present society	-.04	—
attitude present youth	—	-.11
<i>(9) memory test</i>		
total memory test score	-.19	-.18

“—” means: variable not selected at this cycle

latter number is slightly smaller due to a decrease in power in the smaller sample. The variables selected will be included in the second and third analysis steps.

The background variables in fields (1) and (2) show only a minimally significant association with survival time. The health care use, medical history and disability variables in fields (3), (4) and (5) appear to have greater impact. Notably, the non disease-specific variables show considerable correlation with survival time, a correlation that increases from cycle one to cycle two. While at cycle one, the disease-specific variables selected in these fields are predominantly related to heart disease, this is not true for the variables selected at cycle two. Here, variables

relating to a wider range of diseases are selected. From the anthropometric and bio-medical variables in field (6), blood sedimentation rate shows the largest correlation with survival time; this is, again, a non disease-specific variable showing a slightly higher correlation at cycle two. Systolic blood pressure is the only heart disease related variable selected at cycle two. Note the inverse relationship between body mass index and RPD<sub>2</sub>. Among the physical examination variables (field (7)), objective health shows the largest zero-order correlation with survival time in the study. Again, at cycle two, specifically heart disease related variables are not selected from this field. In field (8), the psycho-social variables most related to survival time are those related to physical functioning. Next in importance is the value a subject attaches to present life. The reversal of the sign of the correlation between relationship with spouse and survival time may be an artifact due to the small number of elderly who at cycle two admitted that their relationship has worsened (2%). From the memory test (field (9)), several subscales were as strongly associated with survival time as the overall score. However, most of the subscales are highly intercorrelated. To avoid collinearity, only the total memory test score is selected.

When not specifically noted above, all univariate associations are in the expected direction. Thus, for instance, the higher the income, the lower the RPD, and the more dependency is expressed by the living arrangements, the higher the RPD. Also, the more use is made of health care, and the more disability is recorded, the higher the RPD. Conversely, the more active a subject, and the better the memory test performance, the lower the RPD.

The results of analysis step two are shown in Table 3. For each cycle, the standardised regression coefficients are listed, so that the magnitudes of the coefficients can be compared within each cycle. The variables are regrouped into three general fields: those directly indicating disease (*symptoms*: fields (4), (6), (7), (9)), those indirectly relating to health (*indicators*: fields (3), (5)) and *social and psychological co-factors* (fields (1), (2), (8)).

At both cycles, independent predictors can be observed in all three groups. At cycle one, two of the strongest independent predictors of survival time can be found among the *symptoms*: objective health and memory test score. Other independent predictors have regression coefficients smaller than 0.10. These are the *symptoms* systolic murmur, abnormalities of heart and large blood vessels, and blood sedimentation rate, the *indicators* time since last medical treatment, health care use for cancer, instrumental ADL and continued working, and the *social and psychological co-factors* evaluation of (physical) aging, value of present life, relationship with spouse and attitude toward present society. One variable appears irregular: year of birth. The magnitude of the independent effect of this variable on RPD<sub>1</sub> is surprising, considering its small zero-order correlation (cf. Table 2). Moreover, an association between RPD<sub>1</sub> and year of birth is not expected, because

**Table 3. Independent predictors of realised probability of dying at cycles one and two respectively from stepwise regression analysis: standardised beta-coefficients ( $p < .05$ ), ages 70 and over.**

variable	cycle one*	cycle two*
<i>SYMPTOMS</i>		
objective health	.14	.14
abnormalities heart and major blood vessels	.06	—
systolic murmur	.04	—
systolic blood pressure	—	.08
dyspnea	.09	
inguinal hernia	—	.12
asthma	—	.07
albuminuria	—	.12
memory test score	-.14	-.12
<i>INDICATORS</i>		
regular doctor's visit		.08
time since last medical treatment	-.09	—
health care use cancer	.05	.09
instrumental ADL	.07	
physical ADL		.12
recreational activity		-.09
continued working	-.22;.18**	—
<i>SOCIAL AND PSYCHOLOGICAL CO-FACTORS</i>		
year of birth	.21	.14
age of spouse at death		-.09
relationship spouse	-.04	.09
evaluation of aging	-.06	
value of present life	-.06	-.13
attitude present society	-.04	
attitude present youth	—	-.09
total variance explained	19.9%	24.8%

“—” means: variable not included in analysis

blank means: variable included in analysis but not significant

\* all variables not listed were not significant in either cycle one or cycle two

\*\* for this variable, both linear and quadratic terms were selected, with first and second regression coefficient listed, respectively



the realised probability of dying controls for year of birth. The finding, however, can be explained to reflect a selection bias in the study sample (Deeg et al. 1989).

At cycle two, objective health again has the largest independent effect on survival time (regression coefficient 0.14). Other regression coefficients above 0.10 are shown for the *symptoms* albuminuria, inguinal hernia, and memory test score, for the *indicator* physical ADL, and for the *psychological co-factor* value of present life. Independent predictors with regression coefficients smaller than 0.10 are: the *symptoms* systolic blood pressure and asthma; the *indicators* regular doctor's visit, health care use for cancer and recreational activity; and the social and psychological co-factors age of spouse, relationship with spouse and attitude toward present youth. As inferred from the independent effect of year of birth, the sample selection bias is again still present in cycle two, but not as strongly as in cycle one (non-standardised regression coefficients 0.00043 and 0.00027 for the quadratic term of year of birth at cycles one and two, respectively).

A comparison of the independent predictors at cycle one and cycle two suggests, first, that the symptoms at cycle two pertain to a wider range of diseases. The same was noted from univariate analysis. Second, among the *indicators*, at cycle two a somewhat stronger effect of both health care use for cancer and disability can be noted (non-standardised regression coefficients 0.16 and 0.07 at cycle one versus 0.34 and 0.12 at cycle two). As the independent effects of health care use may be interpreted to represent a "proxy" for diseases not explicitly examined in the study, this finding may be interpreted to confirm the observation that at cycle two a wider range of diseases is associated to survival time than at cycle one. This point will be considered further in the Discussion section.

A final observation from this analysis step is the amount of variance explained. At cycle one, 20% of the variance can be explained, while at cycle two this percentage is improved by 5%. Possible explanations of this difference are given in the Discussion section.

The results of analysis step three are shown in Table 4. First, all variables listed in Table 2, as measured at cycle one, are entered into the regression equation. For the variables with significant regression coefficients in this first part of the analysis, the regression coefficients at part one as well as at part two of the analysis are listed. In the second part of the analysis, out of those 49 variables that are listed in Table 2 and measured at cycle two, in a forward, stepwise manner only those variables are additionally entered into the regression equation that contribute to the variance explained beyond the cycle one variables already in the equation. For these significant variables, again, the regression coefficients at part one as well as at part two are listed. Also are listed the percentages of variance explained in the subsequent parts of the analysis.

Out of all cycle one variables entered into the regression equation in the first part of the analysis, only six variables have an independent predictive value for

**Table 4. Independent predictors of realised probability of dying after cycle two from a regression model with all cycle one variables forced into the regression equation and forward, stepwise addition of cycle two variables only if significant beyond the cycle one variables: standardised beta-coefficients ( $p < .05$ ).**

variable	standardised regression coefficient		increase in variance explained
	part one	part two	
<b>part one</b>			
<i>symptoms</i>			
systolic blood pressure	.15	.12	
inguinal hernia	.13	.12	
memory test score	-.16	-.15	
<i>indicators</i>			
—			
<i>social and psychological co-factors</i>			
evaluation aging	-.09	-.07*	
value present life	-.09	-.06*	
year of birth	.16	.21	
variance explained			15.4%
<b>part two</b>			
<i>symptoms</i>			
objective health	.01	.19	5.6%
abnormalities heart and major blood vessels	.03	.11	.8%
<i>indicators</i>			
health care use cancer	-.02	.15	1.4%
physical disability	.11	.19	2.0%
continued (motor) bicycling	.05	.17	.6%
<i>social and psychological co-factors</i>			
—			
total variance explained			25.7%

\* marginally significant ( $p = .10$ )

survival time as measured from cycle two onward at significance level  $p < 0.05$ . These include three *symptoms*: systolic blood pressure, inguinal hernia and memory test score, and three *social and psychological co-factors*: a person's evaluation of (physical) aging, the value a person attaches to present life and year of birth. No *indicators* are independently predictive of survival time as measured from cycle two onward.

From the cycle two variables, subsequently entered in the regression equation, five other independent predictors are revealed. These new independent predictors are the *symptoms*: objective health and abnormalities of heart and major blood vessels, and the *indicators*: health care use for cancer, physical disability and continued (motor) bicycling. Note the relatively large standardised regression coefficient for objective health and physical disability at cycle two (both 0.20). No cycle two *social and psychological co-factors* appear to be independently predictive of survival time; the regression coefficients of both evaluation of aging and value of present life even drop to marginal significance ( $p = 0.10$ ). This may be due to the partly psychological connotation of the *indicators* newly entered in the regression equation. From their cycle one regression coefficients, it can be inferred that the cycle two predictors were not significant at cycle one. (Although the cycle one regression coefficient of physical disability is relatively large, its standard error is too large for it to be significant.)

The cycle two predictors added to the regression equation, can be interpreted as reflecting a change in level of the variables concerned since the time of cycle one, i.e. a change over five years, regardless of the initial level recorded at cycle one. For instance, when a person's objective health rating changed from good to moderate, or from moderate to poor (together in 22% of all subjects), this person will be likely to survive a shorter period than persons whose objective health rating stayed stable (75%) or improved (3%). The initial level of objective health appears to have no significant predictive value. When this information is combined with the information from analysis step two (Table 2), where objective health was observed to be one of the most powerful predictors of survival time from both times of measurement onward, it can now be inferred that objective health is a short term predictor of survival time. The same is true for abnormalities in heart and major blood vessels, and for the — predominantly behavioural — *indicators* health care use, physical disability and continued bicycling. It is from recent declines that these variables obtain their predictive value.

On the other hand, the cycle one predictors that stay significant throughout the second part of the analysis, can be considered long term predictors. For instance level of memory test score, also an important independent predictor of survival time in analysis step two (Table 2), is predictive even if survival time is measured only from a point in time five years later. Thus, a relatively poor performance on the memory test, or a high blood pressure, as more or less stable characteristics,

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have a shortening effect on the life span. The same is true for a medical history of inguinal hernia, and — to a lesser extent — for the extent to which a person is satisfied with the fact of aging and with present life.

While all cycle one variables explain 15.4% of the variance, the total variance explained in this analysis is 25.7%. This means, the variance explained when incorporating change in the regression model (step three) is hardly improved compared to models which do not incorporate change (step two). The fact that linear and not quadratic regression analysis is applied, only accounts for a slight loss of variance explained. When no quadratic terms were employed at analysis step two, only 0.5% of variance explained was lost. Note, also, the smaller total number of independent predictors emerging from the third compared to the second analysis step (11 versus 15). While it is not immediately clear why this difference exists, it might contribute to the lack of increase in variance explained in analysis step three.

## Discussion

In the course of the three analysis steps reported in this paper, it has been possible to increasingly specify the findings concerning predictors of longevity. At the first step, variables at two point in time were identified which showed a zero-order correlation with the realised probability of dying. The second analysis step provided independent predictors of the RPD at two points in time as well as their relative importance in the presence of other independent predictors. With the last step, it was possible to specify for some of these independent predictors: those which obtain their predictive value through recent decline in levels on the one hand, and those which are rather stable characteristics predicting survival time in the long run on the other hand.

Several aspects of the analyses call for further discussion. First, there are some substantial differences in the predictor variables selected at both points in time. At the second cycle, significant variables reflect a greater variety of diseases than at the first cycle, in which mainly variables pertaining to heart disease were selected. Possibly, the larger sample size at cycle one accounts for a larger variability, causing only the very strong predictors to emerge as significant. While other specific disease-related variables may not be captured by more general variables like health care use or disability, this may also explain the lesser variance explained at cycle one compared to cycle two.

A second aspect for discussion is the justifiability of the inferences made from analysis step three. The conclusion from the stepwise selection of cycle two variables into the regression equation, that the variables thus selected reflect change in levels since ascertainment at cycle one, presupposes that they are still

reliably measuring the same construct. If this is not true for some variable, this would be a reason for it to be selected from the cycle two variables. One way to evaluate the similarity of the constructs measured at cycles one and two, is a comparison of the factor structures at each cycle (Cunningham 1982).

Applying the principal component method, it turns out that the number of factors extracted at both cycles is six when the minimal eigenvalue is set at 1.4, which appears to yield the best interpretable factor structures. The factor loadings are presented in Tables 5a and 5b (only those with absolute magnitude larger than 0.40 are listed). There is considerable similarity between both factor structures, but they are not identical. We will only discuss the position in the factor structures of the variables of concern here.

The most important variable in the second part of analysis step three, objective health, clearly does not change position in the factor structure. At both cycles, it is associated with subjective health, health care use and heart disease. The variable next in importance, physical disability, shows similar associations with other disability and activity variables at both cycles. But also, it is more strongly associated with cancer at cycle one than at cycle two. Health care use for cancer is also selected in the regression equation, thus likely reflecting the change in association with disability since cycle one and thus a change in construct measured. Of the other two cycle two variables in the regression equation, continued (motor) bicycling shows the same position in the factor structure. The variable abnormalities of heart and major blood vessels however, is associated with other heart-related variables at cycle one, but shows no clear associations at cycle two. Thus, the selection of this variable in the regression equation may reflect a change in construct measured rather than a "real", recent change in health status predictive of survival time. In summary, possibly two of the cycle two variables earlier interpreted to reflect change in health status, may actually be based on an artifact. Conversely, more confidence can be put into the interpretation of objective health, physical disability and continued (motor) bicycling as short term predictors of longevity.

A third aspect of the analyses worth discussing is the amount of variance explained. Comparable studies show similar outcomes (e.g. Palmore 1974, Botwinick et al. 1978, Hodkinson & Piper 1981, Abramson et al. 1982). However, these studies only focus on examination data at one point in time with mortality follow-up at a future point in time. The variance explained in this study hardly surpasses 25%, which is somewhat disheartening since it could be expected that when change is incorporated in the statistical model, a greater predictive power would be obtained than when change is not taken into account. After all, aging is a process in which changes take place, especially when death is near. Some improvements in study design may improve the predictive power, especially in the realm of data quality: better scales, and less inter-observer variability. As it stands now, it seems that the prediction of survival time is subject to great uncertainty whether or not change

### II.3 Change and stability in predicting longevity

over time is considered. This poses a challenge to future research: can the variance explained be increased by a study design capturing the "right" predictor variables, or do the changes in characteristics determining death occur only so close to death that they can not be captured by a prospective study?

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## II.4

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# THE ASSOCIATION BETWEEN CHANGE IN COGNITIVE FUNCTION AND LONGEVITY IN DUTCH ELDERLY

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## Abstract

The association between rate of change in cognitive function and longevity was investigated with data from the Dutch Longitudinal Study among the Elderly. A group of 211 Dutch persons, aged 65-84 years at baseline (1955-1957), was re-examined twice during an eight-years follow-up period, after which mortality was ascertained through 1983. Cognitive function was assessed based on an adaptation of the Wechsler Memory Scale. Rate of change in cognitive function during the eight years of follow-up was determined by regression on time for each individual. Cognitive function declined significantly over the eight year period (mean yearly change  $-0.28$  units, with 95% confidence interval  $-0.34$  to  $-0.22$ ). The rate of decline in cognitive function was strongly associated with subsequent survival time in the ages 70 years and over, with those with a large decline having a short survival time. No association could be demonstrated in the age group 65-69 years. Adjustment for potential confounders did not affect the magnitude of the association. These findings suggest that the rate of decline of cognitive function is an independent predictor of longevity in older persons.

*Keywords:*

aged / cognitive function / epidemiologic method / longevity / longitudinal study



## Introduction

Evidence that cognitive function declines in older age has accumulated over the past decades (1-5). However, some recent studies report no decline in healthy individuals (6,7). The issue of whether cognitive decline is part of “normal” aging or a sign of pathology associated with premature death has not been resolved. Whereas evidence of an association between change in cognitive function and subsequent mortality was found in a sample of dementia patients (8), reports of longitudinal studies relating change in cognitive function to survival in samples of the general population are contradictory. Some investigators have suggested that there is a “critical” decline in cognitive function which separates survivors from non-survivors (9-11). Other investigators did not find any relationship between change in cognitive function and survival (12,13). In the present study, the association between change in cognitive function and longevity was investigated in 211 Dutch elderly subjects in the general population who were followed a maximum of 28 years.

## Materials and methods

**Study design.** From 1955 through 1957, a probability sample of 3149 subjects was examined in the first cycle of the Dutch Longitudinal Study among the Elderly. The sample was distributed over the Netherlands and was sex- and age-stratified, such that age-categories of 65-69, 70-74, 75-79, and 80-99 years contained approximately equal numbers of men and women. The subjects were examined by their own general practitioner; a total of 374 general practitioners cooperated. The initial study objective was to describe the health status of the elderly in the general population, as well as related mental and social factors (14). The data collected included an adapted version of the Wechsler Memory Scale (15).

There were six follow-up examination cycles, in which traceable elderly subjects were re-examined when their general practitioners were willing and able to continue cooperation. The number of subjects examined was 658 in cycle 2 (1960-1962) and 304 in cycle 3 (1963-1965). The small proportion of subjects re-examined not only reflects increasing sample mortality, but also the fact that the study originally was not intended to be longitudinal and lacked sufficient administrative support. In 1983, an effort was made to ascertain vital status and causes of death for all subjects. This effort was successful for 2645 of the 3149 initially examined subjects (84%). These subjects are similar to the total Dutch population with respect to survival time (16).

For the current study, analyses were restricted to those subjects examined in the first, second and third cycles whose vital status was known in 1983 (n=231). For

these subjects, examination data were available spanning a period of eight years, with mean subsequent survival follow-up of 19 years. As will be shown later, the health related characteristics at baseline of these subjects were not appreciably different from the baseline characteristics of those subjects who survived during eight years but were not re-examined twice. The age of the subjects at the time of the third cycle was 73 years and older. The key variable of interest in this report, rate of change in memory test score, was calculated when scores at all three cycles were available. The present analysis was based on those 211 subjects who fulfilled this criterion.

### Measurements

**Rate of change in cognitive function.** The Wechsler Memory Scale (15) was abbreviated and adapted to the Dutch situation, as described in detail previously (14). This adapted version (further referred to as “memory test”) comprised 17 items, evaluating personal orientation, time orientation, general orientation, logical memory, auditive memory and visual reproduction. Since the focus of the present study is on cognitive function at large, all 17 items were summed to one scale. The minimum score, then, was 0 (= only errors), the maximum score 25 (= no errors). The rate of change in memory test score was determined by least squares regression of test score on time for each individual. The regression coefficient indicates the yearly rate of change in memory test score for each subject.

**Potential confounders.** The relation between memory test score and survival may be confounded by other factors. As potential confounders the baseline values of the following variables, measured as reported previously (14), were taken into account: age, sex, current income, living arrangements (independent or dependent), health status as rated by the examining physician, frequency of medical treatment, blood sedimentation rate, physician’s findings of abnormalities of heart and large blood vessels, physician’s findings of systolic murmur, subject’s perception of problems related to aging, subject’s evaluation of life in retrospect. These variables proved to be independent predictors of longevity in previous reports from the Dutch Longitudinal Study among the Elderly (17).

**Measures of survival.** Three measures of survival were used: (1) the percentage of subjects deceased within 5 years subsequent to cycle three, (2) the relative risk from Cox’ proportional hazard model based on the statistical analysis of survival time data (18), and (3) the Realized Probability of Dying (RPD), an individual measure of survival time relative to the total population and based on sex and age at cycle three (16). For example, the value of an individual’s RPD is 0.8 if at the time of his death 80% of his cohort is still alive.

**Data analysis.**

The relation between rate of change in memory test score and longevity was evaluated in two ways. First, within three age groups the survival was determined for those subjects with a rate of change below the median and those subjects with a rate of change above the median yearly change. The median rates of change are  $-0.11$ ,  $-0.29$ , and  $-0.33$  for the age groups 65-69, 70-74, and 75+ years respectively. Survival in both groups was expressed as percentage of subjects deceased within 5 years, as relative risk derived from the Cox model, and as mean RPD.

Second, the association between rate of change in memory test score as a continuous variable and survival after cycle three was analyzed. Two types of regression model were used: the Cox regression model with survival time as the dependent variable, and the multiple regression model with the logit of the RPD (LRPD) as the dependent variable, the latter having an approximately normal distribution. Separate analyses were performed, with rate of change in cognitive

**TABLE 1 Comparison of cycle 1 characteristics of subjects examined at cycle 1 and re-examined at cycles 2 and 3 with complete memory test scores with subjects examined at cycle 1 and surviving through cycle 3 but not re-examined twice. Dutch Longitudinal Study among the Elderly 1955-1983.**

Variable	Complete (N=211)	Not re-examined (N=916)
Mean age	72.7	72.9
Females (%)	43.6	50.3
Married (%)	60.7	58.6
Low income (%)	14.7	22.0
Living independently (%)	67.3	67.6
Mean height (m)	1.64	1.63
Mean weight (kg)	70.1	69.4
Mean body mass index (kg/m <sup>2</sup> )	26.2	26.1
Mean blood sedimentation rate	10.7	10.1
Mean hemoglobin (g%)	14.0	13.7
Mean pulse rate	74.6	75.4
Mean systolic blood pressure (mm Hg)	161.9	165.5
Mean diastolic blood pressure (mm Hg)	89.4	91.7
Mean memory test score	19.9	19.0

**TABLE 2** Description of the study sample at cycles one and three in terms of variables potentially related to survival time, by age at cycle one. Dutch Longitudinal Study among the Elderly, 1955–1983.

Variable	Age 65-69 (N=63)		Age 70-74 (N=79)		Age 75+ (N=69)	
	Cycle 1	Cycle 3	Cycle 1	Cycle 3	Cycle 1	Cycle 3
Females (%)	49.2	49.2	44.3	44.3	37.7	37.7
Married (%)	73.0	57.1	58.2	43.0	52.2	27.5
Low income (%)	0.0	4.8	19.0	7.7	23.2	23.5
Living independently (%)	79.4	68.3	63.3	55.7	60.9	37.1
Mean height (m)	1.72	1.72	1.69	1.67	1.70	1.64
Mean weight (kg)	64.5	63.3	63.3	62.1	62.9	61.2
Mean body mass index (kg/m <sup>2</sup> )	26.7	26.9	25.7	25.4	26.4	24.6
Mean blood sedimentation rate	9.4	13.0	10.3	12.6	12.3	15.2
Mean hemoglobin (g%)	14.0	13.7	14.0	13.6	14.0	13.7
Mean pulse rate	73.9	76.8	75.1	75.7	74.6	75.1
Mean systolic blood pressure (mm Hg)	156.6	164.0	160.4	165.8	168.6	166.8
Mean diastolic blood pressure (mm Hg)	89.9	93.0	88.5	89.2	90.0	88.0

function conditional on initial test score (at cycle one), and conditional on attained test score (at cycle three).

In order to examine possible selection bias, general baseline characteristics of those 916 subjects surviving but not re-examined twice and those 211 re-examined twice with complete memory test scores were compared (Table 1). It appeared that those who did not participate in cycles 2 or 3 were slightly more likely to be female and to have a lower income. No significant differences in health related variables were observed. The subjects who were not re-examined twice had lower memory test scores at cycle 1 than those who were re-examined. The mean RPD of the 211 subjects re-examined twice was 0.50 with standard deviation 0.28, indicating a uniform distribution on the interval (0,1) and therefore reflecting the distribution of survival time in the general population (16). Thus, the 211 subjects may be considered representative of the population with respect to survival time, given their age and sex.

**TABLE 3** Description of the study sample at cycles one and three in terms of variables potentially related to survival time, by sex. Dutch Longitudinal Study among the Elderly, 1955–1983.

Variable	Males (N=119)		Females (N=92)	
	Cycle 1	Cycle 3	Cycle 1	Cycle 3
Mean age	72.9	80.9	72.4	80.4
Married (%)	73.9	55.5	43.5	25.0
Low income (%)	12.6	9.4	17.4	15.2
Living independently (%)	68.9	58.0	65.2	48.9
Mean height (m)	1.71	1.69	1.69	1.65
Mean weight (kg)	68.5	67.1	57.1	55.6
Mean body mass index (kg/m <sup>2</sup> )	25.0	24.7	27.8	26.9
Mean blood sedimentation rate	8.5	12.8	13.5	14.6
Mean hemoglobin (g%)	14.3	14.0	13.5	13.3
Mean pulse rate	72.1	73.9	77.8	78.4
Mean systolic blood pressure (mm Hg)	158.0	157.7	167.0	175.8
Mean diastolic blood pressure (mm Hg)	87.4	86.9	91.9	93.8

## Results

General characteristics of the study sample at cycles one and three are presented for the three age categories (Table 2) and for males and females (Table 3). In this sample, the proportion of females decreased across age groups (Table 2). The proportion of subjects still married decreased across age as well as over time. Also, the percentage still married was considerably lower among females (Table 3). The percentage of persons with low income increased across age groups (Table 2). Most variables related to health status showed a downward trend across age as well as across time. The health related variables indicated, in addition, a worse health for females than for males (Table 3).

Change in memory test score across the three cycles is presented by age and by sex in Table 4. Means and standard deviations are given of test score at each cycle in addition to the average yearly change in cognitive function. Across cycles, the mean scores clearly decreased in each age group. For the total sample, the mean memory test score was 19.9 at cycle 1 (95% confidence interval 19.5 to 20.3), 18.8 at cycle 2 (95% confidence interval 18.3 to 19.3) and 17.3 at cycle 3 (95% confidence interval 16.7 to 17.9). The standard deviations of all scores increased

**TABLE 4 Mean memory test scores at cycles 1, 2 and 3 and memory test score change across cycles 1 through 3 for the total sample and by age and sex (standard deviations in parentheses). Dutch Longitudinal Study among the Elderly 1955–1983.**

	Memory test score				N
	Cycle 1 Year 1	Cycle 2 Year 5	Cycle 3 Year 8	Change Year 1-8	
Ages 65-69	20.7 (2.4)	19.8 (3.5)	19.4 (3.8)	-0.14 (0.43)	63
Ages 70-74	19.7 (2.9)	18.7 (3.2)	16.9 (3.9)	-0.30 (0.40)	79
Ages 75+	19.3 (3.8)	18.1 (4.7)	15.9 (5.1)	-0.40 (0.48)	68
Test for age trend	$p = 0.011$	$p = 0.014$	$p = 0.000$	$p = 0.001$	
Males	20.1 (2.8)	19.1 (3.4)	17.6 (4.2)	-0.28 (0.43)	119
Females	19.6 (3.5)	18.5 (4.3)	17.0 (4.9)	-0.30 (0.47)	92
Test for sex difference	$p = 0.287$	$p = 0.211$	$p = 0.276$	$p = 0.621$	
Total	19.9 (3.2)	18.8 (3.8)	17.3 (4.5)	-0.28 (0.46)	211

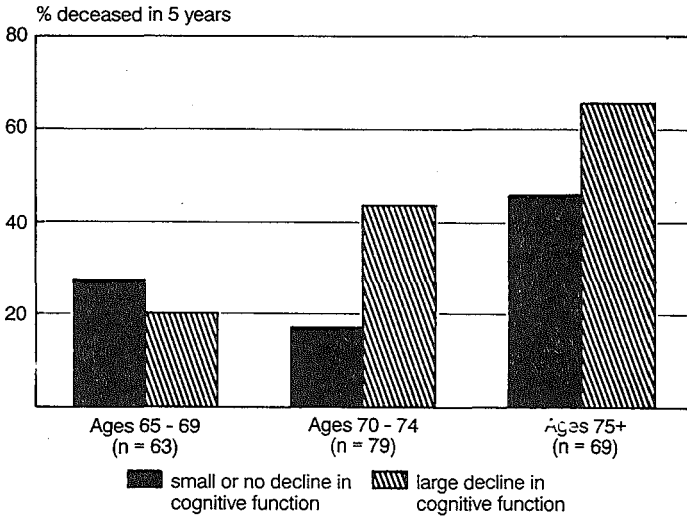
over time, as well as across age groups. Tests for linear trend indicated that all scores differed significantly across age groups ( $p < 0.05$ ). There was no evidence of sex differences. Overall, the yearly decline of  $-0.28$  was significantly different from 0 (95% confidence interval  $-0.34$  to  $-0.22$ ). The quartile points of overall yearly decline were  $-0.48$ ,  $-0.24$ , and  $0.00$ , respectively.

Rate of change in memory test score below or above the median was found to be related to longevity in the ages 70 years and over at cycle one (Figures 1 and 2); in the youngest age group no significant association was found with any of the methods used. The three measures of survival performed slightly differently in the age groups 70-74 years and 75 years and over. The difference in 5-year mortality between those subjects whose rate of change was below the median and those whose rate of change was above the median did not reach significance in the age-group 75 and over (difference 20%, SE of difference 13%), the Cox relative risk did not reach significance in the age-group 70-74 (RR = 1.16, 95% confidence interval 0.92 to 1.46). The differences in mean RPD, however, were in both age groups significant.

Regression analysis of survival on rate of change in cognitive function as a continuous variable showed a significant association: a regression coefficient of 0.32 (95% confidence interval 0.12 to 0.52) in the Cox model and of  $-0.85$  (95%

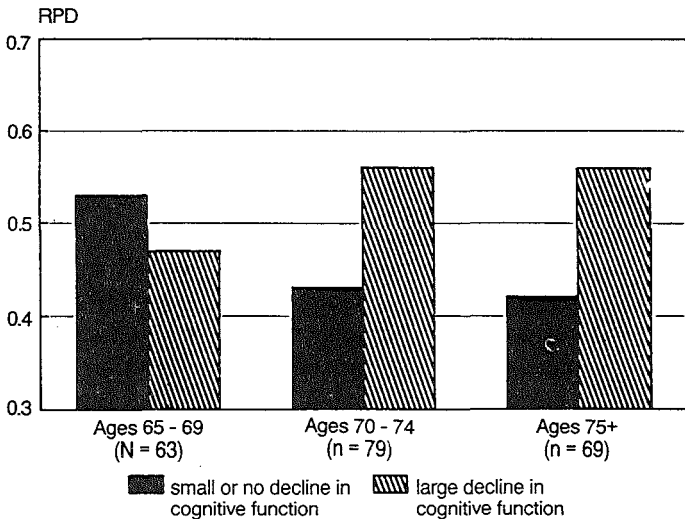
**Figure 1. Association of memory function change with five-year mortality, by age. Dutch Longitudinal Study among the Elderly, 1955-1983**

“Small or no decline” represents a rate of change above the median;  
 “large decline” represents a rate of change below the median.



**Figure 2. Association of memory function change and realized probability of dying, by age. Dutch Longitudinal Study among the Elderly, 1955-1983**

“Small or no decline” represents a rate of change above the median;  
 “large decline” represents a rate of change below the median.



confidence interval  $-1.32$  to  $-0.38$ ) in the LRPD-model. Addition of initial level of memory test score to the two regression models did not change the magnitude of the relation of rate of change in test score to survival time (Tables 5 and 6). However, in the Cox regression model, rate of change in memory test score was no longer significantly related to survival time with the level of memory test score at cycle three included in the model; in this model, neither rate of change nor level was significantly associated with survival time. By contrast, in the regression model with LRPD as the dependent variable, the magnitude of the relationship between rate of change in memory test score and survival time did not change notably when level of memory test score at cycle three was substituted for initial level of memory test score. Adjustment for potential confounders pertaining to physical and mental health resulted in only slight changes in the magnitude of the regression coefficient of survival time or LRPD on rate of change in memory test score (Tables 5 and 6).

## Discussion

The findings in this study suggest that rate of change in cognitive function, measured by a memory test over a period of eight years, is an independent predictor of subsequent survival. The predictive ability of rate of change in cognitive function for survival appears stronger than that of level of cognitive function. Adjustment for potential confounders appears not to alter the observed relationship.

The major methodologic issue in this study is that the analysis is based on only 211 of the initially examined subjects. It should therefore be considered whether the observed association may be due to selection bias. Although this possibility cannot be fully ruled out, we consider it unlikely for the following reasons. First, the main reason for the attrition was that a number of general practitioners who had collaborated in the study by examining sample members were no longer available. It is unlikely that factors which contributed to the discontinuation of the physicians' collaboration were associated with their patients' cognitive performance or longevity. Second, the 211 subjects with complete memory test scores through cycle three and therefore included in this analysis were found to be not different from the general population with respect to survival time, given their age and sex. Third, comparison of baseline characteristics between the 211 subjects included in this analysis and those 916 subjects who were examined at baseline, survived eight years, but were not re-examined twice (Table 1), revealed no major differences with two exceptions. The first one is that the study sample included a relatively small percentage of females. Since there was no significant difference in cognitive test performance between women and men, this should not have affected the results. The second exception is a slightly better cognitive function in the study



**TABLE 5** Cox regression coefficients of survival time on memory test score change in three models, unadjusted and adjusted for potential confounders (95% confidence interval in parentheses). Dutch Longitudinal Study among the Elderly, 1955–1983.

	Cox regression coefficient	
	Unadjusted	Adjusted*
Model 1: Change alone	0.32 (0.12,0.52)	0.31 (0.08,0.54)
Model 2: Change + initial level <sup>#</sup>	0.36 (0.16,0.56)	0.31 (0.08,0.54)
Model 3: Change + attained level <sup>#</sup>	0.19 (-0.06,0.44)	0.27 (-0.08,0.62)

\* Adjusted for: age at cycle 1, living independently, income, health status, regular medical treatment, blood sedimentation rate, abnormalities heart, systolic murmur, perceived problems related to aging, and evaluation of life in retrospect.

<sup>#</sup> initial level = score at cycle 1; attained level = score at cycle 3

**TABLE 6** Regression coefficients of LRPD\* on memory test score change in three models, unadjusted and adjusted for potential confounders (95% confidence intervals in parentheses). Dutch Longitudinal Study among the Elderly, 1955–1983.

	Unstandardized regression coefficient	
	Unadjusted	Adjusted <sup>¶</sup>
Model 1: Change alone	-0.85 (-1.32,-0.38)	-0.71 (-1.16,-0.26)
Model 2: Change + initial level <sup>#</sup>	-0.87 (-1.34,-0.40)	-0.77 (-1.28,-0.26)
Model 3: Change + attained level <sup>#</sup>	-0.77 (-1.43,-0.11)	-0.57 (-1.00,-0.14)

\* Logit of the Realized Probability of Dying. A positive value of the LRPD indicates that an individual has lived a short time relative to his or her age and sex peers in the total population; a negative value indicates a relatively long survival time.

<sup>¶</sup> Adjusted for: age at cycle 1, living independently, income, health status, regular medical treatment, blood sedimentation rate, abnormalities heart, systolic murmur, perceived problems related to aging, and evaluation of life in retrospect.

<sup>#</sup> initial level = score at cycle 1; attained level = score at cycle 3

sample. This may affect the results as follows. It is possible that those with a better cognitive function at baseline show a higher rate of cognitive function decline (19,20). This possibility was not seen to influence the association of rate of cognitive function change and longevity: when baseline level was entered into the model, the regression coefficient did not change.

The arguments given above support the view that the present findings are not due to selection bias. However, the generalizability of the findings may be limited by another feature of the study design. Only subjects who survived at least eight years were included in the present analyses. By comparison, the majority (57%) of the initial sample had died by cycle three. With only one measurement available for the majority of those who died, there is no way of determining how their cognitive function changed and how this change was related to their longevity. The rate of change observed in the study sample is likely to be an underestimation of the rate of change experienced by the total initial sample (21-23,11).

A further methodologic issue concerns the operational definition of rate of change in cognitive function. This parameter was estimated by linear regression of memory test score on time. This approach entailed making the assumption of a linear change of memory test score over time. Undoubtedly, this is not correct for all subjects. In Table 4 it can be seen that the decrease in mean scores between cycles two and three is at least as large as the decrease between cycles one and two, although the latter interval involves five years and the former only three years. Therefore, a true relation between rate of decline in cognitive function and shortened survival time may have been diluted.

The association of change in cognitive function with longevity appears stronger than that of level of cognitive function. As shown in Tables 5 and 6, this is especially true with respect to initial level. With attained level in the model, the association of cognitive function change and longevity is somewhat weaker. This is not unexpected, because it seems plausible that what really matters for survival is not where one came from, but where one ended up (24). Also, at cycle one the study sample was relatively homogeneous (cf. the relatively small standard deviations of memory test score in Table 4), which makes it difficult to distinguish clearly at cycle one those who are to decline and those who are to maintain their level of cognitive function. The larger standard deviation at cycle 3 reflects a greater heterogeneity, which makes clearer distinction possible.

An increase in variability of various measures of cognitive function over time has also been noted in other studies (25,26). It may be argued that across the whole life span a continuous diversification of personal characteristics occurs, and thus, that the noted increase in variability of cognitive function is inherent to normal aging. In the current study, one quarter of the subjects maintains or even improves its level of cognitive function over eight years, while the others show declines. The latter are likely to have a shorter survival time than the former. The increase in

variability in cognitive function may therefore mainly be an expression of the fact that some individuals live longer than others.

The results of the present study are obtained by employing three measures of survival. The first two measures (5-year mortality and relative risk based on Cox proportional hazards model) provided partly contradictory results even in one and the same sample. It has been argued elsewhere (16) that these two measures are sensitive to sample variation with respect to age and sex, because they are aggregate measures. To control for age and sex in the analyses does not fully solve this problem. In addition, both measures have a limited capacity to detect differences between shorter and longer survivors when almost all sample members have died. By contrast, the third survival measure (RPD) is not an aggregate, but an individual measure. Because it is based on age and sex, it takes sample variation directly into account, thus providing results that are comparable across samples of different age and sex composition. Moreover, the RPD performs better as the percentage deceased becomes larger. These advantages lend greater reliability to the results obtained with the RPD.

In summary, the current study provides evidence of an association between rate of decline in cognitive function and subsequent survival. The magnitude of the association is virtually unaffected after adjustment for putative confounding variables. Therefore, this study's findings are compatible with the view that change in cognitive function is an independent predictor of longevity.

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## II.5

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# LONGEVITY IN LATE LIFE: PREDICTIVE ABILITY OF INDICATORS OF HEALTH AND ILLNESS IN NHANES I

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## Abstract

Data from the First National Health and Nutrition Examination Survey (NHANES I) were used to predict longevity in White subjects aged 65-74 years at baseline, 1971-75. At follow-up in 1986, vital status was known for 98.7% of the sample ( $n = 3137$ ). At that time, 49.5% had died. The NHANES I design involved collection of data from examination, interview and laboratory testing, such that more detailed data were collected in representative subsamples.

The majority of factors found to be independent predictors reflected cardiovascular conditions and allied risk factors. Others included indicators of activity, anthropometric variables, and laboratory measures of physiologic functioning. The percentage of variance explained was 34.1% (19 independent predictors) in the subsample for which the most detailed data were available ( $n = 682$ ). In the total sample, with least complete data, only 17.6% of the variance could be explained (21 independent predictors). In analyses of the total sample, the dominant predictors tended to be global indicators of ill health, including high sedimentation rate, poor skin evaluation, high pulse rate, high systolic blood pressure, abnormal findings from blood and urine analysis, drug use, low daily carbohydrate intake. When analyses were limited to the most fully studied subsample, a somewhat different set of predictors were revealed, including specific symptoms, signs, and history of disease (ECG findings, history of stroke, dyspnea without exertion, diabetes, kidney trouble, recent weight loss). Across all subsamples, an indicator of good health (worked in two weeks prior to examination) was a consistent predictor. Identification of these markers of health and illness offers a further specification of life-threatening conditions in older persons to which preventive measures may be directed.

## Introduction

Epidemiologic studies of longevity in older persons can roughly be described as having two underlying objectives. The first involves the recognition of groups at high risk as a means for facilitating intervention, treatment, or prevention. The second objective involves the identification of markers of aging. Those interested in prevention often base their studies in the community or use nationally representative samples. They usually include only limited clinical and biological information in addition to social and behavioral data, in order to maintain sufficient response rates (Mossey & Shapiro 1982, Parnes 1981, Kaplan & Camacho 1983, Cornoni-Huntley et al. 1986, Branch 1988, Jagger & Clark 1988). Researchers interested in markers of aging usually collect extensive clinical and biological information, and thus are forced to limit their study to (healthy) volunteers willing to undergo extensive and repeated testing (Bell et al. 1972, Libow 1974, Hale et al. 1980, Shock et al. 1984, Busse & Maddox 1985). The combination of both a nationally representative study sample and extensive clinical and biological information is rarely realized (Epstein et al. 1970, Rinder et al. 1975, Bengtsson et al. 1978, Dawber 1980, Tibblin et al. 1982, Haavisto et al. 1984).

The evidence from prior studies concerning predictors of longevity has not always been unequivocal, and has sometimes been contradictory. Possibly, this has resulted from the different objectives and, consequently, different quality and quantity of information collected across these studies. In addition, these studies differed with respect to methodological characteristics such as sampling frame, measurement instruments, follow-up time, and analytic method. The question of whether the different results across studies should be attributed to methodological differences or to different quality and quantity of information available can only be addressed when methodological characteristics are held constant. Such endeavor should shed light on questions such as to what extent prevention is really aimed at mechanisms favorable to continued good health or at those leading to premature death, and to what extent markers of aging are meaningful across all population groups.

The First National Health and Nutrition Examination Survey (NHANES I) and its follow-ups contain a wide range of health and social data on representative samples of Americans aged 1-74 years at baseline. Although some information is lacking that is considered specifically appropriate for older ages, such as cognitive and physical functioning (Branch & Jette 1981, Chirikos & Nestel 1985, Spitzer 1987), the clinical and biological information included in this dataset is potentially relevant to longevity.

The design of NHANES I involved collection of a core set of data for all participants, with supplementary and more detailed data being obtained for defined subsets of the total sample. This design allows the comparison of results

based on information of different quality and quantity, other design characteristics being equal. Thus, the opportunity exists to shed some light on observed differences in findings across studies. This paper addresses two questions related to the prediction of longevity: 1. What predictors predominate in the total sample versus subsamples? 2. Does the more extensive and detailed information available in subsamples add to the prediction of longevity compared to the more global information available for the total sample? In order to reach a maximum predictive ability, or alternatively, a maximum of variance explained, an approach is taken that capitalizes on ascertainment of predictors as systematic and complete as possible.

## Methods

**Study design.** The First National Health and Nutrition Examination Survey was conducted from 1971 to 1975 by the U.S. National Center for Health Statistics (NCHS). It was based on a national probability sample of 23,808 persons (25% of the original target population), aged 1-74 years, from the civilian, non-institutionalized population of the coterminous United States, excepting those persons residing in Indian reservations. Certain population groups thought to be at high risk of malnutrition, including the elderly, were oversampled (NCHS 1979a and b).

The main data collection took place from 1971 to 1973 in a subsample consisting of 65 locations (referred to as “locations 1-65”). Demographic information was obtained by means of a household questionnaire. Nutritional information was obtained by interviews as well as a questionnaire. A general medical history and medical examination, dental and dermatological examinations, anthropometry, and hematological, blood chemistry, and urological laboratory determinations provided clinical and biological information. An ophthalmological examination was conducted in the subsample consisting of locations 1-35.

On a random subsample across locations of adults aged 25-74 years, referred as the “detailed sample”, more clinical data were collected. These consisted of a medical history supplement, an extended medical examination, additional laboratory determinations, x-rays of the chest and hip and knee joints, goniometry, spirometry, electrocardiography, questionnaires concerning arthritis, respiratory and cardiovascular conditions (when applicable), and a health care needs questionnaire. A general well-being questionnaire to this sample provided the only psychological information available in the NHANES I.

After the nutrition survey was completed, the detailed examination was continued in 1974 and 1975 until the total number of persons examined in detail was approximately double the number of examinees who received the detailed exami-



nation during the nutrition survey (NCHS 1978). This augmentation sample is indicated as “locations 66-100”. Several items were added to this final survey component, including the Center for Epidemiologic Studies Depression scale (CES-D).

In 1981, the NCHS and the National Institute on Aging, in collaboration with seven other NIH-Institutes and agencies of the United States Public Health Service, initiated the NHANES I Epidemiologic Follow-up Study (NHEFS) of all subjects aged 25-74 during NHANES I. The data collection took place in 1982-84. Information was obtained on 93% of the survivors, while death certificates were obtained for 96% of the decedents (Madans et al. 1986). For participants aged 55 years and over at baseline, telephone follow-up interviews have been conducted annually since 1986. This report uses vital status information from the 1986 wave of this NHANES I Continued Follow-up Study of the Elderly, which was available for 98.2% of all eligible sample members examined at baseline (Cadell et al. 1987).

In order to enable comparison with a previous study of predictors of longevity in Dutch persons aged 65 and over (Deeg et al. in press), this report makes use of data on White persons aged 65-74 years at baseline whose vital status was known as of 1986. Sample sizes in each of the subsamples by year of examination and by 5-year age group and sex are displayed in Table 1. The total sample included 3137 subjects (98.7% of Whites aged 65-74 years at baseline), while subsample sizes ranged from 340 (locations 66-100) to 2797 (locations 1-65). The detailed sample included 1022 subjects.

**Table 1** National Health and Nutrition Examination Survey I Continued Follow-up of the Elderly. Numbers of White persons aged 65-74 at baseline with vital status known as of 1986 in total sample and subsamples, by year of examination and by age group and sex.

sample*	total	year of examination					ages 65-69		ages 70+	
		71	72	73	74	75	M	F	M	F
total	3137	410	1145	1011	354	217	859	937	627	714
total: ls. 1-35	1240	410	830	—	—	—	332	380	264	264
total: ls. 1-65	2797	410	1145	1011	231	—	773	843	552	629
detailed	1022	103	282	239	181	217	285	308	207	222
det.: ls. 1-35	302	103	199	—	—	—	80	98	59	65
det.: ls. 1-65	682	103	282	239	58	—	199	214	132	137
det.: ls. 66-100	340	—	—	—	123	217	86	94	75	85

\* abbreviations: ls. = locations, det. = detailed

Baseline information that was considered potentially relevant to longevity is summarized in Table 2. The information was grouped into four categories: {I} *objective assessments* of signs of disease from physical and laboratory examination; {II} *symptoms* of disease from *self reports* (medical history); {III} other *indicators* of health, namely activity and health care use; {IV} social and psychological *co-factors*, including life style and demography. Each category is further divided into two or more sub-categories, henceforth referred to as “fields”, of which there are 16 in total.

**The measurement of longevity.** The concept of longevity was expressed as the Realized Probability of Dying (RPD), a function of survival time, sex and age at baseline (Deeg et al. 1989). This function was designed to make the survival time of sample subjects of different sex and age comparable. The RPD compares each individual subject’s survival time with the survival curve of those peers in the total population who have the same age and sex and who were still alive at the baseline examination. Possible values of the Realized Probability of Dying are between 0 and 1. These values introduce a rank order among all sample subjects. For example, the value of an individual’s RPD is 0.7, if at the time of his or her death 70% of the population comparison group is still alive. If the RPD is uniformly distributed on the interval (0,1), the survival distribution of the sample represents that of the total population. Uniformity requires that the mean is 0.50 and the standard deviation, 0.29. For the samples used in the current study, the RPD was indeed approximately uniformly distributed (Table 3).

Figure 1 depicts, as an illustration, two survival curves: one for all white American men aged 65 years in 1971 and one for all white American men aged 75 years in 1971. The survival curves are based on the population mortality rates in the successive years following baseline through 1986 as provided by the National Center for Health Statistics. It can be derived that a man aged 65 in 1971 (the year of his baseline examination) who dies 14 years after baseline (in 1985) has a RPD of approximately 0.5, or 50%, because 50% of the members of his birth cohort still alive in 1971 survived until 1985. For a man aged 75 in the same year of baseline examination, the RPD would be 0.5, when he would have lived approximately 8 years following baseline.

For those 50.5% of subjects still alive at the end of the study (1986), a value of the Realized Probability of Dying was imputed. The RPD for these subjects was estimated by assuming that their remaining survival time corresponded to the median population survival time from end-of-follow-up onward. This amounted to multiplying the probability of reaching their age in 1986 by one half. For instance, a man aged 65 when examined in 1971, reached the age of 80 (in 1986) with probability 0.48; his imputed RPD is 0.24, implying that he was expected to die when only 24% of his cohort would still be alive.

**Table 2** National Health and Nutrition Examination Survey I Continued Follow-up of the Elderly. Baseline information representing aspects of health status potentially relevant to longevity and subsamples in which available.

category and field	subsample*				
	total	detailed			
		ls. 1-35	ls. 1-65	ls. 1-35	ls. 1-65
<b>{I} Objective Assessments</b>					
{1} physical examination	partly	partly	yes	yes	partly
{2} electrocardiograms	no	no	yes	yes	yes
{3} anthropometry	partly	partly	yes	yes	yes
{4} bio-chemistry	partly	partly	partly	partly	partly
{5} dermatology	yes	yes	yes	yes	no
{6} ophthalmology	yes	no	yes	no	no
{7} spirometry	no	no	yes	yes	yes
<b>{II} Symptoms, Self-report</b>					
{8} medical history	partly	partly	partly	partly	partly
{9} med. hist. supplement	no	no	partly	partly	partly
{10} arthritis	no	no	yes	yes	yes
<b>{III} Indicators Of Health</b>					
{11} activity	partly	partly	partly	partly	partly
{12} health care use	partly	partly	partly	partly	partly
<b>{IV} Social And Psychological Co-factors</b>					
{13} nutrition	yes	yes	yes	yes	no
{14} life style	partly	partly	partly	partly	partly
{15} well-being	no	no	partly	partly	yes
{16} demography	partly	partly	yes	yes	partly

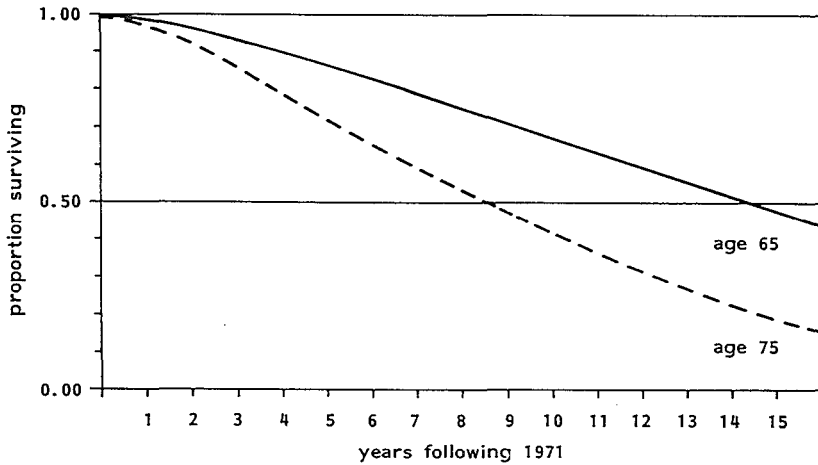
\* ls. = locations  
 yes = all variables in this field are available in this subsample  
 partly = some but not all of the variables in this field are available in this subsample  
 no = no variables in this field are available in this subsample

**Statistical methods.** Because the Realized Probability of Dying was uniformly distributed, the logit of the RPD (LRPD) was approximately normally distributed with mean 0. By consequence, the LRPD could be used as the dependent variable in regression analysis, the main analytical method in this study.

The data analysis was carried out in two steps:

1. selection of a set of independent variables for further analysis;
2. multivariate evaluation of factors related to the LRPD.

**Figure 1** Survival curves for U.S. males aged 65 and 75 in 1971



The first step involves examination of the variables within each field. The number of variables per field ranged from 6 to 126, amounting to a total of 780 potential predictor variables. The main predictors of longevity were selected in several phases. Initially, variables with more than two response categories were

**Table 3** National Health and Nutrition Examination Survey I Continued Follow-up of the Elderly. Mean and standard deviation of the Realized Probability of Dying in total sample and subsamples.

sample	mean	standard deviation
total	0.49	0.26
total: locations 1-35	0.50	0.28
total: locations 1-65	0.49	0.27
detailed	0.49	0.26
detailed: locations 1-35	0.51	0.27
detailed: locations 1-65	0.50	0.27
detailed: locations 66-100	0.49	0.25

recoded such that the categories obtained a rank order according to a monotonously increasing or decreasing estimated impact on longevity. Then, within each field, independent predictors of the LRPD were identified by forward stepwise regression analysis. This method of analysis guarantees a systematic evaluation, and brings the large number of variables down to a manageable number while maximizing predictive ability (Leigh 1988). To provide for possible non-linear relationships, the quadratic term of each independent variable with more than two categories was included in addition to the linear. Only variables adding significantly ( $p < 0.05$ ) to the percentage of variance explained were retained.

In the majority of the fields, observations were missing for less than 1% of subjects. Electrocardiograms were missing for 8.4% of subjects (detailed sample). Bone density variables (detailed sample) were missing for 11.2% of subjects. For this reason, and because of their considerable correlation with the upper arm girth and sitting height ( $r = 0.65$  and  $0.57$  respectively), bone density variables were omitted from further analysis. The highest percentage of missing values occurred in hematological variables (10.9 — 52.6%). Specifically, in the red and white blood cell counts many observations were missing. These two variables were omitted from further analysis. Valid spirometry measures were available only on 71.8% of all persons examined in the detailed sample. Despite their relatively strong univariate association with longevity and their only moderate correlations with other variables (the highest with sitting height:  $r = 0.48$ ), these variables were omitted from further analysis. Finally, those variables that were only available for locations 66-100 were also omitted from further analysis, because in a multivariate model including other variables with even a small percentage of observations missing, the total number of subjects with complete information would have been reduced to the extent that predictions would become unstable. This concerned specifically the CES-D scale, of which the zero-order correlation with the LRPD was fairly high ( $r = 0.27$ ).

A final selection criterion for the set of variables for further analysis was that no collinearity between independent variables across fields should occur. Collinear variables were detected by calculating zero-order correlations ( $r$ ) and by factor analytic methods. When collinearity ( $r \geq 0.60$ ) between two or more variables occurred, the variable was retained for further analysis which had the highest zero-order correlation with the LRPD, or — in case of equal correlations — which loaded highest on the common factor.

In the second step of the data analysis, the selected variables — i.e. their linear as well as their quadratic terms — were entered as independent variables in forward stepwise regression analysis with the LRPD as the dependent variable. This analysis was performed in the total sample, the total sample: locations 1-65, the detailed sample, and the detailed sample: locations 1-65 respectively, each time using the variables selected from the information available for the specific sample.

Those independent variables are reported that added significantly to the percentage of variance explained. To facilitate comparison among the significant predictors in terms of their relative importance, their standardized regression coefficients are reported.

Because the NHANES I sample is a national probability sample, with probability of selection varying by age, sex, residence, and income, sample weights should be used if one should wish to obtain estimates which are representative of the US population. However, because the use of such weights presents additional analytic complexity, and because the purpose of the present analyses is to compare predictors across subsamples rather than estimate the magnitudes of their effects, the results of unweighted analyses are reported.

## Results

The variables that proved to be independent predictors of longevity in four subsamples after performing both analysis steps are listed in Table 4. The information contained in Table 4 is discussed first with regard to the nature of the predictors, and second with regard to their predictive ability.

**Nature of predictors.** The number of independent predictors in each sample turned out to be approximately equal, ranging from 19 to 22. In contrast, the number of variables included in the second analysis step increased from 32 in the total sample to 68 in the detailed sample: locations 1-65. The independent predictors tended to be more specific in the detailed samples as compared to the total sample, thus superseding the more general variables available for the total sample. The number of objective assessments and self-reported symptoms having independent predictive ability increased from 12 in the total sample to 15 in the detailed sample, whereas the number of indicators and social and psychological co-factors having independent predictive ability decreased from 9 in the total sample to 4 in the detailed sample: locations 1-65. For example, usual day activity (non-recreational) appeared no longer as an independent predictor in the detailed sample. Note also the supersedence of blood pressure in the detailed sample where information was available on symptoms based on chest auscultation such as systolic murmur (intercorrelation  $r = 0.17$ ) and electrocardiography such as ST-T depression (intercorrelation  $r = 0.13$ ). Similarly, all biochemistry variables were superseded in the detailed samples. Erythrocyte sedimentation rate, for example, was intercorrelated with shortness of breath when walking (ordinary pace on a level surface), and with ST-T depression (both  $r = 0.11$ ), while glucose was intercorrelated with taking insulin and with hepatomegaly ( $r = -0.15$  and  $-0.16$ , respectively). A frequently cited predictor of (cardiovascular) mortality, total serum cholesterol, was not selected for analysis in step 1. Another cardiovascular risk factor, body

mass index, was selected for analysis in step 2, but did not appear to have independent predictive ability.

Among the several social, psychological, and life style variables, only cigarette smoking, daily carbohydrate intake, and insurance for medical care were independently predictive of longevity. The lack of independent predictive ability of other social and psychological co-factors such as well-being may be attributable to correlations between these and other factors; for example, both subjective health and freedom from health worry were correlated with usual day activity ( $r = 0.27$  and  $0.21$ , respectively, detailed sample). The intercorrelations of well-being with work in past two weeks, were slightly lower but still significant:  $r = 0.15$  (subjective health) and  $r = 0.09$  (freedom of health worry). Similarly, the influence of variables reflecting socio-economic status may have been weakened as a result of their association with other independent predictors such as cardiovascular risk factors: the zero-order correlation coefficients of number of years of schooling with systolic blood pressure and glucose were small but significant ( $r = -0.08$  for both, total sample). The number of persons per room in the household, another indicator of socio-economic status, was correlated with the independent predictor ST-T depression ( $r = 0.11$ , detailed sample: locations 1-65).

The direction of the effect of these predictors was generally in accordance with expectation: the worse the condition (findings upon cardiovascular evaluation, greater shortness of breath, more medication, etc.) the shorter the longevity (indicated by a higher LRPD). However, associations of upper arm girth and total carbohydrate with the LRPD were negative: the smaller the girth and the lesser the carbohydrate intake, the shorter the survival time. These findings might suggest that, in this age group, overweight was not as much a risk factor as was low nutritional intake. The indicator medication for upset stomach/indigestion (coded: regularly — occasionally — no) had a small, reversed association with the RPD.

The persistent, negative correlations of age at baseline with the RPD need some further consideration. The fundamental reason for employing the RPD was to adjust survival time for the influence of age and sex, thereby allowing men and women of all ages to be pooled for the prediction of longevity. The negative correlation probably reflects an age-dependent selection bias for participation in the survey. The sex- and age-specific survival curves against which individuals are compared as their RPD's are calculated were established for the general population, including institutionalized and impaired persons. In contrast, participation in NHANES I required that the subject not be institutionalized, and that he or she tolerate a rather extensive examination and interview. Since the prevalence of both institutionalization and impairments increases with advancing age, older survey participants will be progressively more selected for relatively good health.

In contrast, the negative correlation of month of examination with the RPD is not likely to reflect either a substantive association or a selection bias. Since the

**Table 4** Independent predictors of longevity in four NHANES I samples: standardized regression coefficients (beta's).

variable label	available in sample <sup>2)</sup>	standardized beta (order of term <sup>1)</sup> )			
		total sample		detailed sample	
		all n=2852 a	ls. 1-65 n=2163 +	all n=904 *	s. 1-65 n=559 +*
<i>Objective assessments</i>					
cardiovascular evaluation	a	-.06	-.06	n.s.	-.08
chest evaluation	+		-.08		-.15
chest auscultation	*			.08	n.s.
systolic blood pressure (sitting)	a	-.33,.40	.05	n.s.	n.s.
irregular pulse	a	.06	n.s.	n.s.	n.s.
systolic murmur	*			.08	n.s.
hepatomegaly	a	-.05	n.s.	-.08	n.s.
abdominal evaluation	a	n.s.	n.s.	n.s.	-.08
pulse palpation femoral	*			n.s.	.11
left lateral bending cervical	*			.08	.10
skin evaluation	a	-.06	n.s.	n.s.	n.s.
ST-T depression non-specific	*			.11	.12
Q-S duration	*			.09	n.s.
mean heart rate	*			.07	n.s.
upper arm girth	a	-.92,.85	-.77,.61	n.s.	-.80,.74
sitting height	a	n.s.	n.s.	-.08	n.s.
sedimentation rate	+		.10		n.s.
glucose (urine dipstick)	a	.08	n.s.	n.s.	n.s.
albumin (urine dipstick)	a	.06	.06	n.s.	n.s.
serum albumin	+		-.06		n.s.
serum magnesium	a	-.63,.57	n.s.	n.s.	n.s.
total iron binding capacity	+		.06		n.s.
<i>Symptoms — self report</i>					
ever/still chron.bronchitis or emphysema	a	-.04	n.s.	-.05	-.06
ever/still diabetes	+		-.08		-2.55,2.44
ever/still high blood pressure	+		-.05		n.s.
ever/still benign tumor, growth, cyst	a	-.07	-.06	-.09	n.s.
years since stroke	a	.12,-.09	.05	.09	.14
maximum weight ever	+		.11		n.s.
age at minimum weight	+		n.s.		-.55,.67
difficulty swallowing ≥ 3 days/month	a	n.s.	-.04	n.s.	n.s.
any health problem now	*			.06	n.s.



Table 4 (continued)

variable label	available in sample <sup>2)</sup>	standardized beta (order of term <sup>1)</sup> )			
		total sample		detailed sample	
		all n=2852 a	ls. 1-65 n=2163 +	all n=904 *	s. 1-65 n=559 +*
shortness of breath when walking on level surface	*			-.10	-.12
possible heart or circulation problems	*			n.s.	.15
kidney or bladder trouble, pain when urinating	*			-.11	-.14
frequency of adventitious noises in ear past year	*			.09	.05
<i>Indicators</i>					
activity usual day (non-recreation)	a	-.21, .33	-.24, .36	n.s.	n.s.
physical activity past 24 hours	a	-.04	n.s.	n.s.	n.s.
work in past two weeks	a	.05	.05	.08	.11
medication for weak heart	a	-.11	-.10	-.08	n.s.
take medicine while chestpain when walking	*			n.s.	-.09
medication for water loss (fluid pills)	a	-.07	-.07	n.s.	n.s.
take insulin	*			-.11	n.s.
time from first chest/lung trouble to doctor	*			n.s.	.10
medication for upset stomach/indigestion	a	.05	.05	n.s.	n.s.
medication for pains other than headache	a	-.04	n.s.	n.s.	n.s.
<i>Social and psychological co-factors</i>					
total carbohydrate 24 hour recall	+		-.06		n.s.
smoke cigarettes now	*			-.82, .71	n.s.
insurance for medical care	*			.08	n.s.
age at baseline examination	a	-.11	-.11	-.09	-.11
month of examination	a	-.08	-.07	-.06	n.s.
number of variables		21 (9+3+7+2)	22 (8+6+5+3)	22 (8+7+3+4)	19 (7+8+3+1)
total percent variance explained		17.6%	20.9%	24.4%	34.1%

1) .nn = dichotomous variable  
 .nn = linear term  
 .nn = quadratic term

2) a = total sample  
 + = locations 1-65  
 \* = detailed sample

RPD was calculated on a yearly basis, it was only “exact” for those examined in the middle of the year. By consequence, the survival time of those examined early in the year was shortened, while that of those examined late in the year was lengthened by a few months.

**Predictive ability.** Information on the predictive ability of the joint independent predictors is provided by the total variance explained in the LRPD. This statistic increased from 17.6% in the total sample to 34.1% in the detailed sample: locations 1-65. Thus, not only were the predictors in the detailed samples more specific, they also explained a greater percent of variance.

The standardized regression coefficients of the predictors (beta’s) indicate the relative effect on the LRPD when controlling for the other predictors selected into the model. For several predictors the quadratic rather than the linear term was selected; for a few predictors, both linear and quadratic terms were selected. In the latter case, an approximation of the relative effect of the predictor can be obtained by summing both beta’s. The standardized regression coefficient of usual day activity, then, was the largest one in those samples where this variable was selected as an independent predictor (beta  $\approx$  0.12). Usual day activity also showed the largest zero-order correlation with the RPD ( $r = 0.22$ , total sample). In the detailed samples, the standardized regression coefficient of chest evaluation ranked among the largest beta’s (beta =  $-0.15$ ). Chest evaluation also showed a high zero-order correlation with the RPD ( $r = -0.19$ , detailed sample: locations 1-65). A beta of similar magnitude was associated with self-reported heart or circulation problems.

Closer inspection of the quadratic relationships found may lead to some interesting tentative interpretations, to be investigated in more focussed analyses. In the first group of variables (*Objective assessments*), systolic blood pressure showed such a quadratic relationship with the LRPD, indicating that there was no association with survival time in the lower ranges of pressure, or alternatively, that there was a slight inverse association in the lower ranges (J-shaped association). The same may be true for mean heart rate. Upper arm girth showed a reversed J-shaped association with longevity, reflecting a stronger association in the lower ranges. The quadratic association of erythrocyte sedimentation rate indicates that this physiologic variable was associated with decreased longevity particularly in the higher ranges. Serum magnesium, on the other hand, was associated with shorter survival time particularly in the lower ranges.

In the group *Symptoms — self report*, the quadratic associations in those items reporting ever/still high blood pressure and ever/still benign tumor, indicated that having had the condition in the past was not associated with risk of shorter survival time as compared to never having had the condition, whereas the risk was concentrated in those currently having the condition. Maximum weight ever showed a J-shaped association indicating that the risk was particularly concentrated in the

more extreme overweight range, while the J-shaped association of age at minimum weight indicated that the more recent the minimum weight, the greater the risk. This is equivalent to an association between recent weight loss and survival time.

In the *Indicators* group, usual day activity was coded according to decreasing activity. Therefore, its J-shaped association indicates that the excess mortality risk was concentrated in the category “quite inactive”. The medication variables were coded “regularly — occasionally — no”. Thus, occasional medications for weak heart and water loss were not associated with shorter survival time as compared to no medication, whereas regular medication was.

Finally, among the social and psychological *co-factors*, the life style predictor current smoking was coded “yes — not currently — never”. Its reversed J-shaped association with the LRPD therefore indicates that having smoked in the past did not increase mortality risk as compared to never having smoked, but that the increased risk was concentrated in current smokers.

More detailed and specific analyses of the continuous variables showing non-linear associations with longevity will be necessary to determine threshold values. The purpose of this report is to evaluate the independent predictors of longevity as systematically and completely as possible. This purpose would have fallen short had quadratic associations been disregarded.

To summarize the results presented, the detailed information available in subsamples did in fact add to the prediction of longevity as compared to the more global information available in the total sample. The variance explained rose from 17.6% to 34.1%, despite the fact the number of independent predictors stayed around 20. The information available in the detailed sample appeared to be more directly relevant to longevity; variables conveying more specific health/illness information tended to replace less specific variables available for the total sample. A major portion of this information concerned cardiovascular conditions and allied risk factors, such as ECG findings, systolic murmur, history of stroke, diabetes, dyspnea without exertion, and kidney trouble. Other illness-related independent predictors were being underweight, having chronic bronchitis, and having a (benign) tumor. The one independent predictor indicating good health that stood out in all samples was “worked in past two weeks”.

Comparing these independent predictors with those in the total sample where less detailed information was available, it is evident that cardiovascular conditions and allied risk factors still account for the largest portion of the predictive value. In the total sample, these conditions are indicated in less direct ways, e.g. by systolic blood pressure, pulse, and medications taken. In addition, a greater proportion of the independent predictors are markers of non-specific disease, such as skin evaluation, albumin in urine, physical activity, non-specific drug use. Erythrocyte sedimentation rate, only available in locations 1-65, is a similarly non-specific

independent predictor in the total sample: locations 1-65, but no longer in the detailed sample: locations 1-65.

## Discussion

In this report, physical as well as behavioral variables were shown to be related to longevity in the elderly over approximately 13 years of follow-up. The more specific the information contained in the variables available, the greater was the predictive ability and the more parsimonious the model. The amount of variance explained in longevity was 18 — 34%, depending on the information available in the subsample examined. This amount is comparable to findings in other studies among elderly (Palmore 1970, 1974, Botwinick et al. 1978, Hodkinson & Piper 1981, Abramson et al. 1982, Palmore 1982). However, since this study aimed at maximizing the variance explained, this outcome does not seem quite satisfactory. Several aspects of the study design may have prevented an optimal result.

First, many observers were involved in the data collection. Although no assessment is available of inter-observer variation, there is reason to assume that it is non-negligible. The “noise” that is thus introduced is likely to decrease the variance explained.

Second, the ordering of response categories may be improved. As these were originally designed for a cross-sectional, descriptive study, recoding of the categories was needed such that they were ordered according to expected association with survival time. Ideally, for simplicity of analysis and interpretation, the new order results in a linear relationship between the variable and longevity. Because in many instances knowledge of the relative effects of specific categories was lacking, the order decided upon may not always have allowed the true influence of the predictor to be apparent. By applying quadratic instead of linear regression analysis, loss of explained variance due to quadratic relationships has been prevented.

Third, exact survival time was known for 49.5% of the sample (death having occurred), remaining survival time, and thus RPD, being imputed for subjects alive at the end of the follow-up period. The rank order thus introduced among subjects may not correspond to the true one, and consequently obscure significant associations.

Apart from the magnitude of the predicted effect, some comments on the content of the predictors are in order. Although cardiovascular conditions and allied risk factors were the predominant predictors of longevity, only a modest role was played by established risk factors such as high serum cholesterol, a high systolic blood pressure, smoking, and being overweight (Truett et al. 1967, Pooling Project Research Group 1978, Leaverton et al. 1987). Moreover, in the biochemistry field,

cholesterol was superseded by other predictors already in the first selection step. Furthermore, the risk of being underweight was shown to be greater than that of being overweight. Possibly, these discrepancies are due to the age of the current sample: the well-known risk factors cited were established in samples of middle aged as opposed to elderly subjects. There is some evidence that the effects of these risk factors are not as strong in older age groups as they are in younger ones (Semenciw et al. 1988). The effect of systolic blood pressure and serum cholesterol on all-cause mortality has been shown to be decreased or absent in older age groups (Agner 1983, Kessler & Reimer 1987, Shibata et al. 1988). This may be due to a greater homogeneity in extent of atherosclerosis among progressively older persons. In a study of persons of mean age 88 years, Mattila et al. (1988) even found an inverse relation of both diastolic and systolic blood pressure with mortality, which suggests that a moderately elevated blood pressure may indicate an adaptive cardiovascular phenomenon. The J-shaped relationship of systolic blood pressure with survival time, the independent predictive ability of a reduced or non-palpable femoral pulse, and the consistent predictive ability of cardiovascular abnormalities observed by examination in the present study are compatible with this view.

Our results concerning the predictive ability of other specific clinical measurements for longevity in older persons is mostly supported by previous evidence. A meaningful gain in predictive ability by considering ECG findings in addition to routinely available clinical information has also been demonstrated by Velema et al. (1985). However, the specific ECG abnormalities reported to have maximal predictive ability differ across studies, possibly due to differences in coding and selection of endpoints. ST-T abnormalities showed a clear predictive value for survival time in our data, confirming the findings of Knutsen et al. (1988) of an independent association with incidence of cardiovascular disease. Q-S duration showed a weaker, but still independent, association in our data. Prolonged Q-S duration has not been consistently reported as a predictor of cardiovascular disease. Although intraventricular conduction defects were not found to be associated with CVD incidence by Knutsen et al. (1988), an association with cardiac death was found by Schneider et al. (1980), Velema et al. (1985), and Hinkle et al. (1988). The prognostic significance of elevated heart rate and irregular pulse (various arrhythmias) for cardiac death has been observed by others (Berkson et al. 1970, Ruberman et al. 1981, Velema et al. 1985).

Serum glucose level, self-reported diabetes, and particularly insulin medication has been shown to predict both cardiovascular and all-cause mortality (Agner 1983, Harris et al. 1988a, Kleinman et al. 1988, Benfante et al. 1989). Erythrocyte sedimentation rate has been observed to be an independent predictor of survival time (Campbell et al. 1986, Deeg et al. in press). Decreased serum albumin as well as albuminuria have also been found to be associated with mortality (Libow 1974,

Hodkinson & Piper 1981, Heinämäki et al. 1986, Caradoc-Davies 1987, Shibata et al. 1988). The demonstrated adverse effects on longevity of low serum magnesium and total iron binding capacity, like those of a small upper arm girth (an indirect measure of muscular mass), “recent weight loss” (age at minimum weight) and low total carbohydrate intake, may be interpreted as signs of sub-optimal nutrition, possibly reflecting lack of physical activity and underlying disease (Marton et al. 1981, Menotti et al. 1987, Harris et al. 1988b) or depression (Braun et al. 1988).

The self-reported conditions found to have independent predictive ability correspond with the four leading causes of death among older U.S. citizens: heart disease, stroke, cancer and chronic lung disease (e.g., Manton & Soldo 1985, Brody et al. 1987). The number of years since stroke, a consistent predictor across samples, suggests that the longer the cerebrovascular disease has existed, the shorter the remaining life time. Difficulty swallowing and hearing adventitious noises appeared to be correlated with diabetes and chest conditions such as emphysema and shortness of breath; persons mentioning these symptoms were particularly likely to rate their health as poor and to use medication frequently. Shortness of breath has been shown to predict survival in studies focussing on forced expiratory volume (Marcus et al. 1989), even independent of smoking status (Cook 1987, Menotti et al. 1987, Ebi-Kryston 1988). Our results suggest that self-reported shortness of breath without exertion is also an independent predictor of longevity (cf. Kaplan & Kotler 1985).

The first three Indicators showing independent predictive ability are related to physical activity. In studies of the elderly, physical functioning is usually measured by more detailed scales of activities of daily living, measuring degrees of dependency with respect to self-care and adaptation to the environment (Branch & Meyers 1987, Fillenbaum 1987). Some studies use measures of more vigorous activity, also referred to as “health practices”, which can be considered markers of good rather than poor health (Belloc & Breslow 1972, Mor 1987). In the present study, work in past two weeks, a consistent, independent predictor can be interpreted as a marker of good health, singling out those who have above-average health rather than those who have below-average health. In studies of survival time with a relatively long follow-up, this distinction becomes meaningful (cf. Kaplan et al. 1987, Deeg et al. in press).

The most notable group of factors apparently lacking significant associations with longevity are social and psychological co-factors. Both subjective health and health worry lack of significant predictive ability, although these variables were in fact included in the detailed samples analyses. Yet, many previous reports bear witness to the importance of these factors in longevity in the elderly (Lehr 1982, Mossey & Shapiro 1982, Kaplan & Camacho 1983, Deeg 1987, Kaplan et al. 1988). Our analyses did not include a measure of depressive symptomatology. Information from the CES-D scale, an instrument to identify depressive symptoms, was

only available in the smallest subsample (locations 66-100), which sample was not analyzed because of its small size and the instable estimates which might result. The CES-D scale has indeed been shown to have such independent predictive ability for physical health (Berkman et al. 1986). The remaining subjective and psychosocial variables available for analysis may not have been those most pertinent to longevity in older age groups. Data on cognitive functioning and social connectedness, to name two psychosocial factors contributing importantly to longevity (Palmore 1974, Botwinick et al. 1978, Berkman & Syme 1979, Cohen & Brody 1981, Blazer 1982, House et al. 1982, Schoenbach et al. 1986) were not collected. The NHANES I was designed to include all ages up to 74 years, and was not specifically intended to provide information relevant to older age and longevity. Yet, the present findings suggest that conclusions with regard to the importance of social factors for the prediction of longevity should be suspended until pertinent information on concomitant health- and illness-related factors is available.

Some final comments should address the question of the relevance of our findings to the prevention of premature death in late life. Current health care delivery philosophy advocates the targeting of health care to groups identified on the basis of social or economic characteristics. However, our findings suggest that these characteristics at most have an indirect effect on longevity. The direct identification of persons with evidence of disease may represent a more efficient means for targeting limited health care resources. Direct identification might be realized by periodic disease screening programs for older persons. A community screening program for the older age group, however, does not satisfy the criteria that are generally accepted for a screening to be feasible, the most important problem being that there is not one clearly defined target disease for the detection of which one specific test is available (Wilson & Jungner 1968). Moreover, the occurrence of “false positives” may result in needless disturbance and costs (Frederiks 1986).

Alternatively, preselection of persons at risk of health decline may be effectuated in the context of general practice or community nursing (Huygen 1986). Assessment of the predictors identified in this study among selected persons will help to obtain a more detailed picture of specific health risks incurred. This strategy of consultation-based screening then, sometimes referred to as “case finding” (Freer 1987, Buckley & Williamson 1988), benefits from a systematic ascertainment of markers of poor health such as was performed in the present study.

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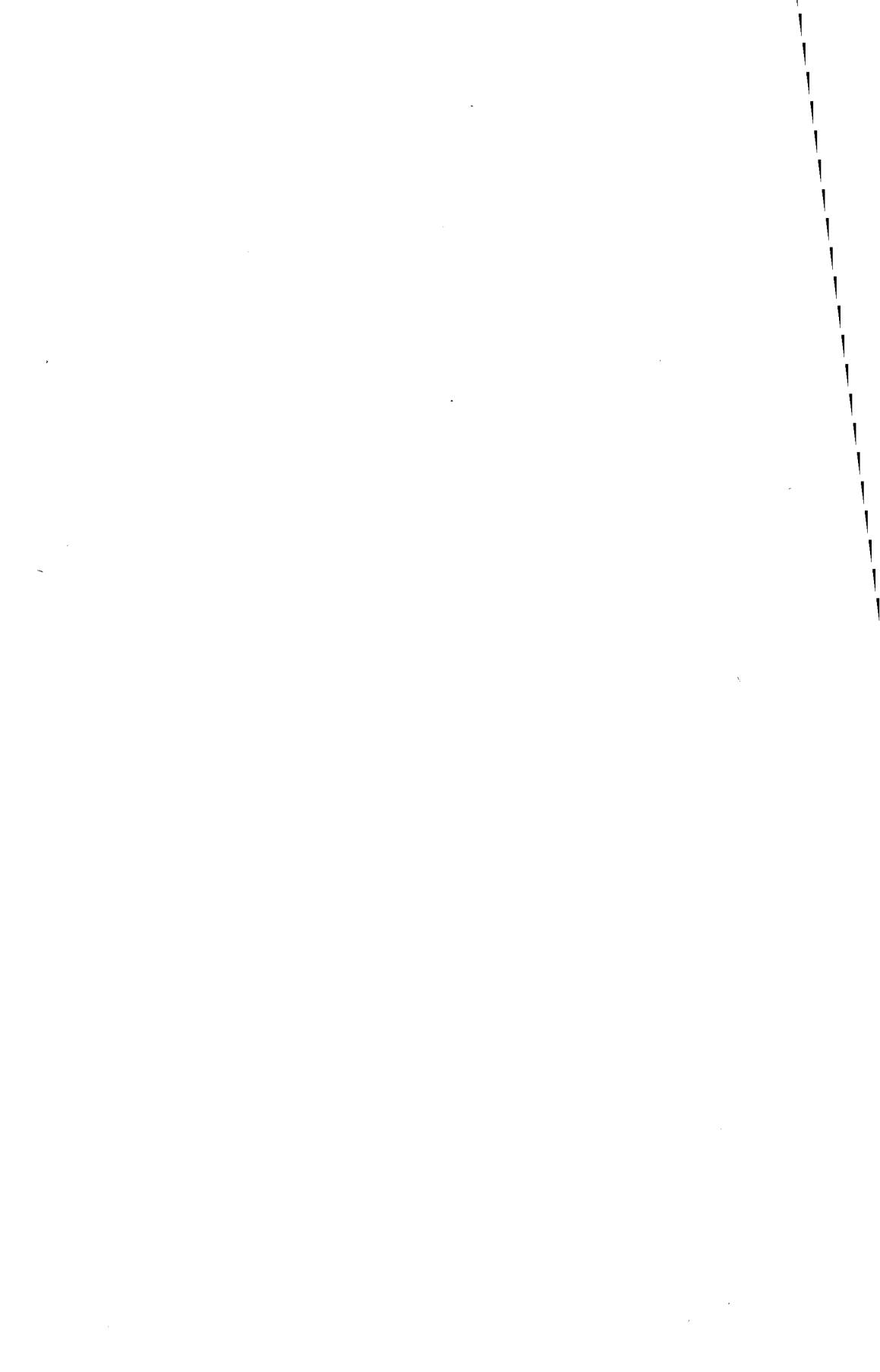
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II.6

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THE PREDICTION OF SURVIVAL TIME OF  
ELDERLY IN A  
RESIDENTIAL HOME

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## Summary

In a study of survival time of residents in a Dutch home for the elderly, 298 residents of mean initial age 83 years were followed during 4½ years. The survival time of 80% of residents was below the median survival time of the general population. There appeared to be a clear gradient of mean RPD across age categories, indicating an increasingly shorter survival time for younger ages as compared to the general population. From age-specific multiple regression models, survival time in residents aged 80 years and over appeared to be associated with physical disability and morale in addition to age and admission year, while in residents younger than 80 years no predictors of survival time other than age were found. Thus, younger residents died relatively sooner and were more homogeneous with respect to survival time than older ones. These findings indicate that stricter admission criteria may have been used for younger residents and that older residents may be more similar to the general population.



## Introduction

Studies of survival of residents in long-term care institutions have accumulated over the past decades (Kay et al. 1956, Costello & Tanaka 1961, Lieberman 1961, Goldfarb et al. 1966, Kral & Müller 1966, Epstein 1971, Brody et al. 1972, Van den Heuvel 1977, Brauer et al. 1978, Diesfeldt 1979, Uhlmann 1987). Typically, characteristics of interest to the investigators are assessed at some point in time (*baseline*), upon which after a certain time period mortality and survival are ascertained and related to baseline characteristics. The follow-up period may last from six weeks to over ten years. In most studies, but not in all, age plays a predominant role among the resulting predictors of survival (exceptions: Lieberman 1961, Goldfarb et al. 1966, Diesfeldt 1979). The older the residents, the smaller their probability of survival. Generally, this result is considered not surprising, because the same association holds in the general population. However, it is not evaluated how the study population compares to the general population. Since admission to a long-term care institution is not a random process and is often based on criteria related to diminished self-reliance and increased disability, it is neither evident that characteristics of residents of long-term care institutions should resemble those of the general population nor that the same associations with survival should hold in both populations. Moreover, since admission criteria differ across institutions, characteristics of residents and associations with survival may well differ accordingly (Goldfarb et al. 1966).

The present study started from the position that the residential population of a home for the elderly differs from the general population, and investigated: 1. the extent of the difference with respect to survival time between residents of a large home in the Netherlands and the general Dutch population; 2. the consequences of the demonstrated difference for the prediction of survival time or longevity in this home. Special consideration was given to subgroups of residents who may have been admitted to the home based on different criteria.

As of 1981, less than 5% of the total Dutch population below age 80 resided in a home for the elderly. This percentage increased dramatically in the ages 80 and over, and reached a high of 35% for males and 43% for females in the age group 90 and over (Huijsman 1988). It is hypothesized that persons of ages younger than 80 were likely to have been admitted for different reasons than persons over age 80. Younger applicants may have been more in need of the services offered by the home because they were no longer able to live independently. Relocation to the home may not as much have been their choice but instead, their only alternative. The year 1977 marks the institution of the so-called "Assessment Committees Homes for the Elderly" with the task to assess the disability of applicants to homes for the elderly. Admission to a home was now dependent on the degree of disability of applicants. Residents older than 80 years in 1981 may have chosen to live in the

home before 1977 when selection criteria were not yet established. They may have continued living their fully independent lives, and not have declined. Alternatively, older persons may have been admitted by way of precaution, because they were living alone and had no support system available in case their health would decline (Van der Does 1988).

These hypothesized differences between younger and older residents, and similarly between residents admitted prior to 1977 and since 1977 may be reflected in different findings when attempting to predict survival time. Therefore, factors associated with survival time in younger and older residents ( $\leq 79$  and  $\geq 80$  years) and in residents more and less recently admitted (prior to and since 1977) were evaluated separately.

## Material and methods

### Study sample and design

All residents of a large residential home for the elderly in the Netherlands were assessed by staff members at three month intervals during four and a half years. Of those 298 residents living in the home at baseline (June 1981), vital status and, in case of death, date of death were ascertained up to January 1986. The average age at baseline was 83.7 years (standard deviation 5.6 years); the average duration of residence was 6.5 years (standard deviation 5.9 years); 72% were women; 74% were widowed.

### Baseline measurements

The three-monthly ratings of each resident by staff members pertained to physical, mental and social functioning. Physical functioning was assessed using an instrument developed to estimate the need of care of individual residents as well as the demands on the staff in Dutch homes for the elderly (Twijnstra & Gudde 1978). From this routinely applied instrument, seven items were combined to reflect Activities of Daily Living, i.e. self maintenance (bathing, dressing, making the bed, eating, tidying up the room, getting to and from the toilet) and incontinence. Both aspects have been shown to be informative of physical disability and mortality outcome both in community living elderly (Jagger et al. 1986, Koyano et al. 1986) and in elderly in institutions (Goldfarb 1966, Brody et al. 1972, Brauer et al. 1978). Each item was scored from 0 (no help needed) to 2 (fully dependent). For the items bathing and dressing, the scale was extended to 3. The latter items are considered the most basic activities of daily living and are included in most other scales of physical functioning (Branch & Meyers 1987). The seven items were summed to

a scale (maximal score 16), defined as Activities of Daily Living — Personnel (ADLP). The test-retest reliability of this scale over the full study period was 0.77 (Van Loveren-Huyben et al. 1988a, p. 25). Other assessments of physical functioning pertained to the amount of nursing provided, such as administering drugs, dressing of simple wounds, and bandaging. These were dichotomous items.

An instrument to rate psychosocial functioning was especially developed to evaluate the quality of life of the residents with the ultimate goal of adjusting the care provided by the staff (Van Loveren-Huyben & Van der Bom 1983, Van Loveren-Huyben et al. 1988b). It contains 35 items indicating problematic behaviors, e.g.: is confused, needs to be watched, complains, is suspicious, lacks interest in environment. The scores of each item ranges from 0 (never) to 4 (very often). Based on the results of factor analysis, 23 items were summed to three scales indicating cognitive functioning (maximal score 44), morale (maximal score 28), and social functioning (maximal score 20). The test-retest reliabilities over the full study period are 0.78, 0.74, and 0.69 for cognitive functioning, morale, and social functioning respectively (Van Loveren-Huyben et al. 1988a, p. 25). The items not constituting one of the three scales included behaviors such as daydreaming, nightly restlessness, using abusive language, and the sensory functions hearing, vision, and speech.

### **The measure of survival**

Survival time is operationally defined as the Realized Probability of Dying (RPD), a function of survival time, sex and age at baseline (Deeg et al. 1989a). This function is designed to compare the survival time of residents to that of the general population, and to achieve comparability of the survival time of residents of different sex and age. The RPD compares each individual subject's survival time with the survival curve of those age and sex peers in the general population who were still alive at the baseline examination. Possible values of the Realized Probability of Dying are between 0 and 1. These values introduce a rank order among all sample subjects. For example, the value of an individual's RPD is 0.7, if at the time of his or her death 70% of the population comparison group is still alive. If the RPD is uniformly distributed on the interval (0,1), the survival distribution of the sample represents that of the general population. Uniformity requires that the mean is 0.50 and the standard deviation 0.29.

For those 182 subjects still alive at the end of the study (January 1986), a value of the Realized Probability of Dying is imputed. The RPD for these subjects is estimated by assuming that their remaining survival time corresponds to the median population survival time from end-of-follow-up onward. This amounts to multiplying the probability of reaching their age in 1986 by one half. For instance, a woman aged 80 at baseline in 1981, reaches the age of 85 (in 1986) with

probability 0.69; her imputed RPD will be 0.35, implying that it is expected that she will die when only 35% of her population comparison group is still alive. This approach is derived from standard actuarial methods.

**Statistical analysis**

Mean and standard deviation of the RPD are direct indicators of the sample's representativeness of the general population regarding survival time. Differences in mean RPD among subgroups of residents are tested by means of *F*-tests. Pertinent subgroups are categorized according to age ( $\leq 74$ , 75-79, 80-84, 85-89, and  $\geq 90$  years), sex, marital status, and duration of residence ( $< 4.5$  and  $\geq 4.5$  years). The latter categorization is based on admission before or since 1977.

The predictive ability of baseline assessments for subsequent survival time was evaluated using forward, stepwise multiple regression models with the logit of the RPD (LRPD, approximately normally distributed) as the dependent variable. Baseline assessments were summarized as ADLP, cognitive functioning, morale,

**TABLE 1 Mean Realized Probability of Dying (RPD) for all residents and subgroups of residents.**

Subgroup		RPD		N
		Mean	SD	
Total		0.66	0.19	298
Ages	$\leq 74$ years	0.86	0.07	14
	75-79	0.80	0.10	52
	80-84	0.68	0.13	103
	85-89	0.60	0.17	84
	$\geq 90$	0.48	0.20	45
Admitted	$< 1977$	0.63	0.19	162
	$\geq 1977$	0.69	0.18	136
Males		0.63	0.20	83
Females		0.67	0.18	215
Married		0.64	0.19	46
Never married		0.68	0.16	22
Widowed		0.66	0.19	221
Divorced		0.68	0.14	8

and social functioning as described above. More detailed analyses including the separate assessment items were performed to improve the interpretation of the associations found. Separate analyses were performed for residents aged 79 years and younger ( $n = 66$ ) and 80 years and over ( $n = 232$ ), and for those admitted before ( $n = 136$ ) and since 1977 ( $n = 162$ ).

## Results

### Comparison of survival time

The mean RPD appeared to be 0.66 (standard deviation 0.19) for the total group of residents as of June 1981 (Table 1). Therefore, residents had decreased survival times as compared to their sex and age peers in the general population. Only 20% had survival times in excess of the population median (RPD < 0.5). For an individual female resident aged 80 at baseline, for example, the RPD value of 0.66 translates into a decrease in life expectancy at age 80 from 7.1 to 5.0 years.

Comparison of mean RPD among subgroups showed interesting differences. There was a clear, significant gradient of decreasing RPD with increasing age, the oldest age group (ages 90 years and over) showing the closest correspondence to the general population. Younger residents appeared to constitute a progressively negative selection of the general population with regard to survival time. In addition, duration of residence, or alternatively admission year, was significantly associated with the RPD, indicating that those admitted in 1977 or after had decreased survival times as compared to those admitted earlier. Differences

**TABLE 2 Independent predictors of survival time (Logit of the Realized Probability of Dying) from multiple regression analysis on four scales of physical and psychosocial functioning, age at baseline and admission year for all residents.**

Variable	Standardized regression coefficient
Age at baseline	-0.54
ADLP <sup>¶</sup>	0.16
Morale	0.11
Total variance explained:	33.2%

<sup>¶</sup> Activities of Daily Living — Personnel

**TABLE 3 Independent predictors of survival time (Logit of the Realized Probability of Dying) from multiple regression analysis on all assessment items for all residents.**

Variable	Standardized regression coefficient
Age at baseline	-0.59
Admission year	0.12
Incontinence	0.14
Administering drugs	0.15
Dropping of ears	0.18
Bandaging	0.11
Dressing simple wounds	-0.20
Exactingness	0.10
Inconsistent speech	0.11
Not knowing the way	-0.11
Wandering	-0.10
Daydreaming	0.16
Speech	-0.13
Total variance explained:	46.8%

among sex or marital status groups did not prove to be significant. Since age and duration of residence may confound the associations between baseline assessments and LRPD, both variables are included in the subsequent regression analyses.

#### **Prediction of survival time**

From forward, stepwise multiple regression analysis, age appeared to be the predominant predictor of survival time c.q. LRPD (Table 2). The association corresponded to the above findings: younger residents were likely to have relatively shorter survival times than older residents. The effect of age was three to five times as large as that of the other independent predictors: ADLP and morale (standardized regression coefficients 0.54, 0.16, and 0.11, respectively). Neither cognitive nor social functioning entered into the model as independent predictors. The total variance explained was 33.2%.

**TABLE 4 Independent predictors of survival time (Logit of the Realized Probability of Dying) from multiple regression analysis on four scales of physical and psychosocial functioning, age at baseline and admission year for residents aged younger than 80 years and 80 years and over.**

Variable	Standardized regression coefficient	
	Ages ≤ 79 years	Ages ≥ 80 years
Age at baseline	-0.43	-0.33
Admission year	n.s.	0.13
ADLP <sup>†</sup>	n.s.	0.18
Morale	n.s.	0.15
Total variance explained:	18.9%	19.9%

<sup>†</sup> Activities of Daily Living — Personnel

More detailed analysis including all assessment items (Table 3), revealed that the one ADLP-item having an independent effect on LRPD was incontinence. Similarly, only one item of the morale scale had an independent effect on LRPD: exactingness. Three items of the cognitive functioning scale now appeared to have independent predictive ability: inconsistent speech, wandering, and not knowing the way. Note, however, that the latter two items had a reversed association with LRPD.

In addition to items constituting one of the four scales, other items showed independent predictive ability. Notably, this was the case with items indicating some amount of nursing: administering drugs, dropping of ears, bandaging, and dressing of simple wounds. Note, however, that the latter item's association with LRPD was reversed. Of the other psychosocial and sensory items, two showed independent effects: daydreaming and speech. The latter item had a reversed association with LRPD. In this more detailed regression model, year of admission appeared to be independently predictive of LRPD in the sense that the more recently admitted residents had a poorer prognosis in terms of survival time.

### Prediction by age and duration of residence

In residents younger than 80 years, no factors other than age appeared to be independently predictive of LRPD (Table 4). In residents aged 80 years and older, age had a decreased, although still considerable independent effect in addition to

**TABLE 5 Independent predictors of survival time (Logit of the Realized Probability of Dying) from multiple regression analysis on four scales of physical and psychosocial functioning, age at baseline and admission year for residents admitted prior to 1977 and since 1977.**

Variable	Standardized regression coefficient	
	Admitted < 1977	Admitted ≥ 1977
Age at baseline	-0.59	-0.52
Admission year	n.s.	0.15
ADLP <sup>†</sup>	0.23	n.s.
Morale	n.s.	0.19
Total variance explained:	28.9%	34.7%

<sup>†</sup> Activities of Daily Living — Personnel

ADLP, morale, and year of admission. The total variance explained was 18.9% in younger and 19.9% in older residents.

Both among residents admitted since 1977 and among those admitted prior to 1977 (Table 5), age showed an independent effect on LRPD of similar size (standardized regression coefficient over 0.50). Morale and admission year appeared to have independent effects in the more recently admitted. In contrast, in those admitted longer ago ADLP was the only additional independent predictor of LRPD. The total variance explained was 28.9% in the recently admitted, and 34.7% in those admitted longer ago.

## Discussion

The results presented above provide evidence that the population of a residential home for the elderly is not a random selection of the general elderly population, but has a poorer prognosis with respect to survival time. Moreover, while residents aged 90 and over had survival times similar to the general population, the survival times of younger residents deviated progressively toward shorter survival times with decreasing age. In addition, residents admitted since 1977, a year in which admission policy became stricter, had shorter survival times as compared to the general population than those admitted earlier. In multiple regression analyses, the latter effect appeared to be independent of the effect of age.



National statistics on residential homes for the elderly show a steady increase in the percentage of residents aged 85 years and over since 1965, while the proportion of those younger than 80 decreases (Huijsman 1988). The amount of help needed by the residents increases accordingly. Our data suggest, however, that this trend can not be attributed solely to the increased age of the residents, but to a large extent also to the decreased validity of younger residents.

The purpose of this study was to explore the consequences of selectivity in the study sample for the prediction of survival time. The greater selectivity of residents younger than 80 years proved to have a parallel in the prediction of survival time for this group: other than age, no predictors were found among indicators of physical and psychosocial functioning. It may be concluded that younger residents are a rather homogeneous group, and that the criteria which lead to their admission to the home override other possible determinants of survival time. The same conclusion applies partly to those admitted since 1977, because physical disability, the main criterion for admission, was not associated with survival time among this group. However, a psychosocial indicator of quality of life — morale — did contribute independently to the variance explained in this group.

By comparison, residents aged 80 and over demonstrated more variability with respect to survival time, resulting in independent effects of both physical and psychosocial functioning on survival time. These results correspond to predictors of longevity found in samples based on the general population (Libow 1974, Palmore 1974, Deeg et al. 1985, Lehr et al. 1987). The finding that physical functioning was the predominant predictor of survival time in residents admitted prior to 1977 is in line with other studies which show the greater importance of physical functioning for survival time as compared to psychosocial factors (Palmore & Cleveland 1976, Diesfeldt 1979, Abramson et al. 1982).

In contrast to the evidence from many studies in samples of the general population (Jarvik et al. 1962, Riegel et al. 1967, Hall et al. 1972, Botwinick et al. 1978, Siegler et al. 1982, Berg 1987), no predictive ability was found for cognitive functioning in the present study. However, in institutionalized populations, this finding is not uncommon (Siegler 1975). Upon closer examination, several items constituting the cognition scale had reversed associations with survival time, thereby cancelling out the effects of other items in the scale which did show anticipated associations. To explain this "anomaly", it might be argued that a second selection mechanism is at work in the study sample. Those residents with some signs of cognitive dysfunction such as wandering and not knowing the way, may otherwise be in good health, and therefore not eligible for relocation to a psychogeriatric nursing home. It has been shown elsewhere (Deeg et al. 1989b), that decreased cognitive functioning in the absence of further physical or psychosocial health problems is not associated with decreased survival time. On the other hand, cognitive functioning items such as inconsistent speech are likely to be

associated with severe health problems. Residents with co-morbid conditions are more likely to be relocated to a nursing home. Unfortunately, no detailed information on the nature of physical impairments was available in this study.

The association of psychosocially problematic behaviors with survival time needs some further consideration. The behavior included in the morale scale showing an independent effect in the single item analysis, exactingness, was noted by the staff in 19% of residents. Like most other psychosocial problems, its occurrence increased in the course of the study period (Van Loveren-Huyben et al. 1985). After several reorganizations aiming at improving the quality of life of residents in the home (Van Loveren-Huyben & Van der Bom 1988), the proportion of residents showing exactingness dropped back to the initial level. Similarly, the behavior of daydreaming, which showed an independent effect on survival time, was noted in 20% of residents at baseline, which percentage increased subsequently and dropped to 18% after the reorganizations. The improvements occurred particularly in those who exhibited occasional, as opposed to frequent, problematic behaviors. Thus, psychosocial problems of residents are to some extent amenable to change, which may not only improve quality of life, but increase survival time as well.

Social functioning, the third psychosocial scale, did not show any independent effect on survival time. This finding is in contrast with studies demonstrating the beneficial effect of social support on longevity in samples of the general population (Berkman & Syme 1979, House et al. 1982, Orth-Gomér & Johnson 1987, Seeman et al. 1987). In contrast, two studies conducted in nursing homes found a reversed relationship (Kral & Müller 1966, Van den Heuvel 1977). Meanwhile, problems in social functioning were among the problems most frequently noted among residents of the home (Van Loveren-Huyben et al. 1985). Providing an environment that is conducive to social functioning, therefore, may not increase survival time, but may certainly add quality to the remaining time of life.

In conclusion, survival time in residents of a home for the elderly was found to be independently associated with age, duration of residence, physical functioning, and morale. However, in residents younger than 80 years no factors other than age were found to be independently predictive of survival time. These residents appeared to be a rather homogeneous group with respect to factors that have been shown to predict longevity in other samples. Similarly, in residents admitted after stricter admission criteria based on disability were introduced, physical functioning was no longer independently predictive of survival time. Cognitive functioning problems were not found to be related to survival time, probably due to relocation policy: those residents who have additional health problems — and thus decreased life expectancy — are relocated to nursing homes, while those without further health problems — and thus no decreased life expectancy — are maintained in the residential home. In generalizing results from studies based on institutionalized

samples, then, due consideration should be given to factors associated with the specific selectivity of the sample, such as age, admission criteria, and relocation criteria.

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## II.6 Survival time of elderly in a residential home

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*II.6 Survival time of elderly in a residential home*

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## II.7

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# CHANGES IN HEALTH RELATED FACTORS DURING THE LAST YEAR OF LIFE

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## Summary

Factors associated with mortality in the elderly have often been ascertained several years prior to death. These studies provide no information about how these factors change in individuals as death is approached. This paper describes data collected on physical and psychosocial function at three month intervals on 495 residents of a Dutch residential home for the elderly over a 4½ year period. During this period, 153 residents died, of whom 88 had four complete evaluations in the year prior to death. Evaluations are summarized in terms of physical functioning, cognitive functioning, morale, and social functioning. Multivariate analysis of variance methods for repeated measurements demonstrate a significant decline of all factors during the last year of life; decline in physical, cognitive, and social functioning, but not in morale, is of greater magnitude than the decline seen in those who survived the study period. Furthermore, the decline in physical functioning seen in the last year of life accelerates in the months just prior to death. This accelerated decline is most pronounced in those who, at the beginning of their last year of life, had little physical disability.

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## Introduction

Traditionally, precursors of death are studied in prospective designs in which survival subsequent to observation in a "baseline" year is ascertained. In such studies, baseline characteristics are determined which discriminate those subjects who survive a shorter time from those who survive a longer time. However, no information is obtained about changes in characteristics during the phase of life just prior to death, i.e. about trajectories that in the end lead to death. Better knowledge of this last phase of life is not only desirable from a purely scientific point of view, but also from the point of view of geriatric practice: it may lead to improved case management, placement decisions, and therefore improved quality of life.

The time span in which changes leading to death are likely to occur has not been agreed upon by different authors, and may range from seven years (Siegler et al. 1982) or five years (Riegel & Riegel 1972, Berg 1987) to less than one year (Botwinick et al. 1978). Neither does agreement exist about the kind of change that occurs prior to death: is it a gradual, age-related decline (*terminal decline*) or an accelerated, health-related one (*terminal drop*)? Most of the discussion on this subject revolves around cognitive change (Jarvik & Blum 1971, Steuer et al. 1981, Siegler et al. 1982, Uhlmann et al. 1987), although also change in personality characteristics (Riegel & Riegel 1972) and in physical and social functioning (Palmore & Cleveland 1976, Botwinick et al. 1978, Schmitz-Scherzer 1987) prior to death are reported. Whatever the area of interest, methodological differences between studies make comparison difficult. The number of observations as well as the time interval between successive observations may be at variance. The study samples may be selective, with a bias towards either above-average or below-average health. Age at death may or may not have been taken into account (Siegler 1975).

Prospective study of changes in the last phase of life calls for at least three observations such that distinction can be made between linear, gradual and non-linear, accelerated change. Only then can terminal decline and terminal drop be distinguished. Moreover, the last observation needs to be at a distance to death that is approximately equal for all subjects studied. Because individuals die at different, previously unknown times, the interval between observations needs to be fairly short. A sample of deceased subjects that is large enough for statistical evaluation can either be obtained by long-term study of a limited number of subjects, or by short-term study of a large number of subjects. The sample size needs to be large enough to enable evaluation of effects of age at death and health status (Siegler 1975).

The present study draws on data collected at three month intervals over a 4½ year period on 495 residents of a Dutch residential home for the elderly. Obser-

uations are made on physical functioning, cognitive functioning, morale, and social functioning. Four issues are addressed: 1. Can changes in health related and behavioral factors be detected during the last phase of life? 1.a. Do the observed trajectories represent a gradual or rather a precipitous change (*terminal decline* or *terminal drop*)? 2. Are these changes more exacerbated than those in subjects who did not yet enter the last phase of life? 3. Do subjects who experience their last phase of life at younger ages show different trajectories than those who die at older ages? 4. Can different trajectories during the last phase of life be demonstrated for those subjects whose initial health status was satisfactory and those who entered the last phase of their lives in poor health?

## Material and methods

### Population

All residents of a medium sized home for the elderly in the Netherlands were assessed by staff members at three month intervals during four and a half years (June 1981 through September 1985). The capacity of the home amounts to approximately 300 residents. Observations are available on a total of 495 individuals. During the study period, 207 persons dropped out due to death or relocation, and a similar number of new residents were taken in. A number of 151 residents was present from the start of the study throughout the study period. Three-fourth of those individuals dropping out died ( $n=153$ ). The average age at death is 85.5 years (standard deviation 6.0 years); 55% of the deceased are women; 78% is widowed.

Since availability of complete observations up to death is necessary, those residents who died early in the study period could not be included in the current study. As a compromise between number of subjects available for study and length of series of available observations, a period of one year (the equivalent of four observations) is chosen for the evaluation of changes prior to death. Twenty-three residents died during the first study year, which leaves 130 residents eligible for inclusion in the study. On 88 of these, four complete observations are available. These 88 residents form the study sample. Their average age at death is 85.9 years (standard deviation 6.3); 58% are women, and 80% is widowed. Those residents with incomplete observations during the year prior to death dropped out of the study temporarily because of a stay in a hospital or nursing home. Thus, although the study sample's demographic characteristics do not differ appreciably from those of all residents eligible for this study, its health status may be above average.

## Measurements

The three-monthly ratings of each resident by staff members pertained to physical, mental and social functioning. Physical functioning was assessed using an instrument developed to estimate the need of care of individual residents as well as the demands on the staff in Dutch homes for the elderly (Twijnstra & Gudde 1978). From this routinely applied instrument, seven items were selected for use in the current study, reflecting self maintenance (bathing, dressing, making the bed, eating, tidying up the room, getting to and from the toilet) and incontinence. Both aspects have been shown to be informative of physical disability and mortality outcome both in community living elderly (Jagger et al. 1986, Koyano et al. 1986) and in elderly in institutions (Brody et al. 1972, Brauer et al. 1978). Each item is scored from 0 (no help needed) to 2 (fully dependent). For the items bathing and dressing, the scale is extended to 3. The latter items are considered the most basic activities of daily living and are included in most other scales of physical functioning (Rosow & Breslau 1966). The seven items are summed to a scale (maximal score 16), defined as Activities of Daily Living Personnel (ADLP). The test-retest reliability of this scale over the full study period is 0.77 (Van Loveren-Huyben et al. 1988a, p. 25).

An instrument to rate psychosocial functioning was especially developed to evaluate the quality of life of the residents with the ultimate goal of adjusting the care provided by the staff (Van Loveren-Huyben & Van der Bom 1983, Van Loveren-Huyben et al. 1988b). It contains 35 items indicating problematic behaviors, e.g.: is confused, needs to be watched, complains, is suspicious, lacks interest in environment. The scores of each item ranges from 0 (never) to 4 (very often). Based on the results of factor analysis, 23 items were summed to three scales indicating cognitive functioning (maximal score 44), morale (maximal score 28), and social functioning (maximal score 20). Those items that did not load clearly on any of these three factors were discarded from this study. The test-retest reliabilities over the full study period are 0.78, 0.74, and 0.69 for cognitive functioning, morale, and social functioning respectively (Van Loveren-Huyben et al. 1988a, p. 25).

## Statistical analysis

Changes in each of the four scales are evaluated using the Time Data Analysis Program for repeated measurements (Oud et al. 1986), which follows a MANOVA approach. A quadratic curve is fitted to enable the detection of accelerated change. In a first series of analyses, it is tested whether the curve significantly departs from the horizontal line of *no change* (null hypothesis  $H_0: \beta = 0$ ), and whether the change is linear or quadratic. A second series of analyses is conducted to test whether the study group's trajectory departs from the trajectory that reflects the

II.7 Last year of life

average change in those residents surviving with complete observations during the full study period (n=141). The latter change is approximated by a linear curve (Van Loveren-Huyben et al. 1988a, annex 4.19). Significant departure from this curve is tested (null hypothesis  $H_0: \beta = \beta_0$ ), again fitting a quadratic curve in the study group. A third series of analyses addresses the question whether differences in trajectories can be demonstrated between younger and older subjects (ages  $\leq 79$ , n=16 and  $\geq 80$  years, n=72), and between those who had only minor physical disability at one year before death (ADLP  $\leq 4$ , n=24) and those who had major physical disability at one year before death (ADLP 5, n=64). It is tested whether the curve of the older group departs significantly from the curve of the younger group, and similarly whether the curve of the disabled group departs significantly from the curve of the non-disabled group (null hypothesis  $H_0: \beta = \beta'$ ). The trajectory of each group, again, is estimated by a quadratic curve.

**Table 1.** Trajectories of physical functioning, cognitive functioning, morale, and social functioning during the last year of life by age: mean scores on four subsequent observations prior to death (standard deviations in brackets).

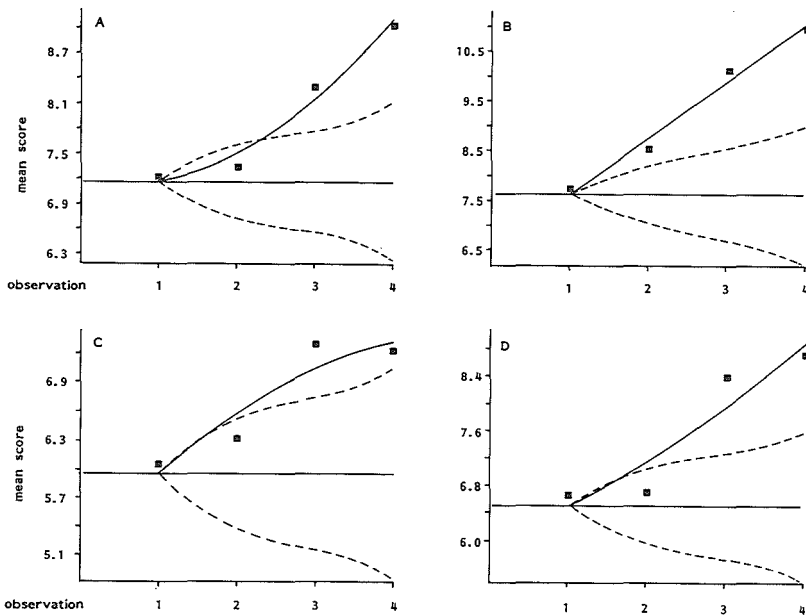
	observation				N
	1	2	3	4	
<i>physical functioning</i>					
ages $\leq 79$	6.5 (4.2)	6.2 (4.2)	7.2 (4.6)	7.6 (4.5)	16
ages $\geq 80$	7.4 (3.8)	7.6 (4.2)	8.5 (4.1)	9.4 (4.3)	72
total	7.2 (3.9)	7.3 (4.2)	8.3 (4.2)	9.2 (4.3)	88
<i>cognitive functioning</i>					
ages $\leq 79$	2.9 (6.6)*	3.1 (6.4)*	4.4 (10.0)*	4.4 (10.2)*	16
ages $\geq 80$	8.8 (10.0)*	9.8 (10.6)*	11.4 (11.0)*	12.5 (11.6)*	72
total	7.7 (9.5)	8.5 (10.0)	10.1 (10.8)	11.0 (11.3)	88
<i>morale</i>					
ages $\leq 79$	3.5 (3.7)*	3.7 (3.8)*	4.5 (5.8)*	4.6 (5.7)	16
ages $\geq 80$	6.6 (6.7)*	6.9 (6.9)*	7.9 (7.2)*	7.8 (7.1)	72
total	6.0 (6.3)	6.3 (6.5)	7.3 (7.0)	7.2 (6.9)	88
<i>social functioning</i>					
ages $\leq 79$	2.8 (3.6)*	2.7 (3.5)*	3.6 (4.5)*	3.9 (5.0)*	16
ages $\geq 80$	7.5 (6.2)*	7.6 (6.4)*	9.5 (6.4)*	9.8 (6.7)*	72
total	6.7 (5.8)	6.7 (6.0)	8.4 (6.1)	8.8 (6.4)	88

\* age difference (columnwise) is significant,  $p < 0.05$

## Results

The average scores on physical functioning, cognitive function, morale, and social functioning on each of the four observations prior to death are presented by age in Table 1. As distance to death decreases, the mean scores on all factors can be seen to increase. Those who enter their last phase of life at older ages clearly have more problems than those who do so at younger ages. The age difference is most pronounced with respect to social and cognitive functioning; with respect to morale, the age difference does not stay significant throughout the year; the age difference in physical functioning is not significant.

**Figure 1** Trajectories of residents in their last year of life, estimated by a quadratic curve: A. physical functioning; B. cognitive functioning; C. morale; D. social functioning.



### Gradual versus precipitous decline

For each factor, the four mean scores together with the estimated quadratic curve and its confidence interval are shown in Figures 1a-d. The decline on each factor appears to depart significantly from the horizontal line of *no change* as the moment of death is approached. Evidence of an accelerated decline (*terminal drop*) can

only be found for physical functioning. The fit of the quadratic curves, evaluated by introducing a cubic term and testing its significance, appeared satisfactory for the first three factors. For social functioning, however, the cubic term was significantly negative ( $p < 0.05$ ).

**Decedents versus survivors**

Table 2 gives the estimated linear change on the four factors for those who were observed over the full study period of 18 observations and were alive at the end of this period ( $n = 141$ ). The regression coefficients  $b$  will serve as the “normal” values against which the estimated curve parameters for the last year of life will be compared. Note, that also in the group of survivors significant declines occur, with the exception of physical functioning.

**Table 2.** Estimated linear change in physical functioning, cognitive functioning, morale and social functioning of residents observed over 4½ years and alive at the end of this period ( $n = 141$ ): intercept ( $a$ ), regression coefficient ( $b$ ) with 95% confidence interval ( $b-,b+$ ), and estimated level attained at the end of the study period ( $a + 18*b$ ).

	$a$	$b$	$(b-,b+)$	$a + 18*b$
physical functioning	5.7	-0.02	(-0.06,0.02)	5.3
cognitive functioning	3.2	0.27	(0.18,0.37)	8.0
morale	4.1	0.16	(0.09,0.23)	7.0
social functioning	4.0	0.18	(0.10,0.26)	7.2

**Table 3.** Departure of the estimated quadratic trajectory of subjects in their last year of life from the estimated linear change in those surviving during 4 ½ years: intercepts ( $a$ ), difference of linear regression coefficients ( $b_1$ ), and difference of quadratic regression coefficients ( $b_2$ ), including 95% confidence intervals ( $a-,a+$ ), ( $b_1-,b_1+$ ), and ( $b_2-,b_2+$ ).

	$a$	$(a-,a+)$	$b_1$	$(b_1-,b_1+)$	$b_2$	$(b_2-,b_2+)$
physical functioning	7.2	(6.3,8.0)	0.20	(-0.30,0.69)	0.16	(-0.02,0.34)*
cognitive functioning	7.6	(5.6,9.7)	0.85	(0.26,1.44)	0.01	(-0.18,0.19)
morale	5.9	(4.6,7.3)	0.56	(-0.07,1.19)*	-0.09	(-0.30,0.13)
social functioning	6.5	(5.2,7.8)	0.42	(-0.18,1.01)	0.07	(-0.13,0.26)

\* borderline significant ( $0.05 < p < 0.10$ )

The magnitude of the departure of the trajectory in the last year of life from the “normal” trajectory is given by the coefficients in Table 3. The intercepts represent the estimated, average levels at the time of observation 1. They show that, already upon entry into the last year of life, a resident is likely to have more physical disability than a survivor at the end of the study period. This is, however, not true for psychosocial functioning. Furthermore, as compared to the survivors’, the study group’s physical functioning declines more quickly and in an accelerated fashion (the difference of quadratic coefficients is borderline significant). Although there is a strong suggestion that all three psychosocial functions decline more quickly in the study group than in the survivors, the difference of linear coefficients only

**Table 4.** Departure of the estimated quadratic trajectory of subjects in their last year of life aged 80 and older, from the estimated quadratic trajectory of those aged 79 and younger: difference of intercepts ( $a$ ), difference of linear regression coefficients ( $b_1$ ), and of quadratic regression coefficients ( $b_2$ ), including 95% confidence intervals ( $a-,a+$ ), ( $b_1-,b_1+$ ), and ( $b_2-,b_2+$ ).

	$a$	$(a-,a+)$	$b_1$	$(b_1-,b_1+)$	$b_2$	$(b_2-,b_2+)$
physical functioning	0.9	(-1.3,3.1)	0.23	(-1.08,1.52)	0.02	(-0.46,0.50)
cognitive functioning	5.9	(0.7,11.1)	0.51	(-1.02,2.04)	0.07	(-0.42,0.55)
morale	3.1	(-0.4,6.5)*	0.27	(-1.37,1.92)	-0.06	(-0.62,0.49)
social functioning	4.7	(1.5,7.9)	0.48	(-1.05,2.03)	-0.02	(-0.53,0.50)

\* borderline significant ( $0.05 < p < 0.10$ )

**Table 5.** Departure of the estimated quadratic trajectory of subjects in their last year of life with major physical disability ( $ADLP \geq 5$ ,  $n = 64$ ) from the estimated quadratic trajectory in those with minor physical disability ( $ADLP \leq 4$ ,  $n = 24$ ): difference of intercepts ( $a$ ), difference of linear regression coefficients ( $b_1$ ), and quadratic regression coefficients ( $b_2$ ), including 95% confidence intervals ( $a-,a+$ ), ( $b_1-,b_1+$ ), and ( $b_2-,b_2+$ ).

	$a$	$(a-,a+)$	$b_1$	$(b_1-,b_1+)$	$b_2$	$(b_2-,b_2+)$
physical functioning	6.7	(5.5,7.9)	0.10	(-1.03,1.23)	-0.34	(-0.75,0.06)*
cognitive functioning	7.4	(3.1,11.8)	0.85	(-0.46,2.17)	-0.20	(-0.62,0.21)
morale	4.1	(1.1,7.0)	1.48	(0.09,2.87)	-0.48	(-0.94,-0.01)
social functioning	3.1	(0.3,6.0)	0.45	(-0.88,1.79)	-0.14	(-0.59,0.31)

\* borderline significant ( $0.05 < p < 0.10$ )

becomes significant with respect to cognitive functioning, and marginally significant with respect to morale.

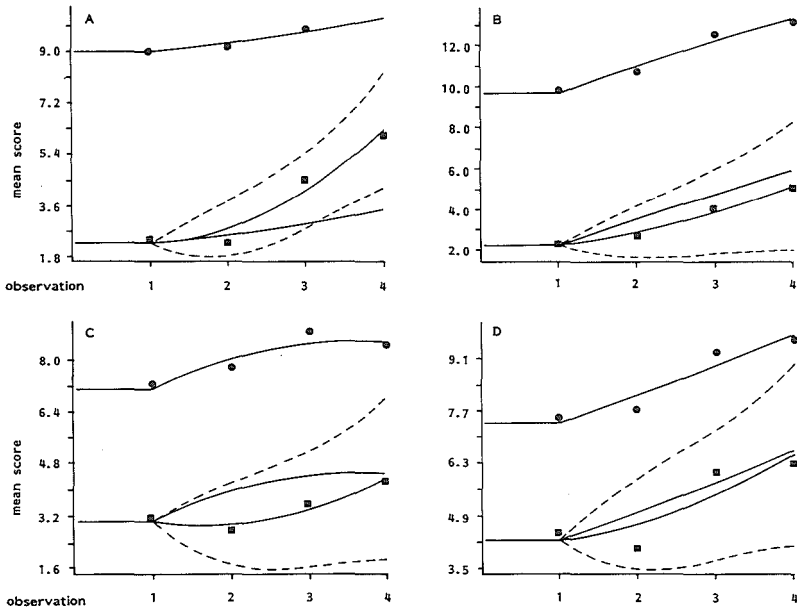
**Older versus younger**

Possible age differences in trajectories are examined in Table 4. Significant differences in the linear and quadratic coefficients are lacking, indicating that the rate of decline is similar across age. Thus, the differences in level of functioning are maintained throughout the last year of life.

**Better versus poorer health**

The relation between health status, indicated by physical functioning, and trajectories in the last year of life is examined in Table 5. The magnitudes of the intercept differences show that the presence of major physical disability is associated with

**Figure 2** Comparison of trajectories of residents in their last year of life, estimated by quadratic curves: A. physical functioning; B. cognitive functioning; C. morale; D. social functioning. Comparison groups: those with minor initial physical disability (■) versus those with major initial physical disability (●).





significantly poorer psychosocial functioning. The negative difference of quadratic coefficients for physical functioning indicates that residents who enter their last year of life with only minor physical disability experience an accelerated decline in physical functioning subsequently. Morale shows an accelerated decline for the same group. However, the significant positive difference of linear coefficients for morale indicates a stronger decline for the initially more disabled group. Thus, the actual difference in trajectories is rendered insignificant (cf. Figure 2c). The disability level of the initially less disabled group does not, on the average, surpass that of the initially more disabled group (cf. Figure 2a). The initial differences in cognitive and social functioning are maintained throughout the last year.

## Discussion

These results indicate declines in physical as well as psychosocial functions during the year just prior to death in residents of a residential home for the elderly. Residents entering this last phase of their lives can be distinguished from survivors by their, on the average, higher degree of physical disability, and by their more pronounced decline in physical and cognitive functioning and in morale. Residents who experience their last phase of life at ages 80 and over show, despite their poorer levels of functioning, declines similar to the declines seen in those whose last phase comes prior to age 80. Residents with only little physical disability at the beginning of their last year show more accelerated declines in physical disability and morale than those who already had major physical disability.

In order to enable a distinction between *terminal decline* and *terminal drop*, a quadratic curve was fitted. If the quadratic coefficient differed significantly from zero, this was interpreted as evidence of a terminal drop, or accelerated decline. The second degree polynomial curve appeared to fit the data adequately, except in the case of social functioning. Here, a third degree polynomial curve appeared more appropriate. However, the authors are not aware of a gerontological theory supporting an S-shaped decline. The anomaly may be tentatively explained as a fluctuation in a decline that occurs over a period of much longer than one year. The onset of decline in social functioning, then, may occur at a longer distance to death than in the other factors. The period of one year prior to death has proven to be a useful entity for the detection of a certain amount of terminal change. Nevertheless, the current results do not preclude that significant terminal changes occur at a distance to death of more than one year.

Two notes on the study sample need to be made. First, 130 residents were eligible for inclusion in the study, because potentially they had four observations prior to death. However, only 88 residents fulfilled the criterium of having four complete observations. The most frequent reason for missing observations in the remaining

42 residents is temporary absence due to either admission to the in-house hospital, to the adjacent nursing home, or to the city hospital. It has been demonstrated that also in community dwelling elderly hospital admission is a frequently occurring phenomenon during the last year of life (Shapiro 1983).

The selectivity of the study group towards better health bears not only on the generalizability of results, but also on the variability remaining in the sample. Several earlier studies of terminal decline in nursing homes did not provide significant results, perhaps due to the lack of variability in the sample (Siegler 1975). However, sufficient variability remained in the present sample for significant results to emerge. One can safely assume that the results would have been more significant, had those residents with missing observations been included.

The second note on the study sample concerns its size. The analysis of variance methods employed require normally distributed variables and, in the case of two groups, equal covariance matrices. However, provided that the number of subjects is not too small and the group sizes are equal, the significance tests are unaffected by violations of these assumptions (Oud et al. 1986). What can be understood as a "not too small" number, depends on the specific study design. Aspects determining required sample size are: the desired significance level and power, the interindividual and intraindividual variance and reliability of the instrument used for study, the anticipated magnitude of decline, and the number of observation times (Schlesselman 1973a, Guyatt et al. 1987, Overall 1987). The required sample size decreases if requirements on the significance level and power are slackened, the interindividual variance is smaller, the reliability of the instrument is larger, the anticipated magnitude of decline is larger, and the number of observation times is larger. The relatively large number and frequency of observation times is certainly a strong aspect of the current study (Schlesselman 1973b). In the absence of knowledge about the crucial element of anticipated decline, however, the proof of the current results lies in their replication in other studies, in which use can be made of the rough estimates of declines provided by this study.

The choice of age 80 as the cut-off point for the age comparison may be disputable, as it results in two groups of quite unequal sizes and, on some factors, unequal variances (cf. Table 1). However, this choice is made in order to conform to current thinking in gerontology about *young-old* and *old-old*, between which the transition is to occur between 75 and 80 years of age (Neugarten 1975, Chappell & Havens 1980). The sizes of the groups with minor and major physical disability are less unbalanced, but still not ideal. The cut-off point of ADLP = 5 was chosen, because this is the median performance of all residents across the study period (Van Loveren-Huyben et al. 1988a, p. 28). If those residents who experience their last year of life are to be recognized among all other residents, it seems better to relate the cut-off point to the total group of residents rather than just to the terminal group.

The lack of more detailed information on health status in this study may be felt as a shortcoming. Although physical disability measures have been shown to be good indicators of general health status in frail elderly (Guralnik et al. in press), additional information on e.g. the presence of a heart condition (Berg 1987, Rubenstein et al. 1988), of organic brain dysfunction (Steuer et al. 1981), or the suddenness of death (Siegler 1975) are desirable. However, the data collection for the present study was not originally designed to address questions of terminal change. It is recommended that new investigations in this area take medical conditions into account.

Finally, a discussion of the implications of the findings is in order. In the first place, they confirm the conclusion of several other investigators that decline in physical and psychosocial function is not an aspect of normal aging, but rather indicates the approach of death (Jarvik & Blum 1971, Riegel & Riegel 1972, Palmore & Cleveland 1976, Siegler et al. 1982). In addition, the findings indicate that terminal decline occurs in more than one aspect of human functioning (Beigler 1957, Schmitz-Scherzer 1987, Uhlmann 1987). Of particular interest is the finding of a precipitous decline in physical functioning, whereas psychosocial functioning declines more gradually. It should be noted that the specific population studied here experienced declines in psychosocial functioning, even when they survived the full study period (Van Loveren-Huyben et al. 1985). The declines in the survivors, however, are likely to be contingent on the environment provided by the residential home, and may be halted (Van Loveren-Huyben & Van der Bom 1988). In any case, the terminal group showed greater declines than the group that survived the full study period.

Some differences in trajectories prior to death are found according to initial physical disability. Initially less physically disabled residents show greater declines than initially more physically disabled residents. Although age difference in decline could not be demonstrated, and older age is by no means identical to physical disability in this group (the correlation coefficient is 0.21,  $p < 0.05$ ), no difference is made for the purpose of the following tentative interpretation. Younger residents seem to more frequently succumb to diseases with a sudden onset, limiting the period of disability prior to death to a minimum. By contrast, older residents may have one or more disabling conditions for a longer, stable period. Aggravation of one of these conditions, or onset of a new, minor condition, may trigger off an accelerated decline ultimately leading to death. The value of a differentiation into these trajectories as outlined, again, needs to be tested in other samples.

This study's findings, if confirmed elsewhere, can constitute the basis of improved geriatric assessment and care. Recognition of the onset of a trajectory specified as shortly leading to death, can for instance bring a new element in the decision making about a new treatment or about relocation. A new treatment may represent an extra burden for the resident which is unnecessary at this point

because of the diminished prospects of recovery. Similarly, relocation to the theoretically more appropriate environment of the nursing home may impose an unwarranted burden on the resident, thus unnecessarily reducing the quality of his or her last phase of life.

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### III

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## DISCUSSION

The evidence from the various studies of longevity presented in part II can now be reviewed in the light of the central theme of this book: Is prediction of longevity in the elderly possible at a satisfactory level of predictive ability? Striking the balance, the answer should not be too optimistic. At the current state of knowledge, the best answer might be: "To a certain extent." This answer will be explained below. Further on, it will be discussed how this "certain extent" can be made useful to the promotion of health among the elderly, and whether it can be considered meaningful to spend more scientific resources on further study of longevity or if attention would be more profitably focussed on alternative concepts that are more pertinent to the underlying objectives.

### III.1 Summary of findings

By way of summary of the evidence and continuation of the discussion broached in part II, the issues comprising this dissertation's research agenda will first be evaluated. These issues were formulated in part I as follows:

1. What is an optimal operational definition of longevity in a long-term follow-up study of the elderly?
2. Which predictors of longevity can be identified consistently across different studies?
3. What can be concluded regarding total predictive ability across studies of different design?
4. Do predictors of longevity based on studies of institutionalized populations correspond to predictors based on studies of non-institutionalized populations?
5. Does inclusion of (rates of) change in characteristics improve the prediction of longevity as compared to levels of characteristics?

### *III.1 Summary of findings*

6. Are factors showing changes just prior to death the same as those which are found to be predictive of longevity in the longer run?
7. Which characteristics of the aging process can account for the observation that longevity studies attain a predictive ability of far less than 100%?

#### **Issue 1. The operational definition of longevity**

As discussed in II.1, samples of elderly subjects are usually quite heterogeneous with regard to age. The age range may amount to four decades. Since expected survival time decreases with increasing age, the age composition of the sample confounds the relationship between baseline characteristics and subsequent survival time. The same argument goes for the sex composition of the sample, since women have a greater life expectancy than men. An often chosen solution is to study this relationship while controlling for age and sex in multivariate regression models. However, this method involves the pooling of data across age and sex groups, with consequent loss of power of statistical tests. Moreover, comparison of age-sex-controlled results from different studies is hampered because of unknown effects of differences in underlying age and sex distributions. Furthermore, in studies with a long follow-up period, the sampling error in ranking the survival times of subjects increases across the study period due to the decreasing number of subjects "at risk".

To meet these problems, a measure of survival time was developed which assigns to each individual subject a number corresponding to the percentile of the survival distribution for his or her age and sex peers in the total population who were still alive at the time of the baseline examination. Thus, the measure is based on conditional survival probabilities, taking into account that individuals who died before the starting date of the study were not observed. In terms of the statistical analysis of failure time data, this is called left truncation (Tsai et al. 1987) or left censoring (Kurtzke 1989). The proposed measure, termed the realized probability of dying (RPD), allows comparison of sample members' survival times independent of their age and sex, and in addition comparison of the sample distribution of survival time to that of the total population. The latter property enables the researcher to examine sample selectivity with regard to survival.

Conceptually, using the RPD is attractive since it is an individual measure of survival time, and therefore corresponds to individual longevity. For a person of given age and sex, the value of the RPD is easily transformed into number of years lived subsequent to baseline; similarly, a difference in RPD found to be associated with the presence or absence of a life-threatening characteristic can be expressed in number of years lost due to the characteristic for a given age and sex.

Calculation of the RPD involves multiplication of age-specific survival probabilities in the consecutive years following baseline until the year of death. The



survival probabilities are derived from population life tables covering the years of the follow-up period. The RPD, then, is a longitudinal measure: the changes in population mortality which may occur during the study period are taken into account.

For those subjects still alive at the end of the study period, no date of death is known. Their survival times are right censored in terms of the statistical analysis of failure time data. In order to retain the information these persons contribute, their RPD is imputed by multiplying the survival probabilities until the final year of the study, and multiplying this number with the expected RPD from end-of-study onward. In a non-selective sample, the expected RPD is 0.5, regardless of age, sex, or length of follow-up.

In II.4, where the association between rate of change in cognitive function and longevity is studied, the results using two frequently applied methods for testing the association under study are compared to the results using the RPD. By using the first method, the comparison of five-year mortality rates, all information on rank order among individual subjects with respect to survival time is discarded, except the information whether survival time exceeded five years or not. Not surprisingly, the association between change in cognitive function and five-year mortality is only significant in one age group. By using the second method, the Cox proportional hazards model, the statistical model tests the association between change in cognitive function and longevity while controlling for age (five-year groups) and sex. Because the model only roughly controls for age, no full use is made of information on each individual's age-based contribution to survival time. In addition, some loss of power is introduced by controlling for age and sex. Again, the association studied only reaches significance in one age group. Interestingly, this is not the same age group as when comparing five-year mortality rates. By contrast, using ordinary regression analysis with the RPD as the dependent variable, the association studied reaches significance in both age groups. Furthermore, upon introducing the level of cognitive function at the most recent time of measurement into the model, the association between change of cognitive function and survival time loses its significance when using the Cox model, whereas this association continues to be significant when using the RPD. Thus, assuming that no error of type I is introduced, the RPD method is more sensitive in rejecting the null hypothesis of no association.

Review of the results obtained by application of the RPD in three different samples raises three issues. These are: the role of age, the treatment of right censored data, and the suitability of the RPD in studies based on clearly selective samples.

**The role of age.** A inverse association of age at baseline and RPD was noted in all samples without exception, despite the operational definition of the RPD as independent of age at baseline. As probable causes for this association several

### *III.1 Summary of findings*

circumstances were indicated: selective preference of the examining physicians to examine those younger-elderly with whom they were in regular contact in a family physician based sampling frame (II.1-4), increasing rate of institutionalization with age in a non-institutionalized sample (II.5), and decreasing rate of disability on admission to a residential home for the elderly with age in an institutionalized sample (II.6). However, sample selectivity may not constitute a fully adequate explanation of the considerable and persistent association between age and RPD. Moreover, multivariate regression models showed that the partial correlation between RPD and age, allowing for other factors associated with the RPD, was considerably larger than the zero-order correlation. A complementary explanation of this association between age and RPD, related to an important assumption underlying the RPD concept, must therefore be considered.

The definition of the RPD assumes that predictors of longevity differentially affect persons of different ages at baseline. This assumption can be illustrated by comparing a man aged 65 years with a man aged 85 years in 1956 (at baseline in DLSE), both having the same, poor performance on a predictor of longevity — for example shortness of breath. Based on population survival probabilities, the expected survival time of the first man is a little over 15 years, while that of the second is just 4.5 years (II.1, Figure 1). A predictor of longevity is assumed to influence the survival time of both men proportionally. Let the mean RPD for a person without any shortness of breath be 0.44, and the mean RPD for a person with shortness of breath without exertion be 0.68 (Deeg et al. 1985, p. 282). For the younger man, his suffering of shortness of breath without exertion translates into an expected survival time of 11.5 years whereas his age peer without any shortness of breath can expect to live another 16.5 years, implying a loss of approximately 5 years. The similar condition for the older man amounts to an expected survival time of 3 years as compared to 5 years for his age peer without any shortness of breath, implying a loss of only 2 years.

The issue, then, is whether the assumption of proportionality is warranted, or whether both men really have the same expected survival time given their poor condition, regardless of their age difference. In the latter case, in the following referred to as the similarity assumption, the age correction implicit in the RPD does not correspond to reality. A good argument in favor of the proportionality assumption is that younger persons, and perhaps females, have more reserves and can therefore better resist the lethal effects of a poor condition than older persons and males. An alternative argument speaks in favor of the similarity assumption: when a condition hits, it is likely to hit every person equally hard.

A recent study of survival time following hip fracture (Magaziner et al. 1989) exemplifies this argument. After one year, the difference between the observed and expected mortality rates appeared to be greater in patients younger than 75 years than in older patients: mortality was elevated with a factor 6 in patients aged

65-74 and with a factor 1.7 in those aged 85 years and over. The authors write: "Patients older than 84 years of age have 2.6 times the risk of dying within three months of hip fracture as patients between ages 65 and 74 years, decreasing by six months after fracture. [...] the expected death rate for persons 85 years of age and older is nearly six times the mortality rate for persons between ages 65 and 74 years (14.6 per cent versus 2.5 per cent)." (p. 275). Although the authors call this finding "noteworthy", they do not attempt to explain it. According to the similarity assumption, however, this finding is not surprising. If the crude mortality effect of a hip fracture is nearly as great in younger persons as in older ones, this means a considerable increase in mortality for younger persons, whereas for older persons the excess mortality is limited because of the sheer magnitude of usual mortality at that age.

Another argument in favor of the similarity assumption derives from the increasing selectivity of the population with age. Older persons, having survived diseases that have made their age peers succumb, may be considered the fittest of their generation, and therefore constitute an increasingly selective "elite" (Riegel & Riegel 1972). Thus, they may be at least as resistant to lethal effects of diseases as are younger persons. In terms of the statistical analysis of failure time data, this observation casts doubts on the assumption of independence of left truncation time (= age at baseline) and conditional survival time (Tsai et al. 1987).

In some cases, then, it may be preferable to utilize absolute years instead of a relative measure of survival time. The dilemma of choosing between either the proportionality assumption or the similarity assumption cannot be solved in the context of longevity studies alone. Longitudinal research on intra-individual age-related decline of reserves and resilience in the face of physical and psycho-social hardship will help to clarify to what extent either assumption applies, given the particular sample and predictors under study. Most likely, the dilemma will not be decided in favor of either assumption, but a combination of both assumptions will prove the most viable. The proportionality assumption may be appropriate for some predictors, the similarity assumption for others. E.g., different assumptions may be appropriate for short-term versus long-term predictors, for social versus clinical predictors, or even for different clinical predictors such as those directly related to ill-health conditions and those indicating elevated risk of ill health.

**Treatment of right censored data.** The second issue that comes to light upon reviewing the application of the RPD in three different samples pertains to the method followed when imputing an RPD-value for individuals still alive at end-of-follow-up. The assumption underlying the imputation method is that these survivors are a non-selective group as compared to the total population alive at that time. While this assumption may be valid in initially representative samples, such as those of DLSE and NHANES I (II.1 and II.5), its validity must be seriously doubted in samples that are selective to begin with. As is described in II.6, this

applies to the SDHE sample. The issue becomes more urgent in studies with a relatively short follow-up time, implying a relatively large proportion of subjects with right censored survival times. Again, this applies to SDHE. A suboptimal treatment of right censored data may change the rank order among subjects, and thus the associations between baseline characteristics and RPD.

The problem is, then, how to find more appropriate imputation criteria? One approach is to calculate the mean RPD for those subjects having died, and use this mean as the last multiplication factor in the calculation of the imputed RPD. However, using this mean leads to underestimation of the survival times of right censored subjects, whose survival time up to this point already exceeded that of deceased subjects and whose expected remaining survival time may be more favorable due to excess mortality among those who have died. On the other hand, the approach taken in II.6, where right censored subjects are attributed an expected remaining survival time corresponding to the population mean, is likely to lead to overestimation of their survival times. A more complicated, multi-step approach is to start with imputation based on the population mean survival time (i.e. 0.5), to calculate the mean RPD for the total sample (0.66 in SDHE), and subsequently to recalculate the RPD's of the right censored subjects substituting this mean for the last multiplication factor. The new sample mean is then calculated, and its value is compared to the original mean. If the difference between original and new mean RPD's is still considerable, e.g. greater than a preset level, then the procedure is repeated. This iterative process stops when the difference between the mean RPD's calculated at the  $(n-1)$ th and  $n$ th step is sufficiently small, i.e., when stability is reached.

**Selective samples.** A final issue is: does the rank order introduced among sample members, which is based on direct comparison with the population survival distribution, correspond to the true rank order of survival times corrected for age and sex in the sample? In other words, is the transformation from the population survival distribution to the sample survival distribution a monotonic one? In highly selective samples, this may not be the case. The question is, however, which rank order is to be preferred. Although a rank order based on the sample itself seems to be the natural one, and therefore preferable, there are potent arguments speaking in favor of a rank order derived from the total population. First, a rank order based on the total population is less dependent on the arbitrary composition of the particular sample. Second, it indicates the extent of selectivity of the sample. And third, it improves comparability of the study findings to findings from other studies.

**Issue 2. Predictors of longevity showing consistency across studies**

Aspects of activity are the foremost independent predictors of longevity showing consistency across the three studies. In DLSE, these aspects were instrumental activities of daily living (such as housekeeping) and still working; in NHANES I, they were non-recreational activity and again, still working; in SDHE, they were primary activities of daily living (such as self-maintenance). This finding is compatible with the emphasis on various activities of daily living and indicators of more robust activity in recent gerontological research (Branch & Jette 1981, Chirikos & Nestel 1985, Fillenbaum 1987, Mor 1987, Guralnik in press). There is an emerging consensus that activity, as an indicator of physical functioning, is an important tool to monitor the overall health status and quality of life of the older population. Its importance has long been recognized in clinical medicine and in long-term care, where the level of performance of activities of daily living is clearly connected with the severity of a condition and the amount of care that should be provided. The recognition of its usefulness for monitoring the general population was accompanied by the recognition of the need to develop indicators of physical functioning that differentiate not only at the disabled end of the spectrum, but also at the able end (Guralnik 1987). The predictive ability for longevity of still working, as demonstrated in DLSE and NHANES I, underlines the meaningfulness of differentiating among persons with high levels of physical functioning.

Proponents of monitoring levels of physical functioning in older populations generally point to the equal importance of monitoring cognitive, emotional, and social functioning (Spitzer 1987). This is in line with the often-quoted definition of health by the World Health Organization as a "state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" (WHO 1947). Several measurement instruments have been developed for survey of the general elderly population that combine all four aspects of functioning (Index of Well-being — Kaplan et al. 1976, Older Americans Resources and Services methodology — Duke Center for the Study of Aging 1978, Rand General Health Perceptions Scale — Brook et al. 1979, Sickness Impact Profile — Bergner et al. 1981, Philadelphia Geriatric Center Multilevel Assessment Instrument — Lawton et al. 1982, Comprehensive Assessment and Referral Evaluation — Gurland & Wilder 1984, Self-Evaluation of Life Function — Linn & Linn 1984). In part II of this dissertation, independent predictive ability for longevity was observed for cognitive functioning as measured by a memory test (DLSE) and emotional functioning as indicated by satisfaction with aspects of life such as health and income (DLSE) and by morale (SDHE). Neither cognitive nor emotional functioning could be evaluated with respect to predictive ability in NHANES I, because no information was available on these aspects. Cognitive functioning did not independently differentiate among shorter and longer lived persons in SDHE perhaps because of selectivity of the sample. Aspects of social functioning were

### *III.1 Summary of findings*

not found to independently predict longevity in any study, partly because information on social contacts and social activities lacked (NHANES I), partly because they were superseded by other predictors (DLSE, SDHE).

Physical information was available in most detail in NHANES I. It is therefore not surprising that the large majority of predictors of longevity in this study are related to physical impairments and conditions. In the following, only those predictors will be discussed that also played an independent role in either of the other studies. Shortness of breath is one of the strongest, independent predictors of longevity in both NHANES I and DLSE. Further independent predictors in both studies are cardiovascular findings, which corresponds to abnormalities of heart and major blood vessels upon percussion in DLSE, and systolic murmur. Erythrocyte sedimentation rate proved to be one of the most stable predictors in DLSE. However, in NHANES I it was a predictor only in the total sample, and did not reach significance in the sample with the most detailed information available. Possibly, its predictive ability would have persisted if older age groups had been included in NHANES I. Detailed analyses in DLSE (Deeg et al. 1985) revealed that this parameter is a predictor especially in persons aged 75 and over having heart disease and pneumonia among their causes of death, in addition to persons of all ages dying of cancer. Health care use and use of medications were independent predictors in all three studies, although the amount of detail in the indicators varied. From NHANES I, it can be concluded that the medication use most predictive of longevity is related to heart disease and diabetes.

All in all, there is a reasonable consistency among predictors of longevity considering the diversity of the data available. Note, that this consistency exists in spite of the different mean ages of the study samples. While age ranges overlap, mean ages at baseline were 75, 69, and 82 years in DLSE, NHANES I, and SDHE, respectively, thus showing considerable differences. The DLSE sample allowed comparison of predictors in the age groups 65-74 and 75 and over (Deeg et al. 1985). An important difference was revealed: among predictors in the older age group, general characteristics predominated which were not related to one specific disease, such as physician-rated overall health status and memory function; in the younger age group, by contrast, the majority of predictors were related to specific disease, namely cardiovascular disease. This finding can be interpreted as a caution against extrapolation of predictors of longevity determined in younger elderly to older elderly.

In summary, independent predictors of longevity consistent across studies appear to be related to all aspects of general health status and quality of life, except social functioning. The vast majority of disease-related, independent predictors pertain to cardiovascular diseases.

**Issue 3. Predictive ability of factors associated with longevity**

Comparison of the predictive ability of the joint predictors found across the different studies described in part II (Table 1), leads to the conclusion that improvement above the level of 20% variance explained is in fact possible. The experience in both NHANES I and SDHE shows that inclusion of more detailed, especially health-related, information is crucial in improving the predictive ability. The predictive ability of the joint NHANES I predictors might have been even greater if an indicator of cognitive function and better indicators of emotional status and physical function, in particular activities of daily living, had been available. Thus, predictive ability is contingent on the information available. Upon closer examination, however, several caveats should accompany this conclusion. These caveats pertain to sample selectivity, sample size, and length of follow-up.

**TABLE 1 Percent variance explained in three studies of longevity in the elderly**

<hr/>	
DLSE (n=2645)	
including objective health	20.2%
excluding objective health	19.5%
NHANES I	
total sample (n=2852)	17.6%
total sample, locations 1-65 (n=2163)	20.9%
detailed sample (n=904)	24.4%
detailed sample, locations 1-65 (n=559)	34.1%
SDHE (n=298)	
four scales	33.2%
all assessment items	46.8%
<hr/>	

**Sample selectivity.** First, it may not be justified to compare percents of variance explained directly across the studies (Table 1). Recall that the variance explained in SDHE is greatly contingent on the excessive influence of age in this sample. Since the samples of DLSE and NHANES I are less selective, the 33-47% of variance explained in SDHE cannot be directly compared to variances explained

### *III.1 Summary of findings*

in DLSE and NHANES I. Variance explained, then, is contingent on sample selectivity.

**Sample size.** An opportunity to systematically examine the contingency of the percent of variance explained on the information available in the context of one single study based on non-selective subsamples was presented in NHANES I. While in the total NHANES I sample mostly global health related information was collected, collection of more detailed information was realized in various random subsamples. Direct comparison of the percents of variance explained across subsamples, however, is hampered by the decreases in sample size. It is a well-known empirical phenomenon that the percent of variance explained increases as the sample size decreases, due to small sample fluctuations. Associations found in smaller samples are more likely to be due to chance.

**Length of follow-up.** While the follow-up period in DLSE was of such length that virtually all subjects had died, both in NHANES I and SDHE just one half of the subjects were still alive at end-of-follow-up. In DLSE, then, the distribution of the RPD reached uniformity on the interval (0,1) with mean 0.5 and standard deviation 0.29 (II.1, Figure 2). In NHANES I, although the mean RPD was approximately 0.5, the standard deviation was somewhat smaller. The necessity to impute the RPD of one half of all subjects clearly had a decreasing effect on its variance. In SDHE, the standard deviation in the RPD was even smaller than in NHANES I, indicating a greater clustering around the sample mean which may in addition reflect the selectivity of the SDHE sample. A decreased standard deviation of the RPD has consequences for the amount of its variance explained, which introduces a difficulty in comparing percents of variance explained across studies of different length of follow-up.

As has been argued in II.1, differences in length of follow-up play a larger role when using methods to predict longevity which are based on pooling of data instead of an individual measure of survival time. Using pooled data, the rank order of survival times of groups of subjects is not as finely tuned as in observing individual subjects. Consequently, changes in length of follow-up may cause larger shifts in rank order, thereby affecting the associations between predictor variables and longevity to a greater extent. Although the "harm done" by using the RPD, then, is minimal, it could be further reduced by weighting the right censored subjects such that they exert less influence on the results than subjects whose RPD does not need to be imputed. The latter approach is similar to the treatment of censored data in standard life-table analysis, where they are weighted by 0.5 (Kurtzke et al. 1989).

Given the diversity of sample selectivity, sample size, and length of follow-up across studies, final conclusions regarding the baseline information maximizing predictive ability should be guided by the principles of interpretability and reproducibility of the results.



**Interpretability.** The first principle of interpretability, then, is most pertinent to the study giving rise to the most far-reaching conclusions: NHANES I. How can the supersedence of more global risk factors by clinical assessments associated with longevity, by which process the total predictive ability appears to increase, be interpreted? As indicated in II.5, the clinical assessments are more directly related to ill health and therefore to premature death. Indicators of health and psychosocial co-factors, on the other hand, may be best described as predisposing factors that trigger health declines leading to death. Factors directly related to longevity are likely to have greater predictive ability than predisposing factors which are only indirectly related.

**Reproducibility.** The second principle, concerning reproducibility, can again best be examined in the context of NHANES I by observing that supersedence as more detailed information becomes available takes place across all three sub-samples. Furthermore, the same process of supersedence can be observed in the SDHE sample when more detailed, health-related information is included in the analysis.

#### **Issue 4. Institutionalized versus general populations**

As already has become clear when discussing Issue 2, a correspondence of the predictors of longevity observed among residents of a home for the elderly with those among older subjects in the general population can certainly be noted. This applies in particular to indicators of physical and emotional functioning, and to health care needs. Of course, this conclusion is only valid as far as comparable information is available.

At this point, it is relevant to consider a difference between indicators of physical functioning showing predictive ability in SDHE and DLSE respectively. In SDHE, the indicator concerned the performance of activities of daily living for self-maintenance (ADL). More detailed analysis demonstrated that the item incontinence was in particular responsible for the association between ADL and longevity, thus superseding items such as bathing and transferring. Although in DLSE indicators of both ADL and of instrumental activities of daily living (IADL) were included in the regression analysis, only IADL proved to be independently predictive of longevity. As has been pointed out by authors who compared different ADL indicators, there is a hierarchical relationship between IADL and ADL in terms of personal assistance needed, with IADL representing less severe dysfunction (Spector et al. 1987). Prevalence estimates show that fewer persons have ADL disability as compared to IADL disability; the underlying distribution of ADL is more skewed than that of IADL. Presumably, although ADL disability has more severe health consequences, in a general population the cut-off point between able and disabled is at too low a level of functioning for ADL to become independently

### *III.1 Summary of findings*

predictive. In other words, ADL disability does not sufficiently differentiate in a general population. In contrast, ADL is more evenly distributed and therefore differentiates sufficiently among residents of a home for the elderly. Moreover, incontinence has been observed to be even higher in the dysfunction hierarchy in studies where it was not included in the ADL scale (Koyano et al. 1986). Not unexpectedly, then, incontinence proves to be the best differentiator between short- and long-survivors in a relatively disabled population.

It can be concluded that different indicators of ADL apply to different ranges of the total spectrum of physical functioning. The choice of indicator of physical functioning should therefore depend on the disability level of the particular population under study (Branch & Meyers 1987). Although the available measurement instruments of functioning in other areas, such as the cognitive and the emotional, were not sufficiently similar to allow comparison, it may be expected by analogy that the same differential principle applies to these areas.

#### **Issue 5. The predictive ability of change**

Thus far, the evidence has been reviewed from those studies in part II which included only baseline information to predict subsequent survival time. The question of whether the inclusion of change in predictors improves the prediction of longevity, can be answered in the affirmative. However, with respect to predictive ability not too much is gained: the percent of variance explained when including change is only slightly larger than the variance explained when predicting longevity in the same subsample using only information collected at the most recent time of measurement (25.7% versus 24.8%, Tables 4 and 3, II.3). The benefit of including change in addition to baseline information lies in the increased understanding of why a factor is a predictor. When only baseline information is available, the observed level of a predictor may either reflect a recent decline or a stable, health-threatening condition. In the first case, the predictor exerts a short-term influence, in the second case a long-term influence.

When information on two times of measurement is available, it appears that predictors in the first category are change in physician-rated health, change in physical disability (ADL) and change in more robust activity such as bicycling. Predictors in the second category are level of systolic blood pressure, level of cognitive function, presence of inguinal hernia, and level of satisfaction with present life. These findings are highly relevant to the identification of groups at risk. They imply that general health status and physical functioning should be monitored on a regular basis, while there is no immediate need for regular monitoring of other risk factors.

Closer study in II.4 of one of the predictors categorized as having a stable, long-term effect in II.3 yields a seemingly contradictory result. Rate of change in

cognitive function is shown to be a better, independent predictor of longevity than level of cognitive function either at baseline or at most recent time of measurement. This contradiction may be explained by two circumstances. First, rate of change in cognitive function in II.4 is calculated for each individual subject, whereas in II.3 only aggregate change is considered, indicated by a shift in the distribution from the first to the second time of measurement. In the aggregate approach, changes have to be more dramatic to be detected. Second, the calculation of rate of change in II.4 is based on three instead of two times of measurement, thus decreasing the likelihood of observing change or lack of change due to measurement error. Third, II.4 deals with change over a period covering eight years, whereas in II.3 change covering only five years is considered. During eight years, greater changes can occur which subsequently may have greater significance with regard to longevity. In conclusion, the findings of II.4 are more pertinent to processes associated with longevity.

In analogy to the case of cognitive function, it may be useful to conduct more detailed studies of individual changes or rates of change both in factors which in II.3 were identified as long-term and in those identified as short-term predictors of longevity. Findings from such studies may disclose the shapes of particular trajectories preceding death.

#### **Issue 6. Are factors showing change just prior to death predictors?**

SDHE, with its repeated observations on all residents at three month intervals, lends itself very well to the study of this issue. Comparing findings from II.6 and II.7, there does not seem to be a direct one-to-one correspondence between independent predictors of longevity and factors showing decline in the last year of life. Whereas only physical functioning and morale have independent predictive ability, both these factors and cognitive functioning show significant declines as compared to surviving residents.

In attempting to explain why (level of) cognitive functioning did not predict subsequent survival time in residents of a home for the elderly, reference was made to the particular selectivity of this population: residents who, in addition to cognitive function problems, have health problems — and thus decreased life expectancy — are likely to be relocated to nursing homes, while those having cognitive function problems but no further health problems are likely to be maintained in the residential home. As has been observed elsewhere (Deeg et al. 1989), a poor cognitive function alone does not contribute to decreased survival. However, the often reported decreased survival in persons having poor cognitive function should be attributed to comorbid conditions, the impact of which is likely to be greater in those having poor as compared to normal cognitive function. When observing the total population at baseline resident in a home for the elderly,

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therefore, an association of cognitive function and longevity is likely to be obscured because those residents with comorbid conditions are not part of this population.

In addition, as could be shown in DLSE, rate of change appeared to have better predictive ability than level of cognitive function in a sample from the general population (II.4). This may equally apply to the institutionalized population.

A further question of interest is, whether the distinction made in II.6 between factors showing *terminal decline* (i.e. gradual, age-related decline) and those showing *terminal drop* (i.e. accelerated, health-related decline) in the last year of life has any relevance for the understanding of predictors of longevity as evaluated from baseline observation over a period extending over many years. A terminal drop was seen in physical functioning, particularly in those in relatively good health at one year prior to death. In the latter subgroup, a terminal drop was also seen in morale. Cognitive and social functioning only showed a terminal decline, not a terminal drop. Thus, the two predictors of longevity least ambiguous in long-term follow-up studies were seen to decline in an accelerated fashion during the last year of life. This finding suggests the hypothesis that a predictor of longevity as ascertained in a baseline-follow-up study be understood as a factor declining in an accelerated fashion prior to death.

It seems advisable to undertake further study to decide whether associations detected between longevity and factors declining only gradually are to be understood as causal relationships. For example, the reported association between cognitive function and longevity may be due to other factors not included in the analyses. Alternatively, a period of one year prior to death may not be long enough to detect changes that could be interpreted as accelerated declines. Indeed, several authors have suggested that declines leading to death become apparent over a period as long as five or more years prior to death (Riegel & Riegel 1972, Siegler et al. 1982, Berg 1987). Referring to the similarity and proportionality assumptions discussed under Issue 1, it might well be that the period across which terminal declines occur is not of a fixed length regardless of age at death, but shortens with increasing age. Alternatively, in analogy to the suggestion under Issue 1, the length of the terminal period may vary with the particular characteristics under study.

Further studies, similar in design to SDHE, but extending over a longer period and including additional factors believed to predict longevity, should help the understanding of truly causal relationships with regard to longevity.

### **Issue 7. Characteristics of the aging process and the feasibility of predicting longevity**

As has been discussed under Issue 3, the magnitude of the variance explained in longevity is not independent of specific study characteristics. Leaving the distorting effects of sample size, sample selectivity, and length of follow-up for what they are, the variance explained can be improved particularly by including detailed, clinical

information at baseline. In NHANES I, a maximum of 34% variance explained is reached. However, this study neither included measures of cognitive functioning, nor appropriate measures of physical and emotional functioning. Inclusion of such measurement instruments will most likely improve the predictive ability of the joint predictors. The maximum of total variance explained in any study using optimal baseline measurements and controlling for age and sex, then, may be expected to surpass 40%. However, is not likely to exceed one half of the total variance. Thus, lest no break-through will occur in basic fields of science such as cell biology or immunology, chance will continue to play a major role in determining the longevity of an individual, especially in late life.

Conceivably, the estimated maximum percent of variance explained in longevity cannot be improved due to the fact that the study pertains to *elderly*. Persons in the older age groups were able to resist diseases and circumstances which caused the premature death of some of their late contemporaries. Causes of death are likely to be more clear-cut in younger than in older persons (Manton & Stallard 1984, Mackenbach 1988). Moreover, several aspects of what is indicated by the collective noun of "aging" are likely to hamper improvement of prediction of longevity in late life.

First, persons in their seventies or older have a relatively short remaining life expectancy. Therefore, only small differences in survival time are to be explained.

Second, death may result from disorders that have a hardly noticeable impact on younger persons. Threshold values beyond which disorders may become life-threatening are lower in older age. Furthermore, the time of occurrence of these disorders, as well as their particular appearance, may be largely due to chance.

Third, an increasing diversity among individuals of increasing age has been noted repeatedly (e.g., Maddox & Douglass 1974, Maddox 1987). Consequently, it is increasingly difficult to identify general patterns of aging. This diversity not only pertains to the particular shape of trajectories in the last phase of life, but also to particular levels of disturbance (thresholds) that undermine the resistance of individuals and thus threaten their lives.

Fourth, there is considerable interdependence among factors associated with health and longevity in the elderly. This hampers the distinction of factors directly associated with longevity from those indirectly associated. Factors indirectly associated with longevity may weaken associations as compared to directly associated factors. Particularly in psychosocial factors, it is difficult to distinguish direct from indirect effects on longevity, because little is known about the mechanisms or pathways leading from decreased psychosocial functioning to death.

A final difficulty arises from the distinction between normal or non-pathologic aging and pathologic aging or chronic disease (e.g., Shock et al. 1984). Normal aging is considered to be more or less age-related, with individual differences in rate of aging, perhaps based on genetic make-up, perhaps on environmental

### *III.2 Further research*

factors, perhaps both (Adelman 1980). Pathologic aging, by contrast, is contingent on the time of onset of a chronic disease which is not essentially age-related (although for many diseases a correlation with age exists, cf. White et al. 1986). A non-selective older sample, then, consists in part of individuals not characterized by pathology, in part of individuals characterized by pathology. However, “markers” of non-pathologic aging are often identical to risk factors for chronic disease and death (Borkan & Norris 1980). The association between longevity and the former type of factors may still be of a different nature than that between longevity and the latter type (e.g., linear vs. non-linear), thus clouding the prediction of longevity when it is attempted on the basis of a sample in which both types inevitably play a role. Identification of factors determining longevity which can be clearly classified as either markers of aging or as risk factors for chronic disease only seems possible in a rigorously defined, experimental sample which does not represent a mixture of both types of aging.

In conclusion, it seems that students of determinants of longevity have to content themselves with a set of predictors of necessarily less-than-perfect predictive ability. On another note, it may be considered fortunate that human individuals are only partially able to predict their own life spans. The observed “predictors” of longevity, however, may give sufficient guidelines to set up programs to prevent health declines and improve quality of life in population groups. This is elaborated in the next section.

### III.2 Further research

While summarizing main findings, several suggestions for further research have been made. Some of these suggestions were aimed at more detailed study, using more appropriate measurement instruments, of questions left open in this dissertation’s studies. Other suggestions left the realm of prediction of longevity and addressed underlying questions related to aging processes. Both kinds of further research will be discussed in greater detail in this section, with a special view on how they can be made useful to the identification of groups at risk and to the promotion of health and the prevention of health declines among the elderly.

#### **Research clarifying predictors of longevity**

The concern was raised that a baseline predictor, observed only once, does not convey information on the source of its predictive ability (cf. Issue 5). Does an observed level represent a stable condition which in the long run affects longevity? Or alternatively, does an observed level appear to affect longevity because it

represents a "snap shot" of a deteriorating process, so that it is the deterioration rather than the precise level from which the predictive ability derives?

While we were able to present some clarification with regard to several predictors, this issue deserves further study. It was suggested to conduct more detailed studies of individual changes or rates of change in various predictors. Findings from such studies may disclose the shapes of particular trajectories prior to death. E.g., there may be "*critical*" rates of decline in some factors which indicate imminent death (Jarvik & Blum 1971). For prevention purposes, factors known to have such critical rates should be monitored on a regular basis. Adverse consequences of health changes may then be prevented if changes are detected in an early stage. Other factors may have *critical levels* which have detrimental effects on longevity in the long run, even without further decline. If such a level has come to light in an individual, interventive measures to improve the level may be devised. Below, the effectiveness of interventive measures in older persons aimed at selected risk factors reported in literature will be discussed in a separate paragraph.

Another concern was raised with regard to causality in relation to the trajectory of factors showing predictive ability (cf. Issue 6). Is the observation of a gradual decline of a factor sufficient proof of a causal relationship with death? Or should a factor show a precipitous decline prior to death to be marked as a causal agent? For example, cognitive function was shown to decline gradually (as opposed to precipitously) in the last year of life, while evidence was cited that the often reported association between cognitive function and longevity may have to be attributed to concurrent factors not included in the analyses. Further study was suggested to decide what kind of trajectories are indicative of causal relationships between the factor and longevity. In particular, clarification is needed regarding the hypothesis that predictors of longevity are characterized by an accelerated decline prior to death. If this hypothesis gets support, further research is needed into the influence of concurrent factors on those predictors showing only a gradually declining trajectory.

In pursuing such research, data are needed from prospective studies with frequent times of observation, from which series of observations prior to death are selected for those who died during the total study period. A series of observations spanning a period of one year prior to death, as chosen in our own study (II.7), may not be long enough to detect changes that could be interpreted as accelerated declines. It might well be that the period across which terminal declines occur is not characterized by a fixed length regardless of age at death, but shortens with increasing age. Moreover, the length of the terminal period may vary with the particular factor under study. For example, terminal declines on some psychosocial factors may be apparent over a much longer period than those on physical factors. Better knowledge of the characteristics of trajectories of predictors of longevity

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will enhance possibilities for prevention or, more modestly, stabilization of health and quality of life at an acceptable level.

Trajectories cannot be studied separately. Decline in one factor below a critical level can trigger off declines in other factors and vice versa. Terminal decline is a multivariate phenomenon, with some factors having a direct effect, others having an indirect effect on the rate in which death approaches. To elaborate on the example of the relation between cognitive decline and longevity, it might be hypothesized that persons experiencing cognitive decline are more vulnerable to life threatening diseases, such as infections. These incident diseases may be the factor directly causing death, while the prior cognitive decline may be an indirect, or predisposing factor.

Particularly in psychosocial factors, it is difficult to distinguish direct from indirect effects on longevity. E.g., the role of social contacts appears controversial when contrasting the lack of association shown by the studies reported in this dissertation and the positive association reported from other studies. For health promotion purposes, it might be more effective to concentrate on indirect, but possibly triggering, factors than on factors directly associated with terminal decline: it might be too late for intervention if the declining process is already well underway. For example, decreases in the quality and quantity of social contacts may decrease motivation to leave the home and therefore increase immobility. The next step in this causal chain may be the onset of depression which may make the older person more vulnerable to a fatal illness. Clearly, prevention in this example of a deterioration process is most effectively directed at the triggering factor, to the effect of compensation for social contacts lost.

In conclusion, it is essential to study physical, mental and social factors in their simultaneous relation to longevity. However, the information provided by a "snap shot" of these factors is not sufficient. It is paramount to study pathways during the last phase of life. Such pathways or trajectories include both transitions within factors and the mechanisms by which a change in one factor affects changes in other factors. By careful study, it may be possible to determine stages in the process of decline that are still amenable to intervention.

#### **Research aimed at underlying aging processes**

A theoretical question raised by reviewing the results of the studies in part II is: Does a given condition affect a person's longevity proportional to his or her age or is its effect independent of age? (Cf. III.1, Issue 1.) This question has been termed the dilemma between the proportionality and the similarity assumption. An argument in favor of the proportionality assumption is that younger persons have more reserves and can therefore better resist the lethal effects of a poor condition than older persons. An argument in favor of the similarity assumption



hypothesizes that when a condition hits, it hits every person equally hard. A further argument in favor of the similarity assumption is that older persons may be considered the fittest of their generation, and therefore constitute an increasingly selective "elite".

It has been suggested that the dilemma of choosing between either the proportionality or the similarity assumption cannot be solved within the context of longevity studies alone. Longitudinal research on intra-individual age-related decline of reserves and resilience in the face of physical and psycho-social hardship should help to clarify the dilemma. It is important that this research be longitudinal, because it deals with initially healthy individuals whose adaptive responses to physical and psycho-social challenges are observed. This might be an area of research which is most promising with regard to gaining knowledge on aging processes (Adelman 1980). The proportionality assumption may turn out to be appropriate for some predictors, the similarity assumption for others. E.g., different assumptions may be appropriate for short-term versus long-term predictors, for social versus clinical predictors, or for different pathophysiological predictors. For health promotion purposes, knowledge concerning age-related adaptability in the face of morbid conditions seems essential for the formulation of realistic goals and successful intervention in individual persons.

Another theoretical question, broached at the end of section III.1, can be restated as follows: Is there a difference between markers of aging and predictors of premature death, and if so, how can the two be distinguished empirically? Making this distinction implies that aging is viewed as a process that varies among individuals who may be characterized by a *rate of aging*. It has to be added that each individual will be characterized by more than one rate of aging, depending on the factor studied. E.g., his lung volume may decrease at a different rate than his bone density. Furthermore, aging is viewed as a process that is not necessarily related to mortality. Conceptually, a relation between aging and mortality exists only then, when the rate of aging rises above a certain critical or threshold rate or when the aging process has proceeded so far that the factor studied has decreased below a certain critical or threshold level (*rate - and point of no return*, respectively). The threshold marks an increased vulnerability of the individual, e.g. for a lung infection or a hip fracture with a fatal outcome. Had the threshold not been reached, the outcome would not have been fatal, and most likely the event of infection or fracture would not have occurred at all.

It has been suggested above that predictors of (premature) death show a non-linear trajectory over a period of time prior to death, while factors showing a linear trajectory over time may be characterized as markers of aging. An empirical study designed to distinguish both types of factor will have a design similar to the study of trajectories in the last phase of life, proposed earlier in this section. It should be based on a series of observations on factors related to longevity and/or

the aging of the human system, at regular intervals starting at an age where functional capacity is still near its maximum in most individuals (e.g., age 40), and including individuals without apparent pathology (e.g., normotensives). This study should be conducted over a period long enough (e.g., 30 years) to determine rates of aging, i.e. the rate of change in the factors studied. These rates, then, should be correlated with the endpoint of the dichotomy *normal* — *pathologic*. (Note, that the dichotomy *alive* — *dead* is not applicable because the rates have to be determined in those subjects who survived the full study period.) For a factor to be a marker of aging, it should show a significant decline without being correlated with the endpoint. For a factor to be predictive of premature death, it should show a significant decline, and the rate of decline should be correlated with the endpoint. Further evaluation of trajectories of predictors of premature death in those who died during the study period may reveal evidence bearing on the hypothesis of non-linear or accelerated (terminal) decline.

The suggested long-term research, however, is difficult to realize and requires data sets and methodologies that may not be readily available as it stands (Deeg 1989). Serious commitment and long-term investment are needed for its realization. The discussion presented here is intended to draw attention to some as yet unresolved issues. The study of these issues will certainly pay off in terms of better knowledge of the aging process per se and of possibilities to intervene in unfavorable trajectories.

#### Prevention and intervention in older persons

In chapter I (Introduction), the studies reported in this dissertation were classified as “basically descriptive studies attempting to identify groups at risk of premature death.” While a number of factors associated with risk of premature death in older persons were ascertained in chapter II, it is not immediately obvious how groups characterized by these factors should be identified, and how subsequently their risk could be decreased. Asking these questions, the area of prediction of longevity is left and the area of prevention is entered. Nonetheless, it is considered appropriate to present a brief discussion of issues related to prevention in the elderly in this context, because of its close relation to the basic goal of predicting longevity.

Prevention in the elderly has only recently received the attention of policy makers and researchers. Among the several issues surrounding this area, perhaps the most prominent one is the difficulty of quantifying the effectiveness of prevention. Evaluation of conventional effect measures such as a decreased incidence or mortality of diseases (Gunning-Schepers 1988) does not tell the full story. Since older persons are characterized by increased susceptibility to multiple diseases, prevention of one disease may imply the accelerated advent of another disease due to the cumulation of risk factors in late life (Fries et al. 1989). Moreover,

reduction of a risk factor for one disease may also reduce its protective effect for another disease. A most extreme example of this phenomenon is represented by some diseases related to obesity in older women. Obesity is an established risk factor for cardiovascular diseases (Lew & Garfinkel 1979, Hubert et al. 1983, Lapidus et al. 1984, Harris et al. 1988) and for degenerative joint disease or osteoarthritis (Davis et al. 1988, Everett et al. 1989). Non-obese older women, in contrast, are more likely to suffer from adverse consequences of osteoporosis such as fractures: obesity is a protective factor for fractures (White et al. 1986, Farmer et al. 1987). Prevention of obesity in an attempt to reduce morbidity due to some diseases, then, may result in an increased susceptibility to other diseases (for additional examples, see Gunning-Schepers 1988).

Thus, the effectiveness of prevention in older persons is not easily determined. The use of an effect measure such as disease incidence or total mortality may result in too optimistic or too pessimistic a conclusion. One could even doubt the use of prevention in the elderly at all if its effects cannot be measured by conventional methods. Consequentially, some authors in the past proposed a rather arbitrary age, e.g. 70 years, as a reference point against which to measure premature death, implying that beyond this age — by definition — premature death does not occur (Doll 1973, Romeder & McWhinnie 1977, Hickman & Estell 1979). Prevention in the elderly was thus marked a non-issue. More recently, however, prevention in the elderly has emerged as an issue of increasing priority. Even though an increased duration of life is not a primary goal, certainly an improved quality of remaining years of life is a stated health planning goal (Fries et al. 1989, Ministry of Welfare, Health and Cultural Affairs 1989). Quality of life is contingent on minimization of the burden of diseases. Proponents of prevention in the elderly argue that there is no age-defined cut-off point beyond which risk attributes are no longer modifiable (Kannel & Vokonas 1987, Rowe & Kahn 1987).

Meanwhile, it is a given fact that excellent health is only realized in a minority of older persons, a minority which decreases with advancing age. The goal of prevention should therefore be restated to include the majority of older persons. Thus, rather than a disease-free state, a state of optimal health — given a certain level of disability — should be envisaged. In this context, obviously, health is not considered to be restricted to absence of physical impairments, but rather to include physical, cognitive and psychosocial functioning, or quality of life (Ford et al. 1988, Guralnik 1988). A more appropriate description of prevention for older persons may be given by the term *health promotion*. Health promotion in older persons is understood here as the stabilization of functioning and quality of life at

an acceptable level, or equilibrium state.<sup>1</sup> In this sense, it is most closely related to the concept of *tertiary* prevention (Kane 1988). The effects of health promotion may be determined by assessing levels of functioning in the target population on a regular basis. A decreased number of persons with declining levels may then indicate a positive effect of health promotion.

As tools for health promotion, preventive and interventive measures may be applied. The former should be devised to stop further decline of functioning, or to prevent extension of decline to areas of functioning that did not show declines yet. The latter is a specific type of prevention, devised to improve levels of health and functioning so as to move out of a “danger zone” of irreversible decline. The first question to be addressed, however, is how those groups or individuals who should be considered for prevention are to be identified.

**Preventive measures.** The question of to whom preventive measures should be directed has been subject to considerable debate with regard to all age groups. Central to the debate is the controversy between the total population and the risk group approach, aiming to reduce the level of risk factors by a small amount overall and to move risk factors below a defined threshold level, respectively (Rose 1981, Oliver 1986, Kane 1988). The latter approach is relevant in the present context.

The risk group approach starts from identification of groups generally at risk based on social and demographic characteristics such as age, income position, housing condition, social isolation or recent life events. Based on age, all older persons would have to be considered at risk. Further useful differentiation may be based on other social and demographic characteristics. However, these characteristics lack sufficient predictive ability, and generally almost as much disease is found in groups which on this basis are classified as *not* being at risk (Taylor 1987). As readily available social and demographic characteristics do not provide useful differentiation, one would have to look for direct risk factors themselves (*secondary* prevention). This approach entails the screening of all persons in the population above a certain age. Such screening, however, does not satisfy the criteria generally accepted for population screening (Wilson & Jungner 1968), the most problematic being the absence of one clearly defined target disease for the detection of which one specific test is available, and for the treatment of which effective interventions are known. Moreover, screening is likely to cause needless disturbance (Frederiks 1986). A viable alternative may be a screening strategy which utilizes existing health care resources and is not targeted at clinical disease but instead at functional disability.

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1 In recent, mostly American, publications the term health promotion has been used in a more narrow sense, indicating the education of the population with respect to personal health habits.

It has been proposed to select persons at risk in the context of general practice or community nursing (Huygen 1986), perhaps with the support of a geriatric consultation center (Braak et al. 1989). This approach of "case finding" (Freer 1987, Buckley & Williamson 1988) is estimated to reach 75% of all persons aged 60 and over in the course of one year (United Kingdom). In twelve general practices in the Netherlands, in the course of one year contacts were recorded with as many as 82% of all persons aged 65 and over registered in the practices (Meyboom-de Jong 1989). Although those elderly who do not initiate contacts with their general practitioner are believed to be healthy (Ebrahim et al. 1984), additional high-risk individuals may be reached by a letter asking a few simple questions about physical and psychosocial functioning (Barber & Wallis 1982, Taylor 1987). In groups thus classified as being at risk of declined functioning, assessment of those factors previously identified as predictors of longevity (cf. III.1, Issue 2) may then serve to obtain a more detailed picture of health risks incurred.

One question remains: does not this procedure involve costs that are virtually as high as those of a mass screening? Based on evidence of clustering of chronic diseases in a restricted number of individuals (Epstein & Holland 1983), it may be expected that case finding will actually reduce the target group for preventive or interventive measures considerably. Reports from a geriatric screening program indicate that only 15% of all volunteer attenders were eventually treated (Rubenstein et al. 1986).

In addition to treatment of those with diagnosed disease, general practitioners or community nurses may stimulate (preventive) health behaviors such as self-care, risk avoidance, and use of resources in all screenees (Rakowski et al. 1987, Ramsdell et al. 1989). The encouragement of smoking cessation has gained wide support as the most promising preventive strategy to fend off a number of diseases (Kannel & Vokonas 1987, Kane 1988). While the evidence regarding the effect of personal health behaviors other than smoking cessation on mortality is contradictory (Branch & Jette 1984, Kaplan et al. 1987), the relationship of these behaviors with physical, cognitive and psychosocial functioning has not been investigated. Moreover, little information is available on the willingness of older persons to improve their health behaviors. Further research needs to address issues such as the kinds of health behaviors that should be stimulated given certain health risks and levels of functioning, and the social and psychological characteristics of older persons at risk that are associated with the effectiveness of these strategies.

**Interventive measures.** Once groups or individuals having levels of health and functioning in the "danger zone" are identified, intervention is called for. However, results of large scale intervention trials, mostly concerning cardiovascular diseases, have given rise to a continued debate about the effectiveness of interventive measures (most notably, the Multiple Risk Factor Intervention Trial: MRFIT

Research Group 1982). While most intervention trials are conducted in middle-aged persons, questions about the effectiveness of intervention in older persons are even more unresolved. There is only limited experience with intervention in older persons. This experience will be described briefly, so far as it pertains to predictors of longevity as ascertained earlier: blood pressure, ADL, and morale.

With regard to blood pressure, the focus of prevention has moved from decreasing both diastolic and systolic pressure to decreasing systolic pressure in those having normal levels of diastolic pressure (Working Group on Hypertension in the Elderly 1986, Kannel & Vokonas 1987). The prevalence of this "isolated systolic hypertension" increases to relatively high levels in the elderly, and there is evidence that this type of hypertension is more predictive with respect to mortality than diastolic hypertension (Working Group on Hypertension in the Elderly 1986, Van den Ban et al. 1989). This evidence is confirmed by our studies to the extent that diastolic blood pressure was not found to be independently associated with longevity, whereas systolic blood pressure proved to be an independent predictor of longevity, albeit not consistently (II.2, 3 and 5). With respect to intervention, several reports confirm evidence of only marginal beneficial effects of reduction of diastolic blood pressure, in addition to both physical and psychological adverse side-effects (Cutler et al. 1985, Milne et al. 1985, Cruickshank et al. 1987). The final results of an isolated systolic hypertension intervention trial are still underway (Curb et al. 1985, Hulley et al. 1986).

While evidence of the existence of an association of high blood pressure with mortality is not unequivocal, no evidence exists pertaining to an association with functional disability (Ford et al. 1988). However, no studies have been performed on the differential effect of isolated systolic versus diastolic hypertension on functional disability. Of all cardiovascular disorders, the effects of stroke particularly do affect physical functioning (Ford et al. 1988, Gosman-Hedström 1988). Of all diseases, stroke shows the greatest increase in incidence with advancing age (Manton & Soldo 1985, Schellekens 1989). Since hypertension is the major factor underlying stroke (Working Group on Hypertension in the Elderly 1986, Kannel & Vokonas 1987), intervention with respect to high (systolic) blood pressure should not be neglected.

A main aspect of physical functioning is the ability to perform activities of daily living. Direct intervention in this aspect includes provision of technical aids, realization of modifications of the home, meals on wheels, and physical therapy. Of these, the provision of technical aids and modifications in the home were observed to bring significant benefits in a Danish intervention study (Hendriksen et al. 1984), as measured by hospital and nursing home admissions, and deaths. In addition, this type of intervention produced important increases in confidence and therefore quality of life. The results of another, more broadly oriented Scandinavian intervention study are underway. This study addresses the possibilities of

improving physical, mental and social functioning or retarding the development of handicaps and reducing the need for medical and social services (Eriksson et al. 1987). These results should be highly relevant for the effectuation of intervention with regard to physical, cognitive and psychosocial functioning as proposed above.

In institutionalized populations, there is a longer tradition of research based on intervention experiments than in community living populations. These experiments especially evaluate the effect on life satisfaction of measures enhancing the control and competence of elderly residents (Schulz 1976, Langer & Rodin 1976, Schulz & Hanusa 1979). A recent Dutch intervention study in a residential home measured the effects of organizational changes which should stimulate social contacts and provide the residents with more control (Van Loveren-Huyben & Van der Bom 1988). A clear improvement was noted not only in social functioning, but also in morale, particularly in newly admitted residents. An unexpected additional effect was that the number of residents referred to a nursing home significantly decreased after the intervention. Since morale proved to be an independent predictor of longevity in this population, both quantity and quality of life are likely to increase by this intervention.

### Active life expectancy

In the course of this chapter, it has become increasingly clear that instead of a quantitative indicator of years of life lived, a qualitative indicator of health during the remaining years of life is needed. Despite increases in life expectancy during the past decades (cf. II.1, Table 1), there is no evidence that the burden of morbidity has decreased accordingly (Manton 1982, Verbrugge 1984). Some recent evidence is even indicative of an increased proportion of life spent in dependency (Stout & Crawford 1988). Although it has been suggested that a "compression of morbidity" is soon to occur (Fries 1980), this "soon" may have to be understood as a moment in the distant future, and will only happen through intensive research and prudent policy aimed at improving health and functioning during the added years of life (Schneider & Guralnik 1987). It is therefore a matter of pressing importance to develop concepts which will be instrumental in such research.

One concept which has recently gained wide acclaim is *active life expectancy* (Katz et al. 1983). Similar to the familiar demographic concept of life expectancy, active life expectancy indicates the age at which half of the initially independent members of a cohort lose their independence due to death, admission to a nursing home, or by having to rely on others for help in performing activities of daily living while remaining at home. Thus far, however, this concept has only been used to describe the disability-free life expectancy of aggregate groups (Colvez & Blanchet 1983, Van Ginneken & Van Sonsbeek 1989). Although a few recent studies attempt

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to predict good health and functioning for individual persons in older age from baseline data collected at middle or older age (Benfante et al. 1985, Guralnik & Kaplan 1989, Harris et al. 1989), no approach has been developed yet to predict the *time* of transition from good to poor health and functioning, or active life expectancy. It is proposed here, that a method similar to the one presented in this dissertation to predict longevity (II.1) will serve to predict active life expectancy. Analogous to the realized probability of dying (RPD), a measure indicating the *realized probability of functional disability* (RPF) should be developed. As the RPD is based on population life tables, which indicate age- and sex-specific rates of transition between life and death, the RPF should be based on age- and sex-specific rates of transition between ability and disability to perform selected functions. Such transition rates can be derived from population based, longitudinal studies of functional ability (cf. Manton 1988). In fact, the development of more than one RPF should be recommended, each one based on a different component of functioning, because different impairments and circumstances may lead to different disabilities (Jette & Branch 1985). The distinction is essential to design preventive and interventive strategies. Thus, the availability of appropriate data permitting, four RPF's should be constructed:

RPF<sub>physical</sub>, RPF<sub>cognitive</sub>, RPF<sub>emotional</sub>, and RPF<sub>social</sub>.

To develop these proposals further would reach far beyond the context of this dissertation. However, it is hoped that the preceding discussion will provide the reader with sufficient "food for thought" and some tools to develop important insights in the areas of longevity per se, active life expectancy, prevention and intervention.

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## Summary

Longevity research, traditionally, is concerned with health status, of which longevity is considered an indicator. Factors associated with longevity, or survival time, are considered to be associated with health status as well. The search for such factors is the topic of this dissertation. Physical, mental and social characteristics of individuals observed at one point in time (the baseline examination) are related to these individuals' subsequent survival time as ascertained after a follow-up period. Those characteristics which are significantly associated with survival time are termed *predictors*.

The main issue addressed is the feasibility of the predicting of longevity in older persons: what are its possibilities, what its limitations? As is explained in **Part I**, this issue is addressed from a concern with both the scientific value and the practical applicability of the findings. Aspects of the issue include: the available material (selectivity of the study sample, scope of the information collected), the method (measurement of the baseline characteristics, definition of the measure of survival time, statistical model), and comparability of results across different studies.

Results of three longitudinal studies are compared with respect to both the nature of the predictors and their predictive ability in terms of variance explained in longevity. These studies are: the Dutch Longitudinal Study among the Elderly (DLSE), the First United States National Health and Nutrition Examination Survey (NHANES I), and the Study of Disability in a Home for the Elderly (SDHE). Further use is made of the longitudinal design of the first and third studies by evaluating change in characteristics in relation to longevity. This allows ascertainment of pathways or trajectories prior to death, which supplements the ascertainment of predictors of longevity based on a "snap shot" at baseline.

The material covered is summarized into seven questions:

1. What is an optimal operational definition of longevity in a long-term follow-up study of the elderly?
2. Which predictors of longevity can be identified consistently across different studies?
3. What can be concluded regarding total predictive ability across studies of different design?
4. Do predictors of longevity based on studies of institutionalized populations correspond to predictors based on studies of non-institutionalized populations?

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5. Does inclusion of (rates of) change in characteristics improve the prediction of longevity as compared to levels of characteristics?
6. Are factors showing changes just prior to death the same as those which are found to be predictive of longevity in the longer run?
7. Which characteristics of the aging process can account for the observation that longevity studies attain a predictive ability of far less than 100%?

**Part II** of this dissertation consists of seven sections, each taking up one aspect of the prediction of longevity. **Section II.1** deals with the operational definition of a measure of longevity. Since studies of predictors of longevity in the elderly are usually based on samples with a wide age range and some selectivity, this is not a trivial matter. One is faced with the problem of constructing a measure of longevity that:

1. makes subjects in the sample comparable regarding survival time, independent of their age and sex;
2. can be used to check the absence or presence of selectivity of the sample with regard to longevity;
3. is suitable for long-term follow-up studies;
4. can take the mortality development over time into account;
5. improves the comparability of studies with different designs and sampling schemes.

An individual measure of survival time is presented that satisfies these requirements: the Realized Probability of Dying (RPD). Its construction is described. The RPD is derived from population life tables based on age, year of birth, and sex. For each subject, the relative position on the survival curve within the birth cohort is determined. In an illustration, the RPD is applied to data from DLSE, a 28-year longitudinal study of a nationwide, age- and sex-stratified sample of 3149 elderly who were 65-99 years of age at baseline (1955-1957). In 1983, survival time or vital status was determined for 84% of the original sample. The RPD is compared with other survival measures commonly used in this type of studies. It is concluded that the RPD is a powerful and valid measure of longevity in elderly subjects, and that it can be useful in the study of predictors of longevity.

In **Section II.2**, actual predictors of longevity are ascertained in DLSE, using the RPD. Multivariate regression models are used to predict the RPD. Predictor variables include physical, mental and social indicators of health status. The total variance explained is 20.2%. Objective health (rated by the examining physician) shows the strongest relationship with the RPD. Upon removing objective health from the model, 19.5% of the variance remains explained. This indicates that the information contained in objective health largely corresponds to the information in the other independent predictors. Separate analyses are performed for (1) bio-medical, physical and mental examination variables, (2) disability and health care use variables, and (3) social and psychological variables; in each case the variance explained appears to be over 11%, demonstrating considerable interde-



pendence among predictors. Across different regression models, bio-medical and disability variables prove to be the most stable predictors of longevity.

In II.3, a method is presented for an empirical evaluation of the association of changes in characteristics over time and longevity. Essentially, regression analyses are performed with the RPD as the dependent variable, while the independent variables include physical, mental and social characteristics recorded at two cycles five years apart in DLSE (1955-1957 and 1960-1962). Two types of predictors of longevity are distinguished: (1) those deriving their predictive value from a decline in the predictor variable that recently occurred; (2) those deriving their predictive value from a longer lasting, more or less stable level reflecting a poor health condition. Objective health status, physical disability and activity are found to be in the former category. Systolic blood pressure, memory function, inguinal hernia and satisfaction with present life are characteristics found to be in the latter category of predictors.

The association between rate of change in cognitive function and longevity is investigated in II.4, again with data from DLSE. A group of 211 persons, aged 65-84 years at baseline, was re-examined twice during an eight-years follow-up period (1955-1957 through 1963-1965). Their survival time was ascertained over a period of maximally 20 years after the third cycle. Cognitive function was assessed based on an adaptation of the Wechsler Memory Scale. Rate of change in cognitive function during the eight years of follow-up is determined by regression on time for each individual. Cognitive function appears to decline significantly over the eight-years period (mean yearly change  $-0.28$  units, with 95% confidence interval  $-0.34$  to  $-0.22$ ). The rate of decline in cognitive function is strongly associated with subsequent survival time in the ages 70 years and over, with those with a large decline having a short survival time. No association can be demonstrated in the age group 65-69 years. Adjustment for either initial or attained level of cognitive function and for potential confounders does not affect the magnitude of the association.

In II.5, data from NHANES I are used to predict longevity in White subjects aged 65-74 years at baseline, 1971-1975. At follow-up in 1986, vital status was known for 98.7% of the sample ( $n = 3137$ ). At that time, 49.5% had died. The NHANES I design involved collection of data from examination, interview and laboratory testing, such that more detailed data were collected in representative subsamples.

The majority of factors found to be independent predictors of longevity reflect cardiovascular conditions and allied risk factors. Others include indicators of activity, anthropometric variables, and laboratory measures of physiologic functioning. The percentage of variance explained is 34.1% (19 independent predictors) in the subsample for which the most detailed data are available ( $n = 682$ ). In the total sample, with least complete data, only 17.6% of the variance can

## *Summary*

be explained (21 independent predictors). In analyses of the total sample, the dominant predictors tend to be global indicators of ill health, including high sedimentation rate, poor skin evaluation, high pulse rate, high systolic blood pressure, abnormal findings from blood and urine analysis, drug use, low daily carbohydrate intake. When analyses are limited to the most fully studied subsample a somewhat different set of predictors emerges, including specific symptoms, signs, and history of disease (ECG findings, history of stroke, dyspnea without exertion, diabetes, kidney trouble, recent weight loss). An indicator of good health (worked in two weeks prior to examination) appears to be a consistent predictor across all subsamples. Identification of these indicators of health and illness as predictors of longevity leads the way to further specification of life-threatening conditions in the elderly to which preventive measures may be directed.

Section II.6 describes predictors of longevity of residents in a Dutch home for the elderly. In the context of SDHE, 298 residents of mean initial age 83 years were followed during 4½ years. The survival time of 80% of residents appears to be below the median survival time of the general population. There is a clear gradient of mean RPD across age categories, indicating an increasingly shorter survival time for younger ages as compared to the general population. From age-specific multiple regression models, survival time in residents aged 80 years and over appears to be associated with physical disability and morale in addition to age and admission year, while in residents younger than 80 years no predictors of survival time other than age are found. Thus, younger residents die relatively sooner and are more homogeneous with respect to survival time than older ones. These findings indicate that stricter admission criteria may have been used for younger residents and that older residents may be more similar to the general population.

Thus far, factors associated with survival in the elderly have been ascertained several years prior to death. No information is provided about how these factors change in individuals as death is approached. Section II.7 describes data collected on physical, cognitive and social functioning, and morale at three month intervals over a 4½ year period in SDHE. During this period, 153 of a total of 495 residents died, of whom 88 had four complete evaluations in the year prior to death. Multivariate analysis of variance methods for repeated measurements demonstrate a significant decline of all factors during the last year of life; decline in physical, cognitive, and social functioning, but not in morale, is of greater magnitude than the decline seen in those who survived the study period. Furthermore, the decline in physical functioning seen in the last year of life accelerates in the months just prior to death. This accelerated decline is most pronounced in those who, at the beginning of their last year of life, had little physical disability. In this group, also morale showed an accelerated decline.

The empirical findings of part II are “digested” in Part III. In Section III.1, issues bearing directly on the findings are addressed. Thus, the RPD is judged on its merits, particularly with respect to the underlying assumption that an individual’s survival time decreases with age inversely proportional to the increase of population mortality, and with respect to the imputation criteria for those individuals still alive at end-of-follow-up. Predictors of longevity showing consistency across studies are discussed, with special consideration of their predictive ability, given the diversity of sample selectivity, sample size, and length of follow-up. The vast majority of disease-related, independent predictors pertain to cardiovascular diseases. Independent predictive ability for longevity is also observed for physical functioning as assessed by the ability to perform activities of daily living and to continue working, for cognitive functioning as measured by a memory test, and for emotional functioning as indicated by satisfaction with aspects of life such as health and income, and morale.

From a comparison of sections II.6 and 7, it is concluded that the two predictors of longevity which were least ambiguous in II.6 — physical functioning and morale — were seen to decline in a non-linear or accelerated fashion during the last year of life. This finding suggests that an unambiguous predictor of longevity as ascertained in a baseline-follow-up study may be understood as a factor declining in an accelerated fashion during some period just prior to death. Such a factor may be considered a direct predictor of longevity. A predictor showing a stable, poor level or a linear decline, on the other hand, may have to be understood as a factor indirectly predisposing to premature death by increasing the individual’s vulnerability for the life-threatening effect of direct predictors of longevity.

Taking all evidence together, it is estimated that in a study of “ideal” design the joint predictive ability of factors associated with longevity in the elderly will amount to 40-50% of variance explained. Several characteristics of the aging process which hamper further improvement of predictive ability are listed. It follows that in the prediction of an individual’s longevity, chance will continue to play a major role. However, for the prediction of longevity of population groups, i.e. for the identification of groups at risk of premature death, these results provide guidelines which may form a sufficiently sound basis for prevention and health promotion.

In Section III.2, suggestions for further research are brought forward. These suggestions include the clarification of aspects of predictors of longevity such as short-term versus long-term effect, direct versus indirect influence, and mutual interdependence. Further research is also suggested into underlying aging processes and adaptability to physical and psychosocial challenges. In addition, suggestions for further research are made with regard to the practical applicability of predictors of longevity. These include methods to identify groups at risk, to monitor the health status of these groups, and to determine the effectiveness of preventive and interventive measures. It is proposed that, in the elderly, main-

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tenance of functional ability rather than decreased incidence of disease should mark the success of prevention and intervention. Finally, further research is proposed into the prediction of *active* or *disability-free life expectancy*. Thus, not only length of life per se, but also quality of life is considered.

## Samenvatting

Onderzoek naar de overlevingsduur richt zich traditioneel op de gezondheidstoestand: overlevingsduur wordt gezien als indikator van de gezondheidstoestand. Factoren die samenhangen met de overlevingsduur worden ook geacht samen te hangen met de gezondheidstoestand. Deze dissertatie heeft de speurtocht naar deze factoren tot onderwerp. Lichamelijke, psychische en sociale kenmerken van individuen die op een zeker tijdstip (het beginonderzoek) worden waargenomen, worden in verband gebracht met de daaropvolgende overlevingsduur van deze individuen, zoals vastgesteld na een follow-up periode. De kenmerken die significant samenhangen met de overlevingsduur worden *prediktoren* genoemd.

Centraal staat de vraag naar de uitvoerbaarheid van het voorspellen van de overlevingsduur bij ouderen: wat zijn de mogelijkheden, wat de beperkingen? Zoals in **Deel I** wordt aangegeven, wordt deze vraag beschouwd zowel vanuit het standpunt van de wetenschappelijke waarde als vanuit dat van de praktische toepasbaarheid van de resultaten. De volgende aspecten komen aan de orde: het beschikbare materiaal (de selectiviteit van de onderzoeksgroep, de reikwijdte van de verzamelde informatie), de methode (het meten van initiële kenmerken, de definitie van de maat voor de overlevingsduur, het statistische model), en de vergelijkbaarheid van de resultaten over verschillende onderzoeken.

De resultaten van drie longitudinale onderzoeken worden vergeleken met betrekking tot zowel de aard van de prediktoren als hun prediktief vermogen in termen van de verklaarde variantie in de overlevingsduur. Deze onderzoeken zijn: het Nederlands Longitudinale Gezondheidsonderzoek onder Bejaarden (DLSE<sup>1</sup>), de Amerikaanse First National Health and Nutrition Examination Survey (NHANES I), en het Onderzoek naar Hulpbehoevendheid in het Verzorgingshuis (SDHE<sup>1</sup>). Van de longitudinale opzet van het eerste en het derde onderzoek wordt nader gebruik gemaakt door de verandering in kenmerken te bestuderen in verband met de overlevingsduur. Hierdoor wordt het mogelijk “verlopen” of “trajekten” kort voor het overlijden te bepalen, als aanvulling op de bepaling van prediktoren van de overlevingsduur op grond van een “momentopname” ten tijde van het beginonderzoek.

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1 Ter wille van de herkenbaarheid van dit onderzoek in de rest van dit boek, worden in deze samenvatting de engelstalige afkortingen gebruikt.

De onderwerpen die aan de orde komen, kunnen in zeven vragen worden samengevat:

1. Welke operationele definitie van overlevingsduur is optimaal voor gebruik in een follow-up onderzoek van lange duur bij bejaarden?
2. Welke prediktoren van de overlevingsduur blijken uit verschillende onderzoeken consistent naar voren te komen?
3. Welke konklusies kunnen worden getrokken wanneer het totaal prediktief vermogen wordt beschouwd in onderzoeken die verschillen in opzet?
4. Komen prediktoren van de overlevingsduur op grond van onderzoek in geïnstitutionaliseerde bevolkingsgroepen overeen met prediktoren op grond van onderzoek in niet-geïnstitutionaliseerde bevolkingsgroepen?
5. Treedt in de voorspelling van de overlevingsduur verbetering op wanneer naast het nivo van de onderzochte kenmerken de (snelheid van) verandering in die kenmerken in beschouwing wordt genomen?
6. Zijn de factoren die kort voor het overlijden veranderingen laten zien dezelfde als die welke de overlevingsduur op de langere termijn voorspellen?
7. Welke eigenschappen van het verouderingsproces kunnen de bevinding verklaren dat in onderzoek naar de voorspelling van de overlevingsduur veel minder dan 100% aan prediktief vermogen wordt bereikt?

**Deel II** van deze dissertatie bestaat uit zeven secties, die ieder een aspect van het voorspellen van de overlevingsduur belichten. **Sectie II.1** behandelt de operationalisering van een maat voor de overlevingsduur. Aangezien onderzoeken naar prediktoren van de overlevingsduur bij ouderen meestal gebaseerd zijn op steekproeven met een groot leeftijdsbereik en enige selectiviteit, is dit niet een triviaal onderwerp. De onderzoeker wordt gekonfronteerd met het probleem een maat voor de overlevingsduur te konstrueren die:

1. de onderzochten in de steekproef vergelijkbaar maakt wat betreft overlevingsduur, ongeacht leeftijd en geslacht;
2. kan dienen om in de steekproef de aan- of afwezigheid van selectiviteit met betrekking tot overlevingsduur na te gaan;
3. geschikt is voor follow-up onderzoek van lange duur;
4. rekening kan houden met de sterfte-ontwikkeling in de tijd;
5. de vergelijkbaarheid verbetert van onderzoeken die verschillen qua opzet en steekproefsamenstelling.

In deze sectie wordt een individuele maat voor de overlevingsduur die aan deze vereisten voldoet gepresenteerd: de Gerealiseerde Overlijdenskans (RPD). De konstruktie ervan wordt beschreven. De RPD wordt afgeleid uit sterfzetafels van de bevolking op grond van leeftijd, geboortjaar, en geslacht. Voor iedere onderzochte wordt de relatieve positie op de overlevingskromme van het desbetreffende geboortekohort bepaald. In een illustratie wordt de RPD toegepast op gegevens

van de DLSE, een longitudinaal onderzoek gebaseerd op een landelijke, naar leeftijd en geslacht gestratificeerde steekproef van 3149 bejaarden die tijdens het beginonderzoek (1955-1957) 65-99 jaar oud waren. Achtentwintig jaar na het beginonderzoek werd in 1983 de overlevingsduur of de overlevingsstatus vastgesteld voor 84% van de oorspronkelijke steekproef. Er wordt een vergelijking getrokken tussen de RPD en andere overlevingsmaten die in dit type onderzoek gebruikelijk zijn. Gekonkludeerd wordt dat de RPD een krachtige, valide maat is voor de overlevingsduur bij bejaarden, en dat hij nuttige toepassing kan vinden bij onderzoek naar prediktoren van de overlevingsduur.

In *Sektie II.2* worden dan in de DLSE, met behulp van de RPD, prediktoren van de overlevingsduur bepaald. Uit multivariate regressiemodellen komen als prediktoren zowel lichamelijke als psychische en sociale indicatoren van de gezondheidstoestand naar voren. De totale verklaarde variantie bedraagt 20,2%. Objectieve gezondheid (volgens het oordeel van de arts-onderzoeker) vertoont het sterkste verband met de RPD. Na het verwijderen van deze variabele uit het model blijkt nog steeds 19,5% van de variantie verklaard te worden. Dit duidt erop dat de informatie met betrekking tot objectieve gezondheid grotendeels in de overige onafhankelijke prediktoren terug te vinden is. Aparte analyses worden uitgevoerd voor (1) de variabelen uit het biomedisch, het lichamenlijk en het cognitief onderzoek, (2) de variabelen die betrekking hebben op hulpbehoevendheid en gezondheidszorggebruik, en (3) de sociale en psychologische variabelen; in alle analyses blijkt de verklaarde variantie ruim 11% te zijn, hetgeen getuigt van een aanzienlijke onderlinge afhankelijkheid tussen de prediktoren. Wanneer verschillende regressiemodellen worden vergeleken, blijken de biomedische- en de hulpbehoevendheidsvariabelen de meest stabiele prediktoren van de overlevingsduur te zijn.

In *II.3* wordt een methode gepresenteerd om de samenhang van veranderingen in de tijd in de onderzochte kenmerken met de overlevingsduur te bestuderen. Er worden weer regressie-analyses uitgevoerd met de RPD als afhankelijke variabele, terwijl de onafhankelijke variabelen bestaan uit de lichamelijke, psychische en sociale kenmerken die in de DLSE tijdens twee onderzoeken met een tussenpoos van vijf jaar (1955-1957 en 1960-1962) werden waargenomen. Er worden twee typen prediktoren onderscheiden: (1) prediktoren die hun voorspellende waarde ontlenen aan een achteruitgang die kort geleden is opgetreden; (2) prediktoren die hun voorspellende waarde ontlenen aan een reeds langer aanwezig, min of meer stabiel nivo dat op een slechte gezondheidstoestand wijst. Objectieve gezondheid, lichamelijke hulpbehoevendheid en activiteit blijken in de eerste categorie thuis te horen. Systolische bloeddruk, geheugenfunctie, het al of niet hebben van een liesbreuk, en satisfactie met het huidige bestaan blijken tot de tweede categorie te behoren.

De samenhang tussen de snelheid waarmee de kognitieve functie verandert en de overlevingsduur wordt onderzocht in II.4, weer gebaseerd op gegevens van de DLSE. Een groep bestaande uit 211 personen die tijdens het beginonderzoek 65-84 jaar oud waren, kon gedurende een periode van acht jaar (1955-1957 tot 1963-1965) tweemaal opnieuw onderzocht worden. Hun overlevingsduur is bekend tot maximaal 20 jaar na het derde onderzoek. De kognitieve functie werd onderzocht met behulp van een aangepaste versie van de Wechsler Memory Scale. De snelheid waarmee de kognitieve functie gedurende de follow-up periode van acht jaar verandert wordt bepaald met behulp van regressie op de tijd voor ieder individu afzonderlijk. De kognitieve functie blijkt over de periode van acht jaar significant af te nemen (gemiddelde verandering per jaar:  $-0,28$  eenheden, met 95%-betrouwbaarheidsinterval van  $-0,34$  tot  $-0,22$ ). Bij de onderzochten van 70 jaar en ouder hangt de veranderingssnelheid sterk samen met de daarop volgende overlevingsduur, waarbij degenen wier kognitieve functie sterker afneemt een kortere overlevingsduur beschoren is. Een dergelijk verband kan niet worden aangetoond in de leeftijdsgroep van 65-69 jaar. Konstank houden van ofwel initieel ofwel na acht jaar bereikt nivo van kognitief functioneren, en van potentieel versturende variabelen heeft nagenoeg geen invloed op de sterkte van de samenhang.

In II.5 wordt met behulp van gegevens uit de NHANES I de overlevingsduur voorspeld bij kaukasiërs die tijdens het beginonderzoek in 1971-1975 65-74 jaar oud waren. Bij een follow-up onderzoek in 1986 kon voor 98.7% van de steekproef ( $n = 3137$ ) de overlevingsstatus achterhaald worden. Op dat moment was 49.5% overleden. De onderzoekszopzet van de NHANES I is zodanig dat gegevens van lichamelijk onderzoek, interview en bio-medische tests in verschillende representatieve deelsteekproeven in verschillende mate van gedetailleerdheid werden verzameld.

Het merendeel van de factoren die — onafhankelijk van de andere prediktoren — de overlevingsduur blijken te voorspellen, weerspiegelen hart- en vaatziekten en daarmee samenhangende risikofactoren. De overige prediktoren liggen op het gebied van activiteit, anthropometrie en fysiologie. Het percentage verklaarde variantie is 34,1% (19 onafhankelijke prediktoren) in de deelsteekproef waarvoor de meest gedetailleerde gegevens beschikbaar waren ( $n = 682$ ). In de totale steekproef, waarin de minst gedetailleerde gegevens beschikbaar waren, kon slechts 17,6% van de variantie worden verklaard (21 onafhankelijke prediktoren). Uit analyses van de totale steekproef komen als voornaamste prediktoren naar voren globale aanwijzingen voor een verminderde gezondheidstoestand, zoals een hoge bezinkingssnelheid, een slechte huid, een snelle pols, een hoge systolische bloeddruk, abnormale bevindingen bij het onderzoek van bloed en urine, regelmatig medicijngebruik, en een laag gebruik van koolhydraten. Wanneer de analyses beperkt worden tot de meest volledig onderzochte deelsteekproef, komt een



enigszins verschillend beeld naar voren. Prediktoren bestaan nu veeleer uit specifieke symptomen of een anamnese van ziekte (abnormale ECG-uitslagen, hersenbloeding, kortademigheid zonder inspanning, suikerziekte, nieraandoening, en recente gewichtsafname). Een indikator van een goede gezondheidstoestand (werken in de twee weken voorafgaand aan het onderzoek) blijkt in alle deelsteekproeven de overlevingsduur te voorspellen. Nu deze — voornamelijk medische — prediktoren voor de overlevingsduur bij ouderen zijn vastgesteld, wordt het mogelijk in een volgende fase een nadere precisering te bereiken van levensbedreigende factoren waarop preventieve maatregelen gericht zouden kunnen worden.

**Sektie II.6** beschrijft prediktoren van de overlevingsduur bij bewoners van een nederlands verzorgingshuis. In het kader van de SDHE werden 298 bewoners met een gemiddelde leeftijd van 83 jaar gedurende 4½ jaar gevolgd. De overlevingsduur van 80% van deze bewoners bleek beneden de mediane overlevingsduur van de algemene bevolking te liggen. Er bestaat een duidelijk verloop van de gemiddelde RPD over de leeftijd, in de zin van een ten opzichte van de algemene bevolking steeds kortere overlevingsduur naarmate de leeftijd jonger is. Uit leeftijdsspecifieke multipelle regressie-analyses blijkt de overlevingsduur van bewoners die 80 jaar en ouder zijn samen te hangen met de lichamelijke hulpbehoevendheid en de stemming, naast de leeftijd en de verblijfsduur; bij bewoners die jonger zijn dan 80 jaar komen echter naast de leeftijd geen verdere prediktoren van de overlevingsduur naar voren. Jongere bewoners overlijden dus relatief eerder en vormen een homogener groep met betrekking tot de overlevingsduur dan oudere bewoners. Deze bevindingen wijzen erop dat voor de jongere bewoners wellicht strengere toelatingscriteria zijn gebruikt, en dat de oudere verzorgingshuisbewoners als groep meer overeenstemmen met de algemene bevolking.

Tot nu toe zijn de factoren die met de overlevingsduur samenhangen verscheidene jaren voorafgaand aan het overlijden bepaald. Over de wijze waarop deze factoren veranderen wanneer de dood naderbij komt wordt geen informatie verkregen. **Sektie II.7** beschrijft gegevens betreffende het lichamenlijk, cognitief en sociaal functioneren en de stemming van verzorgingshuisbewoners die met driemaandelijke tussenpozen gedurende een periode van 4½ jaar in de SDHE zijn verzameld. In deze periode overleden 153 bewoners op een totaal van 495. Van 88 van de overledenen waren de volledige gegevens op vier tijdstippen tijdens het laatste levensjaar beschikbaar. Multivariate variantie-analyses voor herhaalde waarnemingen laten voor alle onderzochte factoren een significante achteruitgang in het laatste levensjaar zien; de achteruitgang in lichamenlijk, cognitief en sociaal functioneren, maar niet die in stemming, is groter dan de achteruitgang die te zien is bij de bewoners die de onderzoeksperiode overleefden. Voorts neemt de achteruitgang in lichamenlijk functioneren een versneld verloop in de laatste levensmaanden. Deze versnelde achteruitgang is het duidelijkst bij degenen die aan het begin van het laatste levensjaar slechts weinig problemen hadden met hun

lichamelijk functioneren. In deze groep blijkt ook de stemming versneld achteruit te gaan.

De resultaten van het empirisch onderzoek in Deel II worden in Deel III tot een geheel verwerkt. In Sektie III.1 komen enkele problemen aan de orde die direkt uit de resultaten voortvloeien. Zo wordt de RPD op de keper beschouwd, vooral met betrekking tot de onderliggende aanname dat de overlevingsduur van een individu met de leeftijd afneemt, omgekeerd evenredig aan de toename van de sterfte in de bevolking, en met betrekking tot de criteria volgens welke een RPD-waarde toegewezen wordt aan de individuen die aan het einde van de follow-up periode nog in leven zijn. De prediktoren die in ieder onderzoek consequent blijken terug te keren worden besproken, met speciale aandacht voor hun prediktief vermogen gegeven de verschillen in steekproefsamestelling, steekproefgrootte en duur van de follow-up periode. Het merendeel van de onafhankelijke prediktoren die direkt met ziekte verband houden, hebben te maken met hart- en vaatziekten. Als onafhankelijke prediktoren worden daarnaast gevonden: het lichamelijk functioneren gemeten aan het vermogen om algemeen dagelijkse levensverrichtingen uit te voeren en om nog te werken, het cognitief functioneren volgens een geheugenproef, en het psychisch welbevinden zoals aangegeven door de satisfaktie met levensaspecten als gezondheid en inkomen, en door de stemming.

Uit een vergelijking van sekties II.6 en 7 wordt de konklusie getrokken dat de twee meest ondubbelzinnige prediktoren van de overlevingsduur — lichamelijk functioneren en stemming — gedurende het laatste levensjaar een versnelde achteruitgang bleken te vertonen. Deze bevinding doet vermoeden dat een ondubbelzinnige prediktor van de overlevingsduur die naar voren komt in een onderzoek bestaande uit een beginmeting en een follow-up periode waarna de overlevingsduur wordt vastgesteld, begrepen zou kunnen worden als een faktor die een versnelde achteruitgang vertoont gedurende een periode direkt voorafgaand aan de dood. Een dergelijke faktor zou beschouwd kunnen worden als een direkte prediktor van de overlevingsduur. Anderzijds zou een prediktor die een stabiel, ongunstig nivo of een lineaire achteruitgang vertoont wellicht moeten worden begrepen als een faktor die indirekt tot een voortijdige dood leidt, doordat hij de kwetsbaarheid van het individu voor het levensbedreigende effekt van direkte prediktoren van de overlevingsduur vergroot.

Alle resultaten tesamen overziend, wordt de verwachting verwoord dat het gezamenlijk prediktief vermogen van de faktoren die met de overlevingsduur bij bejaarden samenhangen, in een "ideaal" opgezet onderzoek 40-50% van de verklaarde variantie bedraagt. Een aantal kenmerken van het verouderingsproces die het bereiken van een betere voorspelbaarheid bemoeilijken, worden op een rij gezet. Een en ander komt erop neer dat het toeval een overwegende rol zal blijven spelen bij het voorspellen van de overlevingsduur van individuen. Echter,

voor het voorspellen van de overlevingsduur op het nivo van de bevolking, dat wil zeggen voor het bepalen van groepen met verhoogd risico voor een voortijdige dood, kunnen deze resultaten wel degelijk bijdragen tot richtlijnen voor het ontwerpen van preventieve of gezondheidsbevorderende maatregelen.

In **Sektie III.2** worden suggesties voor nader onderzoek over het voetlicht gebracht. Deze suggesties hebben allereerst betrekking op verheldering van aspecten van prediktoren van de overlevingsduur, met name of zij effect hebben op de korte versus de lange termijn, direkte versus indirecte invloed hebben, en hoe zij onderling verweven zijn. Tevens worden suggesties gedaan voor nader onderzoek naar onderliggende verouderingsprocessen en naar het aanpassingsvermogen aan lichamelijke en psychosociale verstoringen. Voorts worden suggesties gedaan aangaande nader onderzoek in verband met de praktische toepasbaarheid van prediktoren van de overlevingsduur. Deze richten zich op methoden om risikogroepen op te sporen, om bij hen de vinger aan de pols te houden, en om de effectiviteit van preventie- en interventie-maatregelen vast te stellen. Er wordt geopperd dat het welslagen van preventie en interventie bij bejaarden afgemeten zou moeten worden aan het handhaven van het nivo van functioneren, en niet aan de afname van de ziekte-incidentie. Tenslotte wordt nader onderzoek gesuggereerd naar prediktoren van *aktieve levensverwachting*, of *levensverwachting zonder beperkingen*. Hiermee zou niet alleen de levensduur op zich, maar ook de kwaliteit van de nog resterende levensduur in beschouwing worden genomen.

## CURRICULUM VITAE

**B**orn in Deventer in 1950, Dorly Deeg finished secondary school (Alexander Hegius Gymnasium Deventer, beta) in 1967. Through a teenage exchange program she spent the subsequent year in the United States of America, where she graduated at Martinsville High School, Indiana. She started the study of applied mathematics at the University of Groningen in 1968, where she obtained the doctoraal examen ( $\approx$ master's degree) in 1979. Several side activities, such as a membership in the Mathematics Subfaculty Council and in various committees concerning improvements in the educational programme, bear witness that she had multiple interests. She complemented her exact study of mathematics by studying (western) sociology at the same university, from 1976 to 1981, when the kandidaats examen ( $\approx$ bachelor's degree) was obtained. Two episodes of teaching mathematics at secondary schools (Groningen 1976-'77, Rotterdam 1980) are also worth mentioning. From 1980 to 1984, she served on the editorial board of the *Tijdschrift voor Vrouwenstudies* and was an editor of *Wetenschap en Samenleving*.

In 1979, she became a researcher at the Department of Public Health and Social Medicine, Erasmus University Rotterdam. Here, she became interested in longitudinal research on aging, specifically the prediction of longevity in the elderly. Her research on the last phase of life of the elderly was continued as a researcher in the Department of Social Gerontology, Catholic University of Nijmegen (1985-'86). In 1986, she went back to the United States as a Visiting Fellow with the Epidemiology, Demography and Biometry Program, National Institute on Aging, National Institutes of Health, Bethesda, Maryland. In 1988, she was contracted by the Netherlands Institute of Gerontology to write a book on longitudinal studies of aging, and started to be a consultant in several longitudinal projects. Currently, she works in the Department of Policy for the Ageing, Ministry of Welfare, Health and Cultural Affairs, Rijswijk, The Netherlands.

## ACKNOWLEDGEMENT

Time plays a crucial role in this book. This is true in more than one sense. Without time, of course there would be no way to measure longevity. Also, without time there would be no longitudinal data sets to study predictors of longevity. Without time, finally, there would have been no opportunity to work with such data sets in different parts of the world.

During the time that has passed since I first started working on the prediction of longevity, I have had support of many different persons and institutions. In each article in Part II, some of those are named, either in the list of co-authors or in the footnotes. At this point, I feel it is appropriate to attempt a more systematic, albeit more global, overview. First of all, there is Dr. Robert van Zonneveld, without whom I might never have entered the field of gerontology. A scientific area in which I would have come to feel better at home is hard to imagine. Then, there is the Institute of Public Health and Social Medicine, Erasmus University Rotterdam, and those who are and have been affiliated with it. They have supported me long after I had left the institute to pursue research activities in other parts of the world. These places are Nijmegen, where I spent an interesting and memorable year with the Department of Social Gerontology, University of Nijmegen, and Bethesda, U.S.A., where the fruitful and enjoyable collaboration with the colleagues at the Epidemiology, Demography and Biometry Program of the National Institute on Aging, National Institutes of Health, have further shaped my abilities as a researcher of aging. This is especially true (and not only in reference to the past) for Dr. Lon White, who paved my way across the ocean. Back in the Netherlands, a spin-off of my temporary affiliation with the Netherlands Institute of Gerontology for work not directly related to this dissertation, was that I learned to use its library, which proved to be valuable for the present work as well. Financial support for my activities was provided by the Netherlands Organization for Scientific Research (grant 93-26 for the work at the Erasmus University, and travel grant L 96-70 for the work at the National Institute on Aging), by the Ministry of Welfare, Health and Cultural Affairs (grant through the Steering Committee for Research on Aging, SOOM, for the work at the University of Nijmegen), and by the National Institute on Aging.

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Rotterdam,  
September 1989

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