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Multimorbidity and healthcare utilization

among the oldest old and centenarians

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Abbreviations

ACE = Angiotensin-Converting-Enzyme

AOK = Allgemeine Ortskrankenkasse (General Local Health Insurance)

COPD = chronic obstructive pulmonary disease

DEAS = Deutscher Alterssurvey (German Ageing Survey)

ECHO-AGE = Extension for Community Healthcare Outcomes for old AGE intervention

ELSA = English Longitudinal Study of Ageing

ENT = ear, nose, and throat; Otorhinolaryngology

ESH/ESC = European Society of Cardiology/European Society of Hypertension

GEDA = Gesundheit in Deutschland aktuell (German Health Update study)

GP = General Practitioner

HRS = Health and Retirement Study

ICD-10 = International Classification of Diseases version 10

interRAI = International Resident Assessment Instrument

NICE = National Institute for Health and Care Excellence

SHARE = Survey of Health, Ageing and Retirement in Europe

UK = United Kingdom

US = United States

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1. Introduction

Although longevity has always been a goal of human desires and endeavors, aging is not perceived as merely positive [1]. This may be largely due to age-associated declines, illnesses, and dependencies. While physical vulnerability is characteristic of advanced age, potential and resilience are genuine characteristics of this phase as well [2]. Centenarians – i.e., those aged hundred years and older – are representatives of a group of individuals with very advanced age. Although the age of hundred years may be considered to be an arbitrary threshold, centenarians have been seen as an exception, being very old yet being relatively healthy [3]. This view has been challenged in recent years [4]; evolving into a multilayered perspective towards this age group. The present work will contribute to a better understanding of the morbidity and healthcare trajectories of very old individuals, including centenarians, using the perspective of potentials of advanced age.

In the following introduction chapter, the epidemiology of the oldest old and centenarians will be outlined (Chapter 1.1). Then, the introduction continues with a review of evidence of multimorbidity in these very old individuals (Chapter 1.2), followed by a summary of healthcare research among the oldest old and centenarians (Chapter 1.3).

1.1 Changing demographics: The oldest old and centenarians

1.1.1 The oldest old

The number of oldest old – i.e., those individuals living beyond the age of 80 or 85, depending on the definition [5, 6]– is exponentially rising in most counties around the world [5]. According to data from the Human Mortality Database, in European countries and the US, the current life expectancy for people 85 years old is more than six years [5]. While joint data from the Health and Retirement Study (HRS), the Survey of Health, Ageing and Retirement in Europe (SHARE), and the English Longitudinal Study of Ageing (ELSA) surveys that 66-72% of the oldest old are female, only 8-14% of the women are married (not yet widowed [5]). In contrast, this figure is 43-57% for men. While genuine surveys that focus on the population of oldest old individuals are still sparse, the California 90+ Study [7], the Leiden 85+ Study [8], and the Newcastle 85+ Study [9] are valuable exceptions. In the California 90+ Study, 72% were women and 74% were aged 90 to 94 [7]; in the Newcastle 85+ Study, 62% were women [9]; in the Leiden 85+ Study 66% of the sample were women [8]. Moreover, in the California 90+ Study for

instance, 74% were widowed and 49% lived alone [7]. This illustrates that there are substantially more oldest old women than men.

In Germany, five percent of the population is over 80 years of age [6]. In this age group, 60% of those aged 80-85 are women; however, this number increases to about 70% for those between 85 and 90 years old. At the time of writing, there exist no population-based surveys focused on the oldest old in Germany. The existing population-based and aging surveys primarily show biases towards overrepresentation of younger cohorts. Two major surveys in Germany are the German Ageing Survey (DEAS [10, 11]) and the German Health Update study (GEDA [12]). Although it is likely that a few centenarians will be in the coming panel cohort of the DEAS, centenarians are still largely underrepresented [10, 11]. The 2014 GEDA had 1107 participants over 80 years of age, yet only two individuals aged 100 years and older; in the 2009 GEDA, there were only 592 participants aged 80 years and older and just a single centenarian [12]. Although wave 6 of the Survey of Health, Ageing and Retirement in Europe (SHARE) survey included 9316 participants equal or older than 80 years, only 19 centenarians were included in the data [13].

1.1.2 Centenarians

Worldwide demographic development regarding the number of centenarians (aged 100 years and older) outperforms growth rates of the oldest old aged 85 years and older. Drawing on data from the 2015 Revision of the World Population Prospects of the United Nations, Robine and Cubaynes report a worldwide total number of 96,000 centenarians in 1990 [14]. This is predicted to increase from 451,000 in 2015 to an estimated 25 million in 2100. Although the model predicts the acceleration will flatten as we approach the year 2100, the number of centenarians will increase extraordinarily. While James F. Fries [15] wrote in the year 1980 that "approximately one in 10,000 persons in developed countries lives beyond the age of 100," current estimates predict every second child born in developed countries in this century to have a life expectancy of 100 years [16]. Centenarians are predominantly female, as of 2015, there are about four times more female centenarians than male [14]. This difference will decrease by 2100, where there will be two female for every one male centenarian [14]. According to the German Federal Statistical Office [17], there were around 17,000 centenarians living in Germany at the end of 2014. Of these, 85% were women. Although this male-to-female ratio is a common finding in the centenarian literature from around the world [4, 14, 18, 19], this ratio is likely to become more balanced in the future as the morbidity trends for men and women converge [14].

Following the increase in numbers of oldest old and centenarians, centenarian research over the last decades has expanded from descriptive studies drawing on small samples that to larger and methodologically comprehensive studies that include the frequent investigation of social and behavioral research questions [20]. According to the review of centenarian research by Poon and

Cheung, the first large centenarian study was a survey of centenarians starting in 1990 in France [21]. The longest-running American centenarian study is the Georgia Centenarian Study [22, 23]. Further major centenarians studies include the Okinawa Centenarian Study [24, 25], the Danish Longitudinal Centenarians Study [26] and the Fordham Centenarian Study [27]. Rasmussen and Andersen-Ranberg [28] and Jopp, Boerner and Rott [29] also give an overview of the major centenarian studies to date.

In Germany, the most relevant, recent, and comprehensive centenarian study are the Heidelberg Centenarian Studies I [30] and II [29]. The first of the two studies was population-based; all centenarians of a previously defined geographical area around the city of Heidelberg were eligible for study participation and were contacted if possible. This study had no exclusion criteria and included – although there were likely underrepresented – centenarians living in nursing homes as well as those with dementia. Of the existing 281 centenarians found in the national registry, which contains basic information on all residents in Germany, 91 centenarians and their proxies constituted the final sample in which interviews were made. Interviews primarily focused on cognitive status, functional capacity, and mental health, with additional time spent on subjective well-being and autonomy. Major findings include the prevalence of dementia in this age group, although individuals with good cognitive status existed as well. Approximately one third of the centenarians showed little or no performance loss. Half of the sample had dementia and 83% received care. The Heidelberg Centenarian Study II was conducted with 112 centenarians from 2011 to 2013. Sampling procedure was carried out following the same procedure as in the Heidelberg Centenarian Study I in 2000 and 2001. In this second study, out of 485 centenarians from the national registry, 112 centenarians participated; 94 of which provided self-reported data; in 78 cases, the relatives provided additional data; in 18 cases, the proxies were the only source of data provision. Of these 112 centenarians, 18 percent lived alone and 58 percent lived in the community. Although these findings provide first insights about the distribution of health and healthcare utilization in German centenarians, the specific health and health care trajectories of centenarians in Germany remain largely unknown.

1.2 Multimorbidity in the oldest old and centenarians

1.2.1 Conceptualization of multimorbidity

In old age, the co-existence of multiple chronic conditions is common. Individuals with no condition or only one major condition remain the exception. Although there are many ways of defining and measuring multimorbidity in health service research, in its most basic form multimorbidity refers to a patient with two or more health conditions at the same time [31]. A systematic review of the literature by the European General Practice Research Network found 132 definitions of multimorbidity, which were then subsequently categorized into themes and summarized in the following definition:

"Multimorbidity is defined as any combination of chronic disease with at least one other disease (acute or chronic) or biopsychosocial factor (associated or not) or somatic risk factor. Any biopsychosocial factor, any risk factor, the social network, the burden of diseases, the health care consumption, and the patient's coping strategies may function as modifiers (of the effects of multimorbidity). Multimorbidity may modify the health outcomes and lead to an increased disability or a decreased quality of life or frailty."[32]

One commonly applied approach of defining multimorbidity in the literature is the combination of two conditions [33]. Using routine data from 314 medical practices in Scotland, Guthrie et al. investigated multimorbidity by creating a matrix of comorbidities, showing the percentage of patients diagnosed with the combination of two specific conditions [34]. They found, for instance, that physical conditions such as cancer, chronic obstructive pulmonary disease (COPD), and coronary heart disease were linked with pain and depression. In general, multimorbidity strongly increased with age, although absolute numbers remained larger in those patients under 65 years of age. Adding complexity, Ward and Schiller not only examined condition dyads but also studied chronic conditions triads [35]. The most common triad was the combination of arthritis, hypertension, and diabetes. Investigating more complex clusters of multimorbidity using data from over 160,000 Danish adults from the general population, the analyses of Larsen et al. suggested seven specific classes of patients, where "complex cardiometabolic disorders" and "complex respiratory disorders" were those with the most complex disease patterns [36]. A further cluster analysis study found five multimorbidity clusters in a population over 85 years; of these five, two complex multimorbidity clusters accounted for 60 percent of the patients, whereas only about 5 percent were classified into the healthier cluster [37]. Finally, approaches that go beyond the mere investigation of the co-existence of morbidities, are, for instance, functional disability [38, 39], frailty [40-42], or the forth age [43, 44]. These concepts will be further outlined in the discussion section.

Regarding the prediction of mortality, multimorbidity is a prime indicator. Several indices of multimorbidity have been established; an overview of the multimorbidity indices has been provided by Diederichs et al. [45]. According to their review, the Charlson Comobidity Index is the most frequently used comorbidity index [46]. The Charlson Comorbidity Index groups ICD-10 diagnoses into 19 disease categories. Measuring multimorbidity, the Elixhauser Comorbidity index has been developed [47] and adjusted [48, 49] to predict hospital mortality. The Elixhauser index groups diseases into 30 categories. When compared, the Elixhauser index, according to Walraven et al. [49], performs slightly superior to the Charlson index when adjusting for multimorbidity, while the Charlson is more parsimonious than the Elixhauser index. However, in populations with advanced age, comorbidities such as dementia and some musculoskeletal diseases are missing in the Elixhauser index. Thus, both indices have specific advantages that justify their use in health service research.

1.2.2 Multimorbidity among the oldest old

According to finding from the Newcastle 85+ Study, beyond geriatric conditions such as hearing (60%) and visual impairment (36%) and urinary incontinence (31%), the most prevalent chronic conditions in the oldest old were hypertension (58%), osteoarthritis (57%), and ischemic heart disease (36%) [37]. In this sample, multimorbidity was defined as the presence of two or more geriatric and chronic conditions. Thereby, a median value of four conditions in this sample of very old patients with an interquartile range from three to six conditions. Investigating multimorbidity clusters, 60% of the patients showed high morbidity rates, while only about 5% were in the few conditions cluster [37].

Concerning multimorbidity, a study drawing on data from the Leiden 85+ cohort defined multimorbidity as the co-existence of two or more of a set of nine common chronic conditions: arthritis, COPD, diabetes mellitus, heart failure, stroke, Parkinson disease, depression, cancer, and myocardial infarction [50]. While multimorbidity was present in 39% of the sample of oldest-old individuals, arthritis was the most common comorbidity with 33% of the sample suffering from this disease. Further, multimorbidity was predictive for physical functioning in those individuals with high level of cognitive functioning, highlighting the modifying role of dementia in the oldest old [50].
The Californian 90+ Study found hypertension (53%) and heart disease (47%) to be highly prevalent in the sample of oldest old. When comparing those with incident dementia (18% at baseline) to those without dementia, hypertension was the only comorbidity that was higher in the subgroup with dementia. The incidence rate of dementia increased exponentially with age and doubled every 5.5 years.

Regarding the health of people over the age of 75 in Germany (GEDA09 [6]), in women, hypertension (59%), osteoarthritis (46%), and hyperlipidemia (44%) were the most common reported conditions. For men, hypertension (51%), coronary heart disease (30%), and osteoarthritis (30%) were the most common conditions. As multimorbidity can be considered an independent predictor for disability [51]. Among those aged 80 years and older, 44% in women and 39% in men had at least one limitation in instrumental activities of daily living (SHARE [6]).

1.2.3 Multimorbidity among centenarians

Centenarians have long been seen as prototypes of successful aging [3]. However, recent evidence challenges the assumption that centenarians commonly suffer from multimorbidity [4, 28, 29]. Jopp et al. [29] gave a narrative overview about the morbidity prevalence in centenarians drawing on data from the following major centenarian studies: the 1895 Cohort of the Danish Centenarian Study [4], the New England Centenarian Study [52], the Georgia Centenarian Study [53], the Ontario Centenarian Study [18], the Sydney Centenarian Study [54], and the Tokyo Centenarian Study [55]. Hypertension was present in 27-63% of the centenarians across studies, heart disease in 18-60%, while heart disease or congestive heart failure was present in 17-37% of the centenarians. Dementia was

only reported in two of the six studies, with a prevalence of 51% and 58%. Likewise, arthritis was reported in two studies with 54% and 56%. Diabetes prevalence was low, 4-19% across studies. Non-skin cancer was prevalent in 5-15% of the studies. In a review of centenarian studies by Rasmussen and Andersen-Ranberg [28], morbidities were compared across a broad range of centenarian studies. The authors conclude that centenarians showed a variety of diseases and cannot be described as healthy, although many centenarians showed good activities of daily living and although healthy exceptions existed. According to their review, hypertension, for example, was present in 25-50%, atrial fibrillation in 17-26%, and heart failure in 31-60% of the centenarians. The authors claim that objective rather than self-report measures are necessary to back up the diagnoses, since objective data showed higher prevalence in most of the studies [28].

For Germany, data from the Heidelberg Centenarian Study II showed a mean number of 5.3 diseases, which were previously defined [29]. Over 37% of the centenarians suffered from more than five conditions, where – besides sensory problems (94%) and urinary system conditions (55%) – cardiovascular (57%) and musculoskeletal diseases (60%) were most prevalent in this sample [29]. Hypertension was found in 45%, heart disease in 31%, and dementia in 33% of the centenarians from Heidelberg; other conditions were not highly prevalent, such as a history of stroke (12%), diabetes (11%), and non-skin cancer (4%). However, due to the selection effects in the recruitment process, diseases such as dementia may be underrepresented in this study.

1.2.4 Compression of morbidity

With increasing life expectancy of the population over the last decades [56] comes the concern that years spent morbidity will raise proportionally. However, the compression of morbidity hypothesis, as proposed by James F. Fries [15, 57, 58], assumes that the onset of morbidity will be postponed and that smaller proportions of the lifespan will be lived with morbidity as life expectancy increases. Effectively, this will result in an increased number of independent and healthy life years. This is mainly achieved by improvements in education, adaptive technologies, and medical treatments [59]. Although studies vary in rigor of testing the compression of morbidity hypothesis, a relative reduction of disability [59, 60] — and to a smaller extent morbidity [59] — can be assumed over the last decades, although population prevalence for many diseases increase with rise of life expectancy [60]. The presumption of a fixed length of life that was further proposed by Fries [15] is objective of debate [56, 61]. Although life expectancy has increased over the decades since Fries first proposed his hypothesis [61], there is epidemiological evidence that this increase flattens continuously over time [56]. Whether the number of comorbidities is compressed in the very old is not well investigated; for a review of the literature on compression of morbidity in centenarians, see the chapter Multimorbidity in Centenarians.

Concerning a compression of morbidity at the limits of the human life span, the classical centenarian study that supported this thesis used retrospective self-report data to compare three morbidity profiles of centenarians that emerged from the data [52]. Andersen et al. [62] distinguished survivors, delayers, and escapers as previously termed by Evert et al. [52]. Survivors were those centenarians who suffered from at least one age-related major disease before the age of 80 years; delayers were those with a disease onset of 80 years and older; and, finally, escapers were those centenarians who reached the age of 100 years without a diagnosis of an age-associated disease. Survivors, delayers, and escapers made up 24%, 44%, and 32% of male and 43%, 42%, and 15% of female centenarians, respectively. Further, Andersen et al. [62] impressively supported the compression of morbidity hypothesis when comparing different age groups of oldest-old patients using a prospective design. Supercentenarians (110 years and older) were compared with semisupercentenarians (105-109 years), centenarians, nonagenarians, and younger controls. Across many diseases, the authors found a delayed disease onset the older the age group was, compressing diseases into the very last years of life. Among centenarians, Kheirbek et al. [63] found the compression of morbidity hypothesis confirmed in centenarian veterans. When comparing those aged 100 years and older with those in their 80s and 90s, lower incidence rates were observed. Similarly, Ismail and colleagues found across longevity studies, i.e., Longevity Genes Project and the New England Centenarian Study, that a compression of morbidity was present [64]. Studies that compared centenarians with younger cohorts of oldest old found lower incidence rates for a broad range of conditions in centenarians [65-67] and for health service utilization [68].

Using a distance-to-death approach which inspects the terminal trajectories before death from the general population sample across more than ten years of observation [69, 70], Gill et al. [51] explored trajectories of disability development in the last years of life. They found no disability, catastrophic, accelerated, progressive, and persistently severe disability trajectories to all be distinct from each other [51]. Interestingly, most of these patterns could not be linked with specific diseases that were leading to death, except for dementia. Dementia showed a persistently severe disability trajectory. For centenarians, data from the Heidelberg Centenarian Study I showed centenarian physical and cognitive functioning to continuously decline with increasing age [71]. Further, while 13% of the centenarians maintained their very good cognitive status until death, for physical health, this was true for 7% only [71].

1.3 Healthcare utilization among the oldest old and centenarians

1.3.1 Healthcare utilization among the oldest old

Among the oldest old, the need for care, long-term care, and the utilization of healthcare including the use of medical care inflates as disability and diseases become substantially more prevalent [66, 72].

Regarding **care utilization**, the data from the Newcastle 85+ Study indicates that 41% of the study population was independent, 12% required professional care, and 8% required intensive care [9]. In this study, 77% of the oldest old lived at home, 13% in sheltered housing and 10% in long-term care facilities [9]. A study utilizing complete health insurance data from the German population in 2015 found about 780,000 individuals were living in long-term care settings, where about 3 out of 4 residents were 80 years and older [73]. Another study that draw on German health insurance data found 8 out of 10 residents in long-term care facilities were over 75 years of age, with most of them aged 85 to 89 years. The study showed a strong decline in absolute numbers in peopled aged 90 to 94 years as well as those aged 95 and older [74]. Factors associated with long-term care use in the oldest old that have been discussed in the literature were age, life satisfaction, and previous service use [75, 76], all which may, in turn, be driven by an increased disease and disability burden [77].

Concerning **healthcare utilization** and medical care among the oldest old, in the Newcastle 85+ Study, clusters of individuals with high and low morbidity burdens were distinguished by health care factors medication count, hospital admissions, and general practitioner consultations [37]. Further, consultation of the general practitioner substantially increased across age groups from 85 to 90 years of age [78]. Investigating the health care use of the oldest old in the last years before death, data from the Leiden 85+ Study suggests that the number of home visits from the general practitioner as well as the frequency and length of contact increased in the last year before death. Thereby, the proximity to death was more closely related with healthcare use than chronological age [8]. Although adequate medication among the oldest old is mostly the preferred treatment choice, polypharmacy (i.e., five or more medications in use simultaneously) is common in this population and is associated with a range of negative health effects including falls, adverse drug events, hospitalization, and mortality [79]. In a community-dwelling sample of oldest old from Belgium, for instance, 58% of the sample took five or more medications (i.e., polypharmacy) and 9% took ten or more medications (i.e., excessive polypharmacy)[80]. At the same time, 67% were underprescribed and 56% had potentially inadequate medication [81]. Thus, underprescribing and polypharmacy are not mutually exclusive, but often occur in combination [82]. Concerning polypharmacy in long-term care, a systematic review found 44 studies reporting a wide range of polypharmacy rates (between 65-91%), depending on the study and the defined number of medications [83]. Predictors of polypharmacy in long-term care were,

among others, disease-related factors such as circulatory and metabolic comorbidities and healthcare-related factors such as a prior hospital discharge or multiple prescribers [83].

1.3.2 Long-term care utilization among centenarians

Long-term care facilities provide intense care for a large number of oldest old individuals. Regarding the proportion of centenarians in long-term care compared to those centenarians living in the community, several studies from different countries indicate that about half of the centenarian population lives in long-term care facilities, with variation across country and study design [4, 18, 19]. High proportions of centenarians living in long-term care were reported in a study from Denmark and two recent studies from Ontario, Canada with 52% [4], 54% [18], and 66% [84] of the centenarians sample residing in long-term care facilities. As data from the available US studies based on non-representative samples, it is likely that these data underestimate the prevalence of long-term care for the US with 37% in Georgia [85] and 26% in New York [27]. In Porto, Portugal [86] and the Heidelberg region of Germany [29], 42% of the centenarians were in long-term care. In Tokyo, Japan [19], this rate was lower (32%). In China [87] only 3% of the centenarians were in long-term facilities, which illustrates cultural differences than the differences in care needs. In the Chinese study, 89% of the centenarians were living with family members, while a minority of 8% lived alone, which may indicate the provision of care by family members. Two studies from Australia reported that 52% [88] and 23% [54] of the centenarians were living in long-term care facilities. The lower rate in the later study may be related to selection bias due to the recruitment strategy. Finally, a study from England, Great Britain [89], which investigated death certificates of centenarians, reported that 27% of the centenarians died in long-term care and a further 27% passed in a hospital, where those who died in a hospital may have been referred from long-term care facilities prior to death.

Regarding the predictors and conditions of those centenarians in long term care compared with those not, Cevenini et al. [90] suggested that cognitive and physical status – which are likely related with dementia and musculoskeletal disorders – are the primary factors that distinguish vary between those in long-term care and those who are not; with those in long-term care showing high rates of both conditions. In two recent studies that made use of routine health data of centenarians from Canada, this assumption was not confirmed in one study, but was supported in the other one [18, 84]. While Rochon et al. [18] found dementia to be present in community-based and long-term care centenarians. Analyzing the interRAI, Freeman et al. [84] found that those centenarians who were in long-term care had poorer cognitive and physical functioning than centenarians who received care in the community. Thus, further investigation is needed.

Along with comorbidity-related factors, sociodemographic and health care factors may be different across care settings. Centenarians in long-term care are more likely to be female; moreover, they may have weaker social and financial resources than those receiving community-based care [84-

86]; whereas no differences regarding educational status were found. Although further evidence is needed, polypharmacy is likely to be lower and physician and hospital visits higher in community-based than in long-term care populations of centenarians [18, 84, 89]. Finally, evidence is missing about the specific patterns of length of stay in long-term care among centenarians compared to younger cohorts of older adults [91].

1.3.3 Medical care among centenarians

Concerning medical care, about one third (33-36%) of centenarians were hospitalized in the previous year, according to data from Australia and Canada [18, 68]. A large proportion of the centenarians (87-98%) had a doctor appointment with their general practitioner (GP) in the previous year [4, 18, 68]. An Australian study reported 11% of the centenarians saw their GP weekly, while 67% saw them irregularly [88].

Using medical data on all living centenarians in Sweden, a study on medication prescription in centenarians found, on average, five drug classes prescribed to the centenarians [92], which corresponds to the threshold of polypharmacy. In this study, centenarians used, for instance, more diuretics and analgesics than octogenarians did, yet centenarians have been prescribed fewer ACE inhibitors, beta-blockers, and antithrombotic medication. In a population-based cohort study, about 11,000 centenarians were investigated, this study showed that one third of those who received medication had at least one potentially inappropriate medication [93]. Whether polypharmacy, underprescriptions, or prescriptions of potentially inappropriate medication in centenarians is more common than in other age groups needs further investigation.

2. Papers

This second chapter provides an overview about the research objectives and the designs of the studies (Chapter 2.1), followed by five empirical chapters: Chronic conditions and use of health care service among centenarians (Chapter 2.2); Multimorbidity profiles among centenarians (Chapter 2.3); Multimorbidity trends among the oldest old and centenarians (Chapter 2.4); Long-term care status among the oldest old and centenarians (Chapter 2.5); Atrial fibrillation and medication among the oldest old and centenarians (Chapter 2.6).

2.1 Research objectives and designs of the studies

2.1.1 Research objectives

As shown in the previous paragraphs, there are only a few pioneer studies on the oldest old and centenarians. Large-scale and longitudinal investigations about health and healthcare status of the oldest old and of centenarians are needed; especially those in long-term care are poorly investigated. For Germany, health insurance routine data provides a unique opportunity for the analysis of real-life data for hard-to-reach populations with low costs, no study drop out or bias of selection, interviewer, reporting, and recognition [94, 95]. An example of a study that made use of routine data from Germany on centenarians in comparison with younger age groups comes from Tamayo et al. [65], which showed the prevalence of diabetes across age groups. Internationally, findings based on administrative data of centenarians is available, for instance, for the US [66], Canada [18, 84], and the UK [93]. Registry data for complete cohorts exist for Swedish and Danish centenarians [96]. To date, a growing though still small number of studies have made use of routine and registry data to examine disease and health service use for the oldest old and centenarians.

This paper aims to shed light on the composition and trajectory of multimorbidity in German centenarians. Further, healthcare utilization among the oldest old compared with centenarians in the presence of multimorbidity was investigated. More specifically, the research objectives were:

1. Gaining a broad overview about morbidity distribution and healthcare utilization was the research objective of the first Paper 1 (Study I [97]). Thereby, morbidities and healthcare utilization for the whole sample as well as broken down by different care setting status, i.e., community-dwelling without care, community-dwelling with private home care, with professional care and in long-term care facilities were distinguished.

2. The second objective was to investigate multimorbidity profiles that are different for subgroups of centenarians by an exploratory approach and to relate these profiles to health care use in centenarians (Paper 2, Study I [98]).

3. Extending the hypothesis of the compression of morbidity, it was assumed that those individuals who died as centenarians show a lower number of comorbidities than the younger

cohorts of oldest old (i.e., those who died between age 80-89 and age 90-99); and that the increase of multimorbidity would less steep in the last years before death (Paper 3, Study II [99]).

4. The forth research objective in Paper 4 (Study II [100]) investigates long-term care patterns (i.e., comparing "long-term care survivors" with "long-term care delayers" and "long-term care escapers") in the oldest old in order to explore the transition rate to long-term care before death as well as the length of stay varies with increasing age among the very old. Although centenarians were expected to show higher rates of care dependency than the younger cohorts of oldest old did, it was assumed that they would show a distinct prediction pattern in terms of morbidities and health care use associated with being in long-term care [100].

5. Concerning medication use, for the sample case of atrial fibrillation, this final research objective (Paper 5; Study II [101]) examined whether the medication rates were lower in centenarians diagnosed with atrial fibrillation compared with the other age groups within the subsample of patients with atrial fibrillation.

2.1.2 Designs of the studies

The present paper and five research questions were based on two consecutive studies that utilized routine data from health and care insurance. An overview of the research questions and design across the Study I and Study II is given in Figure 1.
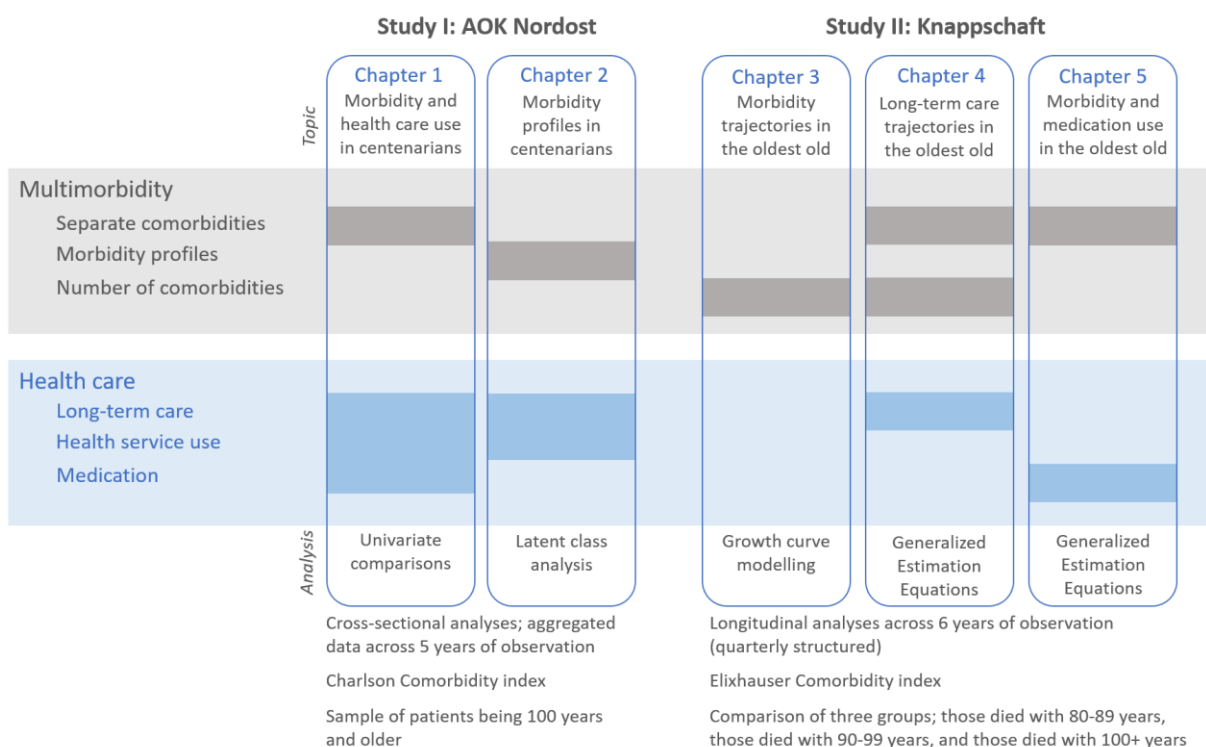

Figure 1 Overview of the research questions

In the first study (**Study I**), health insurance data from N = 1121 centenarians living in the surrounding Northeastern region (i.e., the German federal states of Berlin, Brandenburg, and Mecklenburg-Vorpommern) of Germany have been used [97, 98]. All were policy holders at *AOK Nordost* aged 100 years and older as of December 31, 2013. AOK Nordost insures 52% of the local population above the age of 90 in Berlin, 73% in Brandenburg, and 78% in Mecklenburg-Vorpommern [97]. The Charlson index was calculated to account for multimorbidity using established algorithms [46]. Using ICD-10 diagnoses, these diagnoses were classified into 17 disease categories; these categories were weighted and summed across the 5 years of observation [18, 46, 102, 103]. For validation purposes, each diagnosis had to be recorded at least twice across the observation period and diagnoses indicated as "suspicion" were excluded.

Study II used health insurance data on insurees from the *Knappschaft*, a major health insurance company with insurees from all over Germany with three main clusters [99-101]. Of all oldest old in our study, 36% lived in the Ruhrgebiet Region, 20% came from Lausitz and the surrounding areas, and 6% from Saarland. A further 38% were from other regions across Germany. The sample contained a total of N = 1,398 individuals from Germany for 6 years prior to death. All insured individuals who died as centenarians (between January 01, 2015 and December 31, 2015) were selected for the present study (N = 398 [99-101]). To allow comparison across age groups, two random samples of insured nonagenarians (90–99 years at death; random sample of n = 500 out of N = 9,588) and octogenarians (80–89 years at death; random sample of n = 500 out of N = 19,746) who died in the same period as the centenarian cohort were selected [99-101]. The Elixhauser comorbidity index was calculated [47, 48]. ICD-10 diagnoses were classified into 30 disease categories. Showing a better approximation to the normal distribution, the unweighted number of conditions was used instead of a weighted index [98, 100]. To allow a better comparison of the results from Elixhauser and Charlson, we adjusted our analyses for dementia and musculoskeletal diseases as separate predictors alongside the Elixhauser index [99, 100].

2.2 Paper 1: Chronic conditions and use of health care service among centenarians

This first paper (**Paper 1** [97]) provides a broad overview of multimorbidity and health care utilization in centenarians, including the distribution of Charlson-based multimorbidity, the most frequent diseases, use of care, medication prescription, and health service use such as hospital stays and physician visits. Besides providing a descriptive overview about the health and health care situation among centenarians, this paper is specifically focused on the comparison of multimorbidity and health care use across care settings, i.e., community-based care (no care, private home care, and professional home care) and long-term care.

Drawing on health insurance data on centenarians from the Berlin area (Study I), this paper found distinct health and health care patterns across care settings. Almost half of the sample received care in long-term care facilities, while a minority did not receive any paid care. Dementia and musculoskeletal conditions were among those conditions, which were most prevalent. Moreover, rates of both conditions were largely different between those centenarians being in long-term care facilities and those receiving care in the community. The role dementia and musculoskeletal conditions play in care dependency needs further investigation.

2.3 Paper 2: Multimorbidity profiles among centenarians

Paper 2 [98] further illuminates the morbidity distribution found in Paper II. While Paper 1 [97] merely reported Charlson-based multimorbidity and the separate frequencies of single diseases, this second paper aimed to find subgroups of centenarians that share coherent and complex morbidity patterns. Again, data from Study I have been used for this in-depth analysis.

Using a latent class approach, four morbidity patterns were derived from the data. About one third of the centenarians were classified as suffering from age-associated diseases, while about another third had a low likelihood of suffering from multiple diseases. Almost a further fifth of the centenarians showed a range of diseases. Those with multimorbidity yet without diabetes were classified as multimorbid without diabetes. A final subgroup contained almost a tenth of the centenarians: multimorbid with diabetes. In addition, these morbidity profiles were analyzed according to their relation to health care utilization. This paper further contributes to the understanding of multimorbidity in the oldest old.

2.4 Paper 3: Multimorbidity trends among the oldest old and centenarians

There is a substantial body of evidence that shows centenarians to have lower morbidity rates than younger cohorts of oldest old individuals. These findings are in line with the compression of morbidity hypothesis, which assumes a later onset of diseases in those individuals that are approaching the upper limits of the human life span. While this assumption has been tested in different studies, it is unknown whether the number of conditions follows this pattern as well.

Paper 3 [99] further extended the findings of Paper 1 [97] and Paper 2 [98] by adding a longitudinal and perspective of age group comparisons. Paper 3 [99] investigated the number of comorbidities across six years before death in three groups of oldest old using routine data from Study II. Those who died as centenarians were compared with those who died in their 90s (nonagenarians) and those who died in their 80s (octogenarians). This approach allows for the comparison of differences related to age at death. Simultaneously, the behavior of the primary comorbidity trajectories of the three age groups remain was investigated. We found that centenarians suffered from a smaller number of diseases than the younger cohorts of oldest old. Further, the trajectories did not collapse into each other, but the difference between groups even increased when approaching death, as centenarians showed a less steep increase in the number of comorbidities than the other groups did. Although centenarians had multiple conditions, multimorbidity prevalence appears to be lower in centenarians.

2.5 Paper 4: Long-term care status among the oldest old and centenarians

In Paper 1 [97], we found that about half of the centenarians were in long-term care facilities and that dementia and musculoskeletal conditions were more prevalent in those in long-term care. Consequently, **Paper 4** [100] examines the length of stay in long-term care and the longitudinal prediction patterns related with long-term care status and with the transition from private home into a long-term care facility. Analyzing the data of the oldest old of Study II, the predictors were dementia and musculoskeletal diseases, multimorbidity indicated by the Elixhauser comorbidity index, hospital admission, gender, and age group.

Although we found that centenarians were more often in long-term care than the younger cohorts of oldest old, the length of stay in long-term care was substantially longer for centenarians than for the other cohorts. Those who died as octogenarians and nonagenarians died earlier after admission into long-term care compared with those who died as centenarians. Interestingly, dementia and musculoskeletal diseases were less strongly relates with the transition into long-term care than in the younger comparison groups. Hospital admission in the same and in the previous calendar quarter were significantly associated with the transition into long-term care for all age groups. The long stays and the high proportion of centenarians in long-term care may require care strategies that consider preventive, interdisciplinary, and holistic approaches.

2.6 Paper 5: Atrial fibrillation and medication among the oldest old and centenarians

The first paper provided a comprehensive overview about medication prescription in centenarians. Following **Paper 1** [97], **Paper 5** [101] provides a sample case of atrial fibrillation, investigating the medication prescribing among those atrial fibrillation patients who died as centenarians compared with those patients who died in their 80s and 90s. While we assumed a lower rate of atrial fibrillation in centenarians than in the comparison cohorts, we further expected a relative underprescribing of relevant medication, i.e., antithrombotic and anticoagulant medication, in those deceased as centenarians than in the younger cohorts of very old atrial fibrillation patients.

In line with our assumptions, those with atrial fibrillation who died as centenarians were prescribed less anticoagulant therapy than the comparison cohorts. Surprisingly, receiving anticoagulants was not related with stroke risk with and without taking the risk of major bleedings into account. While our findings lead to a request for more in-depth research on the link between age and prescription rates, the appropriateness of prescribing routines in practice should be investigated in more detail.

3. General Discussion

This final third chapter briefly reiterates the research question and main findings (Chapter 3.1). Then, the present findings will be compared and contrasted with prior evidence, both in terms of multimorbidity (Chapter 3.2) and healthcare research (Chapter 3.3). Finally, strengths and limitations (Chapter 3.4) and conclusions and implications will be discussed (Chapter 3.5).

3.1 Summary of the main findings

The overall aim of the present thesis was to illuminate the structure, trajectories, and associations of multimorbidity and healthcare utilization in the oldest old and in centenarians. In a first study (Study I [97, 98]), centenarians were the subject of investigation; in a second study (Study II [99-101]), those individuals who had died as centenarians were compared with those oldest old who had died as nonagenarians (aged between 90 and 99 years) and those who had died as octogenarians (between age 80 and 89 years).

Multimorbidity was present in most centenarians across the two studies with dementia, musculoskeletal conditions, and heart failure being among the most prevalent conditions (Paper 1 [97] and Paper 3 [99]). While the majority of centenarians showed complex multimorbidity patterns (Paper 2 [98]), a minority showed low multimorbidity (Paper 1 [97]); furthermore, the number of morbidities and the increase over time was lower in centenarians in the last years of life than it was in the younger cohorts of the oldest old (Paper 3 [99]).

Regarding healthcare utilization, a substantial proportion of centenarians were in long-term care in both study samples (Paper 1 [97] and Paper 4 [100]). They spent significantly more time in long-term care facilities years at the end of their lives than the younger cohorts of the oldest old, i.e., more centenarians were "long-term care survivors" than "long-term care delayers" and "long-term care escapers" [100]. In Paper 1 [97] and Paper 4 [100], rates of dementia and musculoskeletal conditions helped to distinguish between centenarians living in the community and in long-term care facilities. Paper 4 [100] showed both conditions to be strongly associated with the transition into long-term care in the younger cohorts, while this association was weaker in centenarians. In terms of medical care, one third of the centenarians had spent time in the hospital in the previous year and almost all of them had seen their GPs [97]. The Otorhinolaryngologist (ENT) was the most frequently consulted medical specialist, where about one in three centenarians had a consultation in the previous year (Paper 1 [97]). In terms of medication use, on average, patients were prescribed more than six medication classes in the previous year [97]. However, prescription rates among centenarians with atrial fibrillation tended to be lower than in younger cohorts, which may indicate underprescribing in centenarians (Paper 5 [101]).

3.2 Multimorbidity among the oldest old and centenarians

Although multimorbidity was common in centenarians in the present two studies; in Study I, according to the cut-off values of the Charlson comorbidity index, about a quarter of centenarians only had a low burden of chronic disease [97]. Thereby, half of the centenarians suffered from heart failure, while about two third have been diagnosed with musculoskeletal conditions and dementia, which were the three most common Charlson-based conditions in our study population [97]. In Study II, in the quarter prior to death, three in four centenarians had hypertension; two in three suffered from dementia, and half from heart failure, which were the three most common Elixhauser-based conditions, when adding dementia and musculoskeletal conditions to the Elixhauser index [99]. In line with our findings, two narrative reviews of disease rates in major centenarian studies reported heart failure (29-70%), hypertension (19-64%), heart disease (29-60%), atrial fibrillation (17-26%), and myocardial infarction (10-16%) as the most common diseases [28, 29]. Within these reviews, more recent studies tended to report higher disease rates than older ones [28, 29]. Geriatric conditions that are not used in the Charlson and Elixhauser indices such as vision and hearing impairments (94%) or incontinence (48-60%) were common in the reviewed studies [29]. However, the reviewed literature on centenarians reports low rates of cancer (5-11%), stroke (2-16%) and diabetes (4-13%), which echoes our findings. Dementia was not addressed in one of the reviews [28], while the other review [29] reported high dementia rate estimates (51-58%). These rates were higher in our data (66% and 68%).

In Study II, hypertension and common conditions such as arrhythmia, renal failure, and COPD were less frequent in centenarians than in nonagenarians and octogenarians while dementia and heart failure were more frequent in centenarians than in the other cohorts [99]. A study that draws on US Medicare data found lower incidence rates in centenarians compared with nonagenarians and octogenarians for the majority of diseases including myocardial infarction, stroke, heart failure, ulcers, diabetes mellitus, asthma, and dementia [66, 99]. This is evidence that is largely in line with our findings, with the exception of heart failure and dementia [99]. It should be noted that the US study reports incidence rather than prevalence rates, which may partly explain the differences in heart failure and dementia rates between studies. This pattern was confirmed in other studies for diabetes [65], atrial fibrillation [67], and for healthcare utilization [68], for example. A delayed onset for multimorbidity in centenarians [52], which is in line with compression of morbidity hypothesis [57, 58, 64, 104] is also supported by our findings [99]. Moreover, a delay in incidence of cardiovascular diseases was even found in the offspring of centenarians, though not for all diseases [105, 106]. Our study adds to these findings by focusing on the individual trajectories in the last years prior to death while comparing patterns across age groups. A centenarian study that has been published very recently

[107], largely supports our findings of lower disease rates in centenarians compared with younger cohorts [99]. In this study, disease patterns of age-at-death groups (i.e., those who died as centenarians, nonagenarians and younger cohorts) were tracked over the last years of life. Thereby, centenarians showed lower disease prevalence rates at each age; and further, dementia differentiated best between those who died at an earlier age and those who died as centenarians.

Concerning the four patterns of multimorbidity found in Study I [98], where three groups showed morbidity patterns that have been found in the centenarian and multimorbidity literature [34, 35, 52, 108], a minority of centenarians showed low morbidity. As Study I investigated a subgroup of centenarians with a low morbidity profile [98], Study II further examined whether centenarians in general show low morbidity compared to younger cohorts of the oldest old [99]. This idea of a lower number of comorbidities in centenarians compared to younger cohorts [99] goes beyond the compression of morbidity hypothesis, which assumes a delayed onset disease when approaching the limits of human lifespan [15, 57]. We, thereby, add to the literature that supports the compression of morbidity hypothesis in centenarians [62, 63, 66] and show that the overall number of conditions remains lower in centenarians until death.

3.3 Long-term and medical care in the oldest old and centenarians

Impressively, in Study I, half of the centenarians lived at home, which may indicate a certain level of independence. The other half were residents in long-term care facilities [97]. Although many chronic conditions were equally present among those in long-term care settings and those living in the community, dementia and musculoskeletal conditions were substantially more prevalent among centenarians in long-term care. In Study II, dementia and musculoskeletal conditions have been used to predict the transition from private home to long-term care in three groups of oldest old, i.e., those died as octogenarians, as nonagenarians, and as centenarians [100]. Remarkably, the association of these conditions with transition into long-term care was less strong in centenarians compared with the association in the nonagenarian subgroup and was strongest in the octogenarian subgroup [100]. Furthermore, although the proportion of centenarians in long-term care was higher than in the other cohorts; the proportion of those long-term care residents who stayed the full six years of observation until death in long-term care (i.e., "long-term care survivors") was four times larger in centenarians than in octogenarians and almost twice as large as in nonagenarians [100].

We found half (Study I [97]) to two third (Study II [100]) of the centenarians were in long-term facilities, which is largely in line with the proportions from the literature of population-based and registry data from Denmark and Canada [4, 18, 84]. In studies from around the world, proportions of centenarians in long-term care range from 3% in China to 66% in Canada [4, 18, 19, 29, 54, 84-89].

Available data from German centenarians show a lower prevalence of long-term care compared with our findings, though this deviation from our findings may be due to selective inclusion of participants in the Heidelberg Centenarian Study II [29]. Thus, we further contribute to the understanding of long-term care status of centenarians.

The role of dementia and musculoskeletal conditions that we found in both of our studies in terms of high prevalence and predictive power for long-term care is in line with evidence that suggests that diabetes and neoplastic diseases are less frequent in centenarians compared with younger cohorts [65, 66]. The long-term care pattern of centenarians in Study II is described by higher long-term care rates, longer staying times, and weaker associations of disease predictors with the transition to long-term care than in the younger cohorts of oldest old [100]. This contributes to the literature on length of stay in the oldest old at the end of life [91, 100].

Concerning medication use, Study I aimed to provide a broad overview of prescribed medication for centenarians from different care settings [97]. Across all care settings, centenarians received, on average, six medication classes [97]. This finding is in line with evidence from other centenarian studies [4, 18, 103]. While diuretics and agents acting with the renin-angiotensin system were the most commonly prescribed medication classes, the majority of medication classes were more frequently prescribed in the long-term care setting than in community settings [97]. Conversely, examining the sample case of medication use in atrial fibrillation, Study II investigated the whether there is a relative underprescribing of antithrombotic and anticoagulant medication in those atrial fibrillation patients who died as centenarians compared with those patients who died in their 80s and 90s [101]. Although the rate of atrial fibrillation was lower in centenarians than in the other cohorts; within atrial fibrillation patients, those who died as centenarians received significantly less anticoagulants compared with the other cohorts [101]. This new finding is largely in line with the finding found in the literature that general medication is often underprescribed in centenarians [92, 109, 110]. A Swedish registry study found, for instance, that 46% of community-dwelling and 51% of institutionalized octogenarians have been prescribed antithrombotic therapy [92]. In centenarians, prescription rates were only at 38% and 35%, respectively [92]. Moreover, analyses of our Study II data revealed potential underprescribing related to heart failure and heart failure in combination with renal failure as well [111].

3.4 Strengths and limitations

The two studies presented have important strengths: they draw on two large samples of a hard-to-reach population [97, 98] and delve into data concerning a relevant topic and use advanced statistical methods that allow to model longitudinal trajectories [99-101]. Further, we made use of routinely collected data of two major health insurance companies from Germany. German health and healthcare insurance routine data is available going back several years [94, 95]. This data is comprehensive and covers overall use of the healthcare system, while avoiding reporting bias, missing data, study drop out, and study burden on the participants [97, 99, 100]. However, the data is limited to ICD-10 codes and information about healthcare transactions; information about the severity of the symptoms, daily life and activities, social network composition, and other components of quality of life are not included [97, 99]. Knowledge concerning data generation, type of health insurance company (e.g., usually limited to a certain region), healthcare system, and socioeconomic structure are needed to interpret the data [112-114]. Moreover, due to poor data quality in the past and due to data protection regulations, routine data can typically only be used from the past 5 to 6 years. Researchers should validate diagnoses for chronic conditions, for instance by using only diagnoses that occurred at least twice or by cross-validating diagnoses with medical treatment claims [115]. Further, we did not investigate geriatric syndromes (e.g., bladder, vision, and hearing problems), only chronic conditions that are linked with mortality risk. Although this procedure was functional for the research questions asked in our studies, future studies should investigate these syndromes as well. Further, since we focused on a broad range of diseases including different concepts of multimorbidity, we were not able to cross validate all diseases using information on medication prescription. Nonetheless, we used multiple entries, hospital diagnoses, and validated diagnoses, a procedure that has been used in other studies in Germany that used routine data [65]. With regards to the availability of data, we were able to draw on data from five (Study I) and six (Study II) years prior, which limited our hypotheses for instance regard incidence (i.e., related with the compression of morbidity) and length of stay in long-term care. Future studies should attempt to replicate our findings using longer intervals of observation and other sources of data. While we studied a relatively young sample of centenarians, we were not able to proof lower prevalence rates at the very end of human life span, e.g., in supercentenarians aged 110 years and older [62, 99]. Nonetheless, we compared differences of three cohorts of very old individuals and found differences on the ageing continuum that likely further expand in individuals beyond the age of 110.

3.5 Conclusions and implications

This part of chapter 3 will elaborate the conclusions (Chapter 3.4.1) of the present findings. Further, implications related to multimorbidity (Chapter 3.4.1) as well as implications for healthcare utilization – more specifically implications for long-term care and medical care (Chapter 3.4.1) – will be discussed.

3.5.1 Conclusions

In the present work, we examined the comorbidity and healthcare patterns of the oldest old, especially of centenarians. Investigating the co-occurrence of morbidities in centenarians, results of Study I found three multimorbidity clusters and a forth cluster with low multimorbidity burden [98]. Moreover, the findings of Study II appear to show the number of morbidities was lower in centenarians than in nonagenarians and octogenarians; and, in addition, this difference did not vanish when approaching death, but further extended, where nonagenarians and octogenarians showed a stronger "terminal increase" in the number of diseases than centenarians [99]. Extending the compression of morbidity hypothesis in centenarians [62, 63, 66], we did not observe the collapsing of morbidity trajectories of the age cohorts at the end of life, but found the differences in the number of diseases to be continuing until death. Our findings appear to show that centenarians, at least to a certain degree, avoid the confounding potential synergistic effects of having multiple chronic conditions, which may prevent individuals from becoming hundred years of age [99]. Since the prevalence of a variety of single diseases in centenarians has been shown to be lower than it is in younger cohorts of oldest old [66], our data confirmed that multimorbidity as indicated by a lower number of diseases is lower as well.

In early centenarian studies, centenarians were assumed to be healthy and an ultimate prototype of successful aging [3]. This view has been extended, where many centenarians can be considered as relatively independent, but not healthy [28]. Factors that contribute to this change in the conclusion of health status of centenarians include that early studies were highly selective with small sample sizes and likely overrepresented healthy centenarians. Moreover, due to the demographic change over the last decades, centenarians are not at the limits of the human lifespan anymore. Those living to 110 years and older are now more likely to have escaped most chronic diseases and to show a pattern of health [62, 116, 117]. Nonetheless, today's centenarians remain, on average, healthier than today's 80-year olds [65-67].

The rate of dementia and musculoskeletal conditions varied between those in long-term care and those who are not; this emphasizes the role of these conditions play in cognitive and physical dependency in the oldest old, which has been suggested in the literature [90, 97, 100]. Cevinini et al.

used data of 1160 oldest old individuals over 90 years of age from an Italian sibling study [90]. In this study, three previously published classification schemes for very old individuals were compared with a simple classification of health status (i.e., healthy/independent, unhealthy/dependent based on the cognitive and functional status). The classification schemes were by Franceschi et al. (i.e., good, intermediate, and bad health status [118]), Evert et al. (i.e., escapers, delayers, and survivors [52]), and Gondo et al. (i.e., exceptional, normal, frail, and fragile [19]). Compared with those three classifications, the simple classification by Cevenini et al. showed good discriminate validity when mortality over six years was predicted [90].

The long-term care pattern of centenarians in Study II is described by higher long-term care rates, longer staying times, and weaker associations of disease predictors with the transition to long-term care than in the younger cohorts of oldest old [100]. Rather than acute events (e.g., falls and stroke), issues that develop more slowly (e.g., frailty of various body systems and dementia) may drive the transition to long-term care for centenarians [89, 100, 119]. Further, the composition of one's social network, including the already advanced age of the children of the centenarians, may play a role in the creation of the long-term care profile found in our second study (Study II [91, 100, 120]).

In our data (Study I [97]), the average of six medication classes exceeds the polypharmacy threshold of five medication classes and, thus, should be noted with concern [121]. The higher prescription rates in long-term care may be due to higher comorbidity burden as well as different healthcare provision [97]. On the other hand, we found low prescription rates of anticoagulation in centenarians compared with the younger cohorts [101]. Wastesson et al. conclude in their study on medication prescription in Swedish centenarians that prescribing rates of cardiovascular medication appears to be out of accordance with guidelines when comparing prescription rates between octogenarians and centenarians [92]. Balancing the risk of bleeding with the benefits of anticoagulants, a study that investigated data from almost nine thousand oldest old atrial fibrillation patients, found a high risk of stroke as well as of bleeding, but patients still appear to benefit from antithrombotic medication in advanced age [122]. Research designs as well as guidelines should put more emphasis on comorbidities and medication interactions [123]. While many practitioners already take the complex situation of the multimorbid patients into account when prescribing different medication, the exclusion of older adults from pharmacological trials limits our knowledge basis regarding optimal prescribing [101, 111, 124].

3.5.2 Implications related to multimorbidity

The examination of multimorbidity patterns in the oldest old shows the relevance of this concept, specifically in conjunction with healthcare research. We found centenarians to have a high number of conditions; yet, this number was lower in centenarians than in the younger cohorts of oldest old. Further, dementia and musculoskeletal conditions were highly prevalent and related with long-term care status as suggested by the finding of both of the studies. Implications of these findings include: the (re)evaluation of the health status of centenarians, the use of the concept of multimorbidity in medical care beyond the single disease approach, and interventional approaches to tackle multimorbidity.

Although centenarians are not healthy, they had "relatively" lower multimorbidity: We found a lower presence of multimorbidity in those who died as centenarians relative to those who died in their 80s and 90s [99]. Although economic analyses were not conducted in the present studies, it is likely that healthcare costs do not inflate linearly with increasing age. Concerning healthcare costs in the last years of life, according to a US study, medical costs among centenarians and very old patients are lower than those of 70-year-old patients. Yet, long-term costs increase exponentially with age [125]. Additionally, data related to dementia should be treated with caution [126], as dementia was highly prevalent in centenarians in our findings and is likely linked with increased costs of care, i.e., for family caregivers, professional home care, and long-term care facilities. However, recent finding imply also decreased rates of cognitive impairment in those with centenarian offspring, which may have positive implications for future rates of cognitive functioning as well [127]. Beyond the impact on healthcare costs, having fewer medical conditions has implications for the disease burden and quality of life of centenarians and their relatives. A selectivity effect could explain the lower number of morbidities in centenarians than in the other cohorts [99, 128]. Future studies should attempt to detangle the effects that lead to a lower number of conditions. The comparison of two groups of 80-year-olds, those who died at the age of 85 and those who survived until 100 would allow for the quantification of the selection effect.

In both our studies, dementia was among the most prevalent conditions in centenarians [97, 99]. Hence, dementia prevention, treatment, and care should be high priority for future research and healthcare planning. Furthermore, hypertension was the most prevalent condition and is a risk factor for developing multiple conditions and, thus, needs to be treated appropriately while taking age, fragility, and individual tolerability into account (the European Society of Hypertension and the European Society of Cardiology [ESH/ESC] guidelines for the management of arterial hypertension, p. 2184 [129]).

A minority of centenarians showed a low number of diseases in our data, those individuals could further be examined in future studies to isolate the preventative factors that contribute to reaching such extreme ages with no or few morbidities.

Beyond the single disease approach: Our findings highlight the importance of multimorbidity in older adults by showing relevant patterns of the co-existence of morbidities [130]. Adapting clinical guidelines to take multimorbidity into account [33, 130] should be an aim for the future. Future research should further analyze complex patterns of the co-existence of morbidities for whole cohorts and for subgroups of individuals. Beyond the multimorbidity approach, multifaceted concepts such as frailty [41, 42], the fourth age [43], or comprehensive approaches of successful aging [39] should be incorporated into future studies of similar scope and aim. Moreover, future studies should use disability assessments alongside multimorbidity assessments. While our data contained no information about disability, routine health data from Canada, for instance, allows for the evaluation of disability [84]. Moreover, the consideration of frailty and multimorbidity could further help us to understand and evaluate the health and healthcare situation of the oldest old [38, 42, 131, 132]. In the context of routinely collected data, ICD-10 frailty indicators have been established and display a possible route for future research [133]. Finally, a more comprehensive concept of successful aging [39, 134] could guide research hypotheses and could further strengthen our understanding of the complex interactions of health and healthcare utilization among the oldest old. This concept could – beyond the evaluation of physical, cognitive, and social functioning – combine fragility of aging, disability, and care needs [39].

Assessing and intervening multimorbidity: Defining multimorbidity as the co-existence of two or more conditions within a patient is straightforward [135], yet the simplicity is balanced with the phenomenon's complexity, especially noticeable when measured [45]. In our studies, we applied weighted sum scores, creating indices of multimorbidity. This strategy allows for parsimonious and accurate estimation in research contexts [45]. Following separate single-disease guidelines in clinical practice is likely to result in polypharmacy and potential negative medication interactions [135]. Single-disease guidelines should thus be adapted to the case of multimorbidity. This could be done by taking the potentially limited life expectancy into account, suggesting when an additional medication is unlikely results in an additional benefit for the patient and considering potential harms [33, 136]. Further, cross-referencing clinical guidelines from one disease to another or even applying holistic syndrome or functioning oriented approaches would account for multimorbidity [33, 101, 111, 136]. Finally, the use of better evidence that is not solely derived from single-disease studies would be a big step in this direction [33, 136].

Regarding interventions for patients with multimorbidity in the community setting [137], a systematic review of ten intervention studies found that the interventions that addressed risk factors of comorbidities and functional status were the most effective. Case management and interdisciplinary collaboration were the predominant intervention strategies in these complex interventions. Other interventions addressed the patient directly, emphasizing self-management behavior or patient

knowledge. In practice, continuity of care, management of multiple diseases and medications, and patient-centered care are key areas that need to be considered when treating older patients with multimorbidity [136].

In the face of multimorbidity, treating all conditions simultaneously should be replaced by a prioritization of a specific set of conditions, a more feasible approach for the patient [38, 135]. To allow this prioritization, integrative medical care wherein each care provider has a comprehensive overview of the patient and communicates with other care providers when possible is needed [130, 138-140]. Care providers could be guided by already established guidelines such as the NICE guideline on multimorbidity [135]. Moreover, treatment goals should be communicated to and discussed with the patient to allow optimal match between treatment goals and patient preferences [130, 136], therefore maximizing quality of life and independence [43]. Overcoming the diagnosis and treatment of separate diseases, a focus on complex syndromes and on individual functioning including capacities and may lead to the right direction [141].

3.5.3 Implications for healthcare utilization: long-term care and medical care

We found that many centenarians spend a substantial amount of time in long-term care – usually many years. This population will increase in the future as the number of centenarians grows exponentially [16]. While dementia and musculoskeletal conditions were frequent in the oldest old and in centenarians in our studies [97, 99]; their association with long-term transition was weaker in centenarians [100]. Implications of this extensive care pattern in centenarians for future long-term care include the interrelation of preventive measures and improved medical, geriatric, and interdisciplinary care in long-term care facilities, implemented in more holistic concepts of care.

Prevention and long-term care: The concepts of prevention and long-term care are not necessarily opposite ends of a healthcare spectrum; in fact, they can work together. Prevention in long-term care facilities as well in the community to avoid or postpone the transition into long-term care may be target points for improvements [100].

Preventive strategies within the long-term care setting should be established in various areas. The reduction of adverse events linked with polypharmacy [83, 121] is a relevant example; centenarians received, on average, more than six medication classes in long-term care in the present study (Study I [97]). Polypharmacy is usually defined as the taking five of more medication classes [83]. According to a meta-analysis that summarized evidence from 21 randomized clinical trials, interventions to reduce polypharmacy in long-term care showed mixed results; the reduction in the number of hospital admissions was among the most promising outcomes [121]. Nonetheless, more research that develops and tests successful interventions to optimize medication treatment for the oldest old is needed.

We found musculoskeletal conditions, which may be linked with immobility and frailty, were frequently present and predictive of residency in long-term care [97]. Concerning mobility maintenance and prevention of immobility and frailty in long-term care, many long-term care residents are not sufficiently active [142, 143]. Maintaining mobility in long-term care through participation in brisk walking groups and muscle-strengthening exercises is likely to improve medical outcomes as well as the quality of life of the residents [144]. These interventions should be combined with nutritional and medical strategies in the community [145] and in long-term care [146]. This especially holds true, as our data shows that centenarians survive long periods of time in long-term care and the transition to long-term care was less closely associated with acute diagnoses such as stroke than for the other cohorts [100]. Finally, there is a link between mobility and decreased cognitive decline in old age [147], which further underpins the need for complex interventions targeting activation.

Postponing the transition from private home to long-term care through preventive and supportive means is a main challenge of present and future long-term care. This could be achieved through community geriatric assessment units, case managers, and general practitioners as well as through better community care including assisted living [148, 149]. In our data, hospital admission was associated with transition into long-term care within the same of subsequent quarter of the admission to hospital. Geriatric assessment to prevent transition into long-term care is recommended by the NICE guidelines for multimorbidity [135] and has been shown to be effective in ambulatory care settings [149] as well as being part of acute geriatric units [100, 150].

Dementia and musculoskeletal conditions have been related with long-term care in our data [97, 100]. These have been linked with cognitive and mobility disability in the oldest old [84, 90] and may be target of interventions to prevent hospitalization [151, 152]. A focus on the treatable prerequisites of dementia, including nutrition, exercise, and social and mental training [153] as well as the treatment of vascular diseases that may be related to dementia would likely to be beneficial for elderly long-term care residents [154] for maintaining cognitive and mobility capacities.

Another important area of prevention is the support for family members, especially if they provide care for their aged relatives [100, 155, 156]. In our study, dementia was more strongly associated with long-term care status in the younger cohorts than in centenarians, which may be due to the decreased availability of social support from family caregivers in centenarians. These family caregivers may be in advanced age themselves and burdened over extended periods of time [100, 120, 157].

Finally, given we found hints that indicate a compression of morbidity, indicated by the reduced number of conditions in centenarians. Healthcare costs may also be positively affected by this compression. In terms of healthcare costs in long-term care facilities, the high proportion of centenarians in long-term care, the substantial length of stay, and the high prevalence of dementia

strongly suggest increased costs [125, 126]. However, this was not addressed in the present research and needs to be investigated thoroughly in future studies.

Medical, geriatric, and interdisciplinary care in long-term care: Preventive approaches that focus on care and approaches that aim to optimize the living conditions of residents of long-term care facilities should be complemented by intensified medical care, as our data have shown multimorbidity is common in the oldest old [100]. Medical care is often not optimal in long-term care facilities in Germany [158]. However, the internationally well-established example of the nursing home doctor is an encouraging example of improving medical care in the nursing home, which has been instrumental in reducing unnecessary emergency admissions [159]. The nursing home doctor "Berlin Project" and its successor "Care Plus" are examples of an optimized care for very old patients [160]. Permanent or visiting GPs who provide medical services in long-term care facilities participating in the model project on the basis of special cooperation agreements have resulted in a decrease of hospital, transportation, pharmaceutical, and medical costs by 33% at the participating institutions per day and resident, compared to non-participating institutions [160]. Avoiding unnecessary hospitalizations among residents of long-term care facilities is a major field to improve quality of care, which should be evaluated in future research [161-164].

Furthermore, geriatric and interdisciplinary treatment in long-term care is needed, e.g., joint activities of the nursing home staff with medical specialists, physiotherapists, and palliative care specialists [100]. A promising strategy to integrate geriatric and interdisciplinary competency into long-term care facilities is the ECHO-AGE geriatric care model [165, 166]. Video-conferencing with interdisciplinary specialists was used to implement behavioral plans and medication adjustments with the care staff. This pilot study found clinical improvements and reduced hospitalization [166]. While physical and occupational therapists in collaboration with the nursing staff can maintain mobility and abilities related to activities of daily living [167, 168], medical specialists would likely improve the oral health status [169] or vision and hearing impairment, which have been found to be associated with dementia, of the residents [170, 171]. Interdisciplinary collaboration could be facilitated by telemedicine and eHealth approaches [172]. Finally, regarding palliative care and end-of-life decision making [119], although this is important for everyone in long-term care, this topic may play a significant role over decades for centenarians [100, 173, 174]. A study that interviewed centenarians about their end-of-life and healthcare situation found considerable need for professional support and protection in some of the interviewed centenarians [174]. We found shorter stays in long-term care in those who died in their 80s and 90s compared with those who died as centenarians, which is indicative of the relevance for palliative care for all cohorts of the oldest old.

Holistic concepts of care: Our data suggests [100] that the oldest old and centenarians spend very long periods in long-term care facilities; therefore, holistic concepts of long-term care that

consider individual and biography-based preferences in care and that allow feeling home and feeling community-based are needed [100]. Tailored [175] or individualized [176] approaches to long-term care should be implemented in order to meet the specific needs of the residents [177]. Further, the gap between long-term care facilities and the community should be bridged. Strengthening the long-term care in the community, 'open' long-term care facilities, dementia-friendly cities, improved home care including new technologies [172, 178] and shared-housing arrangements for the oldest old [179, 180] might further reduce this gap [153]. We applied the well-established categories of survivors, delayers, and escapers [52] to the context of long-term care survival. Thereby, "long-term care survivors" were defined as those individuals who were in long-term care for the full six years of observation; delayers moved from private home care (or from another ambulatory care residency) into a long-term care facility; and escapers did not move into a long-term care facility at the end of their life. Future research should further explore the factors that contribute to these profiles and examine why centenarians show such a unique distribution.

Implications for medical care utilization: Further, there are Implications for medical care utilization across healthcare settings. We found polypharmacy to be common in the present two studies [97, 99]. An appropriate reduction of prescription medication in combination with an improved matching of the medication with optimal functioning of the older patients in practice is needed; e.g., by means of specific medical training and guidelines [33, 130, 136]. Information communication technology that helps physicians to monitor complex multimorbidity profiles and their related medication combinations together with better communication and exchange of information across medical specialists would improve the medication treatment in the oldest old and centenarians [181]. Moreover, our findings suggest underprescribing takes place more often for centenarians than younger cohorts of the oldest old in patients with atrial fibrillation [101]. As a positive relationship between polypharmacy and underprescribing has been described in the literature [82], adequate prescribing needs to balance both under and overprescribing should adjust medication to the specific circumstances of the individual – which may also include the establishment of routines of deprescribing [182]. Provision of adequate medical services to the oldest old, geriatricians as well as GPs and nurses trained in the treatment and care of geriatric patients, especially for those of very advanced age is needed. However, medical specialists would benefit from guidelines that are cross-referenced to comorbidities and from an easy-to-reach geriatric consultation option for other medical disciplines [33, 111, 136]. Future interventions should investigate the relationship between multimorbidity profiles and healthcare utilization of the oldest old.

In conclusion, in the two studies presented above, centenarians suffered from a lower number of conditions than the younger cohorts of oldest old and showed unique patterns of resistance in long-term care while commonly being chronically ill and dependent. Although vulnerability was common, healthy aging appears to be possible for a minority [97]. We found remarkable variation in health status and healthcare utilization across groups of oldest old and in centenarians specifically. Thus, integrating a perspective of vulnerability with views of potentials and resilience in this very advanced population, all major research questions of the present work followed the ideas of positive aging and potentials of aging without ignoring the limitations that are present in very old age [2]. This approach should inform future research on health and aging as well.

4. Summary

Increasingly, people of advanced age — including centenarians — are the focus of research and social discussion. The present work examines the morbidity and health care patterns of the oldest old, focusing on centenarians.

Routinly collected claim data from the health and long-term care insurance programs were analyzed in two consecutive studies. The first study included the morbidity and health care data of 1,121 insured centenarians in AOK Nordost (i.e., cross-sectional aggregation over five years; Study I). The second study utilized routine data of 1,398 oldest old insurees of the Knappschaft (i.e., a total of 34,735 person-calendar quarters; Study II) over their last six years to death. Three groups were formed for the analysis in Study II; those who died as centenarians were compared to random samples of individuals who died in their 80s or 90s. Community-dwelling and institutionalized individuals were included in both studies. Statistical analysis methods included Latent Class Analysis, Latent Growth Curve Modeling and Generalized Estimation Equations.

Aiming at investigating multimorbidity and health care use in the oldest old and in centenarians, five consecutive research findings contribute to our understanding of this very old population.

Outpatient and inpatient medical care and morbidity distribution differ between centenarians in long-term care and those that receive community-based care (**Paper 1**, Study I). Particularly, dementia and musculoskeletal conditions were more frequent in long-term care than in community-based care settings and can thus be used when distinguishing between centenarians in different care settings.

The analysis of comorbidity profiles revealed four classes of centenarians (**Paper 2**, Study I). More specifically, 36% of centenarians were classified as suffering from age-associated conditions including dementia and musculoskeletal conditions; 18% were multimorbid with a variety of comorbidities, but without diabetes; 9% were referred to as multimorbid with diabetes; and 36% showed low morbidity.

Extending the compression of morbidity hypothesis, we found that the number of conditions was lower in individuals who died at the age of one hundred years and older; and the increase the number of morbidities in centenarians was less steep in the last years before death compared to those who died in their 80s or 90s (**Paper 3**, Study II).

Although those who died as centenarians were more likely to be in long-term care facilities than those who passed in their 80s or 90s; the former spent a longer time in long-term care before their death (**Paper 4**, Study II). Moreover, dementia among those who died as centenarians was less strongly associated with long-term care status and with transition from private home into a long-term care facility than it was with the younger cohorts of oldest old.

Atrial fibrillation, which is a stroke risk factor, especially in very old-age patients, has been further investigated for medication treatment (**Paper 5**, Study II). Centenarians with atrial fibrillation received significantly less anticoagulation medication compared to the other age groups. Within the oldest old with diagnosed atrial fibrillation, receiving anticoagulation was not associated with increased stroke risk, even when the risk of bleeding was adjusted statistically.

Insights from this study on the patterns of multimorbidity and health care of the oldest old, and of centenarians in particular, will allow for improved care planning in the future.

4. Zusammenfassung

In unserer Gesellschaft des langen Lebens treten zunehmend Menschen hohen Alters und sogar Hundertjährige in den Blickpunkt von Forschung und Gesellschaft. Die vorliegende Arbeit untersucht die Morbiditäts- und Versorgungsprofile von hochaltrigen Menschen, insbesondere von Hundertjährigen.

Es wurden Routinedaten der Kranken- und Pflegekassen in zwei konsekutiven Studien analysiert. Die erste Studie umfasste die Leistungs- und Morbiditätsdaten von 1.121 in der AOK Nordost Versicherten Hundertjährigen (querschnittliche Aggregation über fünf Jahre; Studie I). Die zweite Studie umfasst längsschnittliche Verläufe von Routinedaten 1.398 hochaltriger Versicherter der Knappschaft (insgesamt 34.735 Personen-Kalenderquartale; Studie II) über sechs Jahre hin zum Tod betrachtet. Dabei wurden für die Analyse drei Gruppen gebildet; diejenigen, die als Hundertjährige starben wurden mit Zufallsstichproben von Individuen verglichen, die in ihren 80ern oder 90er Jahren starben. Zuhause Lebende und institutionalisierte Personen wurden in beiden Studien eingeschlossen. Statistische Analysemethoden waren unter anderem die latente Klassenanalyse, latente Wachstumskurvenmodelle, sowie generalisierte Schätzgleichungen. Mit dem Ziel, Multimorbidität und Gesundheitsversorgung bei hochaltrigen Menschen und Hundertjährigen zu untersuchen, tragen fünf aufeinanderfolgende Forschungsergebnisse zu unserem Verständnis dieser Bevölkerungsgruppe bei.

Die medikamentöse, ambulante und stationäre medizinische Versorgung sowie die Morbiditätsverteilung unterscheidet sich zwischen Gruppen Hundertjähriger mit unterschiedlichem Pflegestatus (**Arbeit 1**; Studie I). So können etwa Erkrankungen des Bewegungsapparats und Demenzen als Unterscheidungsmerkmale zwischen im Pflegeheim wohnenden und zu Hause lebenden Hundertjährigen gesehen werden.

Die Untersuchung von Erkrankungsprofilen ergab vier latente Klassen von Hundertjährigen (**Arbeit 2**; Studie I). So wurden 36% der Hundertjährigen als an „altersassoziierten Erkrankungen" erkrankt eingestuft; 18% hatten eine Vielzahl von Komorbiditäten ohne Diabetes und wurden als „multimorbid ohne Diabetes" bezeichnet; 9% wurden als „multimorbid mit Diabetes" bezeichnet; und 36% zeigten „niedrige Erkrankungs-wahrscheinlichkeiten".

Die Hypothese der Kompression der Morbidität erweiternd, fanden wir, dass die Anzahl der Erkrankungen bei Personen, die im Alter von hundert Jahren und älter verstarben, niedriger war und der Zuwachs in den letzten Jahren vor dem Tod flacher ausfiel, im Vergleich zu denjenigen, die mit 90-99 Jahren oder 80-89 Jahren starben (**Arbeit 3**; Studie II).

Obwohl die hundertjährig Verstorbenen öfter im Pflegeheim waren, als die 90-99-jährig oder die 80-89-jährig Verstorbenen, zeigten Erstere zum einen eine langsamere Progressionsrate, also verbrachten diese längere Zeit im Pflegeheim vor ihrem Tod (**Arbeit 4**; Studie II). Zum anderen waren etwa Demenzen bei den hundertjährig Verstorbenen weniger stark mit dem Heimstatus assoziiert, als dies bei den jüngeren Kohorten Hochartiger der Fall war.

Vorhofflimmern, welches besonders bei hochaltrigen Patienten ein Schlaganfallrisiko darstellt, wurde zu medikamentöser Versorgung eingehender untersucht (**Arbeit 5**; Studie II). Hundertjährige Patienten mit Vorhofflimmern erhielten im Vergleich zu den anderen Altersgruppen signifikant weniger gerinnungshemmende Medikation. Innerhalb der hochaltrigen Patienten mit diagnostiziertem Vorhofflimmern, war das Erhalten von Antikoagulation nicht mit dem Schlaganfallrisiko assoziiert, selbst dann, wenn für das Blutungsrisiko statistisch adjustiert wurde.

Eine genauere Kenntnis der Multimorbiditäts- und der Versorgungsmuster hochaltriger Menschen, insbesondere von Hundertjährigen, erlaubt eine bessere Versorgungsplanung jetzt und in Zukunft, wofür die vorliegende Arbeit einen Beitrag leistete.

5. References

1. Wurm S, Diehl M, Kornadt AE, Westerhof GJ, Wahl H-W. How do views on aging affect health outcomes in adulthood and late life? Explanations for an established connection. Developmental Review. 2017;46:27-43. doi: 10.1016/j.dr.2017.08.002

2. Kruse A. Lebensphase hohes Alter - Verletzlichkeit und Reife. Berlin: Springer; 2017.

3. Hitt R, Young-Xu Y, Silver M, Perls T. Centenarians: the older you get, the healthier you have been. The Lancet. 1999;354(9179):652. doi: 10.1016/s0140-6736(99)01987-x

4. Andersen-Ranberg K, Schroll M, Jeune B. Healthy centenarians do not exist, but autonomous centenarians do: A population-based study of morbidity among Danish centenarians. Journal of the American Geriatrics Society. 2001;49:900-8.

5. Solé-Auró A, Crimmins EM. The Oldest Old: Health in Europe and the United States. Annual Review of Gerontology and Geriatrics. 2013;33(1):1-33. doi: 10.1891/0198-8794.33.3

6. Amrhein L, Heusinger J, Ottoway K, Wolter B. Die Hochaltrigen. Expertise zur Lebenslage von Menschen im Alter über 80 Jahren. Forschung und Praxis der Gesundheitsförderung Band 47. Köln: BZgA; 2015.

7. Lee DR, Kawas CH, Gibbs L, Corrada MM. Prevalence of frailty and factors associated with frailty in individuals aged 90 and older: The 90+ study. Journal of the American Geriatrics Society. 2016;64(11):2257-62. doi: 10.1111/jgs.14317

8. van Houwelingen AH, Cameron ID, Gussekloo J, Putter H, Kurrle S, de Craen AJ, Maier AB, den Elzen WP, Blom JW. Disability transitions in the oldest old in the general population. The Leiden 85-plus study. Age. 2014;36(1):483-93. doi: 10.1007/s11357-013-9574-3

9. Jagger C, Collerton JC, Davies K, Kingston A, Robinson LA, Eccles MP, von Zglinicki T, Martin-Ruiz C, James OF, et al. Capability and dependency in the Newcastle 85+ cohort study. Projections of future care needs. BMC geriatrics. 2011;11:21. doi: 10.1186/1471-2318-11-21

10. Mahne K, Wolff JK, Simonson J, Tesch-Römer C, editors. Alter im Wandel: Zwei Jahrzehnte Deutscher Alterssurvey (DEAS). Berlin: Springer VS; 2017.

11. DZA. Stichproben des Deutschen Alterssurveys (DEAS). Deutsches Zentrum für Altersfragen Berlin, Deutschland. 2018;Retrieved from https://www.dza.de/forschung/deas/stichproben.html on May 25, 2018.

12. Saß A-C, Lange C, Finger JD, Allen J, Born S, Hoebel J, Kuhnert R, Müters S, Thelen J, et al. „Gesundheit in Deutschland aktuell" – Neue Daten für Deutschland und Europa Hintergrund und Studienmethodik von GEDA 2014/2015-EHIS. Journal of Health Monitoring. 2017;2(1). doi: 10.17886/RKI-GBE-2017-012

13. Malter F, Börsch-Supan A. SHARE Wave 6: Panel innovations and collecting Dried Blood Spots. Munich: Munich Center for the Economics of Aging (MEA); 2017.

14. Robine JM, Cubaynes S. Worldwide demography of centenarians. Mechanisms of Ageing and Development. 2017. doi: 10.1016/j.mad.2017.03.004

15. Fries JF. Aging, Natural Death, and the Compression of Morbidity. New England Journal of Medicine. 1980;303(3):130-5. doi: 10.1056/NEJM198007173030304

16. Christensen K, Doblhammer G, Rau R, Vaupel JW. Ageing populations: the challenges ahead. The Lancet. 2009;374(9696):1196-208. doi: 10.1016/s0140-6736(09)61460-4

17. Statistisches Bundesamt. Ältere Menschen in Deutschland und der EU. 2016.

18. Rochon PA, Gruneir A, Wu W, Gill SS, Bronskill SE, Seitz DP, Bell CM, Fischer HD, Stephenson AL, et al. Demographic characteristics and healthcare use of centenarians: a population-based cohort study. Journal of the American Geriatrics Society. 2014;62(1):86-93. doi: 10.1111/jgs.12613

19. Gondo Y, Hirose N, Arai Y, Inagaki H, Masui Y, Yamamura K, Shimizu K-i, Takayama M, Ebihara Y, et al. Functional status of centenarians in Tokyo, Japan: Developing better phenotypes of exceptional longevity. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences. 2006;61A:305-10. doi: 10.1093/gerona/61.3.305

20. Poon LW, Cheung SLK. Centenarian research in the past two decades. Asian Journal of Gerontology and Geriatrics. 2012;7:8-13. doi: hdl.handle.net/10722/198088

21. Allard M, Robine JM. Les centenaires français. Etude de la Fondation IPSEN 1990-2000 Rapport final Paris: Annee Gerontologique. 2000.

22. Poon LW, Sweaney AL, Clayton G, M., Merriam S, B., Martin P, Pless B, S., Johnson MA, Thielman S, b., Courtenay B, C. The Georgia Centenarian Study. International Journal of Aging & Human Development. 1992;34(1):1-17. doi: 10.2190/8M7H-CJL7-6K5T-UMFV

23. Toyoshima A, Martin P, Sato S, Poon LW. The relationship between vision impairment and well-being among centenarians: findings from the Georgia Centenarian Study. International Journal of Geriatric Psychiatry. 2017. doi: 10.1002/gps.4763

24. Willcox BJ, Willcox DC, Suzuki M. Demographic, phenotypic, and genetic characteristics of centenarians in Okinawa and Japan: Part 1-centenarians in Okinawa. Mechanisms of Ageing and Development. 2017;165(Pt B):75-9. doi: 10.1016/j.mad.2016.11.001

25. Arai Y, Sasaki T, Hirose N. Demographic, phenotypic, and genetic characteristics of centenarians in Okinawa and Honshu, Japan: Part 2 Honshu, Japan. Mechanisms of Ageing and Development. 2017;165(Pt B):80-5. doi: 10.1016/j.mad.2017.02.005

26. Andersen-Ranberg K, Jeune B. The Danish Longitudinal Centenarian Study. In: Yi Z, Crimmins EM, Carrière Y, Robine JM, editors. Longer Life and Healthy Aging. International Studies in Population. New York: Springer; 2006. p. 151-72.

27. Jopp DS, Park MK, Lehrfeld J, Paggi ME. Physical, cognitive, social and mental health in near-centenarians and centenarians living in New York City: findings from the Fordham Centenarian Study. BMC geriatrics. 2016;16:1. doi: 10.1186/s12877-015-0167-0

28. Rasmussen SH, Andersen-Ranberg K. Health in centenarians. In: Pachana NA, editor. Encyclopedia of Geropsychology. New York, USA: Springer; 2017. p. 1-13.

29. Jopp DS, Boerner K, Rott C. Health and Disease at Age 100: Findings From the Second Heidelberg Centenarian Study. Deutsches Arzteblatt international. 2016(113):203-10. doi: 10.3238/arztebl.2016.0203

30. Rott C, d'Heureuse V, Kliegel M, Schönemann P, Becker G. The Heidelberg Centenarian Study: Theoretical and methodological foundations of psychosocial research in the oldest old. Zeitschrift für Gerontolgie und Geriatrie. 2001;34:356-64.

31. WHO. Multimorbidity: Technical Series on Safer Primary Care. Licence: CC BY-NC-SA 3.0 IGO. Geneva: World Health Organization; 2016.

32. Le Reste JY, Nabbe P, Manceau B, Lygidakis C, Doerr C, Lingner H, Czachowski S, Munoz M, Argyriadou S, et al. The European General Practice Research Network presents a comprehensive definition of multimorbidity in family medicine and long term care, following a systematic review of relevant literature. Journal of the American Medical Directors Association. 2013;14(5):319-25. doi: 10.1016/j.jamda.2013.01.001

33. Guthrie B, Payne K, Alderson P, McMurdo ME, Mercer SW. Adapting clinical guidelines to take account of multimorbidity. British Medical Journal. 2012;345:e6341. doi: 10.1136/bmj.e6341

34. Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. The Lancet. 2012;380(9836):37-43. doi: 10.1016/s0140-6736(12)60240-2

35. Ward BW, Schiller JS. Prevalence of multiple chronic conditions among US adults: estimates from the National Health Interview Survey, 2010. Prevention of Chronic Diseases. 2013;10:E65. doi: 10.5888/pcd10.120203

36. Larsen FB, Pedersen MH, Friis K, Glumer C, Lasgaard M. A latent class analysis of multimorbidity and the relationship to socio-demographic factors and health-related quality of life. A national oopulation-based study of 162,283 Danish adults. PLoS One. 2017;12(1):e0169426. doi: 10.1371/journal.pone.0169426

37. Collerton J, Jagger C, Yadegarfar ME, Davies K, Parker SG, Robinson L, Kirkwood TB. Deconstructing complex multimorbidity in the very old: Findings from the Newcastle 85+ Study. Biomedical Research International. 2016;2016:8745670. doi: 10.1155/2016/8745670

38. Fried LP, Ferrucci L, Darer J, Williamson JD, Anderson G. Untangling the concepts of disability, frailty, and comorbidity: Implications for improved targeting and care. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences. 2004;59(3):M255-M63. doi: 10.1093/gerona/59.3.M255

39. Tesch-Romer C, Wahl HW. Toward a more comprehensive concept of successful aging: Disability and care needs. Journals of Gerontology Series B: Psychological Sciences and Social Sciences. 2016;72(2):310–8. doi: 10.1093/geronb/gbw162

40. Pel-Littel RE, Schuurmans MJ, Emmelot-Vonk MH, Verhaar HJJ. Frailty: Defining and measuring of a concept. Journal of Nutrition, Health & Aging. 2009;13:390-4. doi: 10.1007/s12603-009-0051-8

41. Xue QL. The frailty syndrome: definition and natural history. Clin Geriatr Med. 2011;27(1):1-15. doi: 10.1016/j.cger.2010.08.009

42. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, et al. Frailty in Older Adults: Evidence for a Phenotype. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences. 2001;56(3):M146-M57. doi: 10.1093/gerona/56.3.M146

43.   Lloyd LIZ, Calnan M, Cameron A, Seymour J, Smith R. Identity in the fourth age: perseverance, adaptation and maintaining dignity. Ageing and Society. 2012;34(01):1-19. doi: 10.1017/s0144686x12000761

44.   Baltes PB, Smith J. New frontiers in the future of aging: from successful aging of the young old to the dilemmas of the fourth age. Gerontology. 2003;49(2):123-35. doi: 10.1159/000067946

45.   Diederichs C, Berger K, Bartels DB. The measurement of multiple chronic diseases: A systematic review on existing multimorbidity indices. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences. 2011;66(3):301-11. doi: 10.1093/gerona/glq208

46.   Charlson ME, Pompei P, Ales KL, MacKenze CR. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. Journal Chronic Diseases. 1987;40(5):373-83. doi: 10.1016/0021-9681(87)90171-8

47.   Elixhauser A, Steiner C, Harris R, Coffey RM. Comorbidity measures for use with administrative data. Medical Care. 1998;36(1):8-27. doi: 10.1097/00005650-199801000-00004

48.   Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luthi JC, Saunders LD, Beck CA, Feasby TE, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Medical Care. 2005;43(11):1130-9. doi: 10.1097/01.mlr.0000182534.19832.83

49.   Walraven Cv, Austin PC, Jennings A, Quan H, Forster AJ. A modification of the Elixhauser comorbidity measures into a point system for hospital death using administrative data. Medical Care. 2009;47(6):626-33. doi: 10.1097/MLR.0b013e31819432e5

50.   Drewes YM, den Elzen WP, Mooijaart SP, de Craen AJ, Assendelft WJ, Gussekloo J. The effect of cognitive impairment on the predictive value of multimorbidity for the increase in disability in the oldest old: the Leiden 85-plus Study. Age & Ageing. 2011;40(3):352-7. doi: 10.1093/ageing/afr010

51.   Gill TM, Gahbauer EA, Han L, Allore HG. Trajectories of Disability in the Last Year of Life. New England Journal of Medicine. 2010;362(13):1173-80. doi: 10.1056/NEJMoa0909087

52.   Evert J, Lawler E, Bogan H, Perls T. Morbidity profiles of centenarians: Survivors, delayers, and escapers. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences. 2003;58A(3):232-7.

53.   Davey A, Elias MF, Siegler IC, Lele U, Martin P, Johnson MA, Hausman DB, Poon LW. Cognitive function, physical performance, health, and disease: Norms from the Georgia Centenarian Study. Experimental Aging Research. 2010;36(4):394-425. doi: 10.1080/0361073X.2010.509010

54.   Sachdev PS, Levitan C, Crawford J, Sidhu M, Slavin M, Richmond R, Kochan N, Brodaty H, Wen W, et al. The Sydney Centenarian Study: Methodology and profile of centenarians and near-centenarians. International Psychogeriatrics. 2013;25(6):993-1005. doi: 10.1017/S1041610213000197

55.   Takayama M, Hirose N, Arai Y, Gondo Y, Shimizu K, Ebihara Y, Yamamura K, Nakazawa S, Inagaki H, et al. Morbidity of Tokyo-area centenarians and its relationship to functional status. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences. 2007;62(7):774-82. doi: 10.1093/gerona/62.7.774

56.   Dong X, Milholland B, Vijg J. Evidence for a limit to human lifespan. Nature. 2016;538(7624):257-9. doi: 10.1038/nature19793

57. Fries JF. The compression of morbidity. The Milbank Quarterly. 1983;61(3):397-419. doi: 10.2307/3349864

58. Fries JF, Bruce B, Chakravarty E. Compression of morbidity 1980-2011: A focused review of paradigms and progress. Journal of aging research. 2011;2011:261702. doi: 10.4061/2011/261702

59. Mor V. The compression of morbidity hypothesis: A review of research and prospects for the future. Journal of the American Geriatrics Society. 2005;53(9 Suppl):S308-9. doi: 10.1111/j.1532-5415.2005.53496.x

60. Crimmins EM, Beltran-Sanchez H. Mortality and morbidity trends: Is there compression of morbidity? Journals of Gerontology Series B: Psycholgical Sciences and Social Sciences. 2011;66(1):75-86. doi: 10.1093/geronb/gbq088

61. Vaupel JW. Biodemography of human ageing. Nature. 2010;464(7288):536-42. doi: 10.1038/nature08984

62. Andersen SL, Sebastiani P, Dworkis DA, Feldman L, Perls TT. Health span approximates life span among many supercentenarians: compression of morbidity at the approximate limit of life span. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences. 2012: 395–405. doi: 10.1093/gerona/glr223

63. Kheirbek RE, Fokar A, Shara N, Bell-Wilson LK, Moore HJ, Olsen E, Blackman MR, Llorente MD. Characteristics and Incidence of Chronic Illness in Community-Dwelling Predominantly Male U.S. Veteran Centenarians. Journal of the American Geriatrics Society. 2017. doi: 10.1111/jgs.14900

64. Ismail K, Nussbaum L, Sebastiani P, Andersen S, Perls T, Barzilai N, Milman S. Compression of morbidity is observed across cohorts with exceptional longevity. Journal of the American Geriatrics Society. 2016;64(8):1583-91. doi: 10.1111/jgs.14222

65. Tamayo T, Brinks R, Hoyer A, Kuss OS, Rathmann W. The Prevalence and Incidence of Diabetes in Germany. Deutsches Arzteblatt international. 2016;113(11):177-82. doi: 10.3238/arztebl.2016.0177

66. Akushevich I, Kravchenko J, Ukraintseva S, Arbeev K, Yashin AI. Age patterns of incidence of geriatric disease in the U.S. elderly population: Medicare-based analysis. Journal of the American Geriatrics Society. 2012;60(2):323-7. doi: 10.1111/j.1532-5415.2011.03786.x

67. Friberg L, Bergfeldt L. Atrial fibrillation prevalence revisited. Journal of Internal Medicine. 2013;274(5):461-8. doi: 10.1111/joim.12114

68. Roughead EE, Kalisch LM, Ramsay EN, Ryan P, Gilbert AL. Use of health services and medicines amongst Australian war veterans: a comparison of young elderly, near centenarians and centenarians. BMC geriatrics. 2010;10:83. doi: 10.1186/1471-2318-10-83

69. Diegelmann M, Schilling OK, Wahl H-W. Feeling blue at the end of life: Trajectories of depressive symptoms from a distance-to-death perspective. Psychology and Aging. 2016:00-. doi: 10.1037/pag0000114

70. Gerstorf D, Ram N. Inquiry into terminal decline: Five objectives for future study. The Gerontologist. 2013;53(5):727-37. doi: 10.1093/geront/gnt046

71. Rott C, Wozniak D. Physical and cognitive functioning at the frontier of the human life span: A longitudinal analysis from the Heidelberg Centenarian Study. Paper presented at the 18th REVES

Conference, Amsterdam, Netherlands. 2006;Retrieved from http://slideplayer.com/slide/8158751/ on August 02, 2018.

72. Thelen M, Scheidt-Nave C, Schaeffer D, Bluher S, Nitsche-Neumann L, Sass AC, Herweck R. [National health target "healthy ageing". Medical, psychosocial and nursing care for elderly people]. Bundesgesundheitsblatt, Gesundheitsforschung, Gesundheitsschutz. 2012;55(8):991-7. doi: 10.1007/s00103-012-1517-0

73. Schwinger A, Behrendt S, Tsiasioti C, Stieglitz K, Breitkreuz T, Grobe TG, Klauber J. Qualitätsmessung mit Routinedaten in deutschen Pflegeheimen: Eine erste Standortbestimmung. In: Jacobs K, Kuhlmey A, Greß S, Klauber J, Schwinger A, editors. Pflege-Report 2018: Qualität in der Pflege. Berlin, Heidelberg: Springer Berlin Heidelberg; 2018. p. 97-125.

74. Kurch-Bek D, Sundmacher L, Gallowitz C, Tenckhoff B. [Treatment by panel physicians of patients in protective institutions and homes : Analysis based on secondary data]. Zeitschrift für Gerontolgie und Geriatrie. 2018;51(2):213-21. doi: 10.1007/s00391-016-1144-8

75. Finlayson M. Changes Predicting Long-Term Care Use Among the Oldest-Old. The Gerontologist. 2002;42(4):443-53. doi: 10.1093/geront/42.4.443

76. Jorgensen M, Siette J, Georgiou A, Warland A, Westbrook J. Modeling the Association Between Home Care Service Use and Entry Into Residential Aged Care: A Cohort Study Using Routinely Collected Data. Journal of the American Medical Directors Association. 2018;19(2):117-21 e3. doi: 10.1016/j.jamda.2017.08.004

77. Tinetti ME, Fried TR, Boyd CM. Designing health care for the most common chronic condition—multimorbidity. JAMA. 2012;307(23):2493-4. doi: 10.1001/jama.2012.5265

78. Yadegarfar ME, Jagger C, Duncan R, Fouweather T, Hanratty B, Parker S, Robinson L. Use of primary care and other healthcare services between age 85 and 90 years: longitudinal analysis of a single-year birth cohort, the Newcastle 85+ study. BMJ Open. 2018;8(1):e019218. doi: 10.1136/bmjopen-2017-019218

79. Fried TR, O'Leary J, Towle V, Goldstein MK, Trentalange M, Martin DK. Health outcomes associated with polypharmacy in community-dwelling older adults: a systematic review. Journal of the American Geriatrics Society. 2014;62(12):2261-72. doi: 10.1111/jgs.13153

80. Wauters M, Elseviers M, Vaes B, Degryse J, Dalleur O, Vander Stichele R, Van Bortel L, Azermai M. Polypharmacy in a Belgian cohort of community-dwelling oldest old (80+). Acta Clin Belg. 2016;71(3):158-66. doi: 10.1080/17843286.2016.1148298

81. Wauters M, Elseviers M, Vaes B, Degryse J, Dalleur O, Vander Stichele R, Christiaens T, Azermai M. Too many, too few, or too unsafe? Impact of inappropriate prescribing on mortality, and hospitalization in a cohort of community-dwelling oldest old. British Journal of Clinical Pharmacology. 2016;82(5):1382-92. doi: 10.1111/bcp.13055

82. Kuijpers MAJ, van Marum RJ, Egberts ACG, Jansen PAF. Relationship between polypharmacy and underprescribing. British Journal of Clinical Pharmacology. 2008;65(1):130-3. doi: 10.1111/j.1365-2125.2007.02961.x

83. Jokanovic N, Tan EC, Dooley MJ, Kirkpatrick CM, Bell JS. Prevalence and factors associated with polypharmacy in long-term care facilities: a systematic review. Journal of the American Medical Directors Association. 2015;16(6):535 e1-12. doi: 10.1016/j.jamda.2015.03.003

84. Freeman S, Armstrong JJ, Tyas SL, Neufeld E. Clinical characteristics and patterns of health deficits of centenarians receiving home care and long-term care services. Experimental Gerontology. 2017;99:46-52. doi: 10.1016/j.exger.2017.09.010

85. Randall GK, Martin P, Macdonald M, Margrett J, Bishop AJ, Poon LW. Comparing the Support-Efficacy Model among Centenarians Living in Private Homes, Assisted Living Facilities, and Nursing Homes. Journal of aging research. 2011;2011:280727. doi: 10.4061/2011/280727

86. Ribeiro O, Araújo L, Teixeira L, Duarte N, Brandão D, Martin I, Paúl C. Health status, living arrangements, and service use at 100: Findings from the Oporto Centenarian Study. Journal of Aging & Social Policy. 2016;28(3):148-64. doi: 10.1080/08959420.2016.1165582

87. Zeng Y, Feng Q, Gu D, Vaupel JW. Demographics, phenotypic health characteristics and genetic analysis of centenarians in China. Mechanisms of Ageing and Development. 2017;165(Pt B):86-97. doi: 10.1016/j.mad.2016.12.010

88. Richmond RL, Law J, Kay-Lambkin F. Physical, mental, and cognitive function in a convenience sample of centenarians in Australia. Journal of the American Geriatrics Society. 2011;59(6):1080-6. doi: 10.1111/j.1532-5415.2011.03404.x

89. Evans CJ, Ho Y, Daveson BA, Hall S, Higginson IJ, Gao W, project GC. Place and cause of death in centenarians: a population-based observational study in England, 2001 to 2010. PLoS medicine. 2014;11(6):e1001653. doi: 10.1371/journal.pmed.1001653

90. Cevenini E, Cotichini R, Stazi MA, Toccaceli V, Scurti M, Mari V, Berardelli M, Passarino G, Jeune B, et al. How to classify the oldest old according to their health status: A study on 1160 subjects belonging to 552 90+ Italian sib-ships characterized by familial longevity recruited within the GEHA EU Project. Mechanisms of Ageing and Development. 2013;134(11):560-9. doi: 10.1016/j.mad.2013.11.001

91. Kelly A, Conell-Price J, Covinsky K, Cenzer IS, Chang A, Boscardin WJ, Smith AK. Length of stay for older adults residing in nursing homes at the end of life. Journal of the American Geriatrics Society. 2010;58(9):1701-6. doi: 10.1111/j.1532-5415.2010.03005.x

92. Wastesson JW, Parker MG, Fastbom J, Thorslund M, Johnell K. Drug use in centenarians compared with nonagenarians and octogenarians in Sweden: a nationwide register-based study. Age Ageing. 2012;41(2):218-24. doi: 10.1093/ageing/afr144

93. Hazra NC, Dregan A, Jackson S, Gulliford MC. Drug utilization and inappropriate prescribing in centenarians. Journal of the American Geriatrics Society. 2016;64(5):1079-84. doi: 10.1111/jgs.14106

94. Smeets HM, de Wit NJ, Hoes AW. Routine health insurance data for scientific research: potential and limitations of the Agis Health Database. Journal of Clinical Epidemiology. 2011;64(4):424-30. doi: 10.1016/j.jclinepi.2010.04.023

95. Schubert I, Koster I, Kupper-Nybelen J, Ihle P. [Health services research based on routine data generated by the SHI. Potential uses of health insurance fund data in health services research]. Bundesgesundheitsblatt, Gesundheitsforschung, Gesundheitsschutz. 2008;51(10):1095-105. doi: 10.1007/s00103-008-0644-0

96. Modig K, Andersson T, Vaupel J, Rau R, Ahlbom A. How long do centenarians survive? Life expectancy and maximum lifespan. Journal of Internal Medicine. 2017;282(2):156-63. doi: 10.1111/joim.12627

97. von Berenberg P, Dräger D, Zahn T, Neuwirth J, Kuhlmey A, Gellert P. Chronic conditions and use of health care service among German centenarians. Age and Ageing. 2017;46:939–45. doi: 10.1093/ageing/afx008

98. Gellert P, von Berenberg P, Zahn T, Neuwirth J, Kuhlmey A, Dräger D. Multimorbidity profiles in German centenarians: A latent class analysis of health insurance data. Journal of Aging and Health. 2017;Epub ahead of print:1-15. doi: 10.1177/0898264317737894

99. Gellert P, von Berenberg P, Oedekoven M, Klemt M, Zwillich C, Hörter S, Kuhlmey A, Dräger D. Centenarians differ in their comorbidity trends during the six years before death compared to individuals who died in their 80s or 90s. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences. 2017;73(10):1357–62. doi: 10.1093/gerona/glx136

100. Gellert P, Eggert S, Zwillich C, Hörter S, Kuhlmey A, Dräger D. Long-term care status in centenarians and younger cohorts of oldest old in the last 6 years of life: Trajectories and potential mechanisms. Journal of the American Medical Directors Association. 2018;19(6):535-40.e1. doi: 10.1016/j.jamda.2018.02.010

101. Kreutz R, Schmidt IM, Dräger D, Brüggen F, Hörter S, Zwillich C, Kuhlmey A, Gellert P. Atrial fibrillation and medication treatment among centenarians: Are all very old patients treated the same? Geriatrics and Gerontology International. 2018;Epub ahead of print:1-. doi: 10.1111/ggi.13531

102. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. Journal of Clinical Epidemiology. 1992;45(6):613-9. doi: 10.1016/0895-4356(92)90133-8

103. Gruneir A, Forrester J, Camacho X, Gill SS, Bronskill SE. Gender differences in home care clients and admission to long-term care in Ontario, Canada: a population-based retrospective cohort study. BMC geriatrics. 2013;13:1-12. doi: 10.1186/1471-2318-13-48

104. Hubert HB, Bloch DA, Oehlert JW, Fries JF. Lifestyle habits and compression of morbidity. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences. 2002;57(6):347-51. doi: 10.1093/gerona/57.6.M347

105. Terry DF, Wilcox MA, McCormick MA, Perls TT. Cardiovascular Disease Delay in Centenarian Offspring. The Journals of Gerontology: Series A. 2004;59(4):M385-M9. doi: 10.1093/gerona/59.4.M385

106. Galioto A, Dominguez LJ, Pineo A, Ferlisi A, Putignano E, Belvedere M, Costanza G, Barbagallo M. Cardiovascular risk factors in centenarians. Experimental Gerontology. 2008;43(2):106-13. doi: 10.1016/j.exger.2007.06.009

107. Doblhammer G, Barth A. Prevalence of morbidity at extreme old age in Germany: An observational study using health claims data. Journal of the American Geriatrics Society. 2018. doi: 10.1111/jgs.15460

108. Davey A, Lele U, Elias MF, Dore GA, Siegler IC, Johnson MA, Hausman DB, Tenover JL, Poon LW, et al. Diabetes mellitus in centenarians. Journal of the American Geriatrics Society. 2012;60(3):468-73. doi: 10.1111/j.1532-5415.2011.03836.x

109. Mazzoleni G, Alessandria I, Receputo G, Patané R, Di Stefano S, Savia S, Cilmi V, Rapisarda R, Rosana C. Multiple pathologies and drug consumption in a group of centenarians from Eastern Sicily. Archives of gerontology and geriatrics. 1996;22:389-92. doi: 10.1016/0167-4943(96)86968-8

110. Simiand-Erdociain E, Lapeyre-Mestre M, Bagheri-Charabiani H, Montastruc JL. Drug consumption in a very elderly community-dwelling population. European Journal of Clinical Pharmacology. 2014;57(9):691-2. doi: 10.1007/s002280100344

111. Schmidt IM, Kreutz R, Dräger D, Zwillich C, Hörter S, Kuhlmey A, Gellert P. Lower prescription rates in centenarians with heart failure and heart failure and kidney disease combined: Findings from a longitudinal cohort study of very old patients. Drugs & Aging. 2018;Epub ahead of print. doi: 10.1007/s40266-018-0581-z

112. Lübke N, Meinck M. [Geriatric multimorbidity in claims data - part 1: analysis of hospital data and long-term care insurance data]. Zeitschrift für Gerontolgie und Geriatrie. 2012;45(6):485-97. doi: 10.1007/s00391-012-0301-y

113. Meinck M, Lübke N. [Geriatric multimorbidity in claims data - part 3: prevalence and predictive power of geriatric conditions in an age-specific systematic sample]. Zeitschrift für Gerontolgie und Geriatrie. 2013;46(7):645-57. doi: 10.1007/s00391-012-0462-8

114. Meinck M, Lübke N, Ernst F. [Geriatric multimorbidity in claims data - part 2: diagnoses of hospitals and diagnoses from physicians in the ambulatory setting]. Zeitschrift für Gerontolgie und Geriatrie. 2012;45(7):647-57. doi: 10.1007/s00391-012-0302-x

115. Schubert I, Ihle P, Koster I. [Internal confirmation of diagnoses in routine statutory health insurance data: concept with examples and case definitions]. Gesundheitswesen. 2010;72(6):316-22. doi: 10.1055/s-0030-1249688

116. Cho J, Martin P, Margrett J, MacDonald M, Poon LW, Johnson MA. Cohort comparisons in resources and functioning among centenarians: Findings from the Georgia Centenarian Study. International Journal of Behavioral Development. 2012;36(4):271-8. doi: 10.1177/0165025412439967

117. Engberg H, Christensen K, Andersen-Ranberg K, Jeune B. Cohort changes in cognitive function among Danish centenarians. A comparative study of 2 birth cohorts born in 1895 and 1905. Dementia and geriatric cognitive disorders. 2008;26(2):153-60. doi: 10.1159/000149819

118. Franceschi C, Motta L, Valensin S, Rapisarda R, Franzone A, Berardelli M, Motta M, Monti D, Bonafe M, et al. Do men and women follow different trajectories to reach extreme longevity? Aging Clinical and Experimental Research. 2000;12(2):77-84. doi: 10.1007/BF03339894

119. Murray SA, Kendall M, Boyd K, Sheikh A. Illness trajectories and palliative care. British Medical Journal. 2005;330(7498):1007-11. doi: 10.1136/bmj.330.7498.1007

120. Brandao D, Ribeiro O, Oliveira M, Paul C. Caring for a centenarian parent: An exploratory study on role strains and psychological distress. Scandinavian Journal of Caring Science. 2017. doi: 10.1111/scs.12423

121. Johansson T, Abuzahra ME, Keller S, Mann E, Faller B, Sommerauer C, Hock J, Loffler C, Kochling A, et al. Impact of strategies to reduce polypharmacy on clinically relevant endpoints: a systematic review and meta-analysis. British Journal of Clinical Pharmacology. 2016;82(2):532-48. doi: 10.1111/bcp.12959

122. Lip GY, Clementy N, Pericart L, Banerjee A, Fauchier L. Stroke and major bleeding risk in elderly patients aged≥ 75 years with atrial fibrillation: the Loire Valley atrial fibrillation project. Stroke. 2015;46(1):143-50. doi: 10.1161/STROKEAHA.114.007199

123. Fitzgerald SP, Bean NG. An analysis of the interactions between individual comorbidities and their treatments--implications for guidelines and polypharmacy. Journal of the American Medical Directors Association. 2010;11(7):475-84. doi: 10.1016/j.jamda.2010.05.008

124. Bourgeois FT, Orenstein L, Ballakur S, Mandl KD, Ioannidis JPA. Exclusion of elderly people from randomized clinical trials of drugs for ischemic heart disease. Journal of the American Geriatrics Society. 2017;65(11):2354-61. doi: 10.1111/jgs.14833

125. Spillman BC, Lubitz J. The effect of longevity on spending for acute and long-term care. New England Journal of Medicine. 2000;342(19):1409-15. doi: 10.1056/NEJM200005113421906

126. Kelley AS, McGarry K, Gorges R, Skinner JS. The burden of health care costs for patients with dementia in the last 5 years of life. Ann Int Med. 2015;163(10):729-36. doi: 10.7326/M15-0381

127. Andersen SL, Sweigart B, Sebastiani P, Drury J, Sidlowski S, Perls TT. Reduced prevalence and incidence of cognitive impairment among centenarian offspring. Journals of Gerontology Series A: Biological Sciences & Medical Sciences. 2018;Epub ahead of print. doi: 10.1093/gerona/gly141

128. Gakidou E, King G. Death by survey: Estimating adult mortality without selection bias from sibling survival data. Demography. 2006;43(3):569-85. doi: 10.1353/dem.2006.0024

129. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Bohm M, Christiaens T, Cifkova R, De Backer G, et al. 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). European Heart Journal. 2013;34(28):2159-219. doi: 10.1093/eurheartj/eht151

130. Hughes LD, McMurdo ME, Guthrie B. Guidelines for people not for diseases: the challenges of applying UK clinical guidelines to people with multimorbidity. Age & Ageing. 2013;42(1):62-9. doi: 10.1093/ageing/afs100

131. Fuchs J, Scheidt-Nave C, Gaertner B, Dapp U, Renteln-Kruse Wv, Saum K-U, Thorand B, Strobl R, Grill E. Frailty in Deutschland: Stand und Perspektiven. Zeitschrift für Gerontolgie und Geriatrie. 2016;8:734-42. doi: 10.1007/s00391-015-0999-4

132. Herr M, Jeune B, Fors S, Andersen-Ranberg K, Ankri J, Arai Y, Cubaynes S, Santos-Eggimann B, Zekry D, et al. Frailty and Associated Factors among Centenarians in the 5-COOP Countries. Gerontology. 2018:1-11. doi: 10.1159/000489955

133. Gilbert T, Neuburger J, Kraindler J, Keeble E, Smith P, Ariti C, Arora S, Street A, Parker S, et al. Development and validation of a Hospital Frailty Risk Score focusing on older people in acute care settings using electronic hospital records: an observational study. The Lancet. 2018;391(10132):1775-82. doi: 10.1016/s0140-6736(18)30668-8

134. Rowe JW, Kahn RL. Successful aging 2.0: Conceptual expansions for the 21st century. Journals of Gerontology Series B: Psychological Sciences and Social Sciences. 2015;70(4):593-6.

135. NICE. Multimorbidity: clinical assessment and management (NG56). NICE Guidline. 2016.

136. Wallace E, Salisbury C, Guthrie B, Lewis C, Fahey T, Smith SM. Managing patients with multimorbidity in primary care. British Medical Journal. 2015;350:h176. doi: 10.1136/bmj.h176

137. Smith SM, Soubhi H, Fortin M, Hudon C, O'Dowd T. Managing patients with multimorbidity: Systematic review of interventions in primary care and community settings. British Medical Journal 2012;345:e5205. doi: 10.1136/bmj.e5205

138. Barry MJ, Edgman-Levitan S. Shared decision making: The pinnacle of patient-centered care. New England Journal of Medicine. 2017;366:780-1. doi: 10.1056/NEJMp1109283

139. Demiris G, Kneale L. Informatics Systems and Tools to Facilitate Patient-centered Care Coordination. Yearbook of Medical Informatics. 2015;10(1):15-21. doi: 10.15265/IY-2015-003

140. Herrmann WJ, Haarmann A, Baerheim A. A sequential model for the structure of health care utilization. PLoS One. 2017;12(5):e0176657. doi: 10.1371/journal.pone.0176657

141. Cesari M, Marzetti E, Thiem U, Perez-Zepeda MU, Abellan Van Kan G, Landi F, Petrovic M, Cherubini A, Bernabei R. The geriatric management of frailty as paradigm of "The end of the disease era". European Journal of Internal Medicine. 2016;31:11-4. doi: 10.1016/j.ejim.2016.03.005

142. den Ouden M, Bleijlevens MH, Meijers JM, Zwakhalen SM, Braun SM, Tan FE, Hamers JP. Daily (In)Activities of Nursing Home Residents in Their Wards: An Observation Study. Journal of the American Medical Directors Association. 2015;16(11):963-8. doi: 10.1016/j.jamda.2015.05.016

143. Kalinowski S, Wulff I, Kölzsch M, Kopke K, Kreutz R, Dräger D. Physical activity in nursing homes - Barriers and facilitators: A cross-sectional study. Journal of Aging and Physical Activity. 2012;20:421-41. doi: 10.1123/japa.20.4.421

144. Raffin J, Barthelemy JC, Barth N, Garet M, Busso T, Feasson L, Devun A, Montuy-Coquard C, Thillays M, et al. Fifteen Minutes Daily Brisk Walk May Be a New Best Target in Very Old Adults: Age Is Not an Excuse to Not Exercise. Journal of the American Medical Directors Association. 2018;19(3):273-5. doi: 10.1016/j.jamda.2017.12.097

145. Yoshimura Y, Wakabayashi H, Yamada M, Kim H, Harada A, Arai H. Interventions for Treating Sarcopenia: A Systematic Review and Meta-Analysis of Randomized Controlled Studies. Journal of the American Medical Directors Association. 2017;18(6):553 e1- e16. doi: 10.1016/j.jamda.2017.03.019

146. Thomas DR, Ashmen W, Morley JE, Evans WJ. Nutritional Management in Long-Term Care: Development of a Clinical Guideline. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences. 2000;55(12):M725-M34. doi: 10.1093/gerona/55.12.M725

147. Klusmann V, Evers A, Schwarzer R, Schlattmann P, Reischies FM, Heuser I, Dimeo FC. Complex mental and physical activity in older women and cognitive performance: A 6-month randomized controlled trial. Journals of Gerontology Series A: Biological Sciences & Medical Sciences. 2010;65A:680-8. doi: 10.1093/gerona/glq053

148. Ebihara S, Freeman S, Ebihara T, Kohzuki M. Missing centenarians in Japan: A new ageism. The Lancet. 2010;376(9754). doi: 10.1016/s0140-6736(10)62133-2

149. Ekdahl AW, Alwin J, Eckerblad J, Husberg M, Jaarsma T, Mazya AL, Milberg A, Krevers B, Unosson M, et al. Long-Term Evaluation of the Ambulatory Geriatric Assessment: A Frailty Intervention Trial (AGe-FIT): Clinical Outcomes and Total Costs After 36 Months. Journal of the American Medical Directors Association. 2016;17(3):263-8. doi: 10.1016/j.jamda.2015.12.008

150. Baztan JJ, Suarez-Garcia FM, Lopez-Arrieta J, Rodriguez-Manas L, Rodriguez-Artalejo F. Effectiveness of acute geriatric units on functional decline, living at home, and case fatality among

older patients admitted to hospital for acute medical disorders: Meta-analysis. British Medical Journal. 2009;338:b50. doi: 10.1136/bmj.b50

151. Papaioannou A, Santesso N, Morin SN, Feldman S, Adachi JD, Crilly R, Giangregorio LM, Jaglal S, Josse RG, et al. Recommendations for preventing fracture in long-term care. Canadian Medical Association Journal. 2015;187(15):1135-44. doi: 10.1503/cmaj.141331

152. Smit D, de Lange J, Willemse B, Twisk J, Pot AM. Activity involvement and quality of life of people at different stages of dementia in long term care facilities. Aging & Mental Health. 2016;20(1):100-9. doi: 10.1080/13607863.2015.1049116

153. Morley JE. The future of long-term care. Journal of the American Medical Directors Association. 2017;18(1):1-7. doi: 10.1016/j.jamda.2016.11.001

154. Snyder HM, Corriveau RA, Craft S, Faber JE, Greenberg SM, Knopman D, Lamb BT, Montine TJ, Nedergaard M, et al. Vascular contributions to cognitive impairment and dementia including Alzheimer's disease. Alzheimer's & Dementia: The Journal of the Alzheimer's Association. 2015;11(6):710-7. doi: 10.1016/j.jalz.2014.10.008

155. Gellert P, Häusler A, Gholami M, Rapp M, Kuhlmey A, Nordheim J. Own and partners' dyadic coping and depressive symptoms in individuals with early-stage dementia and their caregiving partners. Aging & Mental Health. 2017:1-9. doi: 10.1080/13607863.2017.1334759

156. Gellert P, Häusler A, Suhr R, Gholami M, Rapp M, Kuhlmey A, Nordheim J. Testing the stress-buffering hypothesis of social support in couples coping with early-stage dementia. PLoS One. 2018;13(1):e0189849. doi: 10.1371/journal.pone.0189849

157. Freeman S, Kurosawa H, Ebihara S, Kohzuki M. Caregiving burden for the oldest old: A population based study of centenarian caregivers in Northern Japan. Archives of gerontology and geriatrics. 2010;50(3):282-91. doi: 10.1016/j.archger.2009.04.008

158. Flaig TM, Budnick A, Kuhnert R, Kreutz R, Drager D. Physician Contacts and Their Influence on the Appropriateness of Pain Medication in Nursing Home Residents: A Cross-Sectional Study. Journal of the American Medical Directors Association. 2016;17(9):834-8. doi: 10.1016/j.jamda.2016.05.014

159. Van Der Steen JT, Kruse RL, Ooms ME, Ribbe MW, Van Der Wal G, Heintz LL, Mehr DR. Treatment of Nursing Home Residents with Dementia and Lower Respiratory Tract Infection in the United States and the Netherlands: An Ocean Apart. Journal of the American Geriatrics Society. 2004;52(5):691-9. doi: 10.1111/j.1532-5415.2004.52204.x

160. Berliner Projekt. Berliner Projekt – Pflege mit dem Plus 3., aktualisierte Auflage. 2008;Retrieved from https://www.berliner-projekt.de/Modell.html on May 25, 2018.

161. Ouslander JG, Berenson RA. Reducing unnecessary hospitalizations of nursing home residents. New England Journal of Medicine. 2011;365(13):1165-7. doi: 10.1056/NEJMp1105449

162. Ouslander JG, Lamb G, Tappen R, Herndon L, Diaz S, Roos BA, Grabowski DC, Bonner A. Interventions to reduce hospitalizations from nursing homes: evaluation of the INTERACT II collaborative quality improvement project. Journal of the American Geriatrics Society. 2011;59(4):745-53. doi: 10.1111/j.1532-5415.2011.03333.x

163. Hoffmann F, Schmiemann G. Influence of age and sex on hospitalization of nursing home residents: A cross-sectional study from Germany. BMC Health Service Research. 2017;17(1):55. doi: 10.1186/s12913-017-2008-7

164.	McAndrew RM, Grabowski DC, Dangi A, Young GJ. Prevalence and patterns of potentially avoidable hospitalizations in the US long-term care setting. International Journal for Quality in Health Care. 2016;28(1):104-9. doi: 10.1093/intqhc/mzv110

165.	Catic AG, Mattison ML, Bakaev I, Morgan M, Monti SM, Lipsitz L. ECHO-AGE: an innovative model of geriatric care for long-term care residents with dementia and behavioral issues. Journal of the American Medical Directors Association. 2014;15(12):938-42. doi: 10.1016/j.jamda.2014.08.014

166.	Gordon SE, Dufour AB, Monti SM, Mattison ML, Catic AG, Thomas CP, Lipsitz LA. Impact of a Videoconference Educational Intervention on Physical Restraint and Antipsychotic Use in Nursing Homes: Results From the ECHO-AGE Pilot Study. Journal of the American Medical Directors Association. 2016;17(6):553-6. doi: 10.1016/j.jamda.2016.03.002

167.	Tappen RM, Roach KE, Applegate EB, Stowell P. Effect of a combined walking and conversation intervention on functional mobility of nursing home residents with Alzheimer disease. Alzheimer Disease and Associated Disorders. 2000;14(4):196. doi: 10.1097/00002093-200010000-00002

168.	Sackley CM, van den Berg ME, Lett K, Patel S, Hollands K, Wright CC, Hoppitt TJ. Effects of a physiotherapy and occupational therapy intervention on mobility and activity in care home residents: a cluster randomised controlled trial. British Medical Journal. 2009;339:b3123. doi: 10.1136/bmj.b3123

169.	Adam H, Preston AJ. The oral health of individuals with dementia in nursing homes. Gerodontology. 2006;23(2):99-105. doi: 10.1111/j.1741-2358.2006.00118.x

170.	Chen SP, Bhattacharya J, Pershing S. Association of Vision Loss With Cognition in Older Adults. JAMA Ophthalmology. 2017;135(9):963-70. doi: 10.1001/jamaophthalmol.2017.2838

171.	Lin FR, Albert M. Hearing loss and dementia: Who is listening? Aging & Mental Health. 2014;18(6):671-3. doi: 10.1080/13607863.2014.915924

172.	Little MO, Rantz M, Lynn GA. Health information technology in long-term care: Potential for the future. Journal of the American Medical Directors Association. 2016;17(5):379-80. doi: 10.1016/j.jamda.2016.02.029

173.	Boerner K, Kim K, Kim Y, Rott C, Jopp DS. Centenarians' end-of-life thoughts and plans: Is their social network on the same page? Journal of the American Geriatrics Society. 2018. doi: 10.1111/jgs.15398

174.	Eggert S, Kuhlmey A, Suhr R, Drager D. [Centenarians preparing for the end of life?]. Zeitschrift für Gerontolgie und Geriatrie. 2017. doi: 10.1007/s00391-017-1187-5

175.	Schoot T, Proot I, Meulen Rt, Witte L. Recognition of client values as a basis for tailored care: the view of Dutch expert patients and family caregivers. Scandinavian journal of caring sciences. 2005;19(2):169-76. doi: doi:10.1111/j.1471-6712.2005.00327.x

176.	Suhonen R, Välimäki M, Leino-Kilpi H. Individualized care, quality of life and satisfaction with nursing care. Journal of Advanced Nursing. 2005;50(3):283-92. doi: doi:10.1111/j.1365-2648.2005.03391.x

177.	Holtkamp C, Kerkstra A, Ooms M, Van Campen C, Ribbe M. Effects of the implementation of the Resident Assessment Instrument on gaps between perceived needs and nursing care supply for nursing home residents in the Netherlands. International Journal of Nursing Studies. 2001;38(6):619-28. doi: 10.1016/S0020-7489(00)00116-4

178. O'Sullivan JL, Gellert P, Hesse B, Jordan LM, Moller S, Voigt-Antons JN, Nordheim J. Exploring attitudes of healthcare professionals towards ICT-based interventions for nursing home residents with dementia: A mixed-methods approach. Contemporary Nurse. 2018;54(1):13-25. doi: 10.1080/10376178.2017.1421087

179. Gräske J, Fischer T, Kuhlmey A, Wolf-Ostermann K. Dementia-specific quality of life instruments and their appropriateness in shared-housing arrangements: A literature study. Geriatric Nursing. 2012;33(3):204-16. doi: 10.1016/j.gerinurse.2012.01.001

180. Gräske J, Verbeek H, Gellert P, Fischer T, Kuhlmey A, Wolf-Ostermann K. How to measure quality of life in shared-housing arrangements? A comparison of dementia-specific instruments. Quality of Life Research. 2013:1-11. doi: 10.1007/s11136-013-0504-8

181. Clyne B, Bradley MC, Hughes C, Fahey T, Lapane KL. Electronic prescribing and other forms of technology to reduce inappropriate medication use and polypharmacy in older people: a review of current evidence. Clinical Geriatric Medicine. 2012;28(2):301-22. doi: 10.1016/j.cger.2012.01.009

182. Dills H, Shah K, Messinger-Rapport B, Bradford K, Syed Q. Deprescribing medications for chronic diseases management in primary care settings: A systematic review of randomized controlled trials. Journal of the American Medical Directors Association. 2018. doi: 10.1016/j.jamda.2018.06.021

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Erklärung

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