Aus dem Zentrum für Innere Medizin der Universität zu Köln

Klinik und Poliklinik für Innere Medizin II der Universität zu Köln

Direktor: Universitätsprofessor Dr. med. Th. Benzing

Challenges and opportunities in the co-management of older inpatients undergoing high-performance medicine:

Internal Medicine and Geriatrics in the Cologne model "Universitäre Altersmedizin"

Inaugural-Dissertation zur Erlangung der Doktorwürde

der Medizinischen Fakultät

der Universität zu Köln

vorgelegt von

Lena Pickert

aus Fürth

promoviert am 20. Dezember 2022

Gedruckt mit der Genehmigung der Medizinischen Fakultät der Universität zu Köln
2021

Dekan: Universitätsprofessor Dr. med. G. R. Fink
1. Gutachterin oder Gutachter: Universitätsprofessorin Dr. med. Dr. M. C. Polidori Nelles
2. Gutachterin oder Gutachter: Privatdozentin Dr. med. G. Röhrig-Herzog

Erklärung

Ich erkläre hiermit, dass ich die vorliegende Dissertationsschrift ohne unzulässige Hilfe Dritter und ohne Benutzung anderer als der angegebenen Hilfsmittel angefertigt habe; die aus fremden Quellen direkt oder indirekt übernommenen Gedanken sind als solche kenntlich gemacht.

Bei der Auswahl und Auswertung des Materials sowie bei der Herstellung des Manuskriptes habe ich Unterstützungsleistungen von folgenden Personen erhalten:

Frau Prof. Priv.-Doz. Dr. Dr. M. Cristina Polidori Nelles

Frau Dr. med. Anna Maria Meyer

Weitere Personen waren an der geistigen Herstellung der vorliegenden Arbeit nicht beteiligt. Insbesondere habe ich nicht die Hilfe einer Promotionsberaterin/eines Promotionsberaters in Anspruch genommen. Dritte haben von mir weder unmittelbar noch mittelbar geldwerte Leistungen für Arbeiten erhalten, die im Zusammenhang mit dem Inhalt der vorgelegten Dissertationsschrift stehen.

Die Dissertationsschrift wurde von mir bisher weder im Inland noch im Ausland in gleicher oder ähnlicher Form einer anderen Prüfungsbehörde vorgelegt.

Die dieser Arbeit zugrunde liegende prospektive klinische Studie wurden von mir in Zusammenarbeit mit Frau Prof. Priv.-Doz. Dr. Dr. M. Cristina Polidori Nelles, Leiterin des Schwerpunkts für Klinische Altersforschung der Klinik II für Innere Medizin der Uniklinik Köln, Köln, Deutschland, und Frau Dr. med. Anna Maria Meyer, Assistenzärztin der Klinik II für Innere Medizin der Uniklinik Köln, Köln, Deutschland, und unter statistischer Beratung durch Frau Ingrid Becker vom Institut für Medizinische Statistik und Bioinformatik der Uniklinik Köln, Köln, Deutschland, entwickelt.

Die auf der Krankenstation 15.2 der Klinik II für Innere Medizin durchgeführten Untersuchungen im Rahmen der *MPI_InGAH*-Studie habe ich unter Aufsicht der Oberärztin Frau Prof. Priv.-Doz. Dr. Dr. M. Cristina Polidori Nelles vorgenommen. Die im Rahmen der Studie durchgeführten telefonischen Nachbeobachtungen wurden durch mich vorgenommen.

Die Anleitung zur von mir selbst durchgeführten statistische Auswertung der Daten erfolgte durch Frau Ingrid Becker. Die dieser Arbeit zugrundeliegende Publikation „Role of a multidimensional prognosis in-hospital monitoring for older patients with prolonged stay “ in der Zeitschrift *International Journal of Clinical Practice* (Impact-Faktor 2.6) wurden eigenständig von mir verfasst. Eine genaue Darstellung des Eigenanteils kann meiner schriftlichen Erklärung über den von der Doktorandin geleisteten Beitrag zu der Arbeit eingesehen werden, welche von allen Coautoren unterschrieben worden ist.

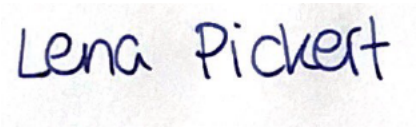
Das Lektorat *Mentorium* hat die Endfassung dieser Arbeit grammatikalisch und sprachlich überarbeitet, hat jedoch weder einen Anteil an der geistigen noch an der inhaltlichen Gestaltung dieser Arbeit.

Falls ich mich im Rahmen dieser Arbeit auf Ergebnisse anderer Arbeiten beziehe, habe ich dies kenntlich gemacht.

Erklärung zur guten wissenschaftlichen Praxis:

Ich erkläre hiermit, dass ich die Ordnung zur Sicherung guter wissenschaftlicher Praxis und zu Umgang mit wissenschaftlichem Fehlverhalten (Amtliche Mitteilung der Universität zu Köln AM 132/2020) der Universität zu Köln gelesen habe und verpflichte mich hiermit, die dort genannten Vorgaben bei allen wissenschaftlichen Tätigkeiten zu beachten und umzusetzen.

Köln, den 24.08.2021

Unterschrift: 

Acknowledgements

First and foremost, I would like to thank the two hundred patients who agreed to participate in the study on which this thesis is based. The contact I have had with these people and hearing their life stories has inspired and shaped me. Such connections and insights that these people have provided me at very vulnerable moments have only deepened my love and passion for patients and medicine.

Furthermore, I would like to wholeheartedly thank my doctoral mother, Prof. Priv.-Doz. Dr. Dr. M. Cristina Polidori for giving me the idea for the title of my thesis and for her constant support. Cristina, your passion for our patients and aging, your warmth and your tireless work have always inspired and motivated me. I am incredibly grateful to you for the trust, support and the love for science you have given me. I would also like to thank Dr. Anna Maria Meyer, without whom this study and this thesis would never have existed. Anna, I am always glad that our paths crossed at Ageing Clinical Research and look forward to a hopefully continuing long and intensive collaboration with you.

I would also like to thank Dipl.-Math. Ingrid Becker for her excellent statistical advice, patience and constant support. Thank you, Mrs. Becker, for letting me come to you with any statistical question and for expanding my mathematical knowledge by quite a bit.

In addition, I would like to thank all co-authors of the paper on which this work is based for their cooperation and support, especially the Director of the Department of Internal Medicine II, Prof. Dr. Thomas Benzing and Prof. Alberto Pilotto. I have learned an incredible amount in the process of writing this paper and am looking forward to a continuing a productive and intensive collaboration.

Finally, I would like to thank all the people who have supported me since the beginning of my studies. My father, without whom this thesis would probably not exist, my mother for her corrections and hints, my brother Paul, Jana, Simon, Leo, Cosi, Tamara, Nina and all those I cannot mention by name here, but who have contributed just as much to this work. Many, many thanks for always being there for me.

Für meine Großeltern, deren Mut und deren Offenheit ich stets bewundert habe.

Und für Layla.

Contents

Abbreviations

EU: European Union

GFR: glomerular filtration rate

BLSA: Baltimore Longitudinal Study on Aging

CKD: chronic Kidney Disease

DNA: desoxyribonucleic acid

KCAL: kilocalories

BMI: Body-mass-index

RCT: Randomized controlled trials

CGA: Comprehensive Geriatric Assessment

MPI: Multidimensional Prognostic Index

UK: United Kingdom

ADL: Activities of Daily living

IADL: Instrumental Activities of Daily living

MNA-SF: Mini Nutritional Assessment – Short form

ESS: Exton Smith Scale

SPMSQ: Short Portable Mental Status Questionnaire

CIRS-CI: Cumulative Illness Rating Scale – Comorbidity Index

CAP: community acquired pneumonia

HCAP: healthcare-associated pneumonia

CAAP: community acquired aspiration pneumonia

HCAAP: healthcare-associated aspiration pneumonia

PIMs: potentially inappropriate medications

PPOs: potential prescribing omissions

FORTA: Fit for the aged

START: Screening Tool to Alert Doctors to start the Right Treatment

STOPP: Screening Tool of Older Persons Potentially Inappropriate Prescription

WHO: World health organization

NMDA: N-methly-D-aspartate

MPI-InGAH: Multidimensional prognostic index – Influence of Geriatric Assessment on hospitalization of older, multimorbid patients

IA: intermediate assessment

i.v.: intravenous

FU: follow-Up

CRP: c-reactive protein

A&E: Accident and Emergency

ICU: Intensive Care Unit

NIA: National Institute of Aging

USA: United States of America

1. Deutsche Zusammenfassung

Altern ist ein Prozess, der die Menschheit und die Wissenschaft seit Anbeginn fasziniert. Warum und wie wir gesund altern, ist bis heute nicht gänzlich verstanden. Aber es ist Fakt, dass in Industrienationen die Lebenserwartung stetig ansteigt und der Anteil der 80-jährigen in diesen Gesellschaften stetig zunimmt. Einige dieser alten Menschen schaffen es, durch eine Kombination aus genetischen und lebensstil-bedingten Faktoren, bis ins hohe Alter gesund und selbstständig zu bleiben. Der größere Anteil dieser Altersgruppe leidet aber an einer oder mehreren chronischen Erkrankungen und benötigt Unterstützung in den Aktivitäten des täglichen Lebens. Diese Menschen sind gebrechlich (frail) oder drohen es zu werden (pre-frail). Chronische Erkrankungen in Kombination mit Gebrechlichkeit führen zu häufigen Krankenhausaufenthalten. Die enormen Kosten, die das Gesundheitssystem durch die meist lange Verweildauer dieser Patienten trägt, ist nur ein Grund, die Prävention und Behandlung von Erkrankungen des höheren Lebensalters zu optimieren. Ziel der modernen Altersmedizin ist es, die Gebrechlichkeit (frailty) der Patienten multidimensional und interdisziplinär zu beurteilen. Den Goldstandard hierfür stellt das Comprehensive Geriatric Assessment (CGA) dar, welches in der vorliegenden Arbeit um den Multidimensionalen Prognostischen Index (MPI) ergänzt wird. Der MPI beleuchtet die physischen, psychischen, funktionellen und sozialen Aspekte älterer Patienten mittels insgesamt acht verschiedener Fragebögen und Scores und ist ein Risikoindex, der Mortalität, Rehospitalisierungen und Institutionalisierungen für einen Monat und ein Jahr nach Erhebung prognostiziert. Hierfür werden die Patienten drei Risikogruppen (MPI-1, niedriges, MPI-2, mittleres und MPI-3, hohes Risiko) zugeordnet. In der vorliegenden Arbeit wurde einerseits durch die Rekrutierung von insgesamt 200 multimorbiden (>2 chronische Erkrankungen) und älteren (>65 Jahre) Patienten in der Klinik II für Innere Medizin der Uniklinik Köln, die Durchführbarkeit und Validität des MPI in einer hochspezialisierten internistischen Klinik bestätigt und es konnte andererseits gezeigt werden, dass der MPI zur Verlaufsbeobachtung von Patienten während des stationären Aufenthaltes herangezogen werden kann und nicht nur Momentaufnahmen abbildet. Durch das dreimalige Erheben des MPIs (bei Aufnahme ins Krankenhaus, nach 7-10 Tagen und bei Entlassung) konnten dynamische Verläufe sichtbar gemacht werden. Interessant war hier, dass besonders Patienten der niedrigsten Risikogruppe (MPI-1) während des Aufenthalts von einer Verschlechterung ihrer Prognose betroffen waren, während Patienten der höchsten Risikogruppe (MPI-3) von einem längeren Aufenthalt eher profitierten. Beide Trends waren bereits nach einer Woche durch den MPI darstellbar und bestätigen das „geriatrische Paradoxon“. Dieses Wissen kann den behandelnden Ärzten und Therapeuten die Möglichkeit geben, Behandlungen maßgeschneidert auf den Patienten anzupassen. Perspektivisch soll der MPI auch in Kombination mit klinischen Aspekten interpretiert werden (wie z.B. Laborparametern), um das Co-Management der Inneren Medizin und Geriatrie zu optimieren. Die Kombination aus internistischer Hochleistungsmedizin und multidimensionaler Altersmedizin wird aktuell in der neu eröffneten Kölner „Universitären Altersmedizin“ auf der Station 17.1 der Uniklinik Köln medizinisch und wissenschaftlich erprobt. Eine derartige Kombination ist die Erste dieser Form in Deutschland und könnte maßgeblich dazu beitragen, den „silbernen Tsunami“, der in den nächsten Jahrzehnten auf die Gesundheitssysteme der Industrienationen zurollt, optimal zu versorgen. Dieses Pilotprojekt wird wissenschaftlich begleitet und die ersten Fallberichte, die im Rahmen des Co-Managements zwischen Innerer Medizin und Altersmedizin veröffentlich wurden, zeigen den positiven Einfluss dieser Zusammenarbeit auf die Prognose älterer gebrechlicher Patienten. Weitere Forschung ist notwendig, um individuelle Behandlungskonzepte für ältere Patienten zu ermöglichen und um ein besseres Verständnis der Einflussfaktoren auf den physiologischen und pathologischen Alterungsprozess zu erlangen. So könnte jedem Menschen die Chance gegeben werden, im hohen Lebensalter selbstbestimmt und individuell zu leben und behandelt zu werden.

2. Introduction

2.1 What is ageing?

We age. Incessantly, day after day, minute after minute. Rose – like most evolutionary biologists – defines ageing as “a persistent decline in the age-specific fitness components of an organism due to internal physiological degeneration” (1) . But is that all that constitutes ageing? A constant, inescapable loss, at the end of which death awaits us?

At some points in their lives, people are desperate to age. It affords people an increase in freedom of action, capacities and options. Children want to become adolescents, adolescents want to finally “grow up”. The ability to drive a car is subject to an age limit in almost every country in the world. The same applies to participation in elections, enrolment in universities or renting your first own apartment. For people in these life situations, ageing is fun; getting older opens up new possibilities. It is not scary at all.

These positive associations with ageing change from at midlife, when people notice a reduction in their cognitive or physical capacity and some are diagnosed with their first chronic condition. The metabolism changes, the daily calorie requirement decreases and often, an increase in body weight occurs. At this point, ageing starts to become scary. For the first time, a loss is sensed, which is described in the above definition of ageing (1).

But doesn’t old age also have its benefits? A wealth of life experience and knowledge? Every person receives answers to at least some of the questions they had when they were younger. Age brings wisdom, as was already known in ancient Greece. Even in old age, the famous Greek philosophers Socrates and Plato drew crowds of students and were eager to spread their lessons. In a similar manner, parents impart knowledge and skills to their children. As in the lyrics of the song “Father and Son” by Cat Stevens, "You're still young, that’s your fault, there's so much you have to know" (2). At the same time, older people need young people, a solidarity that has never been more relevant than during the Corona pandemic; SARS-CoV-2, a highly contagious virus for all humans, is much more likely to be fatal for older people. In this case, it was down to the younger generations to do grocery shopping or to care for older patients when they were affected by the virus. As much wisdom as old age implies, it makes one vulnerable. To use the words of poet Rupi Kaur, “our elders are not disposable” (3). Ageing involves both give and take – one gains something and one loses something.

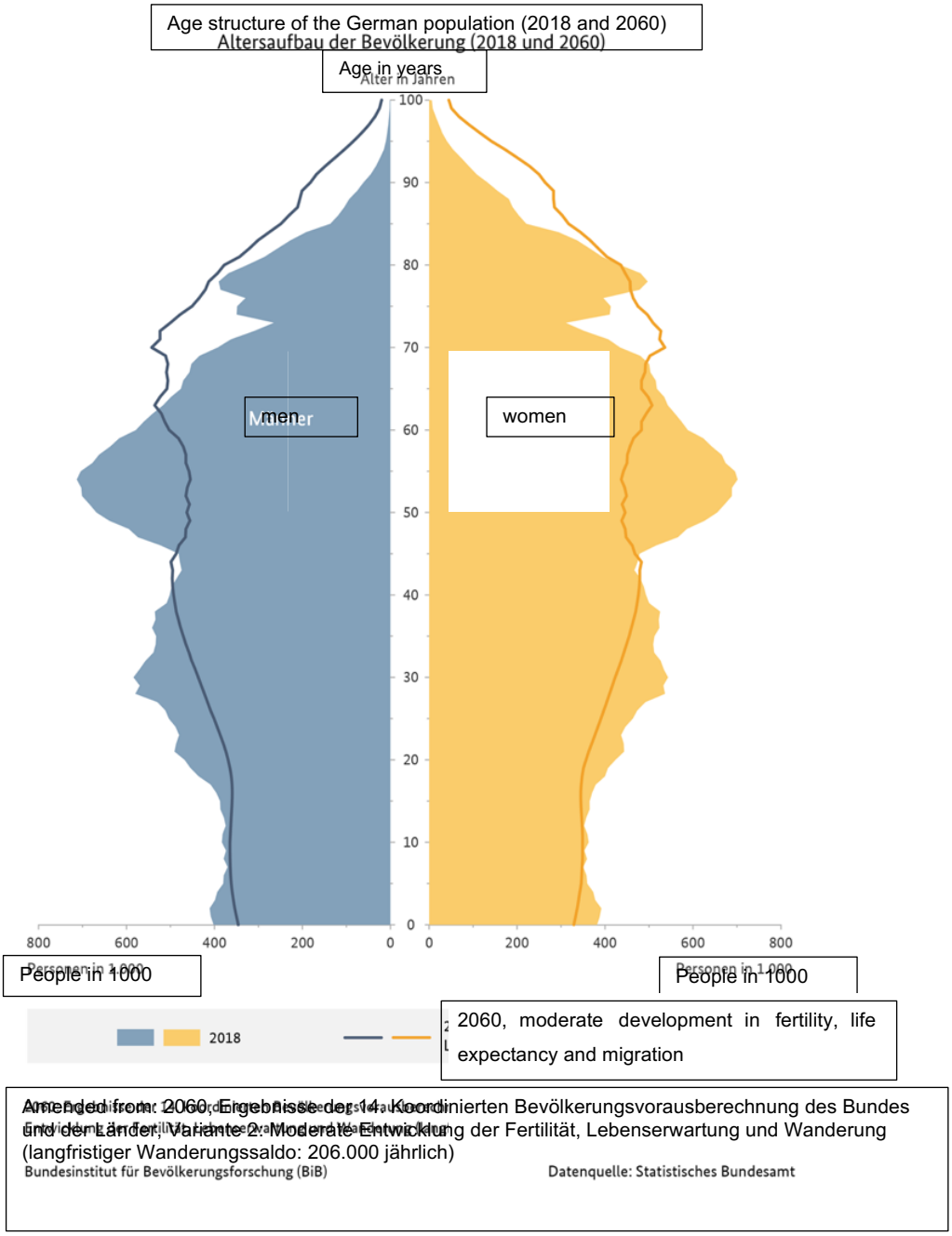
The phenomenon of ageing has fascinated mankind for centuries. Therefore, the various definitions and concepts of ageing involve many different approaches. Three concepts in particular are important for this thesis. Chronological age refers to the counted years after a person's birth, i.e., the age noted on every form when registering at a doctor's office or clinic. Biological age refers to measurement of age according to the functional capacity of the organism (4). Subjective age is the age a person feels (feel age) or thinks they appear to be (look age). (5, 6). Ageing can thus be defined according to time, physical deficits or subjective condition. Clearly, ageing is not a standardized process that can simply be optimized. It is individual and heterogeneous (7). It is multidimensional.

Improved living conditions and better health care lead to ever-increasing life expectancy. Accordingly, there are not only internal factors that influence ageing, but also important external parameters. In the 2010 Georgia Centenarians study by Jonathan Arnold et al. (8), the group of researchers examined 244 centenarians (100-year-olds) and near-centenarians (98 years or older) as well as 80 octogenarians (80-year-olds) (8) and divided them into three groups according to their experience with chronic disease: The *"survivors"*, 43% of the participants, received the diagnosis of a first chronic disease between 0–80 years of age. The *"delayers"*, 36% of the participants, were not diagnosed with a chronic disease until between 80 and 98 years of age. And the *"escapers"*, 17% of the participants, were not diagnosed with a chronic disease until the age of 98.

Since ancient times, people have been fascinated by the idea of immortality. Science has not yet reached the point at which immortality can be promised. But a life of 100 years – without diseases, without restrictions, without sacrifice – is quite some time. So, if it were possible for a person to choose how they will age, many people would certainly take the "escaper" option(8). But how does one become an "escaper"? Is it at all possible to influence the outcome, or is ageing already genetically determined? How can we use the knowledge about the multidimensionality of ageing and the high-performance medicine that exists today to enable people to live a long and self-determined life? This is the major question of Geriatric Medicine in the 21st century.

2.2 An ageing society: epidemiological data

Figure 1: age structure of the population in Germany 2018 and 2060



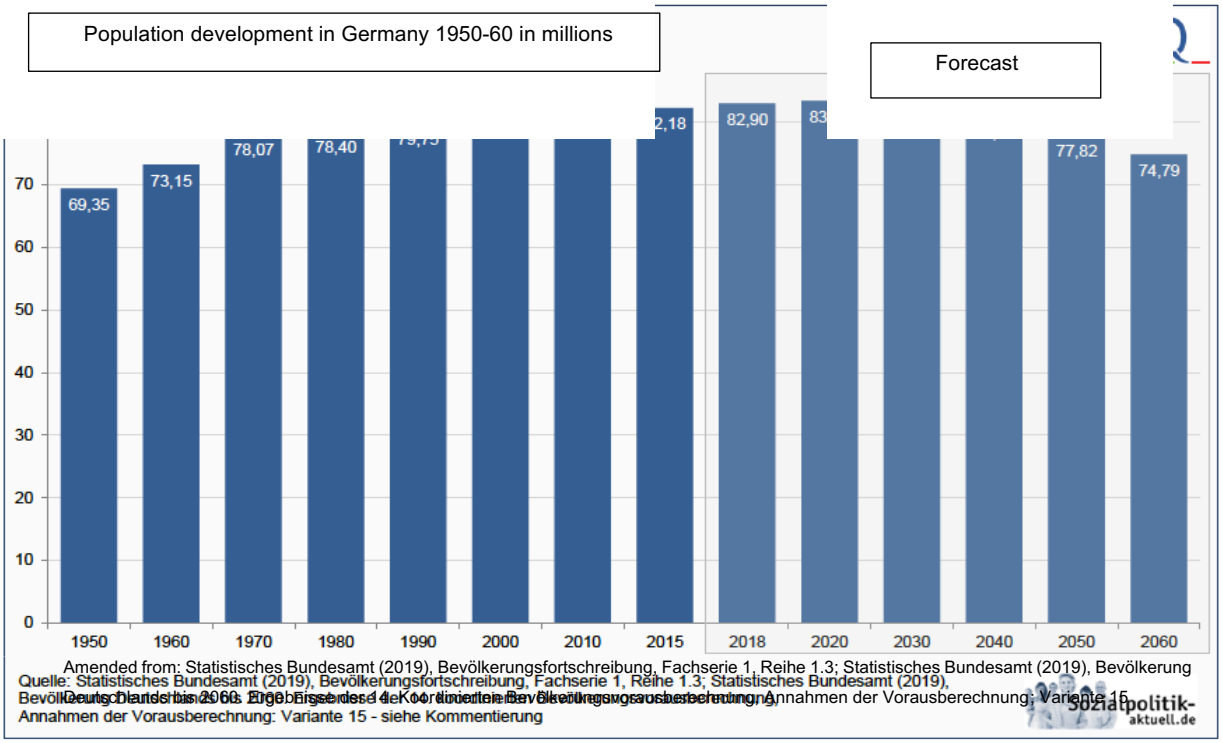
Amended from: 2060. Ergebnisse der 14. Koordinierten Bevölkerungsvorausberechnung des Bundes und der Länder, Variante 2: Moderate Entwicklung der Fertilität, Lebenserwartung und Wanderung (langfristiger Wanderungssaldo: 206.000 jährlich)

Subtitle Figure 1: The male population pyramid is shown on the left, the female on the right. The yellow or blue area represents the actual distribution in 2018, the yellow or blue line the estimated area for the year 2060 assuming moderate development of fertility, immigration and life expectancy. The population pyramid for the year 2018 shows a clear majority of the population between 40 and 60 years old compared to the population between 15 and 25 years old. For the year 2060, a significant increase in the population between 80 and 100 years is expected compared to 2018 (9).

If we compare the population pyramid for 2018 with the expected population pyramid for 2060, which is illustrated in Figure 1, three points stand out. First, the overhang of the persons aged between 45 and 70 years (baby boomers of the 1950s and 1960s) narrows,

and the pyramid gives an almost even picture of the generations in 2060. Secondly, the number of persons between 80 and 100 years old will increase massively in 2060 compared to 2018. Thirdly, the number of births is expected to decline only slightly compared to 2018: while there were almost 800,000 births in 2018, there are expected to be almost 700,000 births in Germany in 2060.

Figure 2: population development in Germany 1950–2060



Subtitle Figure 2: This chart shows the actual population of Germany in millions of people between 1950 and 2015, with statistical projections for the years 2018 to 2060 (10, 11).

The media is currently dominated by headlines reporting that Germany has an “ageing society”, “low-birth cohorts” or an “over-aging population” (12-14). As Figure 1 clearly shows, in 2018, the so-called baby boomers (the generation of people born in the 1950s and 1960s) were between 45 and 70 years old. For 700,000 55-year-olds, there were around 400,000 newborns in 2018. Nevertheless, Figure 2 shows a calculated increase in Germany's population for 2018: from 82.18 million people in 2015 to 82.90 million people in 2018. How can this population increase be explained?

On the one hand, it can be explained by rising life expectancy. In 2018, a newborn girl in Germany had a life expectancy of 83.27 years, while that of a newborn boy was 78.48 years (15). In comparison, the life expectancy of a newborn girl in Germany in 1960 was 72.4 years, with that of a newborn boy in 1960 in Germany being 66.9 years (16). Thus, the population size can remain constant despite less births than deaths. On the other hand,

immigration has the greatest influence on population growth in Germany. The projections of Germany's population figures in Figure 2 of the Federal Statistical Office are based, amongst others, on an expected annual net migration of 221,000 persons (10). This account could still be too low due to the large immigration numbers in 2014.

The two effects described above are not only applicable to Germany, but to the entire European Union (EU). On 10 July 2019, – according to a press release of Eurostat, the EU's statistical office – 513.5 million people were living in the EU, compared to 512.4 million people on 1 January 2018 (17). Although the EU's so-called natural population trend was negative (5.3 million deaths vs. 5.0 million births), the population grew by 1.1 million people. This growth was caused by a positive immigration balance (17).

It can therefore be said that
1. It is expected that by 2060, Germany's population will be reduced to approximately its population level of 1960 (compare Figure 2). This is explained by declining birth rates and rising death rates. Even immigration will not prevent the net decrease in population size.

2. By 2060, there will have been a significant increase in the number of "oldest–old" people (those between 80 and 100 years of age). Which challenges this will pose for society, the health system and politics will be the subject of research in the coming decades.

3. Human life expectancy is increasing every year. This will, as already mentioned in point 2, necessitate changes in both the state health care infrastructure and societal structure.

2.3 Does physiological ageing exist?

Why will rising life expectancy pose challenges to society and the health system? After all, a long life is desirable to most people. Getting older need not be something to be afraid of, as mentioned in chapter 1.1. Many people imagine their retirement in a very idealized way, with lots of time for activities and undertakings that were not feasible in everyday working life – more time for family and for themselves. Everyone would like to age like an "escaper", or at least a “delayer” (8).

The solution may sound simple, but it is not, because how one becomes an "escaper" in old age is not yet understood. What is certain is that it involves an interplay of many factors, some of which can be influenced, some of which are determined from birth (7). Among the factors that influence ageing are genes, lifestyle, diseases, social environment, stress and

trauma. So, the question in the title of this subchapter, "Is there physiological aging?", is not a simple yes or no question (7).

Physiological ageing is widely regarded as a loss of function of various organs and tissues of an organism. However, every organ and every tissue loses its capacity and recovery potential over the course of life, but not at the same rate and to the same extent. Kidney function, for example, decreases continuously from the age of 30 onwards. The fact that the glomerular filtration rate (GFR) – the internationally-established standard value of renal function – continuously decreases with age was first demonstrated for a longitudinal period in the Baltimore Longitudinal Study on Aging (BLSA) (18). Rowe et al demonstrated that for men, the average GFR decreases linearly from 140 ml/min/1.73m^2 at the age of 30 to a value of 97 ml/min/1.73m^2 at the age of 80 (18). Nevertheless, the loss of 43 ml/min/1.73m^2 filtration rate alone is not considered a chronic kidney disease (CKD) or renal failure (19, 20), does not restrict the majority of patients and therefore often goes unnoticed. The physiological renal ageing processes usually have no effect on the individual, unless there are unexpected events such as illness or trauma.

This observation highlights another important fact in the context of ageing and disease. Not every loss of function counts as a handicap (21). Therefore, not every reduction in GFR, for example, needs to be treated, but for some older patients who are impaired by other biomolecular or environmental factors, even this loss signifies a disease worthy of treatment. This illustrates that the algorithm “one-cause-one-mechanism-one-therapy” is not applicable to the older patient (21).

Thus, the ageing of human beings’ largest organ is widely met with fear. The processes of decline are, in this case, visible to everyone – we're talking about our skin. Skin ageing is not only important for the cosmetics industry, but also for medicine. It leads to greater skin fragility, delayed wound healing and the risk of developing skin cancer also increases with age (22). Due to a loss of elastin and collagen fibres or constant exercise of the muscles underneath the skin – particularly notorious here are the laughter lines – wrinkles occur more frequently. The skin is therefore a good example of the difference between the physiological ageing process and the actual age of a person – anyone who has worked a significant amount the sun in the course of his or her life will already have leathery and wrinkled skin at a young chronological age (23). Furthermore, this example can also contribute to an understanding of extrinsic and intrinsic ageing. Intrinsic ageing is difficult to influence, it is largely genetically predetermined, while extrinsic ageing is shaped by external influences. But not every extrinsic impact is synonymous with an externally visible

impact. There can also be extrinsic influence at the cellular level. Consequently, lifestyle factors such as diet, exercise, smoking behaviour and stress or biomolecular aspects like oxidative stress and mitochondrial dysfunction, DNA damage and repair mechanisms or telomere functioning play a major role (21, 22).

Many researchers choose to lay a particular focus on the centenarians and the "escapers" among them for the reasons mentioned above. Their main line of questioning is whether these people exhibit genes that other people are missing or whether mutations cause genes in healthy centenarians to work differently than in people who do not reach this age (24). If differences were to be found here, this could indicate molecular signalling pathways that could be very important in the ageing processes (21, 24).

In order to remain within the scope of this dissertation, only one example of such molecular signaling pathways will be presented here. One approach to elucidate the mechanisms that control intrinsic/physiological ageing is to screen DNA for genes whose expression changes with age, so-called age-related genes (24). Zahn et al. examined skeletal muscles for these age-related genes and were able to establish a molecular profile – and thus a biochemical differentiation – of 250 of these genes (25). This profile was related not only to the physiological age of the specific tissue, but also to the chronological age. The researchers compared the molecular profile they found with profiles of brain and kidney tissue already described in the literature and found astonishing similarities (25). These similarities suggest that there are not only genes that control the ageing of tissue (e.g. the ageing of muscles, kidneys or brain), which can also vary greatly within an individual. Rather, some of these genes are responsible for the ageing of the entire individual (25).

Doctors and therapists who treat old people are therefore faced with a wide variety of challenges. They have to take into account the inter- and intra-individual heterogeneous changes that are based on heterogeneous inter- and intra-individual mechanisms and, in particular, be able to interpret their unpredictable clinical relevance for the patients and their individual risk of mortality or loss of independence (21, 26, 27). So, the goal is to tailor therapeutic approaches (21).

2.4 Resilience

The previous section highlighted the challenge that the individuality of ageing entails. There are approaches and indicators that scientists hope to apply to predict which individual will face which ageing process, which could be a breakthrough in the prevention of age-related diseases and limitations. However, individuality does not manifest only in biology and the biochemical processes of ageing, but also in psychological aspects (28). Body and mind represent a union and far too often, in medicine, the body is treated while the mind is sidelined. And just as every human body ages differently, so does every mind (7). This is where the concept of "resilience" comes into consideration. "Resilience" refers to the ability and capacity of the individual to react to trauma or stress and to recover from it, until the previous physical and mental state is restored (29).

Several studies in fundamental biological and medical research (30, 31) have found indications that there is a systemic, physiological resilience system in addition to individual resilience. If this systemic resilience could be made measurable – e.g. using dynamic resilience biomarkers (29) – this could provide doctors and nurses with indicators to dynamically measure the recovery potential of each individual patient and to intervene directly in the event of changes or an imminent overstrain of the system. However, a serious disease or a hospital stay that results in the loss of independence, even if it is only temporary, is extremely stressful (32, 33).

It has been shown that a slowdown in recovery from an operation or from an acute illness is an indication of the exhaustion of individual resilience and thus a red flag (29). Thus, the dynamic resilience in Geriatrics could be of great importance for the prevention of adverse events in the context of treatments or operations. If the origin and functioning of how systemic resilience works and where it starts were understood, this could provide additional opportunities to strengthen the system and enable more people to grow old as "escapers" (8).

We are living longer and longer, but everyone ages differently. Body and mind are faced with a wide variety of challenges, to which everyone reacts differently, and which affect each of us differently. So, it is clear that there cannot be just *one* treatment for a disease that will work for *every* old person. The keyword is: multidimensionality. To be able to give an old person the proper treatment, we need to know their psychological resilience, their physical abilities, their functional reserves and their social relationships, in order to make the best individual decision for each patient. This is the task of Geriatric Medicine in close

cooperation with every medical specialty that treats older patients – so simple and yet so complex (34-38).

2.5 The Development of Geriatric Medicine

2.5.1 Definition

The term Geriatrics is a combination of the ancient greek word γερων (geron; translated: old person) and ιατρεια (iatreia; translated: medical science). The first mention of the term and the first publications in the geriatric discipline date back to the United Kingdom in the 19th century (39). Up to that point, it was simply not necessary to designate the field of Geriatrics – people were cared for within the family circle, in monasteries or in poorhouses. Many patients did not reach old age and rehabilitation possibilities for older patients were rare. The older the people and especially the better the medical treatment and the equipment of the hospitals became, the more Geriatrics became of interest to the medical profession.

2.5.2 Medical treatment of older patients, past and present

It was less than 100 years ago, in 1943, when Marjory W. Warren published an article in the *British Medical Journal* with the title, "Care of Chronic sick - A case for treating chronic sicks in blocks in a general hospital" (40). The demand that the doctor makes in her article is taken for granted today. She calls for the separate accommodation for the younger chronically ill from the older chronically ill patients and special training of medical and nursing students in dealing with these patients. In addition, she suggests a special diet for the older patients' departments, additional linen for many incontinent patients, staff to help patients cope with daily tasks, and better equipment with walking crutches, wheelchairs and tables for recreation (40).

In the same article, Marjory Warren also presents her “Classification of the Chronic Sick” (40):

> “1. Chronic up patients – that is, patients who get up part or whole days and get about it with some help, but who cannot manage stairs.
>
> 2. Chronic continent bed-ridden patients.
>
> 3. Chronic incontinent patients – such wards are allocated only on the female side.

4. Senile, quietly restless and mentally confused or childish patients required cot beds for their own safety, but not noisy or annoying others.

5. Senile dements – requiring segregation from other patients. “

What was relevant 78 years ago is still relevant today. Of course, this classification is not applicable to the treatment of older patients today, but it is still accurate. After Marjorie Warren established the cornerstones of Geriatric Medicine for the scientific world, other geriatricians followed her, most of them also British (41). Cosin fought for early mobilization of bedridden patients after operations (42, 43) and Howell incorporated the clinical aspects of the ageing process of people into the treatment of his patients (44). These principles were established over 70 years ago, but are still followed one-to-one today (41).

2.6 Modern Geriatric Medicine

There has been no standstill in Geriatric Medicine in recent decades. As already described in the first sections of this thesis on the biochemical processes of ageing and resilience (Section 1.4), geriatricians and scientists are now striving to provide tailored interventions for the needs and diseases of older patients. The approach is not disease-oriented, but patient-oriented.

Certainly, in patient-oriented treatment, the underlying diseases must also play a role. Nevertheless, the needs of the patient within this treatment must also be taken into account. Do the drugs the patient takes have side effects such as dizziness or weakness? Is the patient still able to go about his or her daily routine or is he or she particularly at risk of falls as a result of the treatment or is he or she at risk of becoming immobile? These questions are only some of many examples which demonstrate that the treatment of an underlying disease of an old patient cannot be the same as for a young patient. This is where the cooperation of Geriatric Medicine and high-performance Internal Medicine or surgery needs to take place. In close cooperation, a complex modern treatment can be carried out together with the consideration of the unique characteristics of older people.

Thus, geriatrics today has two guiding concepts: multidimensionality and interdisciplinarity.

2.6.1 The concept of frailty

Frailty is one of the key concepts in modern Geriatric Medicine (45). It describes a state of vulnerability, which is the result of a steady loss of physiological capacity over the course of life (46). A frail patient has no intrinsic capacities and resources left to respond to extrinsic stressors, such as an illness, or any loss of independence. Frailty is therefore also seen as the most extreme form of the ageing process (45) and is associated with multiple adverse outcomes like fall (47), institutionalization to long term care (48), hospitalization (49), impairments in cognition (50), affective disorders (51) and reduced life expectancy (52).

So far, there is no standard definition of frailty. Use of the term in scientific literature began in the 1990s and potential definitions as synonyms with disability (53), comorbidities (54) or simply high age (55) were published. However, the concept of frailty goes much further than a mere comorbidity. The two approaches that were crucial for today's definitions and understanding of frailty were the phenotype approach developed by Fried and colleagues (56) and the stochastic approach of Rockwood and colleagues (46). The frail phenotype, according to Fried et al., has five main characteristics (56):

1. **Weight loss** (more than 10 pounds in the last year, *unintentionally*)

2. **Exhaustion** (measured using the CES-D Depression Scale)

3. **Physical activity** (Any form of physical exercise, such as sport, housework, gardening, etc. measured in kilocalories (kcal) and divided for men (<383 kcal per week) and women (<270 kcal per week))

4. **Walk time** (Gait speed – also divided for men and women)

5. **Grip strength** (stratified for men and women and body-mass-index (BMI) quartiles)

The problem with this definition, which has been extensively validated worldwide, is that the symptoms are one-sided in favor of the physical aspects: According to Fried et al., frailty is a state of very high physical vulnerability (56). Other dimensions, such as cognition or social aspects, are not examined in this model.

The stochastic approach of Rockwood and Mitnitski incorporates deficits in a wide variety of domains and puts them into a mathematical relationship, the frailty index (57). This correlates with a variety of outcomes such as mortality, hospitalization or morbidity. Since

the researchers have made use of the stochastic characteristics of ageing, the index can be influenced not only negatively (by more deficits) but also positively (by robust attributes). This is remarkably close to reality, because frailty is not to be understood as a final dichotomous state but as a continuum (46, 57).

There are also new approaches to characterizing frailty as multidimensional, specifically by thinking of a person as having three layers (21, 58). The inner layer represents the biomolecular side, the physiological aspects of ageing. The middle layer represents the biomarkers and the initial pathophysiological changes that an organism undergoes through ageing and frailty. Neurodegeneration, weight loss, sarcopenia or fatigue would fall under this rubric. And the outer layer, the visible layer, which contains the functional aspects of frailty. In this theory, the inner layer affects first the middle layer, and then finally the outer, visible layer. Here, the emphasis is on the changes and loss an individual has already undergone by the time the outer layer is affected, making clear that in order to treat or prevent frailty, it necessary to provide assisting services not only to the outer layer, but also to make crucial interventions that affect the inner layers (21).

In summary, since the scientific world has not yet reached a consensus on a unified definition of frailty, we are able to make three key statements (59):
First, frailty is multidimensional. Not just physical, but also functional, social and psychological factors play a major role in its development (45).
Second, frailty is related to growing old. But not every person who grows old becomes frail. Frailty is the most significant consequence one can suffer during the ageing process (45).
And third, frailty is a dynamic condition.

In addition, it is clear that frailty is associated with more frequent hospitalizations and higher costs to the health care system (46, 56). Frailty also carries the risk of more frequent rehospitalizations in addition to prolonged hospital stays (60). Thus, a major task of 21st-century medicine will be to understand the concept of frailty, identify patients and, optimally, treat them before they reach a frail state. But how can physicians and nurses identify frailty when there is no standard definition? With a comprehensive approach.

2.6.2 The Comprehensive Geriatric Assessment

The Comprehensive Geriatric Assessment (CGA) has become the gold standard of modern Geriatric Medicine, it originated in the UK in the 1940s, during the advent of Geriatric Medicine (61). Ellis et al. defined the CGA in 2017 as “a multi-dimensional diagnostic and

therapeutic process that is focused on determining a frail older person's medical, functional, mental, and social capabilities and limitations with the goal of ensuring that problems are identified, quantified, and managed appropriately" (34). For a concept with many dimensions – as is the case with frailty – a tool is needed that incorporates these dimensions (34). In addition, the CGA can do something that simple screenings cannot do: provide a treatment approach for Geriatric Medicine (34).

The first systematic review of randomized controlled trials (RCTs) on the CGA, however, was published in 1993 (62). Since then, scientists have been trying to unify and standardize the colorful and broad field of CGA, a necessary step because although there are features in common and specifications as to what a CGA must contain, there is no one standard questionnaire – it is to be understood as a concept and basis for the treatment of geriatric patients. In the following list, the generally accepted characteristics that are common to all studies dealing with Geriatric Medicine or geriatric patients will be outlined (34):

1. **Expertise**: Staff performing the CGA are experienced, trained and confident in performing and interpreting the results.

2. **Multidisciplinary team:** Nurses, doctors (ideally with geriatric training or geriatricians), pharmacologists, social workers, occupational therapists and physiotherapists are needed to gain a comprehensive picture of the patient.

3. **Holistic approach:** The physical, psychological, functional and social capacities and needs of the patient should be recorded.

4. **Treatment plan:** On the basis of the information obtained, a treatment plan should be drawn up together with the patient, his or her relatives and the multidisciplinary team.

5. **Evaluation:** On the basis of weekly team meetings, the established treatment plan is reviewed, and progress or failures are documented and discussed. If necessary or at the patient's request, the treatment plan must be adjusted.

Providing patients with a CGA that includes the characteristics described above requires a lot of training for the team and a setting that facilitates such interventions. This setting is most often found today in acute geriatric wards – a rather German construct, which combines a geriatric clinic with rehabilitation – or geriatric hospitals, but also in stroke units and orthogeriatric wards (35). Outside such specialized settings, while the Geriatric

Assessment is known to most health care professionals, its implementation varies greatly and is hardly standardized (35). Thus, as described in Section 1.2, society is ageing, and hospital admissions of older and potentially frail patients will therefore increase. They will be treated in emergency rooms, on high-performance internal medicine or surgical wards and in outpatient care settings, in which a CGA is not usually performed. Screenings, such as the “Identification of Seniors at risk” (ISAR) screening (63) or the Barthel Index (64), on the other hand, are widely used, even outside Geriatrics. These questionnaires briefly assess the patient's deficits, e.g. in the area of daily living or mobility (64). But a clear distinction must be made here: Screening is not the same as assessment. A screening can reveal deficits or identify patients at risk, but it is not possible to treat patients on their basis. However, treatment is possible on the basis of a Comprehensive Geriatric Assessment, i.e. a multidimensional exploration of the patient. This is because deficits are identified, inquiries are made into diseases and treatments, the patient's social and psychological aspects are explored, and his or her physical and functional capacities are surveyed, thus drawing a multidimensional picture (34, 65-67). On this basis, the best possible treatment recommendation can be made and implemented. For example, a patient is unable to wash and dress him- or herself in the morning. How long this has been the case, whether he or she has a short-term or long-term condition that limits his or her daily living abilities, or whether he or she has help from family or a home care provider remains unclear, even though a screening has been done. A detailed picture can be drawn here by a CGA, upon which tailored therapy options can be built (68).

In order to guarantee the best possible treatment for older patients in these settings, versions of CGA are currently being developed that can be easily and effortlessly integrated into the daily work of non-geriatric wards. One of these projects is the Frailty Index by Pilotto et al. (45) which is now used worldwide and interdisciplinarily: The Multidimensional Prognostic Index (MPI) (69, 70).

2.6.3 The Multidimensional Prognostic Index (MPI)

The MPI aims to draw a multidimensional picture of the patient. A total of 8 items are considered for the calculation of the index. These are: Katz’ Activities of Daily Living (ADL) (71), Lawton’s Instrumental Activities of Daily Living (IADL) (72), the Mini-Nutritional Assessment – Short form (MNA-SF) (73), the short portable mental status questionnaire (SPMSQ) (74), the Exton Smith Scale (ESS) (75), the cumulative illness rating scale – comorbidity index (CIRS-CI) (76), the patient’s living conditions (with relatives/spouse, with

private attendant/institutionalized, alone) and the total number of drugs the patient takes per day.

All values of the indices are divided into the three categories ("low risk", "medium risk" and "high risk") and consequently receive 0, 0.5 and 1 points. The results are added together and divided by the number of indices (8). The MPI thus gives continuous values between 0-1, which are divided into three risk groups MPI-1 (0.00-0.33), MPI-2 (0.34-0.66) and MPI-3 (0.67-1.00) (69).

The MPI is now a globally-used and very well-validated tool for long-term mortality one month and one year after hospitalization, for the length of hospital stay and mortality during hospitalization (77) and for the chance of rehabilitation and institutionalization also one month and one year after the MPI has been carried out (78). Its accuracy has also been proven for a wide range of diseases in older people, such as pneumonia (79), dementia (80), chronic renal failure (81), heart failure or ischemic heart attack (82). In the MPI-Age project funded by the EU, the MPI was conducted mainly in geriatric departments and clinics throughout Europe (83). However, as mentioned earlier, most frail older patients are treated in internal medicine or other specialties, mostly by physicians and nurses without a background in Geriatrics and without performing a CGA upon patient admission. This was the basis for a study, part of the results of which are the subject of this dissertation. After all, the demographic change, the lack of geriatric departments and rehabilitation clinics and the complexity of the multimorbidity and possible frailty of these patients all require multidimensional approaches and geriatric teams not only in specialized departments, but in all clinics and specialist departments (34, 36, 37, 84).

Thus, there are also approaches to make the MPI available to community dwellers over the age of 65, either through their general practitioner (85) or as a questionnaire to be completed independently (86, 87). The focus of these studies is on early detection and prevention of frailty, which enables targeted support by therapists, family and society to avoid hospitalization or adverse events such as falls, sarcopenia and malnutrition. Greater involvement of the preclinical areas could save resources for the clinical area and patients requiring greater professional attention. It could also prevent pre-frail people from becoming frail (88).

Time is one of the biggest concerns in hospitals and by involving patients and their families in the process of prevention, a greater sense of self-determination could be created, which in turn could increase compliance. The ultimate goal, as is well known, is to avoid any non-

essential hospital stay – as these stays are a stressor in themselves for older people (32, 33) – in order to maintain the independence of patients for as long as possible.

2.7 The new interdisciplinarity – co-management in everyday clinical practice

The foundations of Geriatric Medicine, laid in 1940 by Dr. Marjory Warren (40), by her colleagues Fried & Rockwood (46, 56) with the characterization of the term frailty, and by Rubenstein (37) with the implementation of CGA, firmly established in the 1990s to 2000s, are still valid today. However, the wish expressed by Dr. Warren, namely the firm anchoring of Geriatric Medicine in the curriculum of medical studies and the recognition of Geriatrics as an important and aspiring discipline (40), has unfortunately not yet been entirely fulfilled (41). No geriatrician can work without treating the often high number of comorbidities of his patients. And no specialist in neurology, internal medicine or orthopedics without geriatric expertise can treat the majority of his patients and achieve the optimal outcome. The keyword is co-management of patients and as one key concept of this dissertation, the following section will discuss the most frequent interfaces of the above-mentioned disciplines with Geriatric Medicine.

2.7.1 Geriatric Medicine and Internal Medicine: aspiration pneumonia

Pneumonia is a frequent reason for hospitalization of older patients and one of the most frequent adverse events during hospitalization of older patients. The classification of pneumonia is manifold. A distinction is made between community-acquired pneumonia (CAP, onset of symptoms already during hospitalization or up to 48 hours after hospitalization) and healthcare-associated pneumonia (HCAP, onset of symptoms 48 hours after hospitalization). In this paragraph the focus will be on a specific cause of pneumonia, which often occurs in older and frail patients: aspiration pneumonia. The distinction here also applies: community-acquired aspiration pneumonia (CAAP) and healthcare-associated aspiration pneumonia (HCAAP) (89). The etiology of aspiration pneumonia is explained by repeated microaspiration of bacteria from the oropharynx or stomach (90). Not every aspiration causes pneumonia, but repeated aspiration in patients with dysphagia or poorly-controlled gastroesophageal reflux combined with a suppressed cough reflex and insufficient glottal closure leads to these clinical symptoms (90).

According to a systematic review from 2011, the risk factors for aspiration pneumonia are: age, sex, pre-existing lung diseases, severe dementia, angiotensin I-converting enzyme deletion/deletion genotype and poor oral hygiene (91). If these risk factors are present,

symptoms of pneumonia (typical symptoms include fever, cough and dyspnea, which may be absent in atypical pneumonia) and evidence of infiltration in the imaging, the diagnosis of an aspiration pneumonia can be made (89). The differentiation between CAAP and HCAAP is necessary here, especially with regard to the pathogen profile. For HCAAP, anaerobic pathogens such as Pseudomonas aeruginosa or multi-resistant pathogens that require a different therapy than the empirical pathogens of CAAP must also be considered.

The German S3 guideline "Behandlung von erwachsenen Patienten mit ambulant erworbener Pneumonie und Prävention" recommends the parenteral application of ampicillin/sulbactam, clindamycin plus group II/III cephalosporins and moxifloxacin for the treatment of aspiration pneumonia (92). It is pointed out in the guideline that there are no uniformly-accepted diagnostic criteria for aspiration pneumonia and that the criteria listed in the guidelines account for 13-15% of CAP, in nursing home residents up to 50%. The age of the patients is not considered in the therapy recommendation (92).

The severity and seriousness of aspiration pneumonia is shown in a study from 2013, in which patients with CAAP (N=510) were compared with patients with CAP (N=2584) (93). The CAAP patients were significantly older (77 vs. 59 years), had a significantly higher 30-day mortality (19.0% vs. 4.2%), were hospitalized significantly more often (99.8% vs. 57.8%) and had to be treated in an intensive care unit significantly more often (37.1% vs. 14.2%) (93). At present, there is only a small number of published studies for the prevention of aspiration pneumonia. There are approaches for improved oral hygiene (94) or administration of aromatherapy (95) that show promising results, but these still need to be validated in large-scale studies.

2.7.2 Geriatric Medicine and Surgery: falls

Falls, just like pneumonia, are a common reason for hospital admission of older patients (community-dwellers as well as nursing-home residents) and frequent complications that occur during a hospital stay (96). A fall of an older person cannot be compared to the fall of a child who hurts their knees and jumps back onto its bike a short time later: Three quarters of deaths from falls in the United States involve people over 65 years (96). Repetitive falls and general instability are a reliable parameter for admission to a long-term care facility (97). Falls can lead to fear of falling, loss of independence and often to fractures, such as a fracture of the femoral neck (98).

A fracture of the femoral neck generally requires surgery. Undisplaced fractures – regardless of the age of the patient – are treated with internal fixation (2–3 screws or pins), (99) while displaced fractures in older patients are treated with complete or partial arthroplasty (99). Surgery alone is a great risk for this group of patients due to the anesthesia – with consideration of previous cardiac or respiratory disorders – and the often reduced physical and psychological capacity to react to trauma. A fracture of the hip additionally makes every patient who had been independent before the trauma dependent on help for the activities of daily life, presenting patients with great changes and challenges, not only physically but also mentally and socially (100). For orthopedists, physiotherapists and geriatricians, there is a large field of work here and demand will certainly increase in the coming years. A return to the patient's condition before the fall is possible, but it is a long process and not always a given. A larger focus must be devoted to the prevention of falls and the identification of patients at risk in order to avoid their having to undertake the long road to convalescence after falls, fractures and surgery (96). A close cooperation of the orthogeriatric team with the patients and their relatives is key and is already practiced in most orthopedic hospitals.

2.7.3 Geriatric Medicine, Pharmacology and Internal Medicine: polypharmacy

Polypharmacy is one of the best examples of the complexity of treating older, multimorbid patients and at the same time shows the crucial nature of an interdisciplinary and multidimensional approach. Polypharmacy is defined as prescribing and taking five or more drugs daily (101). If a patient suffers from two chronic diseases (such as arterial hypertension and diabetes mellitus type II), this number of drugs is quickly reached. Often, the intake of many drugs leads to side effects or interactions between them, and new drugs must be prescribed to treat these adverse events. Consequentially, there is an ever-increasing number of drugs. An additional problem is the under-representation of patients >65 years or >80 years in clinical trials for drug registration and tolerance. Although this patient population is most often prescribed drugs, the substances are often not approved for use by the older generation or tested for their tolerance and effectiveness (102, 103).

In the meantime, there are several approaches in Europe to prevent over-prescription, to eliminate inadequate prescriptions (potentially inappropriate medications – PIMs) and to prevent the omission of a prescription to avoid a polypharmacy, although treatment or prevention would be necessary (potential prescribing omissions – PPOs) (104). These include the FORTA (Fit for the Aged) list (103), the PRISCUS (Latin for “time-honoured”) list (105) and the START (Screening Tool to Alert Doctors to start the Right Treatment) &

STOPP (Screening Tool of Older Persons Potentially Inappropriate Prescription) criteria (106).

All of these lists contain negative evaluations, while the FORTA and the START criteria also contain positive evaluations. The FORTA list classifies over 200 medications intended for long-term treatment into categories A (Absolutely), B (Beneficial), C (Careful) and D (Don't) (102). The START & STOPP- criteria include 65 PIMs and 22 PPOs, by consensus of a panel of clinical experts (107). With the help of an expert consensus, the PRISCUS list compared the risks of prescription, possible alternatives and instructions for use with a prescription for 83 drugs that were considered as PIMs (105). The processing and modification of a patient's medication list based on the above-mentioned instructions for action requires close cooperation between all health care disciplines. Only if the changes are carried out by *consensus* can it be assured that one discipline will not de-prescribe medication that another discipline then re-prescribes.

2.7.4 Geriatric Medicine and Neurology: dementia

Dementia represents one of the greatest social, medical and societal challenges of an ageing society. First of all, dementia is a very personal challenge for the patient and his or her relatives. Secondly, patients with dementia also have an increased risk for infections, e.g. after an operation, such as pneumonia or urinary tract infection (108), since the symptoms often manifest themselves atypically and the patient cannot adequately determine what is wrong with him or her. In addition, most patients with dementia cannot be given a curative therapy. For Alzheimer's disease, acetylcholinesterase inhibitors and N-methly-D-aspartate (NMDA) antagonists are available, but these can only slow the progression of the disease by a few months (109).

When it comes to dementia, the medicinal focus is on prevention. In 2019, for example, the WHO issued for the first time a guideline on "Risk reduction of cognitive decline and dementia" (110). Since patients usually only visit a doctor at the onset of symptoms in themselves or upon their relatives' urging, the preventive measures are already obsolete in this case.

There are studies showing that with regard to the multimorbidity of older patients, the diagnosis of dementia has a greater impact on health care costs than diabetes mellitus, hypertension and osteoarthritis (111).

2.7.5 Geriatric syndromes

A medical syndrome is clearly defined, but when this syndrome occurs in older patients, the definition is often – as illustrated in the last four sections – difficult, as is the allocation to medical specialties, highlighting the difference between medical syndromes and geriatric syndromes (112). Medical syndromes, on one hand, are linear – symptoms are followed by diagnostics, a diagnosis is followed by a treatment. Geriatric syndromes, on the other hand, are multidimensional (113). They include the diagnosis, the symptoms, the capacities of the patient and the patients' individual treatment needs. This conception of geriatric syndromes makes it possible to summarize the acute illness, the underlying multimorbidity or chronic diseases and the age-related physiological changes (114). These syndromes include instability, cognitive impairment, polypharmacy and swallowing disorders (114). Thus, all of the conditions described above are interfaces of Geriatrics with both geriatric syndromes and other medical disciplines, which illustrates the multidimensionality these syndromes are intended to represent. The focus here is on the treatment of a syndrome and the patient, and thus also on close interdisciplinary co-management.

Recent studies have shown a correlation between geriatric syndromes, patient prognosis and quality of life (114, 115). These results suggest that an inclusion of geriatric syndromes in the evaluation of geriatric patients upon admission to hospital and during their stay should be considered – recording geriatric syndromes in non-geriatric settings could be the first step in implementing a CGA into clinical practice because these syndromes, regardless of the patient's underlying disease, are found in every medical department that treats older patients.

2.8 Integration of Geriatric Medicine and the MPI into the clinical routine of Internal Medicine

2.8.1 The MPI-InGAH studies

The MPI-InGAH (Multidimensional Prognostic Index – Influence of a Geriatric Assessment on Hospitalisation of multimorbid, older patients) study was developed to establish a CGA on a ward for Internal Medicine, to present its possibilities and thus create new opportunities for interdisciplinary cooperation that did not exist before. The study was carried out between August 2016 and August 2019 on the nephrological acute ward of the Clinic II for Internal Medicine, Nephrology, Rheumatology and Diabetology of the University Hospital of Cologne.

In addition to the MPI, the focus of the study was on the admission diagnosis, the length of hospitalization, the patients' medications, examinations during the inpatient stay and the source of referral. After discharge, a follow-up questionnaire was carried out and further telephone follow-ups were added after 3, 6 and 12 months, recording changes in medication intake, renewed hospitalization, increased need for care or falls of patients.

A total of 500 patients were prospectively enrolled in the study. The second amendment, which is the basis of the publication and thus the basis of this thesis, represented an additional third CGA with MPI calculation 7–10 days after hospital admission. The aim of this study was to identify changes in the multidimensional prognosis during hospitalization and to investigate their prognostic relevance, if any, as well as to show how the newly-gained knowledge can be used for a better prevention of adverse events during hospitalization.

There have already been national and international papers on the MPI-InGAH study (114, 116), in addition to the present publication.

3. Presentation of the underlying problem

In recent decades, Geriatric Medicine has made immense progress in the classification of older patients (45, 56). And there is a consensus that a CGA is necessary in order to best understand the geriatric patients' needs, goals and treatment options (34). However, there is a major shortcoming in the indices used: They are static. Once recorded, they remain so until they are measured again, and this usually happens at admission and on discharge. Progress or regression of the patients is nevertheless documented during the treatment and discussed in the therapist's consultation.

The first aim of this thesis is to understand the changes of the MPI during hospitalization of patients on a high-performance Internal Medicine ward. It is intended to examine which group of patients' experiences worsen their multidimensional prognosis during hospitalization and why. At the same time, of course, the patients whose prognosis improves or remains the same will be analyzed. With the help of this information, risk groups could be identified and recommendations for everyday clinical practice could be developed. In this way, the needs of older patients could be included in the treatment of their underlying internal condition or admission diagnosis. In other words, to create interdisciplinarity, in this case between Geriatric Medicine and Internal Medicine.

The second aim of this thesis is to present the already-established interdisciplinary departments that exist within Geriatrics in Germany and to compare them with the Cologne pilot project of University Geriatric Medicine (67). In this section, it is worked out where co-management between the geriatric team and the specialist in Internal Medicine is already taking place and what advantages the collaboration offers for both disciplines and the patients.

The results of the study on which this thesis is based are presented in the original publication shown below. Results that did not find their way into the paper are presented subsequent to the publication in the following section.

4. Results

4.1 Published original work

Received: 19 June 2020 | Accepted: 3 January 2021

DOI: 10.1111/ijcp.13989

ORIGINAL PAPER

GERIATRICS

THE INTERNATIONAL JOURNAL OF CLINICAL PRACTICE WILEY

Role of a multidimensional prognosis in-hospital monitoring for older patients with prolonged stay

Lena Pickert[1] | Anna M. Meyer[1] | Ingrid Becker[2] | Annika Heeß[1] | Nicolas Noetzel[1] | Paul Brinkkötter[1] | Alberto Pilotto[3,4] | Thomas Benzing[1,5] | Maria C. Polidori[1,5]

[1]Ageing Clinical Research, Department II of Internal Medicine and Center for Molecular Medicine Cologne, University of Cologne, Faculty of Medicine and University Hospital Cologne, Cologne, Germany

[2]Institute of Medical Statistics and Computational Biology, Faculty of Medicine and University Hospital of Cologne, Cologne, Germany

[3]Department of Geriatric Care, Orthogeriatrics and Rehabilitation, Frailty Area, E.O. Galliera Hospital, Genova, Italy

[4]Department of Medicine, University of Bari, Bari, Italy

[5]Cologne Excellence Cluster on Cellular Stress-Responses in Aging-Associated Diseases (CECAD), University of Cologne, Faculty of Medicine and University Hospital Cologne, Cologne, Germany

Correspondence
Maria C. Polidori, Ageing Clinical Research, Department II of Internal Medicine and Cologne Center of Molecular Medicine, University Hospital of Cologne, Cologne, Germany.
Email: maria.polidori-nelles@uk-koeln.de

Abstract

Objectives: The Multidimensional Prognostic Index (MPI) is a prognostic tool—amongst others—validated for mortality, length of hospital stay (LHS) and rehospitalisation risk assessment. Like the Comprehensive Geriatric Assessment (CGA), the MPI is usually obtained at hospital admission and discharge, not during the hospital stay. The aim of the present study was to address the role of an additional CGA-based MPI measurement during hospitalisation as an indicator of "real-time" in-hospital changes.

Study design and main outcome measures: Two-hundred consecutive multimorbid patients (128 M, 72 F, median age 75 (78-82)) admitted to an internal medicine ward of a German metropolitan university hospital prospectively underwent a CGA and a prognosis calculation using the MPI on admission and discharge. Seven to 10 days later, an intermediate assessment (IA) was performed for patients needing a longer stay.

Results: The median LHS was 10 (6-19) days. As expected, patients who received an IA had poorer prognosis as measured by higher MPI values ($P = .037$) and a worse functional status at admission than patients who had a shorter stay ($P = .025$). In case of prolonged hospitalisation, significant changes in the MPI were detected between admission and IA, both in terms of improvement and deterioration ($P < .001$). Different overtime courses were observed during prolonged hospitalisation according to the severity of prognosis ($P < .001$).

Conclusion: A CGA-based MPI evaluation during hospitalisation can be used as an objective instrument to detect changes in multidimensional health course. Prompt identification of the latter may enable quick tailored interventions to ensure overall better outcomes at and after discharge.

1 | BACKGROUND

The challenge of treating multimorbid older patients in order to achieve the best possible outcome is a central theme in medicine. It is widely known that hospitalisation itself is an additional risk factor for older patients regardless of their underlying disease.[1] Possible sarcopenia, malnutrition, delirium and polypharmacy often complicate and prolong the hospital stay.[2]

For older people living alone, there is also a risk of longer hospitalisation time.[3] Additionally, because of physiological age-related changes and frailty, adverse events after mild interventions occur more often than in younger adults and can lead patients into

a downward spiral—the so-called *geriatric cascade*—at the end of which death occurs.[4] Although hospitalisation–related risks in advanced age are well recognised,[5] there is still a substantial lack of evidence about the actions to be taken in clinical routine to avoid poor outcomes.[6] In general, the use of the Comprehensive Geriatric Assessment (CGA)[7] is associated with the improvement of a number of key performance indicators including mortality, re-hospitalisation, onset of cognitive impairment and depression and admission in long-term care facilities.[8,9] However, there are numerous barriers to the routine use of the CGA and related instruments in older multimorbid patients and its use is still largely confined to geriatric settings.[10] There is a gap between knowledge of multidimensional needs of older persons with disease and actual organ-centred interventions in usual care. In fact, the geriatric team usually addressing psychosocial and functional aspects beyond (and often behind) the medical burden,[4] remains to date the main instrument of geriatric medicine, not of the medicine of the older person. Accordingly, the CGA is used exclusively in geriatric settings, in its typical performance twice during hospitalisation: at admission and at discharge. However, recently the CGA-based Multidimensional Prognostic Index (MPI)[11] was shown to profoundly impact the characterisation of older multimorbid inpatients admitted to non-geriatric wards.[12-14] In the setting object of our investigation—an acute internal medicine ward of a large German university hospital—admitted patients undergo highly specialised, technology-based, innovative clinical approaches which fall usually within the terminological frame of "high-performance medicine" or "high care", but frequently display high potential for side effects in advanced age.[4,5]

The MPI has previously shown to enable the close monitoring of patients' trajectories after hospitalisation and potentially during hospital stay.[1,15,16] As it is not known to date whether an additional in-hospital MPI calculation aids the clinical evaluation of older multimorbid patients, this study was aimed at measuring the MPI not only on admission and at discharge, but also during the stay of inpatients undergoing "high-performance medicine" in an internal medicine department of a German metropolitan university hospital.

What's known

- The Multidimensional Prognostic Index (MPI) is associated with disease outcomes in advanced age and has been suggested to detect in-hospital disease course fluctuations.
- The Comprehensive Geriatric Assessment (CGA) upon which the MPI bases is usually performed at admission and discharge in geriatric settings.

What's new

- This is the first study adopting the CGA-based multidimensional prognostic evaluation at an additional timepoint with respect to the usual admission- and discharge-examination.
- The MPI evaluation one week after hospitalisation detects and quantifies in "real-time" overall health status changes and can be used to prevent hospital-related complications.

2 | PATIENTS AND METHODS

The study was registered at the German Clinical Trials Register (DRKS00013791) and complies with the Declaration of Helsinki. The Ethical Committee of the University Hospital of Cologne approved the study. All patients (or proxy respondents, when medical record indicated incapacity to give informed consent) signed informed consent to participate.

2.1 | Patients

Two hundred patients were prospectively enrolled in the study between June 2017 and November 2018. Recruitment was carried out in the Department of Nephrology, Rheumatology, Diabetology and General Internal Medicine of the University Hospital Cologne. Inclusion criteria were age over 70 years, at least two chronic diseases and a hospitalisation period longer than four days. Exclusion criteria were a refusal to participate in the study, language barrier and a hospitalisation period of less than 4 days.

2.2 | Comprehensive Geriatric Assessment and Multidimensional Prognostic Index

All patients were enrolled to undergo a CGA with a prognosis calculation using the MPI[11] as previously described.[12,13] Briefly, Activities of Daily Living (ADL),[17] Instrumental Activities of Daily Living (IADL),[18] Mini-Nutritional Assessment-Short Form (MNA-SF),[19] Short Portable Mental Status Questionnaire (SPMSQ),[20] Cumulative Illness Rating Scale (CIRS)[21] and Exton Smith Scale (ESS)[22]—as well as the number of drugs taken by the patient and living conditions[16,23]—were collected to calculate the MPI, which generates continuous values between 0 and 1. These can be divided into three risk groups, MPI-1 (0.00-0.33), MPI-2 (0.34-0.66) and MPI-3 (0.67-1.00), to inform low (MPI-1), medium (MPI-2) and high (MPI-3) risk of mortality, rehospitalisation, admission in long-term care facilities, increase of nursing needs amongst others, 1, 3, 6, 12 months after initial evaluation.[1,13,16,24]

For the purpose of this investigation, the CGA-based MPI was performed at admission and discharge as per standardised procedures in all patients[1,8,9,16] as well as at an additional timepoint after 7-10 days in patients needing a stay longer than one week (intermediate assessment, IA). If patients were about to be discharged on the 7th day of hospitalisation, the IA was not performed.

In all patients, main and secondary diagnoses, geriatric syndromes (including polypharmacy, instability, incontinence, inanition, immobility, irritability/depression, cognitive impairment, insomnia, impoverishment, swallowing disorders, chronic pain, sensorial impairment, irritable colon, iatrogenic disease, social isolation, fluid/electrolyte disorders and incoherence/delirium) and resources (physical resources, good living conditions, social, economic, competence-related, intellectual, spiritual, motivational, emotional and mnestic resources) were also collected as previously described.[13]

2.3 | Statistical analysis

The IBM SPSS 26 software was used for statistical analysis. Descriptive statistics are expressed using absolute numbers and relative frequencies for categorical variables and means (and standard deviation, SD) or medians (and interquartile range, IQR) for continuous variables. All continuous variables were tested for normal distribution using the Kolmogorov-Smirnov test and *t* test or non-parametric tests were used for comparisons amongst groups. Only the number of drugs taken at admission was normally distributed, all other continuous variables were not normally distributed. Rates were compared by Chi-square test or Fisher's exact test.

3 | RESULTS

3.1 | Study population

Of 200 patients, 36% were female. The median age was 78 (75-82) years and the average MPI at admission 0.52 (±0.19) points. The median length of hospital stay (LHS) was 10 (6-19) days and the mean number of medications taken was 9.4 (±3.7) per day. Diagnoses, other clinical characteristics including the most frequent geriatric syndromes observed in our sample are described in Table 1.

3.2 | MPI-prognosis at admission

Sixty-one % of the patients did not receive an IA, as they were discharged after 7-9 days. Thirty-nine % received an IA after 7-10 days. As displayed in Table 1, and as expected, patients with an IA because of prolonged stay showed a significantly poorer multidimensional prognosis at admission with respect to patients with a shorter stay (0.55 IA vs 0.50, **P = .037**). Activities of daily living (ADL) were significantly more impaired and decubitus risk (ESS) significantly increased in patients who had to stay in the hospital for an extended period compared with patients discharged at one week (ADL: 5 (3-6) vs 3 (2-5), **P = .006**; ESS: 16 (13-18) vs 14 (10-17), **P = .020**). Patients in the long-stay group suffered from significantly more geriatric syndromes (5 (3-7) IA vs 6 (5-8), **P = .001**) than those in the short-stay group. Amongst the most frequent geriatric syndromes, immobility was significantly more common in the long-stay group (65.4% IA vs 44.3%, **P = .004**) than in the short-stay group. In line with these findings, significantly more patients with an IA received home care (33.3% IA vs 18.0%, **P = .015**).

3.3 | MPI-Prognosis at discharge

While both patient groups displayed a mild overall health improvement at discharge, the mean MPI of patients without an IA was 0.48 significantly lower than for patients with an IA: 0.54 (**P = .032**). ADL values at the discharge of IA patients were significantly worse compared with those with a shorter stay (**P = .001**). The need for future rehospitalisation (52.8%, **P = .004**) and the number of requested home care services (13.9%, **P = .002**) after discharge were significantly higher in patients receiving an IA compared with patients who did not. MPI domains, distribution of the MPI risk groups and follow-up on discharge are displayed in Table 2.

3.4 | MPI changes during hospitalisation in patients receiving an IA

To assess characteristics and possible reasons for MPI changes between admission and discharge, patients who received an IA were divided for the analysis into three groups: improvement, no change and worsening—referred to as the comparison of the MPI at admission with the MPI at discharge. Three patients were excluded from this analysis because the MPI at discharge was missing. Patients having no change in MPI were significantly older than patients with a change (84 no change vs 78 improvement vs 77.5 worsening, **P = .017**). According to the admission status, patients who had a worsening of MPI were significantly more likely to come as new admission (60% worsening vs 31.6% no change, vs 22.2% improvement, **P = .001**), while patients who entered the ward as an internal referral (ie, admitted from an in-hospital department) had a significantly higher chance of having an improvement in MPI score at discharge than patients from an external ward (69.4% vs 2.8%, **P = .001**). Within the MPI domains, only for the ESS statistical significance could be found at the IA and discharge. Patients with a worsening of MPI had significantly lower ESS values at the IA than patients with an improvement (12.5 (10-16) worsening vs 16 (14.25-18) improvement, **P = .016**) and these values remained almost constant up until discharge (12.5 (10.25-15.75) worsening vs 16.5 (15.25-18) improvement, **P = .002**) (Table 3).

Patients whose MPI did not change between admission and discharge belonged mainly to MPI-2 (47.4%) and 3 (42.1%). The mean MPI at admission and discharge was 0.57, the IA showed a slight improvement to 0.54. This improvement, which was seen in 31.6% of the patients, was relativised until discharge (Figure 1).

Patients whose MPI improved between admission and discharge could be classified to MPI-2 (58.3%) and MPI-3 (41.7%), 77.1%

TABLE 1 Demographic data and MPI prognosis at admission

	Total (N = 200)	No intermediate assessment (N = 122, 61.0%)	Intermediate assessment (N = 78, 39.0%)	*P*-value
Demographic				
Age (y), median (IQR)	78 (75-82)	78 (74-82)	78 (76-83.5)	.428
Female, n (%)	72 (36.0)	41 (33.6)	31 (39.7)	.378
LHS, median (IQR)	10 (6-19)	6 (4.75-9)	19 (13-28.50)	**<.001***
Education (y), median (IQR)	12 (10-15)	12 (11-15)	12 (10-13)	.235
Level of Educational requirements, median (IQR)	2 (2-3)	2 (2-3)	2 (1-3)	.674
Admission status, n (%)				.161
New admission to hospital	90 (45.0)	62 (50.8)	28 (35.9)	
Transferred from internal ward	83 (41.5)	47 (38.5)	36 (46.2)	
Transferred from external ward	21 (10.5)	11 (9.0)	10 (12.8)	
Missing	6 (3.0)	2 (1.7)	4 (5.1)	
Reason for admission, n (%)				.453
Kidney failure	79 (39.5)	48 (39.3)	31 (39.7)	
Acute infection	45 (22.5)	29 (23.8)	16 (20.5)	
Respiratory disease	12 (6.0)	7 (5.7)	5 (6.4)	
Bleeding/Anaemia	9 (4.5)	7 (5.7)	2 (2.6)	
Cardiovascular disease	10 (5.0)	5 (4.1)	5 (6.4)	
Endocrinologic disease	8 (4.0)	5 (4.1)	3 (3.8)	
≥2 diagnoses on admission	127 (63.5)	81 (66.4)	46 (59.0)	.288
MPI groups, n (%)				.058
MPI-1	39 (19.5)	29 (23.8)	10 (12.8)	
MPI-2	107 (53.5)	66 (54.1)	41 (52.6)	
MPI-3	54 (27.0)	27 (22.1)	27 (34.6)	
MPI-value, mean (SD)	0.52 (0.19)	0.50 (0.19)	0.55 (0.17)	**.037***
MPI domains, median (IQR)				
CIRS	5 (4-6)	5 (4-6)	5 (4-6)	.690
ADL	4 (2-6)	5 (3-6)	3 (2-5)	**.006***
IADL	4 (2-7)	4 (2-7)	4 (2-7)	.396
MNA-SF	9 (6-11)	9 (6-11)	8 (6-10)	.237
SPMSQ	1 (1-2)	1 (1-2)	1 (1-2)	.827
ESS	15 (12-17)	16 (13-18)	14 (10-17)	**.020***
Number of medications	9 (7-12)	9 (7-12)	10 (7-13)	.237
Living conditions, n (%)				.299
With relatives (low risk)	131 (65.5)	85 (69.7)	46 (59.0)	
Institutionalised/private attendant (moderate risk)	17 (8.5)	9 (7.4)	8 (10.2)	
Alone (high risk)	52 (26.0)	28 (22.9)	24 (30.8)	
Geriatric Syndromes, n (%)				
Insomnia	106 (53.0)	63 (51.6)	43 (55.1)	.630
Polypharmacy (>6 drugs/d)	171 (85.5)	102 (83.6)	69 (88.5)	.342
Sensorial Impairment	105 (52.5)	61 (50.0)	44 (56.4)	.376

(Continues)

TABLE 1 (Continued)

	Total (N = 200)	No intermediate assessment (N = 122, 61.0%)	Intermediate assessment (N = 78, 39.0%)	*P*-value
Immobility	105 (52.5)	54 (44.3)	51 (65.4)	**.004***
Total number, median (IQR)	5.5 (4-7)	5 (3-7)	6 (5-8)	**.001***
Receiving Homecare, n (%)				**.015***
Yes	48 (24.0)	22 (18.0)	26 (33.3)	

Note: P-value was calculated with non-parametric methods comparisons for continuous variables, rates were compared by Chi-square test or Fisher's exact test, significant at 5% (*).

Abbreviations: ADL, Activities of Daily living; CIRS, Cumulative Illness Rating Scale; ESS, Exton Smith Scale; IADL, Instrumental Activities of Daily Living; LHS, Length of hospital stay; MNA-SF, Mini Nutritional Assessment-Short form; MPI, Multidimensional Prognostic Index; SPMSQ, Short Portable Mental Status Questionnaire.

experienced an improvement up until the IA. At discharge, 19.4% improved up to MPI-1 and 8.3% belonged to MPI-3 (Figure 1).

Patients whose MPI deteriorated between admission and discharge belonged to MPI-1 (35.0%) and MPI-2 (45.0%). In most (73.7%) patients, the prognosis worsened up until the IA. At discharge, 60.0% of the patients were assigned to MPI-2 and 35.0% to MPI-3, none was in MPI-1 (Figure 1).

The Delta-MPI—thus the absolute changes in the MPI score—was statistically significant between the three time points (admission, IA, discharge, ***P* < .001**).

From admission to IA there were major changes (−0.08 (±0.07) improvement, −0.02 (±0.06) no change, 0.08 (±0.11) worsening) compared with between IA and discharge (−0.03 (±0.05) improvement, 0.02 (±0.06) no change, 0.04 (±0.07) worsening) (Figure 2).

4 | DISCUSSION

The present study shows for the first time that the MPI detects in-hospital changes in the multidimensional health of older multimorbid patients. This vigorously supports the evidence that the MPI can function as a monitoring tool during hospitalisation,[15] especially for patients with a prolonged hospital stay. An IA after seven to ten days enables clinical professionals to monitor their patients not only on the basis of organ-related cut-offs, but *multidimensionally*, ie, related to the overall health. If any changes in the MPI are detected, actions can be taken in real-time in order to contrast any clinical deterioration. This observation is particularly relevant, for instance, in case older vulnerable patients are hospitalised, like in the present case, in a non-geriatric setting to undergo "high-performance medicine" as described above. The feasibility of the CGA-based prognosis evaluation also during hospitalisation substantially enriches the already broad spectrum of the MPIs' predictive ability with respect to critical healthcare outcomes including mortality, admission to long-term care facilities, (re)hospitalisation, nursing needs, LHS and healthcare resource use.[1,13,16,24]

This is—to our knowledge—the first study ever in which an IA was performed during the hospitalisation of older, multimorbid patients with prolonged hospitalisation. A previous study by Volpato et al.[15] calculated the possible course of the MPI during prolonged hospitalisation as a function of LHS and reported a high MPI-value at admission, an improvement of the MPI until discharge of patients, who were hospitalised for 1-6 days and a renewed increase until discharge for patients who stayed longer than 6 days.[15] This increase became higher the longer the patients were hospitalised. In contrast, our study showed no significant association between the changes in the MPI (improvement, no change or worsening) and the patients' LHS (***P* = .436**) (Table 3).

For the first time, this study shows that the course of hospitalisation is different for patients according to their initial MPI group at admission (Figure 1). We could observe almost no change for the MPI-2 and we showed that there was a significant improvement for MPI-3 and a significant worsening for MPI-1 (***P* = .006**) ((Figure 1)

Patients whose MPI worsened during a prolonged hospital stay were the youngest compared with patients whose prognosis remained stable or improved [77.5 years (74.25-82) worsening vs 84 (78-87) years no change vs 78 years (74.25-82) improvement, ***P* = .028**]. Patients whose MPI worsened during a prolonged hospitalisation mostly belonged to MPI-1 and −2 (35.0% and 45.0%, ***P* = .006**) and were most frequently hospitalised for acute kidney failure or acute infection (45.0% and 15.0%, *P* = .679). Patients who are admitted acutely to hospital often deteriorated in terms of activities of daily living,[25] physical resources and social support.[26] The fact that the deterioration was most evident in patients with the youngest chronological age shows that a stay in hospital is a high possibility of losing independence, especially for older people who have lived independently up to this point.[27] In addition, this might suggest that chronological health is less critical for the risk of poor outcomes than the multidimensional frailty status, of which the MPI is an indicator[28] and which is a surrogate marker of biological age.[29] In the clinical routine, younger patients might be intuitively considered more robust and fit and this way they may get suboptimal functional training during the hospital stay. Although this group is assumed to be the group with lowest risk of poor outcomes, it is, indeed—based on our findings—the real-risk group.[4,5] Therefore, a comprehensive evaluation and support of the patients during hospitalisation is highly important and should not be primarily based on chronological age.[27] If an IA

TABLE 2 MPI prognosis and follow-up on discharge

	Total (N = 200)	No intermediate assessment (N = 122, 61.0%)	Intermediate assessment (N = 78, 39.0%)	*P*-value[o]
MPI groups, n (%)				.091
MPI-1	44 (22.0)	33 (27.0)	11 (14.1)	
MPI-2	108 (54.0)	61 (50.0)	47 (60.3)	
MPI-3	42 (21.0)	24 (19.7)	18 (23.1)	
Missing	6 (3.0)	4 (3.3)	2 (2.6)	
MPI-value, mean (SD)	0.50 (0.18)	0.48 (0.18)	0.54 (0.18)	**.032***
MPI domains, median (IQR)				
CIRS	5 (4-6)	5 (4-6)	5 (4-6)	.279
ADL	4 (3-6)	5 (3-6)	4 (2-5)	**.001***
IADL	4 (2-7)	4 (3-7)	3.5 (2-6)	.136
MNA-SF	8.5 (3-11)	9 (2-11)	8 (3-11)	.585
SPMSQ	1 (1-2)	1 (1-2)	1 (1-2)	.837
ESS	16 (13-18)	16 (14-19)	16 (12-18)	.159
Number of medications	10 (8-12)	9 (7-12)	10 (7-13)	.315
Follow-Up at discharge, n (%)				
Patient alive	184 (92.5)	112 (91.8)	72 (93.5)	.763
Fall during hospitalisation	8 (4.4)	5 (4.5)	3 (4.2)	1.000
Rehospitalisation planned	73 (39.9)	35 (31.5)	38 (52.8)	**.004***
Institutionalisation requested	5 (2.7)	4 (3.6)	1 (1.4)	.650
Grade of Care requested	9 (4.9)	4 (3.6)	5 (6.9)	.486
Home care requested	12 (6.6)	2 (1.8)	10 (13.9)	**.002***
Medical consultation requested	163 (89.1)	95 (85.6)	68 (94.4)	.061

Note: P-value was calculated with non-parametric methods comparisons for continuous variables, rates were compared by Chi-square test or Fisher's exact test, significant at 5% (*).

Abbreviations: ADL, Activities of Daily living; CIRS, Cumulative Illness Rating Scale; ESS, Exton Smith Scale; IADL, Instrumental Activities of Daily Living; LHS, Length of hospital stay; MNA-SF, Mini Nutritional Assessment-Short form; MPI, Multidimensional Prognostic Index; SPMSQ, Short Portable Mental Status Questionnaire.

reveals deterioration in the MPI, immediate action can be taken. With respect to this, it should be noted that in the setting object of the present investigation, a nephrology department, an initial diagnosis of a nephrological disease is a frequent occurrence. This often represents an important turning point in patients' lives[30] and might contribute to the observed overall worsening, suggesting that not only known high-risk patients, but also apparently milder cases as new admissions[31] should be promptly helped to cope with the new diagnosis.

Patients whose MPI remained stable were, as described above, the oldest patients (84 years (78-87, **$P = .017$**) and belonged mainly to MPI-2 and −3 (47.4% and 42.1%, **$P = .006$**). The most frequent reasons for admission were, again, acute kidney failure or acute infection (42.1% and 15.8%, $P = .679$). Then why is not the prognosis of these patients worsening the same as the patients' prognosis mentioned above? When explicitly looking at the eventual occurrence of any acute clinical events causing the MPI-worsening,[29] it was not possible to detect any in-hospital events which occurred more frequently in the deterioration group than in the stable MPI

TABLE 3 MPI changes during hospitalisation in patients receiving an IA

	Improvement N = 36 (46.1%)	No change N = 19 (24.3%)	Worsening N = 20 (25.6%)	*P*-value°
Demographic				
Age, median (IQR)	78 (74.25-82)	84 (78-87)	77.5 (74.25-82)	**.017***
Female, n (%)	11 (30.6)	8 (42.1)	12 (60.0)	.100
LHS, median (IQR)	17.5 (13-22)	16 (13-26)	24 (12.25-33.5)	.436
Admission status, n (%)				**.001***
New admission	8 (22.2)	6 (31.6)	12 (60.0)	
Internal ward	25 (69.4)	8 (42.1)	3 (15.0)	
External ward	1 (2.8)	4 (21.1)	5 (25.0)	
Missing	2 (5.6)	1 (5.2)	0 (0.0)	
MPI-value, mean (SD)				
Admission	0.58 (0.14)	0.57 (0.17)	0.44 (0.19)	.073
Intermediate assessment	0.51 (0.16)	0.54 (0.19)	0.55 (0.19)	.684
Discharge	0.47 (0.14)	0.57 (0.17)	0.60 (0.17)	**.026***
Delta-MPI, mean (SD)				
Admission-intermediate assessment	-0.08 (0.07)	-0.02 (0.06)	0.08 (0.11)	**<.001***
Intermediate assessment-discharge	-0.03 (0.05)	0.02 (0.06)	0.04 (0.07)	**<.001***
Admission-Discharge	-0.11 (0.06)	0.00 (0.00)	0.12 (0.07)	**<.001***
MPI risk groups at admission, n (%)				**.006***
MPI-1 (low risk)	0	2 (10.5)	7 (35.0)	
MPI-2 (medium risk)	21 (58.3)	9 (47.4)	9 (45.0)	
MPI-3 (high risk)	15 (41.7)	8 (42.1)	4 (20.0)	
MPI risk groups intermediate assessment, n (%)				.857
MPI-1 (low risk)	6 (16.7)	4 (21.1)	4 (20.0)	
MPI-2 (medium risk)	19 (52.8)	7 (36.8)	9 (45.0)	
MPI-3 (high risk)	11 (30.5)	8 (42.1)	7 (35.0)	
MPI changes until intermediate assessment groups, n (%)				**<.001***

(Continues)

TABLE 3 (Continued)

	Improvement N = 36 (46.1%)	No change N = 19 (24.3%)	Worsening N = 20 (25.6%)	*P*-value°
No change	7 (19.4)	11 (57.9)	3 (15.0)	
Improvement	27 (75.0)	6 (31.6)	2 (10.0)	
Worsening	1 (2.8)	2 (10.5)	14 (70.0)	
Missing	1 (2.8)	0	1 (5.0)	
MPI risk groups at discharge, n (%)				.035*
MPI-1 (low risk)	7 (19.4)	2 (10.5)	1 (5.0)	
MPI-2 (medium risk)	26 (72.2)	9 (47.4)	12 (60.0)	
MPI-3 (high risk)	3 (8.3)	8 (42.1)	7 (35.0)	

Note: *P*-value was calculated with non-parametric methods comparisons for continuous variables, rates were compared by Chi-square test or Fisher's exact test, significant at 5% (*).
Abbreviations: LHS, Length of hospital stay; MPI, Multidimensional Prognostic Index.

group. This underlines the advantage of a multidimensional view on patients with respect to the only physical health condition and clarifies the fact that in advanced age a clinical worsening of the general conditions is usually not related to an easily identifiable nosocomial event.[6]

Patients' resilience might also play an important role. Resilience is the personal capacity to react to a stressor—eg, hospitalisation, an acute disease or a relapse of a chronic condition—and the ability to restore the original physical and mental state that the patient had before the stressor.[32,33] Resilience, however, is a factor that is very difficult to quantify,[34] which is why a CGA-based MPI during hospitalisation again seems to make sense in order to create an objective assessment of the patient's condition—physical, psychological, social and functional[9]—for all the actors involved.

Patients whose MPI improved were most often admitted as an in-hospital transfer (69.4%, **$P = .001$**) and belonged only to MPI-2 and 3 (58.3% and 41.7%, **$P = .006$**). In this setting, these patients often were taken over from ICU. They might have received more attention from the very beginning from the doctors, nurses and especially therapists, who usually have accompanied these patients since their time in the ICU. An already formed team could be considered strong support for the patients and a motivation to keep on progressing.[5]

The benefit of everyday clinical practice that can be deduced from this study is relevant. The assessment of the patient's overall potential, ie, physical, psychological, functional and social,[9] is currently the responsibility of experienced doctors and nurses. Up to now, there has been—to our knowledge—no established screening instrument for changes during the hospital stay. A CGA-based MPI could fill this gap.[10] Based on the findings of this study, the major changes show up already after 7-10 days (for improvement −0.08 of −0.11 in total, −0.02 of 0.00 in total for no change and 0.08 of 0.12 in total for worsening, **$P < .001$**), a multidimensional assessment only at admission and discharge might be not sufficient to catch deviations from the expected outcome during therapeutic management. An IA makes intervention possible, through, eg, occupational therapy, physiotherapy or social support and could enable patients to be discharged with multidimensionally improved health beyond "high-performance organ medicine."

As a limitation of the study, it must be considered that the patient population is mostly nephrological patients, which are a particularly vulnerable population.[30,35] They enter the hospital with a focus on this specialised organ-oriented therapy. The goal is to leave the hospital quickly. Thus, patients in this study seem to benefit greatly from the combination of multidimensional organic *and* functional treatment.[10] In addition, the sample of patients who received an IA is 78 relatively low. In order to make precise statements on the improvement of prognosis in patients who have been hospitalised for a longer time, it must be investigated whether prompt identification through an IA during hospitalisation and the treatment of deterioration in multidimensional health of patients leads to improved outcome. The next step will, therefore, be large intervention studies that directly counteract patients when deterioration in

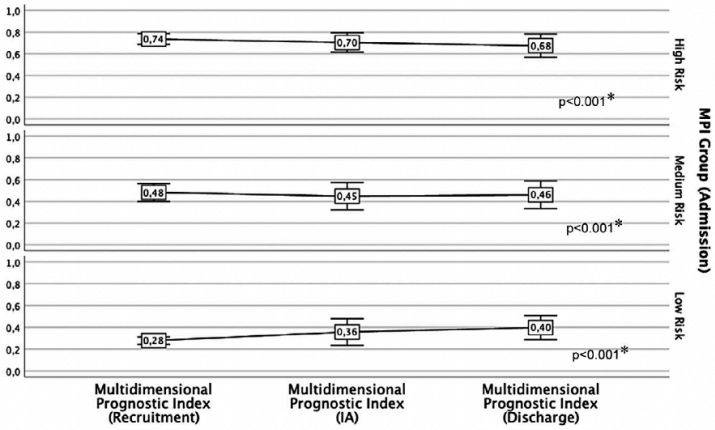


FIGURE 1 Course of the MPI during hospitalisation– subdivided for risk groups. Course of the MPI in patients who received an intermediate assessment. The course is shown separately for the three risk groups: MPI-1 (A, low risk, bottom graph, N = 9), MPI-2 (B, medium risk, middle graph, N = 41), MPI-3 (C, high risk, top graph, N = 27). The scores represent the means (± SD). ***P*-value < .001** for differences between MPI-risk groups (low, medium, high) and MPI at recruitment, MPI at IA and MPI at discharge

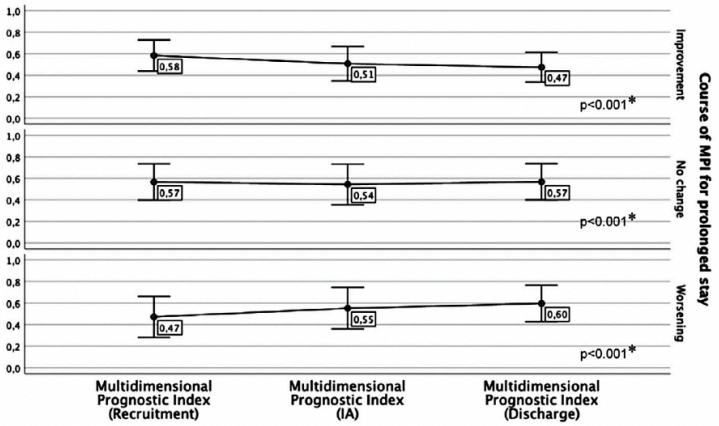


FIGURE 2 Course of the MPI during hospitalisation: improvement, no change and worsening. Course of the MPI in patients who received an intermediate assessment. The course is shown separately for the three possible courses between hospital admission and discharge: Worsening of MPI (X, bottom graph, N = 36), No change in MPI (Y, middle graph, N = 19), Improvement of MPI (Z, top graph, N = 20). The scores represent the means (±SD). The Delta-MPI values for X ($P < .001$), Y ($P < .001$) and Z ($P < .001$) are significant. This graph highlights that already at the time of the IA there is a trend towards improvement or deterioration in the multidimensional health of the patients

their multidimensional prognosis is detected. The outcome of these treated patients may be of great importance for the clinical care of older people.

5 | CONCLUSION

In conclusion, this study shows that the MPI can serve not only as a tool for long-term mortality, rehospitalisation and institutionalisation prediction, but also to dynamically monitor in-hospital changes in multidimensional health of older multimorbid inpatients. In-hospital clinical worsening is often—as outlined in this study—because of functional rather than disease-centred reasons in advanced age. Therefore, the fast uncovering of course change beyond organ cut-offs might enable tailored interventions to achieve the best possible outcome. Especially patients with a "young" chronological age at hospital admission are at risk of overall deterioration. Thus, the identification of patients' frailty—as a predictor of patients' biological age—and the prompt action if worsening of the multidimensional prognosis occurs might be crucial to avoid poor outcomes.

ACKNOWLEDGEMENTS

Open Access funding enabled and organized by Projekt DEAL. WOA Institution: Uniklinik Koln Blended DEAL : Projekt DEAL

DISCLOSURE

The authors declare that they have no competing interests. The results of this study have been presented in part in german at the annual Congress of the German Society for Internal Medicine (DGIM) in Mannheim (14th-17th of April 2018) and the annual congress of the

German Geriatric Society (DGG) in Cologne (7th-11th of September 2018), both as poster presentations.

AUTHORS CONTRIBUTIONS

Conceived and designed the clinical trial: LP, AMM, MCP. Performed the experiments: LP. Analysed the data: LP IB. Wrote the paper: LP. Conception of the manuscript: LP, AMM, MCP, IB. Critical revisions: LP, AMM, IB, AH, NN, PB, AP, TB, MCP.

ORCID

Lena Pickert https://orcid.org/0000-0001-5242-222X

REFERENCES

1. Veronese N, Siri G, Cella A, et al. Older women are frailer, but less often die then men: a prospective study of older hospitalized people. *Maturitas*. 2019;128:81-86.
2. Peterson SJ, Braunschweig CA. Prevalence of sarcopenia and associated outcomes in the clinical setting. *Nutr Clin Pract*. 2016;31:40-48.
3. Agosti P, Tettamanti M, Vella FS, et al. Living alone as an independent predictor of prolonged length of hospital stay and non-home discharge in older patients. *Eur J Intern Med*. 2018;57:25-31.
4. Merten H, Zegers M, de Bruijne MC, Wagner C. Scale, nature, preventability and causes of adverse events in hospitalised older patients. *Age Ageing*. 2013;42:87-93.
5. Besdine RW, Wetle TF. Opportunities to improve healthcare outcomes for elderly people and reduce re-hospitalization. *Aging Clin Exp Res*. 2011;23:427-430.
6. Polidori MC. Geriatrics' turning point. *Eur Geriatr Med*. 2019;10:681-683.
7. Rubenstein LZ, Kane RL. Geriatric assessment programs. Their time has come. *J Am Geriatr Soc*. 1985;33:646-647.
8. Ellis G, Whitehead MA, Robinson D, O'Neill D, Langhorne P. Comprehensive geriatric assessment for older adults admitted to hospital: meta-analysis of randomised controlled trials. *BMJ*. 2011;343:d6553.
9. Ellis G, Gardner M, Tsiachristas A, et al. Comprehensive geriatric assessment for older adults admitted to hospital. *Cochrane Database Syst Rev*. 2017;9:CD006211.
10. Gladman JR, Conroy SP, Ranhoff AH, Gordon AL. New horizons in the implementation and research of comprehensive geriatric assessment: knowing, doing and the 'know-do' gap. *Age Ageing*. 2016;45:194-200.
11. Pilotto A, Ferrucci L, Franceschi M, et al. Development and validation of a multidimensional prognostic index for one-year mortality from comprehensive geriatric assessment in hospitalized older patients. *Rejuvenation Res*. 2008;11:151-161.
12. Meyer AM, Becker I, Siri G, et al. New associations of the Multidimensional Prognostic Index. *Z Gerontol Geriatr*. 2019;52:460-467.
13. Meyer AM, Becker I, Siri G, et al. The prognostic significance of geriatric syndromes and resources. *Aging Clin Exp Res*. 2020;32:115-124.
14. Meyer AM, Polidori MC. Including prognosis evaluation in the management of older patients across different healthcare settings. The Cologne Experience. *Geriatric Care*. 2019;5:8663.65–69.
15. Volpato S, Daragjati J, Simonato M, Fontana A, Ferrucci L, Pilotto A. Change in the multidimensional prognostic index score during hospitalization in older patients. *Rejuvenation Res*. 2016;19:244-251.
16. Pilotto A, Veronese N, Daragjati J, et al. Using the multidimensional prognostic index to predict clinical outcomes of hospitalized older persons: a prospective, multicenter, international study. *J Gerontol A Biol Sci Med Sci*. 2019;74:1643-1649.
17. Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of illness in the aged. The index of ADL: A standardized measure of biological and psychosocial function. *JAMA*. 1963;185:914-919.
18. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist*. 1969;9:179-186.
19. Rubenstein LZ, Harker JO, Salva A, Guigoz Y, Vellas B. Screening for undernutrition in geriatric practice: developing the short-form mini-nutritional assessment (MNA-SF). *J Gerontol A Biol Sci Med Sci*. 2001;56:M366-M372.
20. Pfeiffer E. A short portable mental status questionnaire for the assessment of organic brain deficit in elderly patients. *J Am Geriatr Soc*. 1975;23:433-441.
21. Salvi F, Miller MD, Grilli A, et al. A manual of guidelines to score the modified cumulative illness rating scale and its validation in acute hospitalized elderly patients. *J Am Geriatr Soc*. 2008;56:1926-1931.
22. Bliss MR, McLaren R, Exton-Smith AN. Mattresses for preventing pressure sores in geriatric patients. *Mon Bull Minist Health Public Health Lab Serv*. 1966;25:238-268.
23. Sancarlo D, D'Onofrio G, Franceschi M, et al. Validation of a Modified-Multidimensional Prognostic Index (m-MPI) including the Mini Nutritional Assessment Short-Form (MNA-SF) for the prediction of one-year mortality in hospitalized elderly patients. *J Nutr Health Aging*. 2011;15:169-173.
24. Meyer AM, Siri G, Becker I, et al. The Multidimensional Prognostic Index in general practice: One-year follow-up study. *Int J Clin Pract*. 2019;e13403.
25. Covinsky KE, Palmer RM, Fortinsky RH, et al. Loss of independence in activities of daily living in older adults hospitalized with medical illnesses: increased vulnerability with age. *J Am Geriatr Soc*. 2003;51:451-458.
26. Ha JH, Hougham GW, Meltzer DO. Risk of social isolation among older patients: what factors affect the availability of family, friends, and neighbors upon hospitalization? *Clin Gerontol*. 2019;42:60-69.
27. Creditor MC. Hazards of hospitalization of the elderly. *Ann Intern Med*. 1993;118:219-223.
28. Dent E, Martin FC, Bergman H, Woo J, Romero-Ortuno R, Walston JD. Management of frailty: opportunities, challenges, and future directions. *Lancet*. 2019;394:1376-1386.
29. Pilotto A, Custodero C, Maggi S, Polidori MC, Veronese N, Ferrucci L. A multidimensional approach to frailty in older people. *Ageing Res Rev*. 2020;60:101047.
30. Tonelli M, Wiebe N, Manns BJ, et al. Comparison of the complexity of patients seen by different medical subspecialists in a universal health care system. *JAMA Netw Open*. 2018;1:e184852.
31. Mudge AM, O'Rourke P, Denaro CP. Timing and risk factors for functional changes associated with medical hospitalization in older patients. *J Gerontol A Biol Sci Med Sci*. 2010;65:866-872.
32. Stewart DE, Yuen T. A systematic review of resilience in the physically ill. *Psychosomatics*. 2011;52:199-209.
33. Whitson HE, Duan-Porter W, Schmader KE, Morey MC, Cohen HJ, Colón-Emeric CS. Physical resilience in older adults: systematic review and development of an emerging construct. *J Gerontol A Biol Sci Med Sci*. 2016;71:489-495.
34. Gijzel SMW, Whitson HE, Leemput IA, et al. Resilience in clinical care: getting a grip on the recovery potential of older adults. *J Am Geriatr Soc*. 2019;67:2650-2657.
35. Schoonover KL, Hickson LJ, Norby SM, et al. Risk factors for hospitalization among older, incident haemodialysis patients. *Nephrology*. 2013;18:712-717.

How to cite this article: Pickert L, Meyer AM, Becker I, et al. Role of a multidimensional prognosis in-hospital monitoring for older patients with prolonged stay. *Int J Clin Pract*. 2021;00:e13989. https://doi.org/10.1111/ijcp.13989

4.2 Previously undisclosed results

4.2.1 Reasons for prolonged hospital stay (stay after the intermediate assessment - IA)

After the patients received an intermediate assessment (IA) – seven to 10 days after admission – the medical and nursing documentation was used to record why the patients had to stay in hospital for more than a week. Clarification of home care implies that patients in their current condition cannot be discharged to their previous domestic environment – patients remain in the hospital until the domestic care has been clarified. The same applies for a planned rehabilitation.

Nosocomial infections include pneumonia, urinary tract infection, catheter-associated infections, wound infections or gastrointestinal infections (like diarrhea caused by the bacterium *Clostridium difficile*) (117). If the antibiotic treatment or any other required treatment – especially demanding IV injections – was not yet finished, this was also recorded. Missing or outstanding consultations mean that other disciplines besides Internal Medicine must be consulted before the patient is discharged. In the following Tables 1 & 2, the reasons for patients' prolonged stay are presented, divided into the MPI risk groups (Table 1) and the MPI course groups (Table 2) during hospitalization.

Table 1: Reasons for prolonged hospital stay, subdivided for MPI risk groups

	MPI-1 (N=9, 11.7%)	**MPI-2 (N=41, 53.2%)**	**MPI-3 (N=27, 35.1%)**	**p-value°**
Reasons for prolonged hospital stay				**0.251**
Clarification of home care, n (%)	1 (11.1)	11 (26.8)	4 (14.8)	
Worsening of condition at admission, n (%)	0 (0.0)	9 (22.0)	6 (22.2)	
Nosocomial infection, n (%)	1 (11.1)	2 (4.9)	0 (0.0)	
Treatment not yet finished, n (%)	5 (55.6)	12 (29.3)	11 (40.7)	
New symptoms during hospitalization, n (%)	0 (0.0)	2 (4.9)	3 (11.1)	
Planning of rehabilitation, n (%)	0 (0.0)	1 (2.4)	1 (3.7)	
Missing consultations, n (%)	1 (11.1)	1 (2.4)	0 (0.0)	
Planning of further treatment, n (%)	1 (11.1)	0 (0.0)	0 (0.0)	
Start of dialysis therapy planning, n (%)	0 (0.0)	1 (2.4)	0 (0.0)	
Fall, n (%)	0 (0.0)	1 (2.4)	0 (0.0)	
Reason unclear, n (%)	0 (0.0)	1 (2.4)	2 (7.4)	

Subtitle Table 1: reasons for prolonged stay of patients receiving an IA after 7–10 days, subdivided into MPI risk groups at admission. In total 78 patients were included for this analysis. The p-values° were calculated for rates using the Chi-square test, * significant from p= 0.05.

Table 2: Reasons for prolonged hospital stay, subdivided for course of the MPI during hospitalization (improvement, no change, worsening)

	Improvement (N=36, 48.0%)	**No change (N=19, 25.3%)**	**Worsening (N=20, 26.7%)**	**p-value°**
Reasons for prolonged hospital stay				**0.251**
Clarification of home care, n (%)	9 (25.0)	5 (26.3)	2 (10.0)	
Worsening of condition at admission, n (%)	4 (11.1)	6 (31.6)	4 (20.0)	
Nosocomial infection, n (%)	1 (2.8)	0 (0.0)	1 (5.0)	
Treatment not yet finished, n (%)	16 (44.4)	4 (21.1)	8 (40.0)	
New symptoms during hospitalization, n (%)	1 (2.8)	2 (10.5)	2 (10.0)	
Planning of rehabilitation, n (%)	2 (5.6)	0 (0.0)	0 (0.0)	
Missing consultations, n (%)	0 (0.0)	0 (0.0)	2 (10.0)	
Planning of further treatment, n (%)	0 (0.0)	1 (5.3)	0 (0.0)	
Start of dialysis therapy planning, n (%)	1 (2.8)	0 (0.0)	0 (0.0)	
Fall, n (%)	1 (2.8)	0 (0.0)	0 (0.0)	
Reason unclear, n (%)	1 (2.8)	1 (5.3)	1 (2.8)	

Subtitle Table 2: reasons for prolonged stay of patients receiving an IA after 7–10 days, subdivided for the course of the MPI during hospitalization (admission to discharge). In total, 75 patients were included for this analysis. The p-values° were calculated for rates using the Chi-square test, * significant from p= 0.05.

4.2.2 Follow-up results

The patients included in the present study were followed up for a total period of 12 months. Upon discharge, where the patients were discharged to (home, as an internal transfer in the same hospital or an external transfer to a different hospital, to a rehabilitation clinic, to a nursing home or deceased on ward), their medications, and whether there were changes in the grade of care (118) were all recorded, as well as whether a home care service or a long-term care facility was sought, whether a re-hospitalization was planned and whether the patients fell during their stay in hospital.

After 3, 6 and 12 months, the patients or their relatives were contacted by telephone. During this telephone call, the following was recorded: whether the patients were still alive and if not, the date of death, whether there had been changes in the grade of care, whether the patients were now living in a long-term care facility, whether they were admitted to a hospital again, whether they fell and how many prescriptions they took daily. For each follow-up period, attempts were made to contact the patients or their relatives up to three times. If it was not possible to reach them after the third call, they were considered "Lost to Follow Up" for the respective period. If at the time of follow-up, the patients were again hospitalized in the acute nephrology ward of the University Hospital of Cologne, the follow-up information was obtained from there.

The results of the follow-up are presented in Tables 3 and 4.

*Table 3: results of follow-up at discharge and after 3, 6 and 12 months (**all patients**)*

	MPI-1 (N=39, 19.5%)	**MPI-2 (N=107, 53.5%)**	**MPI-3 (N=54, 27.0%)**	**p-value°**
Follow-up at discharge, n (%)				
Patient alive?	37 (94.9)	101 (94.4)	46 (85.1)	0.060
Discharge status				**0.024***
Home	28 (71.8)	75 (70.1)	22 (40.7)	
Geriatric Rehabilitation	3 (7.7)	8 (7.5)	5 (9.3)	
Transferred to another ward	4 (10.3)	17 (15.9)	18 (33.3)	
Died on the ward	2 (5.1)	3 (2.8)	3 (5.6)	
Missing	2 (5.1)	4 (3.7)	6 (11.1)	
Below: percentages based on the participants who were still alive at that point in time.				
Grade of Care rise requested?	1 (2.7)	4 (4.0)	4 (8.7)	0.349
Home care requested?	1 (2.7)	7 (6.9)	4 (8.7)	0.517
Institutionalization planned?	1 (2.7)	1 (1.0)	3 (6.5)	0.151
Rehospitalization planned?	10 (27.0)	41 (40.6)	22 (47.8)	0.129
Fall during hospitalization?	1 (2.7)	6 (5.9)	1 (2.2)	0.512
Number of medication risk group				**0.002***
<3	2 (5.4)	0 (0.0)	0 (0.0)	
3-5	6 (16.2)	6 (5.9)	1 (2.2)	
>5	18 (48.6)	33 (32.7)	20 (43.5)	
>9	11 (29.7)	62 (61.4)	24 (52.2)	
Missing	0 (0.0)	0 (0.0)	1 (2.2)	
3 months follow-up, n (%)				
Patient alive?	29 (74.4)	80 (74.8)	23 (42.6)	**<0.001***

Below: percentages based on the participants who were still alive at that point in time.				
Grade of Care: yes	7 (24.1)	31 (39.8)	17 (31.9)	**0.001***
Grade of Care rise?	5 (12.8)	15 (18.8)	5 (21.7)	0.852
Home care available?	2 (6.9)	17 (21.3)	8 (34.8)	**0.045***
Institutionalization?	0 (0.0)	2 (2.5)	6 (26.1)	**<0.001***
Rehospitalization?	11 (37.9)	43 (53.8)	13 (56.5)	0.131
Fall in last 3 months?	4 (13.8)	11 (13.8)	1 (4.3)	0.438
Number of medication risk group				0.161
<3	1 (3.4)	0 (0.0)	1 (4.4)	
3-5	6 (20.8)	9 (11.3)	3 (13.0)	
>5	11 (37.9)	17 (21.3)	4 (17.4)	
>9	9 (31.0)	42 (52.4)	12 (52.2)	
Missing	2 (6.9)	12 (15.0)	3 (13.0)	
6 months follow-up, n (%)				
Patient alive?	29 (74.4)	77 (72.0)	19 (35.2)	**<0.001***
Below: percentages based on the participants who were still alive at that point in time.				
Grade of Care: yes	10 (34.5)	37 (48.1)	13 (68.4)	**0.020***
Grade of Care rise?	4 (13.8)	13 (16.9)	2 (10.5)	0.732
Home care available?	3 (10.3)	21 (27.3)	5 (26.3)	0.102
Institutionalization?	1 (3.4)	3 (3.9)	6 (31.6)	**<0.001***
Rehospitalization?	12 (41.4)	31 (40.3)	11 (57.9)	0.223
Fall in last 3 months?	4 (13.8)	12 (15.6)	1 (5.3)	0.520
Number of medication risk group				0.434
<3	1 (3.4)	1 (1.3)	1 (5.3)	
3-5	6 (20.7)	12 (15.6)	3 (15.8)	
>5	9 (31.0)	23 (30.0)	1 (5.3)	
>9	13 (44.8)	36 (46.8)	11 (57.9)	
Missing	0 (0.0)	5 (6.5)	3 (15.8)	
12 months follow-up, n (%)				
Patient alive?	25 (64.1)	62 (57.9)	15 (27.3)	**0.001***
Below: the percentages based on the participants who were still alive at that point in time.				
Grade of Care	8 (32.0)	30 (48.4)	10 (66.6)	0.051
Grade of Care rise?	1 (4.0)	5 (8.1)	3 (20.0)	0.199
Home care available?	0 (0.0)	16 (25.8)	7 (46.5)	**0.001***
Institutionalization?	1 (4.0)	4 (64.5)	3 (20.0)	0.159
Rehospitalization?	8 (32.0)	29 (46.8)	9 (60.0)	0.201
Fall in last 3 months?	0 (0.0)	5 (8.1)	2 (13.1)	0.206
Number of medication risk group				0.384
<3	1 (4.0)	1 (1.6)	1 (6.7)	
3-5	6 (24.0)	8 (12.9)	3 (20.0)	

>5	7 (28.0)	20 (32.3)	1 (6.7)	
>9	11 (44.0)	31 (50.0)	10 (66.7)	
Missing	0 (0.0)	2 (3.2)	0 (0.0)	
Lost to follow-up, n (%)	2 (5.1)	15 (14.1)	12 (22.2)	0.070

Subtitle Table 3: follow-up results of all patients for discharge and after 3, 6 and 12 months. The p-values° were calculated for rates using the Chi-square test, non-parametric methods were used for non-normally distributed continuous variables. * Significant from p= 0.05.

Table 4: results of follow-up at discharge and after 3, 6 and 12 months ***(patients with IA)***

	No change (N=19, 25.3%)	**Improvement (N=36, 48.0%)**	**Worsening (N=20, 26.7%)**	**p-value°**
Follow-up at discharge, n (%)				
Patient alive?	16 (84.2)	36 (100.0)	19 (95.0)	**0.011***
Discharge status				0.283
Home	10 (52.6)	25 (69.4)	9 (45.0)	
Geriatric Rehabilitation	2 (10.5)	3 (8.3)	5 (25.0)	
Transferred to another ward	4 (21.1)	7 (19.5)	5 (25.0)	
Died on the ward	1 (5.3)	0 (0.0)	0 (0.0)	
Missing	2 (10.5)	1 (2.8)	1 (5.0)	
Below: percentages based on the participants who were still alive at that point in time.				
Grade of Care rise requested?	2 (10.5)	2 (5.6)	1 (5.0)	0.625
Home care requested?	5 (26.3)	3 (8.3)	2 (10.0)	0.079
Institutionalization planned?	1 (5.3)	0 (0.0)	0 (0.0)	0.175
Rehospitalization planned?	7 (36.8)	18 (50.0)	13 (65.0)	0.288
Fall during hospitalization?	0 (0.0)	1 (2.8)	2 (10.0)	0.252
Number of medication risk group				0.858
<3	0 (0.0)	0 (0.0)	0 (0.0)	
3-5	1 (5.3)	1 (2.8)	0 (0.0)	
>5	7 (36.8)	15 (41.7)	8 (40.0)	
>9	8 (42.1)	20 (55.6)	11 (55.0)	
Missing	3 (15.8)	0 (0.0)	1 (5.0)	
3 months follow-up, n (%)				
Patient alive?	13 (68.4)	24 (66.7)	13 (65.0)	0.198
Below: percentages based on the participants who were still alive at that point in time.				
Grade of Care: yes	2 (15.4)	11 (45.8)	8 (61.5)	**0.012***
Grade of Care rise?	1 (7.7)	5 (20.8)	5 (38.5)	0.075
Home care available?	3 (23.1)	7 (29.2)	3 (23.1)	0.916
Institutionalization?	1 (7.7)	2 (8.3)	0 (0.0)	0.612
Rehospitalization?	6 (46.2)	14 (58.3)	6 (46.2)	0.740

Fall in last 3 months?	1 (7.7)	3 (12.5)	1 (7.7)	0.887
Number of medication risk group				0.897
<3	0 (0.0)	1 (4.2)	0 (0.0)	
3-5	1 (7.7)	1 (4.2)	0 (0.0)	
>5	4 (30.8)	6 (25.0)	4 (30.8)	
>9	7 (53.8)	14 (58.3)	6 (46.2)	
Missing	1 (7.7)	2 (8.3)	3 (23.0)	
6 months follow-up, n (%)				
Patient alive?	12 (63.2)	21 (87.5)	13 (65.0)	0.754
Below: percentages based on the participants who were still alive at that point in time.				
Grade of Care: yes	7 (58.3)	10 (47.6)	9 (69.2)	0.158
Grade of Care rise?	4 (33.3)	3 (14.3)	2 (15.4)	0.550
Home care available?	4 (33.3)	6 (28.6)	5 (38.5)	0.641
Institutionalization?	0 (0.0)	0 (0.0)	3 (23.1)	**0.018***
Rehospitalization?	4 (33.3)	11 (52.4)	6 (46.2)	0.501
Fall in last 3 months?	2 (16.7)	3 (14.3)	2 (15.4)	0.959
Number of medication risk group				0.549
<3	1 (8.3)	1 (4.8)	0 (0.0)	
3-5	1 (8.3)	3 (14.3)	0 (0.0)	
>5	2 (16.7)	5 (23.7)	1 (7.7)	
>9	8 (66.7)	11 (52.5)	10 (76.9)	
Missing	0 (0.0)	1 (4.8)	2 (15.4)	
12 months follow-up, n (%)				
Patient alive?	8 (42.1)	15 (41.7)	11 (55.0)	0.903
Below: percentages based on the participants who were still alive at that point in time.				
Grade of Care	5 (62.5)	8 (53.3)	6 (54.5)	0.898
Grade of Care rise?	2 (25.0)	1 (6.7)	0 (0.0)	0.200
Home care available?	3 (37.5)	6 (40.0)	3 (27.3)	0.898
Institutionalization?	0 (0.0)	0 (0.0)	2 (18.2)	0.119
Rehospitalization?	6 (75.0)	8 (53.3)	3 (27.3)	0.162
Fall in last 3 months?	3 (37.5)	2 (13.3)	0 (0.0)	0.116
Number of medication risk group				0.894
<3	1 (12.5)	1 (6.7)	0 (0.0)	
3-5	1 (12.5)	3 (20.0)	1 (9.1)	
>5	1 (12.5)	2 (13.3)	1 (9.1)	
>9	5 (62.5)	8 (53.3)	8 (66.7)	
Missing	0 (0.0)	1 (6.7)	1 (9.1)	
Lost to follow-up, n (%)	4 (21.1)	10 (27.8)	0 (0.0)	0.**033***

Subtitle Table 4: Follow-up results of all patients for discharge and after 3, 6 and 12 months. The p-values° were calculated for rates using the Chi-square test, non-parametric methods were used for non-normally distributed continuous variables. * Significant from p= 0.05.

4.2.3 Lab counts

The approach to create a metabolic signature based on the laboratory values of the participants and to combine it with the MPI has already been published by Fontana et al. (119) and was presented in the context of this thesis at the congress of the German Society for Internal Medicine 2019 (Supplementary 3). The results of the laboratory tests are presented in Tables 5 and 6.

Table 5: results of the examination of the laboratory counts on admission of all patients (extract)

	MPI-1 (N=39, 19.5%)	**MPI-2 (N=107, 53.5%)**	**MPI-3 (N=54, 27.0%)**	**p-value°**
Sodium in mmol/l, median (Q1-Q3)	139 (134-141)	137 (134-140)	139 (136.5-142)	0.176
Sodium level pathologic? n (%)	12 (30.77)	33 (30.84)	11 (20.37)	0.393
Creatinine in mg/dl, median (Q1-Q3)	2.43 (1.13-5.76)	3.16 (1.86-4.46)	3.68 (2.03-5.34)	0.203
Creatinine level pathologic? n (%)	29 (74.36)	95 (88.79)	49 (90.74)	**0.007***
Urea in mg/dl, median (Q1-Q3)	73 (54-133.5)	100.5 (51-171)	99 (51.5-146.5)	0.256
Urea level pathologic? n (%)	29 (74.36)	77 (71.96)	41 (75.93)	0.683
CRP in mg/dl, median (Q1-Q3)	26.5 (4.8-74.7)	34 (12.75-119)	37.6 (16.7-104.6)	0.155
CRP level pathologic? n (%)	35 (89.74)	89 (83.18)	43 (79.63)	0.554
White Blood Cells in 1xE9/l, median (Q1-Q3)	8.27 (6.59-9.44)	8.57 (5.49-11.06)	9.52 (7.58-13.37)	**0.002***

White Blood Cells level pathologic? n (%)	10 (25.64)	36 (33.64)	25 (46.30)	**0.050***
Hemoglobin in g/dl, median (Q1-Q3)	11 (9.9-12.6)	9.45 (8.5-11.43)	9.7 (8.55-11.35)	**0.009***
Hemoglobin level pathologic? n (%)	28 (71.8)	89 (83.18)	45 (83.33)	0.054
Hematocrit in %, median (Q1-Q3)	32 (29-37.5)	28 (26-35)	29 (26-34.5)	**0.039***
Hematocrit level pathologic? n (%)	33 (84.6)	91 (85.05)	48 (88.89)	0.170
Albumin in g/l, median (Q1-Q3)	33 (30-36.5)	32 (27-35.25)	31 (23.5-32.5)	**0.017***
Albumin level pathologic? n (%)	29 (74.36)	77 (71.96)	44 (81.48)	0.534

*Subtitle Table 5: Extract of laboratory counts taken on patients' admission. The p-values° were calculated for rates using the Chi-square test, non-parametric methods were used for non-normally distributed continuous variables. * Significant from p</= 0.05. The pathological values were determined according to the cut-off values of the Institute for Clinical Chemistry of the University Hospital of Cologne (120). These were: Sodium 135-145 mmol/l; Creatinine for females 0.5-0.9 mg/dl and for males 0.5-1.1 mg/dl; Urea <50 mg/dl; CRP <0.5 mg/dl; White Blood Cells 4.4-11.3 1xE9/l; Hemoglobin for females 12.0-16.0 g/dl and for males 13.5-18.0; Hematocrit for females 36-45% and for males 42-50%; Albumin 35-52 g/dl.*

Table 6: results of the examination of the laboratory counts on admission of patients with an IA (extract)

	No change (N=19, 25.3%)	**Improvement (N=36, 48.0%)**	**Worsening (N=20, 26.7%)**	**p-value°**
Sodium in mmol/l, median (Q1-Q3)	138 (132.25-141.75)	137.5 (134.5 – 141.5)	140 (137-142)	0.881
Sodium level pathologic? n (%)	6 (31.6)	12 (33.3)	4 (20.0)	0.732
Creatinine in mg/dl, median (Q1-Q3)	3.6 (2.2-4.4)	2.9 (1.4-5.3)	2.5 (1.3-4.8)	0.651

Creatinine level pathologic? n (%)	19 (100.0)	31 (86.1)	14 (70.0)	0.189
Urea in mg/dl, median (Q1-Q3)	110.5 (57.5-137.75)	72.5 (39.75-159.25)	99 (53.5-176.0)	0.681
Urea level pathologic? n (%)	16 (84.2)	24 (66.7)	12 (60.0)	0.446
CRP in mg/dl, median (Q1-Q3)	46.7 (21.8-104.6)	29.0 (9.8-91.6)	23.7 (4.3-208.2)	0.671
CRP level pathologic? n (%)	17 (89.5)	33 (91.7)	17 (85.0)	0.224
White Blood Cells in 1xE9/l, median (Q1-Q3)	12.8 (7.7-15.9)	8.6 (6.1-10.8)	8.3 (5.1-14.3)	0.200
White Blood Cells level pathologic? n (%)	10 (52.6)	12 (33.3)	6 (30.0)	0.420
Hemoglobin in g/dl, median (Q1-Q3)	9.8 (9.1-11.5)	9.1 (8.6-10.8)	9.8 (8.1-12.9)	0.438
Hemoglobin level pathologic? n (%)	17 (89.5)	32 (88.9)	12 (60.0)	0.112
Hematocrit in %, median (Q1-Q3)	29.5 (26.25-34.25)	27.5 (26-32)	31 (24.5-39.0)	0.538
Hematocrit level pathologic? n (%)	18 (94.7)	34 (94.4)	13 (65.0)	**0.036***
Albumin in g/l, median (Q1-Q3)	33.0 (31-34)	31.5 (26-35)	33 (30.5-37.0)	0.342
Albumin level pathologic? n (%)	15 (78.9)	27 (75.0)	13 (65.0)	0.855

*Subtitle Table 6: Extract of laboratory counts taken on patients' admission. The p-values° were calculated for rates using the Chi-square test, non-parametric methods were used for non-normally distributed continuous variables. * Significant from p</= 0.05. The pathological values were determined according to the cut-off values of the Institute for Clinical Chemistry of the University Hospital of Cologne. These were: Sodium 135-145 mmol/l; Creatinine for females 0.5-0.9 mg/dl and for males 0.5-1.1 mg/dl; Urea <50 mg/dl; CRP <0.5 mg/dl; White Blood Cells 4.4-11.3 1xE9/l; Hemoglobin for females 12.0-16.0 g/dl and for males 13.5-18.0; Hematocrit for females 36-45% and for males 42-50%; Albumin 35-52 g/dl.*

4.2.4 Geriatric syndromes and geriatric resources

Only excerpts from the geriatric syndromes and resources (113) have been presented in the above publications; the full results are presented in Tables 7 and 8.

Table 7: results of geriatric syndromes and geriatric resources for all patients

	MPI-1 (N=39, 19.5%)	**MPI-2 (N=107, 53.5%)**	**MPI-3 (N=54, 27.0%)**	**p-value°**
Geriatric Syndromes, n (%)				
Incontinence	8 (20.5)	46 (43.0)	39 (72.2)	**<0.001***
Instability	22 (56.4)	54 (50.5)	24 (44.4)	0.518
Immobility	6 (15.4)	51 (47.7)	48 (88.9)	**<0.001***
Cognitive Impairment	0 (0.0)	8 (7.5)	12 (22.2)	**0.001***
Inanition	7 (17.9)	40 (37.4)	27 (50.0)	**0.007***
Chronic Pain	11 (28.2)	46 (43.0)	21 (38.9)	0.269
Polypharmacy	31 (79.5)	102 (95.3)	52 (96.3)	**0.003***
Irritability / Depression	6 (15.4)	11 (10.3)	7 (13.0)	0.680
Sensorial Impairment	15 (38.5)	54 (50.5)	36 (66.7)	**0.022***
Insomnia	15 (38.5)	66 (61.7)	25 (46.3)	**0.023***
Irritable Colon	10 (25.6)	56 (52.3)	28 (51.9)	**0.012***
Iatrogenic Disease	0 (0.0)	3 (2.8)	1 (1.9)	0.561
Incoherence / Delirium	0 (0.0)	2 (1.9)	9 (16.7)	**<0.001***
Impoverishment	0 (0.0)	6 (5.6)	2 (3.7)	0.308
Isolation	1 (2.6)	3 (2.8)	5 (9.3)	0.142
Fluid/Electrolyte Problems	15 (38.5)	33 (30.8)	21 (38.9)	0.505
Swallowing disorder	0 (0.0)	12 (11.2)	17 (31.5)	**<0.001***
*Number, median (*Q1-Q3*)*	3 (2-5)	5 (4-7)	7 (5.75-8.25)	**<0.001**
*Percentage, median (*Q1-Q3*)*	18 (12-29)	29 (24-41)	41 (34-49)	**<0.001***
Geriatric Resources, n (%)				
Physical	19 (48.7)	28 (26.2)	1 (1.9)	**<0.001***
Good Living Conditions	29 (74.4)	83 (77.6)	33 (61.1)	0.084
Social	37 (94.9)	103 (96.3)	46 (85.2)	**0.030***
Financial	32 (82.1)	73 (68.2)	28 (51.9)	**0.008***
Spiritual	15 (38.5)	31 (29.0)	15 (27.8)	0.479
Motivational	28 (71.8)	62 (57.9)	16 (29.6)	<0.001*
Emotional	26 (66.7)	78 (72.9)	27 (50.0)	**0.015***
Mnestic	4 (10.3)	20 (18.7)	10 (18.5)	0.458
Competence-related	22 (56.4)	49 (45.8)	20 (37.0)	0.179
Intellectual	9 (23.1)	26 (24.3)	9 (16.7)	0.535
Number, median (Q1-Q3)	6 (5-7)	5 (4-6)	4 (3-5)	**<0.001***
Percentage, median (Q1-Q3)	60 (50-70)	50 (40-60)	40 (30-50)	**<0.001***

*Subtitle Table 7: The syndromes and resources were either directly assessed by asking the patients or their relatives, assessed while taking the CGA and MPI, or taken from the patient's medical record. The p-values° were calculated for rates using the Chi-square test, non-parametric methods were used for non-normally distributed continuous variables. * Significant from p= 0.05.*

*Table 8: results of geriatric syndromes and geriatric resources **(patients with IA)***

	No change (N=19, 25.3%)	**Improvement (N=36, 48.0%)**	**Worsening (N=20, 26.7%)**	**p-value°**
Geriatric Syndromes, n (%)				
Incontinence	11 (57.9)	22 (61.1)	10 (50.0)	0.722
Instability	9 (47.4)	20 (55.6)	8 (40.0)	0.526
Immobility	10 (52.6)	24 (66.7)	15 (75.0)	0.332
Cognitive Impairment	2 (10.5)	4 (11.1)	0 (0.0)	0.305
Inanition	7 (36.8)	14 (38.9)	9 (45.0)	0.858
Chronic Pain	9 (47.4)	16 (44.4)	12 (60.0)	0.526
Polypharmacy	16 (84.2)	33 (91.7)	17 (85.0)	0.642
Irritability / Depression	0 (0.0)	2 (5.6)	3 (15.0)	0.160
Sensorial Impairment	11 (57.9)	18 (50.0)	13 (65.0)	0.546
Insomnia	9 (47.4)	22 (61.1)	9 (45.0)	0.426
Irritable Colon	10 (52.6)	20 (55.6)	9 (45.0)	0.749
Iatrogenic Disease	0 (0.0)	1 (2.8)	0 (0.0)	0.578
Incoherence / Delirium	2 (10.5)	2 (5.6)	0 (0.0)	0.342
Impoverishment	1 (5.3)	1 (2.8)	3 (15.0)	0.205
Isolation	2 (10.5)	3 (8.3)	1 (5.0)	0.813
Fluid/Electrolyte Problems	9 (47.4)	6 (16.7)	11 (55.0)	**0.006***
Swallowing disorder	4 (21.1)	4 (11.1)	1 (5.0)	0.297
*Number, median (*Q1-Q3*)*	5 (4-8)	6 (5-7)	6.5 (5-8)	0.861
*Percentage, median (*Q1-Q3*)*	29 (23-47)	35 (29-41)	38 (29-47)	0.811
Geriatric Resources, n (%)				
Physical	1 (5.3)	7 (19.4)	3 (15.0)	0.368
Good Living Conditions	16 (84.2)	26 (72.2)	12 (60.0)	0.242
Social	15 (78.9)	82 (88.9)	19 (95.0)	0.297
Financial	14 (73.7)	21 (58.3)	14 (70.0)	0.459
Spiritual	9 (47.4)	12 (33.3)	7 (35.0)	0.574
Motivational	8 (42.1)	17 (47.2)	14 (70.0)	0.160
Emotional	13 (68.4)	24 (66.7)	14 (70.0)	0.967
Mnestic	3 (15.8)	4 (11.1)	5 (25.0)	0.397
Competence-related	7 (36.8)	16 (44.4)	9 (45.0)	0.838
Intellectual	5 (26.3)	8 (22.2)	3 (15.0)	0.678
Number, median (Q1-Q3)	5 (4-7)	5 (4-6)	5 (4-6)	0.740
Percentage, median (Q1-Q3)	50 (40-70)	50 (40-60)	50 (40-60)	0.740

*Subtitle Table 8: The syndromes and resources were either directly assessed by asking the patients or their relatives, assessed while taking the CGA and MPI, or taken from the patient's medical record. The p-values° were calculated for rates using the Chi-square test, non-parametric methods were used for non-normally distributed continuous variables. * Significant from p= 0.05.*

5. Discussion

5.1 Key findings, limitations and problems along the conduction of the study

First, the study was conducted as formulated in the study protocol, to which No subsequent changes were made. A total of 29 patients (14.5%) were lost over the entire follow-up period of 12 months. The execution of the study on the nephrological acute ward of the Department II for Internal Medicine of the University Hospital Cologne was possible and no problems were encountered.

The first key finding of this study was that it was possible to detect changes in the multidimensional health of patients with an intermediate assessment and a subsequent intermediate MPI calculation. To our knowledge, this was the first study to use the MPI for such an investigation and was one of the first studies to address changes in the multidimensional health of patients that occur during a hospital stay. There was a further study by Volpato et al. (121), who used two MPI calculations – at admission and discharge – to suspect the course during hospitalization. According to Volpato et. al. (121), the longer the patients were hospitalized, the worse their prognosis became with regard to the MPI. In the present study, in contrast, no correlation between changes in the MPI between admission and discharge (improvement, no change, worsening) and the length of hospital stay could be demonstrated (68). This underlines the assertion that frailty should not be seen as a static medical construct, but rather represents a dynamic process of the multidimensional aspects of every patient (45, 59). And this dynamic can be made visible through the MPI, not just in geriatric hospitals, but in all departments that treat older patients, such as a highly-specialized internal university clinic (68) like the one in the present case.

The second key finding was that there were differences during the multidimensional prognosis of patients depending on their MPI risk group (MPI-1 to MPI-3) at admission. The patients belonging to the MPI-1 group, i.e., the patients with the lowest frailty risk scores, had the greatest chance to deteriorate in their multidimensional prognosis until discharge. In contrast, the patients belonging to the MPI-3 group had the greatest chance to improve their multidimensional health scores. This had already been observed in previous studies and is, summarized in the so-called geriatric paradox (34, 65, 66, 122). It is remarkable, however, that these changes were already evident to a large extent at the time of the IA. The MPI-1 group had already deteriorated by +0.08 points (of an overall deterioration of +0.12) and the MPI-3 group had improved by -0.04 points (out of an overall improvement of -0.06). Transitions could be shown through the IA, in the positive or negative direction. This finding emphasizes the importance of reassessments during the hospital stay. After a

one-time, detailed CGA upon admission, a repetition of this as part of the daily visit is possible without additional time, as is the case with blood draw or physical examinations, which are repeated regularly throughout the patient's stay. Therefore, the detection of any changes – positive or negative – could be used by physicians and caregivers to maintain the current treatment plan or to modify treatments to counteract deterioration in the patient's multidimensional prognosis (68, 121). If the patients who received an IA were not divided according to their MPI groups, but according to the course of the MPI between admission and discharge (i.e., improvement, no change, deterioration), the changes in the MPI at all three points in time (admission –IA, IA–discharge, admission–discharge) were statistically significant. Thus, even in this group distribution of patients, a trend of the multidimensional prognosis can already be shown at the time of the IA.

In this study population, patients with the highest chronological age remained stable in their multidimensional health despite hospitalization (68) and patients whose MPI deteriorated during hospitalization often came to the hospital having been previously self-sufficient (68). As mentioned beforehand, this suggests the necessity for a rethink in the classification of geriatric patients. It is not possible to make assumptions about the course and prognosis of geriatric patients based on chronological age, pre-existing conditions or the grade of care alone. As described above, the geriatric paradox is relevant here (122, 123). Patients who seem to have no reserves left and are seriously ill recover better from, for example, a stay in the intensive care unit than previously-independent pensioners (65, 122).

This paradox is also supported in the present study by the fact that it was not possible to find significant differences in the reasons for patients being hospitalized for prolonged periods, neither when the patients were divided according to their MPI groups (Table 1), nor according to their inpatient courses (Table 2). On the one hand, the MPI-3 group did not have to deal with significantly more complications or difficult disease courses than the MPI-1 group. On the other hand, the group of patients whose MPI improved had to wait for a final examination significantly more often and could have been discharged long before they actually were. This emphasizes that not only this study population, but also ageing and frailty in general are all far too heterogeneous for a one-dimensional classification. To return to the core concept of modern Geriatric Medicine as described in the introduction, it is a matter of a multidimensional and interdisciplinary approach (34, 66).

As already confirmed in several studies (78, 85, 116), significant differences in the follow-up of patients depending on their MPI group were also seen in this study (Table 3). When examining the follow-up, depending on the patients' course during the hospital stay, it is

worth mentioning that after 3 months, 61.5% of the worsening group had a grade of care (Table 4) and that after 6 months, 23.1% of the patients from the worsening group moved to a long-term care facility (Table 4). This shows for the first time that a dynamic monitoring of the MPI during hospitalization can also be an indicator of patient progress after hospitalization, regardless of the MPI group, which marks the third key finding of this study.

The attempt to combine laboratory values and their courses with MPI is also not new. Fontana and Pilotto published their "Metabolic signature" in 2013 (79, 124, 125) and were able to show that some laboratory parameters are significantly associated with the MPI. This could also be shown in the present study (Table 5&6), but since the significant differences, e.g. in the white blood cell count, are within the physiological range of normal, this finding is of little clinical use here. Since in the present study the laboratory values are available as a snapshot on admission (Table 5&6), it is quite possible that the course of some parameters can be combined with the course of the MPI during the hospital stay. This remains open to be the subject of further research and will be discussed in the research outlook.

As is typical for empirical research, the implementation of this study was not without limitations. The reassessment of the patients was often challenging. If it was announced that patients were to be discharged on the day of the intermediate assessment (IA) or one day later, no IA was performed. Due to the often-complex disease history of these nephrological patients, the planned discharge day could frequently not be realized, and the patients remained inpatients for more than one week without receiving an IA. Therefore, the number of patients with an IA, 78, is comparatively low, which is also a limitation of this study. In future studies that aim to dynamically detect changes in the multidimensional health of patients, a regular, scheduled examination using CGA and MPI should therefore be carried out until the patients are discharged. These reassessments could be conducted weekly, every three days or daily. Whether the MPI is a suitable instrument for such a daily measurement or whether it is necessary to change to compact, shorter questionnaires could be the subject of further research.

5.2 The Cologne Model “Universitäre Altersmedizin” (University Medicine of older patients)

5.2.1 Geriatric hospitals in Germany

In Germany, there are (as of 20.08.2019) 360 geriatric hospitals with 18,121 beds (126). Just slightly over 18,000 beds seem like a drop in the ocean in light of our ageing population.

It is no wonder that the bed occupancy rate is 89.3%, the highest value in this report from the Federal Statistical Office compared to other disciplines. Internal Medicine also has a high bed occupancy rate of 80.2%, with a total of 150,202 beds available in Germany (126). The majority of these beds in Internal Medicine in Germany are occupied by older patients (over 65 years), and the lack of beds in Geriatrics has been demonstrated by the above-mentioned figures. The only conclusion is a close cooperation with Geriatric Medicine in hospitals or wards specialized in Internal Medicine. These collaborations already exist in many departments, but they are seldom accompanied scientifically.

Research is conducted at universities, while medical research at faculties of medicine. Here, another interface challenge emerges. Medicine can be studied at a total of 35 state universities in Germany. Only 13 (less than 50%) faculties have a department of Geriatric Medicine; at two additional universities there is at least one Geriatric Medicine hospital (127). Only 10 German universities have an academic chair for Geriatric Medicine at all (128), while at the other locations, Geriatrics is mostly assigned to Internal Medicine or neurology. Despite the massive increase in the number of older patients, Geriatrics is still struggling to gain recognition as an independent discipline (41). But maybe that's not the goal at all. After all, it is not a question of who can boast the best reputation in the medical world, but rather how one can optimally treat older patients through close, interdisciplinary co-management.

The Cologne model of “Universitäre Altersmedizin” is unique in Germany to date (67). The aim of this project is to increase the visibility of Geriatric Medicine collaborating with Internal Medicine at a university hospital, to emphasize its interdisciplinary importance and especially to promote teaching in Geriatric Medicine. Students should not only learn medical facts and treatment strategies, but also soft skills in dealing with older patients, their relatives and with colleagues in the specialist departments involved in treatment (67). Geriatric Medicine cannot be carried out without Internal Medicine and – to a large extent – vice versa.

5.2.2 Development of the “Universitäre Altersmedizin” in Cologne

Between 2016 and 2019, 565 older, multimorbid patients were enrolled in the study "Multidimensional Prognostic Index - Influence of a Geriatric Assessment on Hospitalisation of older, multimorbid patients- MPI-InGAH” at the nephrological acute care unit of the Department II for Internal Medicine of the University Hospital of Cologne. The initiators of this study were Anna Maria Meyer and M. Cristina Polidori, head of Ageing Clinical

Research from the Department II for Internal Medicine of the University Hospital of Cologne. The study aimed to demonstrate the practicability and feasibility of a CGA on a high-performance Internal Medicine medical ward (114, 116). To our knowledge, this study was one of the first clinical trials on geriatric patients in Internal Medicine in Germany. Once this project had been successful (67, 114, 116), further studies were conducted under the coordination of Ageing Clinical Research, e.g. in the emergency room (A&E) (129), the Intensive Care Unit (ICU) or the cardiology department of the University Hospital of Cologne.

The complexity of the nephrological patients presented the geriatric team – which in this project consisted of a geriatrician, the nurse, occupational- and physiotherapists, social workers, a pharmacologist and a medical student – with great challenges. Since 2017, the team had co-managed two geriatric patients per week who were hospitalized in the acute nephrology ward. Co-management in this context implies that the treatment of the underlying disease or acute new disease was taken over by nephrology and the patient additionally received – adapted to her needs and functions – geriatric complex treatment (36-38) by the above-mentioned team after a CGA. Nephrological patients are those with the most pre-existing conditions and therefore extremely vulnerable patients for both Internal Medicine and Geriatrics (130). Hemodialysis, for example, is vital for some nephrological patients. After hemodialysis, however, it is usually not possible to expect patients to undergo physiotherapy or occupational therapy because they are already so exhausted. (131, 132).

What became clear through this study – and not only through this one, but also through many years of research in Geriatric Medicine – was that patients' needs do not necessarily correlate with targeted organ medicine. If the medical treatment weakens the patient to such an extent that he or she can no longer bathe on his or her own or needs help when sitting up from a lying position, does the benefit still outweigh the cost? Do we always have to assess the benefit in purely medical terms, or would it not be more helpful to examine several dimensions and to respond to the patient's individual wishes? Would a targeted therapy for older patients be plausible, just like a targeted immunotherapy? Individuality, multidimensionality and co-management, as so often in this thesis, are the key words. Of course, Geriatric Medicine does not work without organ medicine, but neither does organ medicine work without Geriatric Medicine specifically concerning the treatment of older patients. Furthermore, maybe this separation is now out of date. As emphasized so often in this thesis, every medical discipline treats older patients. Therefore, every doctor, excluding pediatricians, is also a doctor of the older population and this group has individual

needs. Patients from a certain age should therefore be assessed in terms of their frailty (56) and, based on these findings, organ medicine should be adapted to the patients' individual condition. Needless to say, this will not be the solution to all of the challenges that the health care system is facing in the coming century, but it can be a way to support and patients and maintain their independence for as long and as well as possible, in turn also saving a lot of money (38, 70, 121).

5.2.3 Ward 17.1

The ward for "Universitäre Altersmedizin", University Geriatric Medicine, opened on 01.10.2019, includes 14 beds and is located on level 17 of the University Hospital of Cologne with a view of Cologne city centre. The patients of this ward are closely monitored by a co-managing team consisting of internal medicine and geriatric doctors, nurses, occupational therapists, physiotherapists, speech therapists, the social services and the pharmacy. The patients' stay should be at least two weeks so that the training program has time to have an effect. Patients can be admitted via the A&E or via referrals from other departments if patients are already hospitalized. Every potential patient is visited in advance by the ward's doctors and nurses and it is determined whether the patient meets the following requirements:

A) The patient is older than 65 years and does not need full-time care.
B) There is still a need for acute medical treatment. The ward is not a rehabilitation facility but practices University Geriatric Medicine.
C) The patient has the potential to return to a self-determined life after hospitalization or has goals and the potential to improve mobility and agility to regain a higher level of independence.
D) The patient is motivated to participate in the training sessions and is cooperative.

The four criteria listed, which patients must meet to be admitted to ward 17.1, are not to be understood as mandatory. Especially regarding the age, there are many frail patients who are younger than 65 years old. Even if a palliative situation arises in the course of the inpatient stay or the patient is terminally ill, this does not exclude treatment in co-management between internal medicine and geriatrics.

On the day of admission, the patient is visited by representatives of almost all disciplines. There is a medical admission, a visit by the senior physician and a detailed Geriatric Assessment (CGA) is taken. It is important to draw a detailed picture of the patient's initial

condition and it is of central importance to determine the individual goals of the treatment together with the patient. Each profession enters their goals and to-dos for the upcoming week into a weekly schedule. These goals and to-dos are evaluated in the large team meeting, which takes place every Tuesday. Problems and successes are discussed together and new goals for the upcoming week are set. Upon discharge, there is again a comprehensive final examination to document the patient's progress in detail. The patients' discharge management can involve either rehabilitation, the home hospital taking over until home care is finally secured or home if home care is already secured or the patient does not need any further help. In the case of the latter, the social services work closely with the patient and his or her relatives to take into account the individual wishes of all parties.

So far, this sounds like nothing tremendously new. Acute geriatric wards exist in many German hospitals and patients are monitored and managed by a geriatric team there as well. But the difference in this setting in Cologne is the co-management of patients between Internal Medicine and the specialists in Geriatrics. These patients have complex internal diseases and additionally require geriatric complex treatment. The aim is to treat patients medically as well as physically, physically, socially and functionally in order to achieve the best personal outcome in close consultation with the patient. This combination of high-performance Internal Medicine and Geriatric Medicine can only be found in the Cologne University Hospital. Other university clinics also have geriatric departments and care for the patients as a specialist department of a university clinic. The integration of Geriatric Medicine into the university hospital in Munich, for example, seems like the project in Cologne - also comparable to Jena and newly opened in Halle in March 2021 (133-135). The big difference between the above-mentioned Geriatric Medicine departments in university clinics and the university Geriatric Medicine in Cologne is the multidimensional co-management. In Cologne, the focus is on the patient, viewed as a multidimensional being (70) with complex needs and serious illnesses that require the special co-management between Internal Medicine and Geriatrics (136, 137). In the other university clinics, the departments of internal medicine and geriatrics are still separately specialized.

In summary, the aim of the stay is to ensure that the patients no longer have any need for any Internal medical action upon discharge, are in their best possible physical, mental and functional condition, and that the social aspects of home care are covered by the nursing service, assistive devices or a move to a retirement home. This pilot project is scientifically accompanied by Ageing Clinical Research of the University Hospital of Cologne (see 4.3 research outlook). At the time of submission of this thesis, the data are still being evaluated. But in two already published case reports – one on granulomatosis with polyangiitis (137)

and the other on primary hyperparathyroidism (136), both as an initial diagnosis in older patients – it is already clear what value ward 17.1 has for high-performance medicine in a university clinic and what opportunities the close co-management between Geriatric Medicine and Internal Medicine offers. In both cases, it was possible to secure and treat the basic diagnosis behind the patient's new frailty. Upon discharge, both patients showed a significantly improved Barthel index and thus have the opportunity to live independently and at home (136, 137). These are already two very positive examples of how co-management between high-performance Internal Medicine and Geriatric Medicine can work.

5.2.4 Other projects of Geriatric Medicine at university clinics in Germany

As described in the previous section, research and clinical practice in Geriatric Medicine is always interdisciplinary. Without the cooperation of different professions, the optimal care of older patients cannot be ensured (34). Therefore, one of the two major research focuses of Ageing Clinical Research at the University Hospital of Cologne is the CGA (113, 138, 139), its possibilities and its clinical applicability. Which other areas are being researched at the university hospitals, where a chair for Geriatric Medicine or at least a clinic for Geriatric Medicine exists, is briefly touched upon in the following paragraph. Due to the significant amount of research on ageing processes, not every team and focus can be named.

In Berlin (under the direction of Prof. Ursula Müller-Werdan) and in Aachen (under the direction of Prof. Cornelius Bollheimer), there were research foci with regard to age and technology. These included, for example, assist-devices, intended to make it easier for patients to take medication, or various apps, intended to enable independent evaluation of the risk of falling or adverse events (140, 141). In Aachen, work is underway on the contactless monitoring of patients at risk of falling (142).

Another major research focus of Geriatric Medicine in Germany is on nutrition and body composition in old age. This includes research on dysphagia, which is carried out in Bochum under Prof. Wirth (143, 144), for example, on sarcopenia, as it is carried out in Dresden under Prof. Hofbauer, among others, and the importance of micronutrients, which is also the focus of research in Cologne (145).

The last research focus to be examined in this section is health services research. This covers a broad spectrum from nursing research to rehabilitation and acute geriatric treatment and is also the area of geriatric research that can have the greatest direct clinical

impact. This focus is represented in almost all geriatric research groups in Germany, for example under the direction of Prof. Drey in Munich. Additionally, in contrast to Cologne, acute geriatrics in Munich focuses particularly on patients suffering from sarcopenia, the resulting geriatric syndromes' immobility and instability and the triggering factors such as malnutrition. The research focus of Prof. Drey is also sarcopenia (134, 135, 146, 147).

Thus, to our knowledge, the "Universitäre Altersmedizin" project in Cologne remains the first of its kind in Germany, which does not focus on a single area of geriatric diseases (such as sarcopenia) and works in a co-management with the nephrology department of the clinic II for Internal Medicine of the University hospital of Cologne. This increases the motivation to demonstrate the effectiveness, efficiency and usefulness of such a holistic approach to Geriatric Medicine in high-performance University Medicine by providing valid clinical data.

5.2.5 COVID-19

When this thesis was conceived and the data for the underlying study was collected, it was not yet clear what fundamental changes and developments the year 2020 would have in store. Life as we knew it was going to change. And co-management between Geriatric Medicine and Internal Medicine, as in the title of this thesis, has become more relevant than ever. The coronavirus pandemic is affecting the entire world's population. A major problem in facing this crisis is the lack of resources of already overburdened or underdeveloped health care systems across Europe and the world that cannot offer sufficient and adequate support or intensive care for patients (148). But it is affecting one population group the most: people over the age of 60 (149, 150). Thus, in the first calendar week of 2021, a total of 2584 men and 2553 women older than 60 years died from or with the SARS-CoV-2 virus (150), in contrast with only 87 men and 50 women in the under-60 age group who died from or with the coronavirus during the same period (150).

The NICE guidelines (151) for COVID-19: critical care in adults, published in March 2020, clearly state that adults should be assessed for frailty on admission to hospital, regardless of their COVID-19 condition (148, 151). Therefore, triage should be based on the biological age and the individual frailty of the patient and not simply on chronological age (148, 149). As tragic as the necessity of triage is during a global pandemic, this concept emphasizes the importance of close cooperation between Internal Medicine and Geriatrics based on the concept of frailty (148, 151). An assessment of patients' frailty, their individual multidimensional risk, their reserve capacities and their resilience, is not a precise

theoretical construct, but enables clear clinical distinction and treatment options for geriatricians, internists and intensive care physicians even during a pandemic (149).

5.2.6 Delirium @ ICU

One geriatric syndrome that concerns ICU physicians, internists, surgeons, and neurologists equally is delirium (113, 152). Delirium is a diagnosis used in medicine and especially in psychiatry and neurology (153). The official definition of the ICD-10 (International Classification of Diseases) code F.05 "Delirium" includes disorders of consciousness that are not caused by alcohol or other psychotropic substances. It can be of various duration (up to 6 months) and intensity and includes at least two of the following disorders: disorders of attention, perception, thinking, memory, psychomotor skills, emotionality or the day-night rhythm (153). Patients with pre-existing cognitive deficits, such as dementia, have a particularly high risk of suffering from delirium during hospitalization (152). However, patients with a severe infection or who even require intensive care treatment also have an increased risk of developing a delirium (154). For these patients, delirium means an increased risk of prolonged hospitalization and increased mortality (154, 155). But because delirium can present itself in very different ways, standardized diagnosis is often difficult (156, 157).

The study "Delirium @ ICU" of Ageing Clinical Research in collaboration with the Clinic I for Internal Medicine of the University Hospital Cologne has addressed this question. For a total of 6 months, patients over 65 years of age who were not ventilated were examined for the presence of delirium in the ICU and the Intermediate Care Unit using the MPI (78) and the validated screening instruments 4-AT (156) and CAM-ICU (157). The aim of the study was to quantify the incidence of delirium in ICUs and the significance of the diagnosis for the prognosis of the patients.

In the context of the first preliminary and as yet unpublished results, it was found that 29.3% of patients suffered from delirium on admission to the IMC or ICU (158). This was significantly related to an increased MPI value of the patients, a worse quality of life and an increased mortality. This emphasizes the importance of recognizing delirium, especially in the prime example of high-performance medicine that is the ICU (158). Here, close collaboration between geriatricians and ICU physicians is immensely important to provide optimal co-management of critically ill patients (159).

5.2.7 Patients' resilience

Clinical ageing research is – as the name implies – supported by its clinical findings and the scientific demand to discover homogeneity in the heterogeneity of its patients (160). Once homogeneities within the patients have been discovered, the geriatrician can begin to examine his or her clinical findings in fundamental scientific research in order to better understand the molecular mechanisms. The path here is from bedside to bench and not, as is often the case in Internal Medicine, the other way around (161). A phenomenon that is often observed in older patients and that is also evident in the present study (see 4.1) is the unexpected improvement in the condition of older patients with the most severe diagnoses and severely limiting geriatric syndromes such as immobility, instability or electrolyte and fluid disorders at hospital admission (162). So why do more severely affected patients sometimes recover better from acute illnesses than outwardly healthier-looking patients?

The concept of resilience, which has already been briefly outlined in the introduction to this thesis, is one approach by Ageing Clinical Research to explaining this phenomenon. A brief reminder: Resilience refers to the ability and capacity of the individual to react to trauma or stress and to recover from it, until the previous physical and mental state is restored (29). Resilience is a construct that is applicable in psychology, biology as well as in medicine; in Geriatric Medicine it is currently gaining in significance. Accordingly, the National Institute of Aging (149) in the USA has put the determination and research of physiological resilience of older patients on the agenda of geriatric research in 2015 (163). Of particular interest for clinical application would be the measurability of the recovery potential of patients after trauma or an acute illness – or a stressor of any kind (162).

The paper on which this thesis is based focussed on changes in the CGA-based MPI during hospitalization – now, the next step is to be taken. In the following study, in addition to the weekly collection of the MPI (a more detailed study description will follow in the next paragraph), weekly physiological parameters (pulse, blood pressure, temperature, oxygen saturation), cognitive tests and calorimetry will be performed (29). In addition, all possible stressors that could strain the patients' capacities are noted. It is hoped that this study will, firstly, provide a more accurate and detailed picture of the changes in the MPI during hospitalization and secondly, establish a link between parameters that could reflect the physiological resilience of the patients and the MPI.

5.3 Research Outlook: making dynamic changes measurable and settings of geriatric patients

The "von nix kütt nix" study was carried out by Anna Maria Meyer in cooperation with M. Cristina Polidori – head of Ageing Clinical Research of the University Hospital of Cologne – and Ingrid Becker from the Institute of Medical Statistics and Computational Biology. The study's initiation coincided with the opening of Ward 17.1, the Department of Geriatric Medicine at the University Hospital of Cologne. The aim was to provide scientific support for this pilot project from the very beginning and to use the knowledge gained to pave the way for Geriatric Medicine in high performance medicine at German university hospitals.

The first main objective of the study was to optimize the discharge management of patients from the hospital through close cooperation and communication within the triad geriatrician – patient – family doctor. After completion of the intervention study in July 2020, the study is ongoing as an observational study. The new main objective is to show the change in the MPI and the Barthel Index during hospitalization. The insights gained in the present investigation are to be used to avoid a deterioration of the prognosis of patients during hospitalization. For this purpose, the MPI is conducted weekly, and the results are reported to the ward physician and the entire team of therapists. In addition, as described in the previous paragraph, not only is the MPI collected weekly, but also vital signs and laboratory parameters that are needed in daily clinical practice. All this information is collected in a questionnaire throughout the stay and follow-up. The idea is to link the multidimensional and interdisciplinary capabilities of the MPI with clinical parameters. During the weekly sessions, changes in the treatment plan can be made based on these results and discussions with the patient and his or her relatives can be held. Thus, on the one hand, a detailed picture of the patients during hospitalization could be drawn without additional effort, and on the other hand, the changes that occur in the MPI could be combined with changes in laboratory parameters or vital signs. This can adapt the geriatric team's interventions even more precisely to the needs of the patients.

How these interventions affect the changes in the MPI, and especially which treatment measures can be taken, cannot be covered by this observational study. It can, however, provide insights into whether the fluctuations are more or less pronounced in an extended hospital stay in Internal Medicine than in an acute geriatric setting, and the patients' courses can be examined in more detail by means of the weekly surveys. Step by step, this could pave the way from a static recording of the CGA at admission and discharge towards a dynamic CGA and MPI that can respond to fluctuating patient needs.

The MPI-InGAH study was able to demonstrate that it is possible to conduct a repeated CGA-based MPI assessment in a highly specialized Internal Medicine hospital. The opening of ward 17.1 will hopefully soon provide scientific evidence that Internal high-performance Medicine and Geriatrics are not mutually exclusive. This has not yet been investigated in large studies in other departments, such as surgery or the emergency department. Based on the results of this study, a comparison of MPI assessments conducted in 5 different settings will show whether a CGA can provide valuable information not only for patients in Internal Medicine, but to what extent patients in the emergency department or intensive care unit can benefit. Furthermore, this survey will shed light on the clinical relevance a CGA and the MPI can have for patients in a wide variety of settings.

5.4 Conclusion

In brief, the following can be concluded:

Using a CGA-based MPI, it is possible to visualize changes and trends that occur during the hospitalization of patients after just one week. This makes tailored and individual treatment plans for older patients possible and allows the interdisciplinary team to adapt to the patients' needs in real time.

Geriatric medicine and high-performance Internal Medicine are not incompatible. On the contrary, patients seem to benefit from a combination and closer interdisciplinary cooperation, they benefit from co-management. In the future, the large number of older patients will only strengthen the necessity for collaboration. Therefore, the great amount of clinical experience that is already available must be scientifically proven and accompanied in order to rethink the characterization of older patients away from chronological to biological age – towards multidimensionality.

It is essential for hospitals and medical staff to rethink the care of older patients in order to cope with the upcoming Silver Tsunami. Concepts such as University Geriatric Medicine can be examples of how geriatric treatment can be made possible in non-geriatric settings. To further advance research in this area, the study "Von nix kütt nix" on level 17.1 of the University Hospital of Cologne was modified to form an observational study. The focus will be on dynamic changes in the MPI and physical parameters that occur during hospitalization. This raises the additional question of whether the MPI can be a suitable instrument for mapping the resilience of geriatric patients or what conclusions the MPI can provide on resilience. This knowledge is necessary to make the interdisciplinary work even more clinically relevant and to scientifically prove that a Comprehensive Geriatric Assessment does not create additional work but is essential for the prognosis and treatment of older, multimorbid patients.

6. References

1. Rose MR. Evolutionary biology of aging. New York: Oxford University Press; 1991.
2. Stevens C. „Father and son“. Tea for the Tillerman. London: Island Records; 1970.
3. Kaur R. home body. London: Simon & Schuster UK Ltd. ; 2020. 188 p.
4. Karasik D, Demissie S, Cupples LA, Kiel DP. Disentangling the genetic determinants of human aging: biological age as an alternative to the use of survival measures. J Gerontol A Biol Sci Med Sci. 2005;60(5):574-87.
5. Uotinen V. I'm as Old as I Feel: Subjective age in Finnish adults, Jyväskylä Studies in Education. Jyväskylä, Finland: Psychology and Social Research, University of Jyväskylä; 2005.
6. Uotinen V, Suutama T, Ruoppila I. Age identification in the framework of successful aging. A study of older Finnish people. Int J Aging Hum Dev. 2003;56(3):173-95.
7. Lowsky DJ, Olshansky SJ, Bhattacharya J, Goldman DP. Heterogeneity in healthy aging. J Gerontol A Biol Sci Med Sci. 2014;69(6):640-9.
8. Arnold J, Dai J, Nahapetyan L, Arte A, Johnson MA, Hausman D, Rodgers WL, Hensley R, Martin P, Macdonald M, Davey A, Siegler IC, Jazwinski SM, Poon LW. Predicting successful aging in a population-based sample of georgia centenarians. Curr Gerontol Geriatr Res. 2010.
9. Bundesinstitut für Bevölkerungsforschung. Altersaufbau der Bevölkerung: 2018 und 2060 Wiesbaden (Germany)2018 [cited 31.03.2020]. Available from: https://www.bib.bund.de/Permalink.html?id=10103712.
10. Institut Arbeit und Qualifikation der Universität Duisburg-Essen. Bevölkerungsentwicklung zwischen 1950 und 2060 Duisburg-Essen2018 [cited 01.04.2020]. Available from: http://www.sozialpolitik-aktuell.de/tl_files/sozialpolitik-aktuell/_Politikfelder/Bevoelkerung/Datensammlung/PDF-Dateien/abbVII100.pdf.
11. Statistisches Bundesamt. Bevölkerung Deutschlands bis 2060. Ergebnisse der 14 koordinierten Bevölkerungsvorausberechnung. 2019;Fachserie 1(Reihe 1.3).
12. Berg L. Wie der Geburtenrückgang das Land verändert Halle (Germany)2021 [cited 12.06.2021]. Available from: http://www.zukunft-mit-kindern.eu/node/139.
13. Beise M. Deutschland altert - na und? München (Germany): Süddeutsche Zeitung; 2017 [cited 12.06.2021]. Available from: https://www.sueddeutsche.de/wirtschaft/alternde-gesellschaft-deutschland-altert-na-und-1.3782066.
14. Thiel G. Mitten im demografischen Wandel Wiesbaden (Germany): Statistisches Bundesamt; 2021 [cited 12.06.2021]. Available from: https://www.destatis.de/DE/Themen/Querschnitt/Demografischer-Wandel/_inhalt.html.
15. Thiel G. Durchschnittliche Lebenserwartung (Periodensterbetafel): Deutschland, Jahre, Geschlecht, Vollendetes Alter Wiesbaden (Germany): Statistisches Bundesamt; 2018 [cited 03.04.2020]. Available from: https://www-genesis.destatis.de/genesis/online?sequenz=tabelleErgebnis&selectionname=12621-0002&zeitscheiben=16&sachmerkmal=ALT577&sachschluessel=ALTVOLL000,ALTVOLL020,ALTVOLL040,ALTVOLL060,ALTVOLL065,ALTVOLL080.
16. Radtke R. Entwicklung der Lebenserwartung bei Geburt in Deutschland nach Geschlecht in den Jahren von 1950 bis 2060 Hamburg (Germany)2019 [cited 03.04.2020]. Available from: https://de.statista.com/statistik/daten/studie/273406/umfrage/entwicklung-der-lebenserwartung-bei-geburt--in-deutschland-nach-geschlecht/.
17. Eurostat. EU-Bevölkerung zum 01.Januar 2019 auf über 513 Millionen gestiegen. Mehr Sterbefälle als Geburten. 2019(5).

18. Rowe JW, Andres R, Tobin JD, Norris AH, Shock NW. The effect of age on creatinine clearance in men: a cross-sectional and longitudinal study. J Gerontol. 1976;31(2):155-63.
19. Palant C, Amdur R, Chawla LS. Acute Kidney Injury and CKD: No Respite for a Weary Kidney. Am J Kidney Dis. 2015;66(4):552-4.
20. Chawla LS, Eggers PW, Star RA, Kimmel PL. Acute kidney injury and chronic kidney disease as interconnected syndromes. N Engl J Med. 2014;371(1):58-66.
21. Polidori MC. Physiology of Aging as a Basis of Complexity in Aging Medicine and Geriatrics. Springer International Publishing; 2020. p. 1-6.
22. Guinot C, Malvy DJ, Ambroisine L, Latreille J, Mauger E, Tenenhaus M, Morizot F, Lopez S, Le Fur I, Tschachler E. Relative contribution of intrinsic vs extrinsic factors to skin aging as determined by a validated skin age score. Arch Dermatol. 2002;138(11):1454-60.
23. Gilchrest BA. Photoaging. J Invest Dermatol. 2013;133(E1):E2-6.
24. Wheeler HE, Kim SK. Genetics and genomics of human ageing. Philos Trans R Soc Lond B Biol Sci. 2011;366(1561):43-50.
25. Zahn JM, Sonu R, Vogel H, Crane E, Mazan-Mamczarz K, Rabkin R, Davis RW, Becker KG, Owen AB, Kim SK. Transcriptional profiling of aging in human muscle reveals a common aging signature. PLoS Genet. 2006;2(7):e115.
26. Craig T, Smelick C, Tacutu R, Wuttke D, Wood SH, Stanley H, Janssens G, Savitskaya E, Moskalev A, Arking R, de Magalhaes JP. The Digital Ageing Atlas: integrating the diversity of age-related changes into a unified resource. Nucleic Acids Res. 2015;43(Database issue):D873-8.
27. Khan SS, Singer BD, Vaughan DE. Molecular and physiological manifestations and measurement of aging in humans. Aging Cell. 2017;16(4):624-33.
28. Olde Rikkert MG, van't Hof MA, Hoefnagels WH. Dispersion measures in biomedical research on ageing: nuances in the meaning of variability. Age Ageing. 1997;26(1):45-52.
29. Olde Rikkert MGM, Melis RJF. Rerouting Geriatric Medicine by Complementing Static Frailty Measures With Dynamic Resilience Indicators of Recovery Potential. Front Physiol. 2019;10:723.
30. Veraart AJ, Faassen EJ, Dakos V, van Nes EH, Lurling M, Scheffer M. Recovery rates reflect distance to a tipping point in a living system. Nature. 2011;481(7381):357-9.
31. Carpenter SR, Cole JJ, Pace ML, Batt R, Brock WA, Cline T, Coloso J, Hodgson JR, Kitchell JF, Seekell DA, Smith L, Weidel B. Early warnings of regime shifts: a whole-ecosystem experiment. Science. 2011;332(6033):1079-82.
32. Hartley P, Romero-Ortuno R, Wellwood I, Deaton C. Changes in muscle strength and physical function in older patients during and after hospitalisation: a prospective repeated-measures cohort study. Age and Ageing. 2021;50(1):153-60.
33. Hartley P, Gibbins N, Saunders A, Alexander K, Conroy E, Dixon R, Lang J, Luckett J, Luddington T, Romero-Ortuno R. The association between cognitive impairment and functional outcome in hospitalised older patients: a systematic review and meta-analysis. Age and Ageing. 2017.
34. Ellis G, Gardner M, Tsiachristas A, Langhorne P, Burke O, Harwood RH, Conroy SP, Kircher T, Somme D, Saltvedt I, Wald H, O'Neill D, Robinson D, Shepperd S. Comprehensive geriatric assessment for older adults admitted to hospital. Cochrane Database Syst Rev. 2017;9:CD006211.
35. Parker SG, McLeod A, McCue P, Phelps K, Bardsley M, Roberts HC, Conroy SP. New horizons in comprehensive geriatric assessment. Age Ageing. 2017;46(5):713-21.

36. Rubenstein LZ, Stuck AE, Siu AL, Wieland D. Impacts of geriatric evaluation and management programs on defined outcomes: overview of the evidence. J Am Geriatr Soc. 1991;39(9 Pt 2):8S-16S; discussion 7S-8S.
37. Rubenstein LZ. Geriatric assessment: an overview of its impacts. Clin Geriatr Med. 1987;3(1):1-15.
38. Rubenstein LZ, Josephson KR, Wieland GD, English PA, Sayre JA, Kane RL. Effectiveness of a geriatric evaluation unit. A randomized clinical trial. N Engl J Med. 1984;311(26):1664-70.
39. Scott CJ. George Edward Day and "diseases of advanced life". Practitioner. 1975;214(1284):832-6.
40. Warren MW. Care of Chronic Sick. Br Med J. 1943;2(4329):822-3.
41. Ribera-Casado JM. Commentary: the history of geriatrics: a model for equity. J Gerontol A Biol Sci Med Sci. 2004;59(11):1166-7; discussion 32-52.
42. Cosin L. Organizing a geriatric department. Br Med J. 1947;2(4538):1044-6.
43. Cosin LZ. Geriatric rehabilitation. Lancet. 1947;2(6483):804.
44. Howell T. Old age. Geriatrics. 1949;4(5):281-92.
45. Hoogendijk EO, Afilalo J, Ensrud KE, Kowal P, Onder G, Fried LP. Frailty: implications for clinical practice and public health. The Lancet. 2019;394(10206):1365-75.
46. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. Lancet. 2013;381(9868):752-62.
47. Kojima G. Frailty as a predictor of fractures among community-dwelling older people: A systematic review and meta-analysis. Bone. 2016;90:116-22.
48. Kojima G. Frailty as a Predictor of Nursing Home Placement Among Community-Dwelling Older Adults: A Systematic Review and Meta-analysis. J Geriatr Phys Ther. 2018;41(1):42-8.
49. Kojima G. Frailty as a predictor of hospitalisation among community-dwelling older people: a systematic review and meta-analysis. J Epidemiol Community Health. 2016;70(7):722-9.
50. Kojima G, Taniguchi Y, Iliffe S, Walters K. Frailty as a Predictor of Alzheimer Disease, Vascular Dementia, and All Dementia Among Community-Dwelling Older People: A Systematic Review and Meta-Analysis. J Am Med Dir Assoc. 2016;17(10):881-8.
51. Soysal P, Veronese N, Thompson T, Kahl KG, Fernandes BS, Prina AM, Solmi M, Schofield P, Koyanagi A, Tseng PT, Lin PY, Chu CS, Cosco TD, Cesari M, Carvalho AF, Stubbs B. Relationship between depression and frailty in older adults: A systematic review and meta-analysis. Ageing Res Rev. 2017;36:78-87.
52. Mousa A, Savva GM, Mitnitski A, Rockwood K, Jagger C, Brayne C, Matthews FE. Is frailty a stable predictor of mortality across time? Evidence from the Cognitive Function and Ageing Studies. Age Ageing. 2018;47(5):721-7.
53. Campbell AJ, Buchner DM. Unstable disability and the fluctuations of frailty. Age Ageing. 1997;26(4):315-8.
54. Winograd CH, Gerety MB, Chung M, Goldstein MK, Dominguez F, Jr., Vallone R. Screening for frailty: criteria and predictors of outcomes. J Am Geriatr Soc. 1991;39(8):778-84.
55. Winograd CH. Targeting strategies: an overview of criteria and outcomes. J Am Geriatr Soc. 1991;39(9 Pt 2):25S-35S.
56. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA, Cardiovascular Health Study Collaborative Research G.

Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001;56(3):M146-56.
57. Rockwood K, Mitnitski A. Frailty in Relation to the Accumulation of Deficits. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences. 2007;62(7):722-7.
58. JD.; FLFEW. Frailty. Halter JB OJ, Studenski S, editor. New York: McGraw-Hill Education; 2017.
59. Dent E, Martin FC, Bergman H, Woo J, Romero-Ortuno R, Walston JD. Management of frailty: opportunities, challenges, and future directions. Lancet. 2019;394(10206):1376-86.
60. Besdine RW, Wetle TF. Opportunities to improve healthcare outcomes for elderly people and reduce re-hospitalization. Aging Clinical and Experimental Research. 2011;23(5-6):427-30.
61. Warren MW. Care of the chronic aged sick. Lancet. 1946;1(6406):841-3.
62. Stuck AE, Siu AL, Wieland GD, Adams J, Rubenstein LZ. Comprehensive geriatric assessment: a meta-analysis of controlled trials. Lancet. 1993;342(8878):1032-6.
63. Scharf A-C, Gronewold J, Dahlmann C, Schlitzer J, Kribben A, Gerken G, Rassaf T, Kleinschnitz C, Dodel R, Frohnhofen H, Hermann DM. Health outcome of older hospitalized patients in internal medicine environments evaluated by Identification of Seniors at Risk (ISAR) screening and geriatric assessment. BMC Geriatrics. 2019;19(1).
64. Mahoney FI, Barthel DW. Functional Evaluation: The Barthel Index. Md State Med J. 1965;14:61-5.
65. Pilotto A, Veronese N, Daragjati J, Cruz-Jentoft AJ, Polidori MC, Mattace-Raso F, Paccalin M, Topinkova E, Siri G, Greco A, Mangoni AA, Maggi S, Ferrucci L, Investigators MA. Using the Multidimensional Prognostic Index to Predict Clinical Outcomes of Hospitalized Older Persons: A Prospective, Multicenter, International Study. J Gerontol A Biol Sci Med Sci. 2019;74(10):1643-9.
66. Polidori MC. Geriatrics' turning point. Eur Geriatr Med. 2019;10:681-3.
67. Meyer AM, Polidori M.C. Including prognosis evaluation in the management of older patients across different healthcare settings: The Cologne Experience. Geriatric Care. 2019;5.
68. Pickert L, Meyer AM, Becker I, Heess A, Noetzel N, Brinkkotter P, Pilotto A, Benzing T, Polidori MC. Role of a multidimensional prognosis in-hospital monitoring for older patients with prolonged stay. Int J Clin Pract. 2021:e13989.
69. Pilotto A, Ferrucci L, Franceschi M, D'Ambrosio LP, Scarcelli C, Cascavilla L, Paris F, Placentino G, Seripa D, Dallapiccola B, Leandro G. Development and validation of a multidimensional prognostic index for one-year mortality from comprehensive geriatric assessment in hospitalized older patients. Rejuvenation Res. 2008;11(1):151-61.
70. Pilotto A, Custodero C, Maggi S, Polidori MC, Veronese N, Ferrucci L. A multidimensional approach to frailty in older people. Ageing Res Rev. 2020;60:101047.
71. Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of Illness in the Aged. The Index of Adl: A Standardized Measure of Biological and Psychosocial Function. JAMA. 1963;185:914-9.
72. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist. 1969;9(3):179-86.
73. Rubenstein LZ, Harker JO, Salva A, Guigoz Y, Vellas B. Screening for undernutrition in geriatric practice: developing the short-form mini-nutritional assessment (MNA-SF). J Gerontol A Biol Sci Med Sci. 2001;56(6):M366-72.
74. Pfeiffer E. A short portable mental status questionnaire for the assessment of organic brain deficit in elderly patients. J Am Geriatr Soc. 1975;23(10):433-41.

75. Bliss MR, McLaren R, Exton-Smith AN. Mattresses for preventing pressure sores in geriatric patients. Mon Bull Minist Health Public Health Lab Serv. 1966;25:238-68.
76. Salvi F, Miller MD, Grilli A, Giorgi R, Towers AL, Morichi V, Spazzafumo L, Mancinelli L, Espinosa E, Rappelli A, Dessi-Fulgheri P. A manual of guidelines to score the modified cumulative illness rating scale and its validation in acute hospitalized elderly patients. J Am Geriatr Soc. 2008;56(10):1926-31.
77. Pilotto A, Sancarlo D, Pellegrini F, Rengo F, Marchionni N, Volpato S, Ferrucci L. The Multidimensional Prognostic Index predicts in-hospital length of stay in older patients: a multicentre prospective study. Age Ageing. 2016;45(1):90-6.
78. Pilotto A, Veronese N, Daragjati J, Cruz-Jentoft AJ, Polidori MC, Mattace-Raso F, Paccalin M, Topinkova E, Siri G, Greco A, Mangoni AA, Maggi S, Ferrucci L. Using the Multidimensional Prognostic Index to Predict Clinical Outcomes of Hospitalized Older Persons: A Prospective, Multicenter, International Study. J Gerontol A Biol Sci Med Sci. 2019;74(10):1643-9.
79. Pilotto A, Dini S, Veronese N, Daragjati J, Miolo M, Mion MM, Fontana A, Lo Storto M, Zaninotto M, Bragato G, Cella A, Carraro P, Addante F, Copetti M, Plebani M. Multidimensional Prognostic Index and pro-adrenomedullin plasma levels as mortality risk predictors in older patients hospitalized with community-acquired pneumonia: a prospective study. Panminerva Med. 2018;60(3):80-5.
80. Pilotto A, Sancarlo D, Panza F, Paris F, D'Onofrio G, Cascavilla L, Addante F, Seripa D, Solfrizzi V, Dallapiccola B, Franceschi M, Ferrucci L. The Multidimensional Prognostic Index (MPI), based on a comprehensive geriatric assessment predicts short- and long-term mortality in hospitalized older patients with dementia. J Alzheimers Dis. 2009;18(1):191-9.
81. Pilotto A, Panza F, Sancarlo D, Paroni G, Maggi S, Ferrucci L. Usefulness of the multidimensional prognostic index (MPI) in the management of older patients with chronic kidney disease. J Nephrol. 2012;25 Suppl 19:S79-84.
82. Pilotto A, Addante F, Franceschi M, Leandro G, Rengo G, D'Ambrosio P, Longo MG, Rengo F, Pellegrini F, Dallapiccola B, Ferrucci L. Multidimensional Prognostic Index based on a comprehensive geriatric assessment predicts short-term mortality in older patients with heart failure. Circ Heart Fail. 2010;3(1):14-20.
83. Angleman SB, Santoni G, Pilotto A, Fratiglioni L, Welmer AK. Multidimensional Prognostic Index in Association with Future Mortality and Number of Hospital Days in a Population-Based Sample of Older Adults: Results of the EU Funded MPI_AGE Project. PLoS One. 2015;10(7):e0133789.
84. Ellis G, Langhorne P. Geriatric wards in acute hospitals. Age Ageing. 2005;34(4):417-8.
85. Meyer AM, Siri G, Becker I, Betz T, Bodecker AW, Robertz JW, Krause O, Benzing T, Pilotto A, Polidori MC. The Multidimensional Prognostic Index in general practice: One-year follow-up study. Int J Clin Pract. 2019:e13403.
86. Cella A, Ferrari A, Rengo G, Solfrizzi V, Veronese N, Puntoni M, Zora S, Pilotto A, Fimognari F, Investigators S-MS. Agreement of a Short Form of the Self-Administered Multidimensional Prognostic Index (SELFY-MPI-SF): A Useful Tool for the Self-Assessment of Frailty in Community-Dwelling Older People. Clin Interv Aging. 2020;15:493-9.
87. Pilotto A, Veronese N, Quispe Guerrero KL, Zora S, Boone ALD, Puntoni M, Giorgeschi A, Cella A, Rey Hidalgo I, Pers YM, Ferri A, Fernandez JRH, Pisano Gonzalez M, Consortium E. Development and Validation of a Self-Administered Multidimensional Prognostic Index to Predict Negative Health Outcomes in Community-Dwelling Persons. Rejuvenation Res. 2019;22(4):299-305.

88. Gordon SJ, Baker N, Kidd M, Maeder A, Grimmer KA. Pre-frailty factors in community-dwelling 40-75 year olds: opportunities for successful ageing. BMC Geriatr. 2020;20(1):96.
89. Makhnevich A, Feldhamer KH, Kast CL, Sinvani L. Aspiration Pneumonia in Older Adults. J Hosp Med. 2019;14(7):429-35.
90. Bartlett JG, Gorbach SL. The triple threat of aspiration pneumonia. Chest. 1975;68(4):560-6.
91. van der Maarel-Wierink CD, Vanobbergen JN, Bronkhorst EM, Schols JM, de Baat C. Risk factors for aspiration pneumonia in frail older people: a systematic literature review. J Am Med Dir Assoc. 2011;12(5):344-54.
92. Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF)- Ständige Kommission Leitlinien. S3-Leitlinie
Behandlung von erwachsenen Patienten mit ambulant erworbener Pneumonie und Prävention – Update 2016 [updated 21.01.2016, cited 10.04.2020]. Available from: https://www.awmf.org/uploads/tx_szleitlinien/020-020l_S3_ambulant_erworbene_Pneumonie_Behandlung_Praevention_2016-02-2.pdf.
93. Lanspa MJ, Jones BE, Brown SM, Dean NC. Mortality, morbidity, and disease severity of patients with aspiration pneumonia. J Hosp Med. 2013;8(2):83-90.
94. van der Maarel-Wierink CD, Vanobbergen JN, Bronkhorst EM, Schols JM, de Baat C. Oral health care and aspiration pneumonia in frail older people: a systematic literature review. Gerodontology. 2013;30(1):3-9.
95. Ebihara T, Ebihara S, Yamazaki M, Asada M, Yamanda S, Arai H. Intensive stepwise method for oral intake using a combination of transient receptor potential stimulation and olfactory stimulation inhibits the incidence of pneumonia in dysphagic older adults. J Am Geriatr Soc. 2010;58(1):196-8.
96. Rubenstein LZ. Falls in older people: epidemiology, risk factors and strategies for prevention. Age Ageing. 2006;35 Suppl 2:ii37-ii41.
97. Mudge AM, O'Rourke P, Denaro CP. Timing and risk factors for functional changes associated with medical hospitalization in older patients. J Gerontol A Biol Sci Med Sci. 2010;65(8):866-72.
98. Cameron ID, Dyer SM, Panagoda CE, Murray GR, Hill KD, Cumming RG, Kerse N. Interventions for preventing falls in older people in care facilities and hospitals. Cochrane Database Syst Rev. 2018;9:CD005465.
99. Wolf O, Sjoholm P, Hailer NP, Moller M, Mukka S. Study protocol: HipSTHeR - a register-based randomised controlled trial - hip screws or (total) hip replacement for undisplaced femoral neck fractures in older patients. BMC Geriatr. 2020;20(1):19.
100. Magaziner J, Chiles N, Orwig D. Recovery after Hip Fracture: Interventions and Their Timing to Address Deficits and Desired Outcomes--Evidence from the Baltimore Hip Studies. Nestle Nutr Inst Workshop Ser. 2015;83:71-81.
101. Wehling M. Arzneitherapie für Ältere. Berlin: Springer; 2019. 357 p.
102. Wehling M. How to Use the FORTA ("Fit fOR The Aged") List to Improve Pharmacotherapy in the Elderly. Drug Res (Stuttg). 2016;66(2):57-62.
103. Wehling M. [Drug therapy in the elderly: too much or too little, what to do? A new assessment system: fit for the aged (FORTA). Dtsch Med Wochenschr. 2008;133(44):2289-91.
104. O'Connor MN, Gallagher P, O'Mahony D. Inappropriate prescribing: criteria, detection and prevention. Drugs Aging. 2012;29(6):437-52.
105. Holt S, Schmiedl S, Thurmann PA. Potentially inappropriate medications in the elderly: the PRISCUS list. Dtsch Arztebl Int. 2010;107(31-32):543-51.

106. Gallagher P, Baeyens JP, Topinkova E, Madlova P, Cherubini A, Gasperini B, Cruz-Jentoft A, Montero B, Lang PO, Michel JP, O'Mahony D. Inter-rater reliability of STOPP (Screening Tool of Older Persons' Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment) criteria amongst physicians in six European countries. Age Ageing. 2009;38(5):603-6.
107. Gallagher P, O'Mahony D. STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions): application to acutely ill elderly patients and comparison with Beers' criteria. Age Ageing. 2008;37(6):673-9.
108. Hu CJ, Liao CC, Chang CC, Wu CH, Chen TL. Postoperative adverse outcomes in surgical patients with dementia: a retrospective cohort study. World J Surg. 2012;36(9):2051-8.
109. Jack CR, Jr., Bennett DA, Blennow K, Carrillo MC, Dunn B, Haeberlein SB, Holtzman DM, Jagust W, Jessen F, Karlawish J, Liu E, Molinuevo JL, Montine T, Phelps C, Rankin KP, Rowe CC, Scheltens P, Siemers E, Snyder HM, Sperling R, Contributors. NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease. Alzheimers Dement. 2018;14(4):535-62.
110. World Health Organization. Risk reduction of cognitive decline and dementia - WHO Guidelines. Genf2019.
111. Chen LT, Lee JA, Chua BS, Howe TS. Hip fractures in the elderly: the impact of comorbid illnesses on hospitalisation costs. Ann Acad Med Singapore. 2007;36(9):784-7.
112. Inouye SK, Studenski S, Tinetti ME, Kuchel GA. Geriatric syndromes: clinical, research, and policy implications of a core geriatric concept. J Am Geriatr Soc. 2007;55(5):780-91.
113. Meyer AM, Becker I, Siri G, Brinkkötter PT, Benzing T, Pilotto A, Polidori MC. The prognostic significance of geriatric syndromes and resources. Aging Clinical and Experimental Research. 2020;32(1):115-24.
114. Meyer AM, Becker I, Siri G, Brinkkotter PT, Benzing T, Pilotto A, Polidori MC. The prognostic significance of geriatric syndromes and resources. Aging Clin Exp Res. 2019.
115. Clerencia-Sierra M, Calderon-Larranaga A, Martinez-Velilla N, Vergara-Mitxeltorena I, Aldaz-Herce P, Poblador-Plou B, Machon-Sobrado M, Egues-Olazabal N, Abellan-van Kan G, Prados-Torres A. Multimorbidity Patterns in Hospitalized Older Patients: Associations among Chronic Diseases and Geriatric Syndromes. PLoS One. 2015;10(7):e0132909.
116. Meyer AM, Becker I, Siri G, Brinkkotter PT, Benzing T, Pilotto A, Polidori MC. New associations of the Multidimensional Prognostic Index. Z Gerontol Geriatr. 2019;52(5):460-7.
117. Garner JJ, William; Emori, Grace; Horan, Teresa; Hughes, James;. CDC definitions for nosocomial infections. American Journal of Infection Control. 1988;16(3):128-40.
118. Bundesministerium für Gesundheit. Pflegegrade Bonn (Germany): Bundesministerium für Gesundheit (BMG)
Referat L7 "Presse"; 2018 [updated 26.06.2018, cited 27.03.2021]. Available from: https://www.bundesgesundheitsministerium.de/pflegegrade.html.
119. Fontana L, Addante F, Copetti M, Paroni G, Fontana A, Sancarlo D, Pellegrini F, Ferrucci L, Pilotto A. Identification of a metabolic signature for multidimensional impairment and mortality risk in hospitalized older patients. Aging Cell. 2013;12(3):459-66.
120. Streichert T. Leistungsverzeichnis Köln (Germany): Institut für Klinische Chemie der Universitätsklinik Köln; 2021 [cited 20.06.2021, Available from: http://www.unsere-uniklinik.de/institute/kchemie/Zentrallabor/Parameter.html.
121. Volpato S, Daragjati J, Simonato M, Fontana A, Ferrucci L, Pilotto A. Change in the Multidimensional Prognostic Index Score During Hospitalization in Older Patients. Rejuvenation Res. 2016;19(3):244-51.

122. Veronese N, Siri G, Cella A, Daragjati J, Cruz-Jentoft AJ, Polidori MC, Mattace-Raso F, Paccalin M, Topinkova E, Greco A, Mangoni AA, Maggi S, Ferrucci L, Pilotto A, Investigators MA. Older women are frailer, but less often die then men: a prospective study of older hospitalized people. Maturitas. 2019;128:81-6.
123. Gordon EH, Hubbard RE. Differences in frailty in older men and women. Medical Journal of Australia. 2020;212(4):183-8.
124. Pilotto A, Dini S, Daragjati J, Miolo M, Mion MM, Fontana A, Storto ML, Zaninotto M, Cella A, Carraro P, Addante F, Copetti M, Plebani M. Combined use of the multidimensional prognostic index (MPI) and procalcitonin serum levels in predicting 1-month mortality risk in older patients hospitalized with community-acquired pneumonia (CAP): a prospective study. Aging Clin Exp Res. 2018;30(2):193-7.
125. Fontana L, Addante F, Copetti M, Paroni G, Fontana A, Sancarlo D, Pellegrini F, Ferrucci L, Pilotto A. Identification of a metabolic signature for multidimensional impairment and mortality risk in hospitalized older patients. Aging Cell. 2013;12(3):459-66.
126. Thiel G. Einrichtungen, Betten und Patienten-bewegung 2017 Wiesbaden (Germany): Statistisches Bundesamt; 2019 [updated 20.08.2019, cited 11.06.2020]. Available from: https://www.destatis.de/DE/Themen/Gesellschaft-Umwelt/Gesundheit/Krankenhaeuser/Tabellen/krankenhaeuser-fa.html.
127. Heppner HJ. Geriatrie an der Universität Köln (Germany): Deutsche Gesellschaft für Geriatrie e.V.; 2021 [Available from: https://www.dggeriatrie.de/wissenschaft/geriatrie-an-der-universitaet.
128. Heppner HJ. Ein Blick auf die Geriatrie an deutschen Universitäten Köln (Germany): Deutsche Gesellschaft für Geriatrie e.V.; 2016 [updated 14.12.2016. cited 15.06.2021 Available from: https://www.dggeriatrie.de/ueber-uns/aktuelle-meldungen/1217-ein-blick-auf-die-geriatrie-an-deutschen-universitäten.
129. Rarek MP, Meyer AM, Pickert L, Pilotto A, Benzing T, Burst V, Polidori MC. The prognostic signature of health-related quality of life in older patients admitted to the emergency department: a 6-month follow-up study. Aging Clinical and Experimental Research. 2020.
130. Tonelli M, Wiebe N, Manns BJ, Klarenbach SW, James MT, Ravani P, Pannu N, Himmelfarb J, Hemmelgarn BR. Comparison of the Complexity of Patients Seen by Different Medical Subspecialists in a Universal Health Care System. JAMA Netw Open. 2018;1(7):e184852.
131. Ko GJ, Obi Y, Chang TI, Soohoo M, Eriguchi R, Choi SJ, Gillen DL, Kovesdy CP, Streja E, Kalantar-Zadeh K, Rhee CM. Factors Associated With Withdrawal From Dialysis Therapy in Incident Hemodialysis Patients Aged 80 Years or Older. J Am Med Dir Assoc. 2019;20(6):743-50 e1.
132. Hall RK, McAdams-DeMarco MA. Breaking the cycle of functional decline in older dialysis patients. Semin Dial. 2018;31(5):462-7.
133. Marzahn D, Pfister W, Kwetkat A. [Influence of nosocomial infections on activities of daily living in acute geriatric inpatients]. Z Gerontol Geriatr. 2018;51(4):440-5.
134. Ganse B, Drey M, Hildebrand F, Knobe M, Degens H. Performance Declines Are Accelerated in the Oldest-Old Track and Field Athletes 80 to 94 Years of Age. Rejuvenation Res. 2020.
135. Braun LT, Fazel J, Zopp S, Benedix S, Osswald-Kopp A, Riester A, Rubinstein G, Seidensticker M, Beuschlein F, Drey M, Bidlingmaier M, Schmidmaier R, Reincke M. The Effect of Biochemical Remission on Bone Metabolism in Cushing's Syndrome: A 2-Year Follow-Up Study. J Bone Miner Res. 2020.

136. Meyer AM, Wiebe L, Faust M, Chiapponi C, Brinkkötter PT, Polidori MC, Bartram MP. Kognitive Störung, Depression und Gangstörung beim internistischen Patienten – geriatrische Syndrome im Akutkrankenhaus. Zeitschrift für Gerontologie und Geriatrie. 2021;54(1):77-80.
137. Ferring A, Stegemann J, Meyer AM. ANCA-assoziierte Vaskulitis beim älteren Patienten. Zeitschrift für Gerontologie und Geriatrie. 2021.
138. Noetzel N, Meyer AM, Siri G, Pickert L, Heess A, Verleysdonk J, Benzing T, Pilotto A, Barbe AG, Polidori MC. The impact of oral health on prognosis of older multimorbid inpatients: the 6-month follow up MPI oral health study (MPIOH). Eur Geriatr Med. 2020.
139. Rarek MP, Meyer AM, Pickert L, Pilotto A, Benzing T, Burst V, Polidori MC. The prognostic signature of health-related quality of life in older patients admitted to the emergency department: a 6-month follow-up study. Aging Clin Exp Res. 2020.
140. Rabe S, Azhand A, Pommer W, Muller S, Steinert A. Descriptive Evaluation and Accuracy of a Mobile App to Assess Fall Risk in Seniors: Retrospective Case-Control Study. JMIR Aging. 2020;3(1):e16131.
141. Steinert A, Eicher C, Haesner M, Steinhagen-Thiessen E. Effects of a long-term smartphone-based self-monitoring intervention in patients with lipid metabolism disorders. Assist Technol. 2020;32(2):109-16.
142. Lueken M, Kate WT, Valenti G, Batista JP, Bollheimer C, Leonhardt S, Ngo C. Estimation of Stride Time Variability in Unobtrusive Long-Term Monitoring Using Inertial Measurement Sensors. IEEE J Biomed Health Inform. 2020;24(7):1879-86.
143. Wirth R, Dziewas R. Dysphagia and pharmacotherapy in older adults. Curr Opin Clin Nutr Metab Care. 2019;22(1):25-9.
144. Rogus-Pulia N, Wirth R, Sloane PD. Dysphagia in Frail Older Persons: Making the Most of Current Knowledge. J Am Med Dir Assoc. 2018;19(9):736-40.
145. Gerger P, Pai RK, Stuckenschneider T, Falkenreck J, Weigert H, Stahl W, Weber B, Nelles G, Spazzafumo L, Schneider S, Polidori MC. Associations of Lipophilic Micronutrients with Physical and Cognitive Fitness in Persons with Mild Cognitive Impairment. Nutrients. 2019;11(4).
146. Geritz J, Maetzold S, Steffen M, Pilotto A, Corra MF, Moscovich M, Rizzetti MC, Borroni B, Padovani A, Alpes A, Bang C, Barcellos I, Baron R, Bartsch T, Becktepe JS, Berg D, Bergeest LM, Bergmann P, Bouca-Machado R, Drey M, Elshehabi M, Farahmandi S, Ferreira JJ, Franke A, Friederich A, Geisler C, Hullemann P, Gierthmuhlen J, Granert O, Heinzel S, Heller MK, Hobert MA, Hofmann M, Jemlich B, Kerkmann L, Knupfer S, Krause K, Kress M, Krupp S, Kudelka J, Kuhlenbaumer G, Kurth R, Leypoldt F, Maetzler C, Maia LF, Moewius A, Neumann P, Niemann K, Ortlieb CT, Paschen S, Pham MH, Puehler T, Radloff F, Riedel C, Rogalski M, Sablowsky S, Schanz EM, Schebesta L, Schicketmuller A, Studt S, Thieves M, Tonges L, Ullrich S, Urban PP, Vila-Cha N, Wiegard A, Warmerdam E, Warnecke T, Weiss M, Welzel J, Hansen C, Maetzler W. Motor, cognitive and mobility deficits in 1000 geriatric patients: protocol of a quantitative observational study before and after routine clinical geriatric treatment - the ComOn-study. BMC Geriatr. 2020;20(1):45.
147. Drey M. Sarcopenia - pathophysiology and clinical relevance. Wien Med Wochenschr. 2011;161(17-18):402-8.
148. Polidori MC, Sies H, Ferrucci L, Benzing T. COVID-19 mortality as a fingerprint of biological age. Ageing Res Rev. 2021;67:101308.
149. Polidori MC, Maggi S, Mattace-Raso F, Pilotto A. The unavoidable costs of frailty: a geriatric perspective in the time of COVID-19. Geriatric Care. 2020;6(1).

150. Wenchel R. COVID-19_Todesfälle nach Sterbedatum Berlin: Robert-Koch-Institut; 2021 [updated 21.02.202127.02.2021]. Available from: https://www.rki.de/DE/Content/InfAZ/N/Neuartiges_Coronavirus/Projekte_RKI/COVID-19_Todesfaelle.html.
151. NICE (National Institute for Health and Care Excellence). COVID-19 rapid guidelines: critical care in adults. NICE Guideline. 2020.
152. Maschke Mea. Delir und Verwirrtheitszustände inklusive Alkoholentzugsdelir, S1-Leitlinie. (Hrsg.) DGfrN, editor. Online: www.dgn.org/leitlinien2020 (cited 24.05.2021).
153. Neufeld KJ, Thomas C. Delirium: definition, epidemiology, and diagnosis. J Clin Neurophysiol. 2013;30(5):438-42.
154. Jackson JC, Pandharipande PP, Girard TD, Brummel NE, Thompson JL, Hughes CG, Pun BT, Vasilevskis EE, Morandi A, Shintani AK, Hopkins RO, Bernard GR, Dittus RS, Ely EW. Depression, post-traumatic stress disorder, and functional disability in survivors of critical illness in the BRAIN-ICU study: a longitudinal cohort study. The Lancet Respiratory Medicine. 2014;2(5):369-79.
155. Heymann A, Radtke F, Schiemann A, Lütz A, Macguill M, Wernecke K, Spies C. Delayed Treatment of Delirium Increases Mortality Rate in Intensive Care Unit Patients. Journal of International Medical Research. 2010;38(5):1584-95.
156. Bellelli G, Morandi A, Davis DHJ, Mazzola P, Turco R, Gentile S, Ryan T, Cash H, Guerini F, Torpilliesi T, Del Santo F, Trabucchi M, Annoni G, Maclullich AMJ. Validation of the 4AT, a new instrument for rapid delirium screening: a study in 234 hospitalised older people. Age and Ageing. 2014;43(4):496-502.
157. Ely EW, Margolin R, Francis J, May L, Truman B, Dittus R, Speroff T, Gautam S, Bernard GR, Inouye SK. Evaluation of delirium in critically ill patients: validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). Crit Care Med. 2001;29(7):1370-9.
158. Nolting Nick Alexander HM, Pickert Lena, Meyer Anna Maria, Becker Ingrid, Benzing Thomas, Kochanek Michael, Polidori Maria Cristina. The CAM-ICU and the 4AT in older critically ill patients: Prevalence of delirium and implication for prognosis. 2021.
159. Landefeld CS. Care of hospitalized older patients: opportunities for hospital-based physicians. J Hosp Med. 2006;1(1):42-7.
160. Martin P, Kelly N, Kahana B, Kahana E, Willcox BJ, Willcox DC, Poon LW. Defining successful aging: a tangible or elusive concept? Gerontologist. 2015;55(1):14-25.
161. Fried LP, Hadley EC, Walston JD, Newman AB, Guralnik JM, Studenski S, Harris TB, Ershler WB, Ferrucci L. From bedside to bench: research agenda for frailty. Sci Aging Knowledge Environ. 2005;2005(31):pe24.
162. Gijzel SMW, Whitson HE, van de Leemput IA, Scheffer M, van Asselt D, Rector JL, Olde Rikkert MGM, Melis RJF. Resilience in Clinical Care: Getting a Grip on the Recovery Potential of Older Adults. J Am Geriatr Soc. 2019;67(12):2650-7.
163. Hadley EC, Kuchel GA, Newman AB, Workshop S, Participants. Report: NIA Workshop on Measures of Physiologic Resiliencies in Human Aging. J Gerontol A Biol Sci Med Sci. 2017;72(7):980-90.

7. Supplements

7.1 List of figures

7.2 List of tables

7.3 Supplement 1

Etablierung eines dreimaligen geriatrischen Assessments im Hinblick auf gezielte Förderung geriatrischer Patienten

Design und vorläufige Ergebnisse der Studie MPI-InGAH II

(Multidimensional Prognostic Index – Influence of Geriatric Assessment on Hospitalisation)

Lena Pickert[1], Anna Maria Meyer[1], Ingrid Becker[2], Thomas Benzing[1] und M. Cristina Polidori[1]

[1]Schwerpunkt Klinische Altersforschung, Klinik II für Innere Medizin, Universitätsklinik Köln;
[2]Institut für Medizinische Statistik und Bioinformatik der Universität zu Köln

Universitätsklinikum zu Köln

Klinik II für Innere Medizin
Schwerpunkt Klinische Altersforschung

1. Einleitung und Problemstellung

Die Erhaltung der Selbständigkeit und Versorgung im häuslichen Umfeld ist bei geriatrischen Patienten oberstes Ziel. In der Akutmedizinischen Versorgung kann das Erkennen prognoserelevanter Veränderungen im Hinblick auf oben genannte Ziele entscheidend sein. Für die Patienten soll so die beste klinische Entscheidung getroffen und eine verlängerte Hospitalisierung vermieden werden.

2. Zielsetzung und Untersuchungsfragen

Die MPI-InGAH II Studie soll den Verlauf der Mobilität, der alltäglichen Fähigkeiten und der kognitiven Fertigkeiten der Patienten während der Hospitalisierung mittels der dreimaligen Erhebung eines geriatrischen Assessment (CGA) und der Berechnung des Multidimensionalen Prognostischen Index (MPI) beobachten und Veränderungen erfassen.

3. Methodik

Erhebung eines Geriatrischen Assessments (CGA) und Berechnung des Multidimensionalen Prognostischen Index (MPI)

- Alltägliche Fähigkeiten (mittels ADL und IADL)
- Ernährung (mittels MNA)
- Mobilität (mittels ESS)
- Kognition (mittels SPMSQ)
- Lebensumstände und Medikation
- Geriatrische Syndrome und persönliche Ressourcen

→ Der MPI ergibt Werte zwischen 0 und 1 und lässt sich in drei Risikogruppen einteilen (Low risk, medium risk, high risk).

Patienten: >70 Jahre, zwei oder mehr chronische Erkrankungen, mindestens 4 Tage auf der nephrologischen Akutstation hospitalisiert

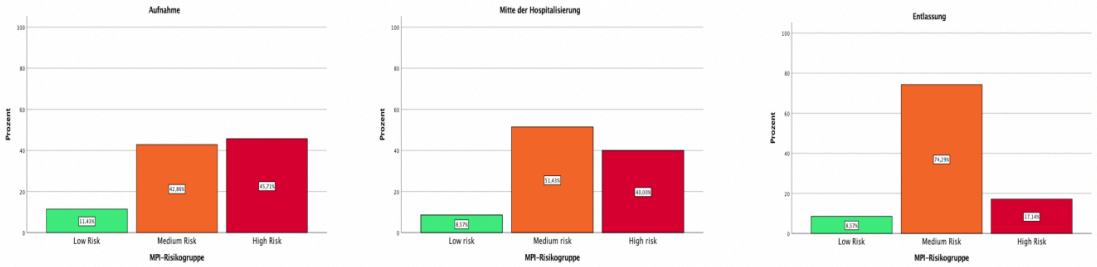
Statistische Auswertung

- IBM Software SPSS

Aufnahme 1. Assessment → Mitte der Hospitalisierung 2. Assessment → Entlassung 3. Assessment → Follow-Up 3/6/12 Monate

4. Vorläufige Ergebnisse: Der MPI verbesserte sich während der Hospitalisierung im Mittel um 0,07 Punkte

Populationsdaten: 104 Patienten (70♂ 79,3 +/- 5,3 Jahre; 34♀ 79,0 +/-5,2 Jahre), Mittlere Hospitalisierungsdauer 15 Tage, die häufigsten geriatrischen Syndrome sind Schlafstörungen und Polypharmazie.



Bisherige Verlaufsbeurteilung: Zwischen Aufnahme und Mitte der Hospitalisierung verbesserte sich der MPI im Mittel um **0,05 Punkte**, zwischen Mitte der Hospitalisierung und Entlassung erneut um **0,02 Punkte**.

5. Ausblick

- Vollständige Rekrutierung der geplanten 200 Patienten (Stand April 2018: 104 Patienten)
- Den optimalen Zeitpunkt des mittleren geriatrischen Assessments anhand der Liegedauer geriatrischer Patienten berechnen
- Genaue Interpretation des Multidimensionalen Prognostischen Index als Verlaufsparameter während einer Hospitalisierung

6. Literatur

1. **Dent E** et al. Frailty measurement in research and clinical practice: A review. Eur J Intern Med, 2016; 31:3-10
2. **Ellis G** et al., Comprehensive geriatric assessment for older adults admitted to hospital: meta-analysis of randomized controlled trials. BMJ, 2011; 343
3. **Pilotto A.**, Development and validation of a multidimensional prognostic index for one-year mortality from comprehensive geriatric assessment in hospitalized older patients. Rejuvenation Res, 2008; 11:151-61
4. **Rubenstein LZ**, Effectiveness of geriatric evaluation unit. A randomized clinical trial. N Engl J Med, 1984; 311:1664-1670
5. **Volpato S**, Bazzano S, Fontana A, Ferrucci L, Pilotto A. Multidimensional Prognostic Index predicts mortality and length of stay during hospitalization in the older patients: a multicenter prospective study. J Gerontol A Biol Sci Med Sci, 2015; 70:325-31

7.4 Supplement 2

Veränderungen des Multidimensionalen Prognostischen Index (MPI) während der Hospitalisierung

Ergebnisse der Studie MPI-InGAH II

(Multidimensional Prognostic Index – Influence of Geriatric Assessment on Hospitalisation)

Lena Pickert[1], Anna Maria Meyer[1], Ingrid Becker,[2] Thomas Benzing[1,3] und M. Cristina Polidori[1]

[1]Schwerpunkt Klinische Altersforschung, Klinik II für Innere Medizin, Universitätsklinikum Köln;
[2] Institut für Medizinische Statistik und Bioinformatik der Universität zu Köln;
[3] Cluster of Excellence – Cellular Stress Responses in Aging-Associated Diseases, University of Cologne

Universitätsklinikum Köln
Klinik II
für Innere Medizin

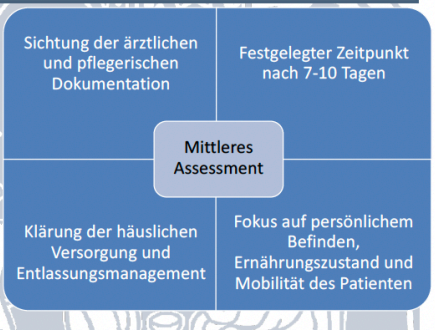
Schwerpunkt Klinische Altersforschung

1. Einleitung

Bei älteren Patienten führen verlängerte Liegedauern häufig zu nosokomialen Infektionen, Dekubiti, oder Stürzen, welche ihrerseits erhöhte Gebrechlichkeit und Verlust der Selbständigkeit zur Folge haben. Die Patienten haben das Risiko, das Krankenhaus mit einer schlechteren Prognose als bei der Aufnahme zu verlassen.

2. Zielsetzung

Detektierung von Veränderungen des Multidimensionalen Prognostischen Index (MPI) während der Hospitalisierung älterer, multimorbider Patienten in der Mitte der geplanten Hospitalisierung



3. Methoden und Patienten

- **Dreimalige Erhebung eines Comprehensive Geriatric Assessment (CGA) mit Berechnung des Multidimensionalen Prognoseindex (MPI)**
- Berücksichtigte Dimensionen: Aktivitäten und Instrumentelle Fähigkeiten des täglichen Lebens (ADL&IADL), Ernährung (MNA-SF), Kognition (SPMSQ), Dekubitusrisiko (ESS), Medikation und Lebensumstände
- Der MPI ergibt Werte zwischen 0-1, die sich drei Risikogruppen **low risk** (0,00-0,34), **medium risk** (0,35-0,66) und **high risk** (0,67-1,00) zuordnen lassen
- CGA bei Aufnahme, erwartete Mitte der Hospitalisierung und Entlassung gefolgt von einem telefonischen Follow-Up nach 3/6/12 Monaten nach Entlassung
- Patienten: >70 Jahre, mind. zwei chronische Erkrankungen, mind. 4 Tage auf nephrologischer Akutstation hospitalisiert
- **Statistik**: Berechnung mittels IBM Software SPSS, p-Werte mittels des Chi-Quadrat-Tests

4. Vorläufige Ergebnisse

Insgesamt: 162 Patienten, **Subanalyse** von 63 Patienten mit drei Assessments: 40♂ (79.6±5.8y), 23♀ (78.9±5.4y), Mittlere Hospitalisierungsdauer 23.5 Tage, die häufigsten geriatrischen Syndrome waren Immobilität (68.3%) und Polypharmazie (66.7%).

	MPI-Verbesserung Aufnahme bis Mittleres Assessment	MPI-Verschlechterung Aufnahme bis Mittleres Assessment	p-Wert	MPI-Verbesserung Mittleres Assessment bis Entlassung	MPI-Verschlechterung Mittleres Assessment bis Entlassung	p-Wert
MPI bei Rekrutierung	31 (49.2%)	9 (14.3%)	<0.001*	18 (28.6%)	12 (19.0%)	0.016*
MPI-1	0 (0.0%)	5 (55.6%)	<0.001*	1 (5.6%)	5 (41.7%)	0.016*
MPI-2	21 (67.7%)	4 (44.4%)	<0.001*	7 (38.9%)	6 (50.0%)	0.016*
MPI-3	10 (32.3%)	0 (0.0%)	<0.001*	10 (55.6%)	1 (8.3%)	0.016*

Pflegegrad	MPI-Verbesserung Aufnahme bis Mittleres Assessment	MPI-Verschlechterung Aufnahme bis Mittleres Assessment	p-Wert	MPI-Verbesserung Mittleres Assessment bis Entlassung	MPI-Verschlechterung Mittleres Assessment bis Entlassung	p-Wert
Kein Pflegegrad	17 (54.8%)	8 (88.9%)	0.040*	8 (44.4%)	10 (83.3%)	0.311
Pflegegrad 1	3 (9.7%)	1 (11.1%)	0.040*	1 (5.6%)	1 (8.3%)	0.311
Pflegegrad 2	5 (16.1%)	0 (0.0%)	0.040*	2 (11.1%)	1 (8.3%)	0.311
Pflegegrad 3	6 (19.4%)	0 (0.0%)	0.040*	4 (22.2%)	0 (0.0%)	0.311
Pflegegrad >=4	0 (0.0%)	0 (0.0%)	0.040*	3 (16.7%)	0 (0.0%)	0.311

5. Fazit

Zwischen Aufnahme und mittlerem Assessment kommt es bei 49.2% der Patienten zu einer statistisch signifikanten Verbesserung des Prognoseindex ($p < 0.001$), zwischen Mittlerem Assessment und Entlassung bei 28.6% der Patienten ($p=0.016$). Die Veränderungen des MPI zwischen Aufnahme und Mittlerem Assessment sind statistisch signifikant mit dem Pflegegrad assoziiert ($p= 0.040$).

Bedacht werden müssen mögliche Einflussfaktoren auf Ergebnisse des Mittleren Assessments: z.B. Persönliches Befinden abhängig von Tagesform, Erhöhung der Medikationsanzahl, Immobilität/Instabilität als Nebenwirkungen einer Therapie

Ausblick: Vollständige Rekrutierung der geplanten 200 Patienten und Fokus der Datenanalyse auf den optimalen Zeitpunkt des mittleren Assessments unter Berücksichtigung der voraussichtlichen Hospitalisierungsdauer

6. Literatur

1. **Dent E** et al. Frailty measurement in research and clinical practice: A review. Eur J Intern Med, 2016; 31:3-10
2. **Ellis G** et al., Comprehensive geriatric assessment for older adults admitted to hospital: meta-analysis of randomized controlled trials. BMJ, 2011; 343
3. **Pilotto A.**, Development and validation of a multidimensional prognostic index for one-year mortality from comprehensive geriatric assessment in hospitalized older patients. Rejuvenation Res,2008;11:151-61
4. **Rubenstein LZ**, Effectiveness of geriatric evaluation unit. A randomized clinical trial. N Engl J Med, 1984;311:1664-1670
5. **Volpato S**, Bazzano S, Fontana A, Ferrucci L, Pilotto A. Multidimensional Prognostic Index predicts mortality and length of stay during hospitalization in the older patients: a multicenter prospective study. J Gerontol A Biol Sci Med Sci ,2015; 70:325-31

7.5 Supplement 3

Können standardmäßig erhobene Laborparameter ein Comprehensive Geriatric Assessment (CGA) ergänzen?

Ein Vergleich der metabolischen Signatur von älteren multimorbiden Patienten

Lena Pickert[1], Anna Maria Meyer[1,3], Ingrid Becker,[2] Selma Bonnekoh[1], Volker Burst[3], Marietta Christiansen[1], Annika Hees[1], Dirk Hoffmann[1], Christie Magnisali[1], Franziska Müller[1], Nicolas Noetzel[1], Marcel Rarek[1], Paul Brinkkötter[3], Alberto Pilotto[5], Thomas Benzing[3,4] und M. Cristina Polidori[1,3]

[1]Schwerpunkt Klinische Altersforschung, Klinik II für Innere Medizin, Universitätsklinikum Köln; [2] Institut für Medizinische Statistik und Bioinformatik der Universität zu Köln; [3] Nephrologie, Rheumatologie, Diabetologie und Innere Medizin, Klinik II für Innere Medizin, Universitätsklinikum Köln; [4]Cluster of Excellence – Cellular Stress Responses in Aging-Associated Diseases, University of Cologne; [5] Department of Orthogeriatrics, Rehabilitation and Stabilization, Frailty Area, Galliera Hospital, Genova, Italy

Universitätsklinikum Köln
Klinik II
für Innere Medizin

Schwerpunkt Klinische Altersforschung

1. Einleitung

In der modernen Medizin ist Zeiteffizienz essentiell. Hochrisikopatienten hingegen, wie gebrechliche und multimorbide alte Patienten, benötigen viel anamnestischen und diagnostischen Aufwand. Das Comprehensive Geriatric Assessment (CGA) ist hierfür im klinischen Setting der Goldstandard. Ob es möglich ist, mithilfe von standardmäßig bei Aufnahme ins Krankenhaus erhobenen Daten, wie Laborparametern, die Aussagekraft eines CGA zu verstärken und dadurch die klinische Entscheidungsfindung während des stationären Aufenthaltes der Patienten zu erleichtern, ist noch relativ unbekannt.

2. Fragestellungen

Frage 1: Gibt es einen Zusammenhang zwischen der Prognoseeinschätzung mittels des Multidimensionalen Prognostischen Index (MPI) und standardmäßig erhobenen Laborparametern?

Frage 2: Lassen sich bei Patienten mit unterschiedlichen Aufnahmediagnosen Laborparameter zu metabolischen Signaturen zusammenfassen?

3. Patienten und Methoden

- **Retrospektive Analyse einer Database mit insgesamt 1074 Patienten, die zwischen 2015 und 2019 prospektiv in mehrere klinische Studien des Schwerpunkts für Klinische Altersforschung der Universitätsklinik Köln eingeschlossen wurden.**
- **Alle Patienten erhielten ein Comprehensive Geriatric Assessment (CGA) mit Berechnung des Multidimensionalen Prognostischen Index (MPI).**
- Berücksichtigte Dimensionen: Aktivitäten und Instrumentelle Fähigkeiten des täglichen Lebens (ADL&IADL), Ernährung (MNA-SF), Kognition (SPMSQ), Dekubitusrisiko (ESS), Medikation und Lebensumstände.
- Der MPI ergibt Werte zwischen 0-1, die sich drei Risikogruppen **low risk** (0,00-0,34), **medium risk** (0,35-0,66) und **high risk** (0,67-1,00) zuordnen lassen.
- Retrospektiv wurden Elektrolyte (u.a. Natrium, Kalium, Calcium), Retentionsparameter (u.a. Harnstoff, Harnsäure, Glutamat-Oxalacetat-Transaminase (GOT), Glutamat-Pyruvat-Transaminase (GPT), Glomeruläre Filtrationsrate (GFR), Kreatinin) und Serumparameter (u.a. Hämoglobin, Hämatokrit, Leukozyten, Erythrozyten) untersucht
- Patienten: >65 Jahre und multimorbide.
- **Statistik**: Berechnung mittels IBM Software SPSS. Signifikanzen wurden mit Hilfe des Chi-Quadrat-Tests, der Korrelation (2-seitig) nach Pearson und der linearen Regressionsanalyse mittels ANOVA berechnet.

4. Ergebnisse

- 47,7% Frauen, Durchschnittsalter 79,67 (+/-6,2) Jahre, Durchschnittliche Hospitalisierungsdauer 14,15 (+/- 14,1)Tage, Durchschnitts-MPI 0,46
- Häufigsten Hauptdiagnosen: 17% Kardiovaskuläre Erkrankungen, 16,9% Akute Infektionen und 15,8% Frakturen
- **Zu Frage 1: Lineare Regressionsanalyse (adjustiert für Alter & Geschlecht)**
- Statistisch signifikant für: Hämoglobin (p<0,001; negative Korrelation), Gesamtprotein (p<0,001; negative Korrelation), HbA1c (p<0,001; positive Korrelation)

Frage 1:

	MPI-1 (N=330)	MPI-2 (N=478)	MPI-3 (N=220)	p-Wert
Hämoglobin (g/dl)	10,95 (+/- 0,48)	10,85 (+/- 0,19)	10,62 (+/- 0,18)	0,001
Gesamtprotein (g/l)	30,27 (+/- 7,00)	28,65 (+/- 5,93)	21,28 (+/- 3,88)	<0,001
HbA1c (%)	9,68 (+/- 0,70)	10,19 (+/- 0,25)	10,41 (+/- 0,21)	<0,001

Frage 2:

	Kardiovaskuläre Erkrankung (N=183)	Akute Infektion (N=181)	Fraktur (N=170)	p-Wert
Natrium (mmol/l)	139,13 (+/-3,79)	137,44 (+/-4,73)	138,46 (+/- 4,13)	0,001
Hämoglobin (g/dl)	12,39 (+/- 2,08)	11,08 (+/-2,70)	11,48 (+/- 2,04)	0,001
Gesamtprotein (g/l)	60,62 (+/- 28,67)	60,58 (+/- 46,07)	18,48 (+/- 27,05)	<0,001

5. Fazit

Standardmäßig erhobene Laborparameter können ein Comprehensive Geriatric Assessment ergänzen:

- Die Höhe der Werte von Hämoglobin, Gesamtprotein und HbA1c kann statistisch signifikant mit den Risikogruppen des MPI korreliert werden.
- Für Aufnahmediagnosengruppen (hier beispielhaft Kardiovaskuläre Erkrankungen, eine Akute Infektion oder eine Fraktur) ist es möglich statistisch signifikante Unterschiede in der Höhe von Laborparametern (hier beispielhaft Natrium, Hämoglobin und Gesamtprotein) festzustellen

- Ausblick: Weiterführende Komplettierung und Analyse der Laborparameter und Zusammenfassung der Laborparameter zu einer metabolischen Signatur von älteren, multimorbiden Patienten mit unterschiedlichen Aufnahmediagnosen

6. Literatur

1. **Dent E** et al. Frailty measurement in research and clinical practice: A review. Eur J Intern Med, 2016; 31:3-10.
2. **Ellis G** et al., Comprehensive geriatric assessment for older adults admitted to hospital: meta-analysis of randomized controlled trials. BMJ, 2011; 343.
3. **Pilotto A.**, Development and validation of a multidimensional prognostic index for one-year mortality from comprehensive geriatric assessment in hospitalized older patients. Rejuvenation Res, 2008; 11:151-61.
4. **Roller-Wirnsberger RE, Singler K, Polidori MC**, Learning Geriatric Medicine (2017), Springer-Verlag, Berlin.
5. **Meyer, A.M.** et al., New associations of the Multidimensional Prognostic Index, Z Gerontol Geriat (2018).
6. **Fontana, L.** et al. "Identification of a metabolic signature for multidimensional impairment and mortality risk in hospitalized older patients." *Aging cell* vol. 12,3 (2013): 459-66.

The role of prognosis for tailored multidimensional interventions in older multimorbid patients: the Multidimensional Prognostic Index

Pickert L[1,2], Meyer AM[1,2], Müller F[1,2], Nötzel N[1,2], Becker I[3], Brinkkötter P[2], Dammertz I[4], Höncke J[4], Karg D[4], Königkamp B[4], Müller M[4], Nano D[2], Ratte-Henn S[5], Pilotto A[6], Benzing T[2,7] and Polidori MC[1,2]

[1]Ageing Clinical Research, Dpt. II for Internal Medicine, University Hospital of Cologne, Cologne, Germany; [2]Nephrology, Rheumatology, Diabetology and Internal Medicine, Dpt. II for Internal Medicine, University Hospital of Cologne, Cologne, Germany; [3]Institute of Medical Statistics and Computational Biology, University Hospital of Cologne, Cologne, Germany; [4]UniReha GmbH, Centre for Prevention and Rehabilitation of the University Hospital of Cologne, Cologne, Germany; [5]Social Services, University Hospital of Cologne, Cologne, Germany; [6]Department of Orthogeriatrics, Rehabilitation and Stabilization, Frailty Area, Galliera Hospital, Genova, Italy; [7]CECAD Excellent in Aging Research, Cluster of Excellence Cluster at the University of Cologne, Cologne, Germany

Universitätsklinikum Köln
Klinik II
für Innere Medizin

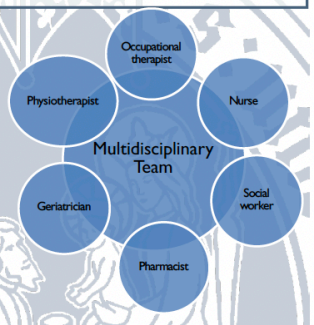
Schwerpunkt Klinische Altersforschung

1. Introduction

As the german society grows older, a higher percentage of patients in non-geriatric wards are aged 65 years and above. As time and facilities for the special needs of geriatric patients is often missing, higher risk of frailty, falls and prolonged hospitalisation might be the result. A multidisciplinary team consisting of geriatricians, physicians of the ward, nurses and therapists is needed to prevent poor outcomes. The instrument used by the geriatric team is the comprehensive geriatric assessment (CGA). Based on a CGA, a Multidimensional Prognostic Index (MPI) can be calculated. The MPI can be used to follow up on intervention efficacy.

2. Aim

To retrospectively assess clinical and prognostic features of older hospitalized patients undergoing a multidomain intervention versus those undergoing usual care as part of a pilot intervention at the Department II of Internal Medicine of the University Hospital of Cologne, Germany.



3. Methods and Patients

MPI: Measurement of 8 domains including comorbidities (Cumulative Illness Rating Scale, CIRS), functions (Activities of Daily Living, ADL & Instrumental Activities of Daily Living IADL), nutrition (Mini Nutritional Assessment-Short Form, MNA-SF), cognition (Short Portable Mental Status Questionaire), pressure ulcer risk (Exton Smith Scale, ESS), living conditions and medication. The MPI classifies patients in low-risk group (0.00-0.34), medium-risk group (0.35-0.65) and high-risk group (0.66-1.00) for one month and one year mortality.

Patients: 56 patients hospitalized for chronic illness or acute relapse of chronic conditions, 23♀(80.4 +/- 6.4 yo), 33 ♂ (78.7 +/-4.9 yo), median length of hospital stay 18.5 days; source of referral was 30.4% new admission, 48.2% from internal ward and 21.4 from external ward;

Statistics: IBM Software SPSS, Chi-Square-Test for frequencies, univariate ANOVA for continuous variables. Statistically significant at 5%.

Multidimensional Interventions: Only two patients could underwent the multidomain interventions at the same time

Inclusion criteria: Age >65 yo, Mobilisation possible Potential, LOS at least 1 week → **Beginning of treatment:** CGA-MPI → Daily visits from occupational therapists physiotherapists, nurses and physicians → Weekly team meeting to report progress ,discuss patients goals and further plan → **Right before discharge:** CGA-MPI

4. Preliminary Results: Red= Admission Green= Discharge

	Multidomain intervention (n=56)	Usual care (n=150)
Age (years, mean, SD)	79.4 (6.0)	78.4 (5.1)
Gender	41.1% Female 58.9% Male	34.0% Female 66.0% Male
MPI (mean, SD)	0.55 (0.16) 0.53 (0.13)	0.51 (0.18) 0.49 (0.17)
MPI-1	10.7% 1.8%	18.7% 22.7%
MPI-2	62.5% 75%	55.3% 56.7%
MPI-3	26.8% 14.3%	26.0% 20.0%
CIRS (median, IQR)	5 (4-7) 6 (4-7)	6 (4-6) 5 (4-6)
ADL (median,IQR)	3 (1-5) 3 (2-5)	5 (3-6) 5 (3-6)
IADL (median, IQR)	4 (2-6) 4 (2-5)	4 (2-7) 4 (2-7)
MNA-SF (median, IQR)	9 (6-11) 10 (8-12)	9 (6-11) 10 (8-12)
MNA-SF MPI-3 (Median, IQR)	7 (5-10) 9 (9-13)	6 (5-7) 8 (5-10)
SPMSQ (median, IQR)	1 (0-2) 1 (0-2)	1 (0-3) 1 (0-3)
ESS (median, IQR)	13 (11-15) 15 (13-17)	15 (12-17) 16 (13-18)
ESS MPI-3 (median, IQR)	10 (9-13) 15 (12-16)	10 (9-12) 12 (11-15)
Medication (median, IQR)	9 (7-13) 11 (9-14)	9 (7-12) 10 (8-12)
Living conditions	69.6% With relatives (low risk) 3.6% Institutionalisation/private attendent (medium risk) 26.8 % Alone (high risk)	67.3% With relatives (low risk) 8.0% Institutionalisation/private attendent (medium risk) 24.7% Alone (high risk)
Length of stay (mean, SD)	23.0 (17.1)	12.4 (9.5)
Care level at admission	67.9% None 7.1% Level 1 12.5% Level 2 8.9% Level 3 3.6% Level 4	58.0% None 12.0% Level 1 14.0% Level 2 8.7% Level 3 6.7% Level 4
Discharge directions	37.5% Home 39.3% Geriatric Rehabilitation 12.5 % Transferred to another ward 1.8 % Gone against medical advice 7.1% died	62.0% Home 11.3% Geriatric Rehabilitation 19.3% Transferred to another ward 0% Gone against medical advice 2.8% died
Patient alive after 3 months	21.3% No 78.7% Yes	18.2% No 78.4% Yes (3.4% Missing)
Rehospitalisation after 3 months	25.0% No 68.2% Yes (6.8% Missing)	46.5% No 43.7% Yes (9.9% Missing)
Falls after 3 months	70.5% No 13.6% Yes (15.9% Missing)	76.1% No 14.1% Yes (9.9% Missing)

5. Interpretation and research outlook

- Multidomain interventions in non-geriatric departments are feasible but need to be adjusted for recovery potential - which is adequately measured by the MPI – and timewindow of the intervention
- Further research is needed to clearly identify implementation gaps.

- A prospective study on the effects of the multidomain intervention on trajectories and outcome of older multimorbid patients hospitalized in non-geriatric acute medical wards as assessed by MPI is beginning in November 2018

6. Bibliography

1. **Dent E** et al. Frailty measurement in research and clinical practice: A review. Eur J Intern Med, 2016; 31:3-10
2. **Ellis G** et al., Comprehensive geriatric assessment for older adults admitted to hospital: meta-analysis of randomized controlled trials. BMJ, 2011; 343
3. **Pilotto A.** , Development and validation of a multidimensional prognostic index for one-year mortality from comprehensive geriatric assessment in hospitalized older patients. Rejuvenation Res,2008;11:151-61
4. **Rubenstein** L.Z. Effectiveness of geriatric evaluation unit. A randomized clinical trial. N Engl J Med, 1984;311:1664-1670
5. **Volpato S**, Bazzano S, Fontana A, Ferrucci L, Pilotto A. Multidimensional Prognostic Index predicts mortality and length of stay during hospitalization in the older patients: a multicenter prospective study. J Gerontol A Biol Sci Med Sci ,2015; 70:325-31

7.7 Supplement 5

Characteristics of geriatric syndromes and geriatric resources of older, multimorbid patients in 4 different settings

Pickert L[1*] and Meyer AM[1*], Becker I[2], Heeß A[1], Hochleitner M[1], Nolting N[1], Rarek M[1], Rudol D[1], Betz T[3], Kochanek M[4], Burst V[5], Brinkkötter P[5], Benzing T[5,6] and Polidori MC[1,6]

[1]Ageing Clinical Research, Dpt. II for Internal Medicine, University Hospital of Cologne, Cologne, Germany; [2]Institute of Medical Statistics and Computational Biology, University Hospital of Cologne, Cologne, Germany; [3] Outpatient Clinic Dr. Thomas Betz, Much, Germany; [4] Intensive and Intermediate Care Units, Department I of Internal Medicine, University of Cologne, Germany; [5]Nephrology, Rheumatology, Diabetology and Internal Medicine, Dpt. II for Internal Medicine, University Hospital of Cologne, Cologne, Germany; [6] Cologne Excellence Cluster on Cellular Stress- Responses in Aging- Associated Diseases (CECAD), University of Cologne, Faculty of Medicine and University Hospital Cologne, Cologne, Germany; *equal contributors

Universitätsklinikum Köln
Klinik II
für Innere Medizin

Schwerpunkt Klinische Altersforschung

1.Introduction

Geriatric syndromes (GS) are very common in older patients and are disclosed through the Comprehensive Geriatric Assessment (CGA). The grouping of complexes geriatric multifactorial conditions under the conceptual framing of GS allows the standardization and thus simplification of the clinical treatment of older patients. Geriatric resources (GR), on the other hand, represent a similar construct in terms of patients' capacities. Neither GS nor GR, however, are currently collected as a standard in everyday clinical practice. Therefore, the actual prevalence of these two entities is largely unknown across settings.

2. Methods and Patients

Patients and settings: In total 950 patients prospectively enrolled in 4 different studies: internal medicine ward (IM, 499 patients, mean age 77.7y (± 5.8),♀ 38.3%), emergency room (A&E, 270 patients, mean age 80.7y (±5.8), ♀ 41.4%), general practice (GP, 125 patients, mean age 79.2y (±6.5),♀ 48.8%), and intensive care unit (ICU, 56 patients, median age 74.8y (±6.5),♀ 53.3%) (p<0.001).

Methods: All patients in this study received a CGA at admission and discharge, as well as GS and GR recording at admission. Patients were all over 65 years of age and had at least two chronic conditions. The syndromes and resources were collected either by direct questioning the patient or relatives, by researching the medical history or by CGA.

Figure 1: How to assess geriatric syndromes & resources in everyday clinical practice

Example Research:
Polypharmacy: Medication plan at recruitment

Example Questions:
Instability: „Do you have difficulty walking, like dizziness, problems with your balance, or do you fall regularly?"

Social isolation: „Are you having regular contact with friends, family or neighbours? Do you have somebody to talk to when you are feeling sad?

Spiritual resources: „Are you a very faithful person and does faith or church give you strength in difficult situations?"

Research & CGA	Questions
• **Syndromes:** ○ Polypharmacy ○ Cognitive Impairment ○ Fluid/Electrolyte problems ○ Incoherence/delirium • **Resources:** ○ Physical resources	• **Syndromes:** ○ Instability, Incontinence, Inanition, Immobility, Irritability/Depression, Insomnia, Impoverishment, Swallowing disorder, Chronic pain, Sensorial impairment, Irritable colon, Iatrogenic disease, social isolation, • **Resources** ○ Good living conditions, Social, Economical, Competence-related, Intellectual , Spiritual, Motivational, Emotional, Mnestic

3. Results: Both the number and the distribution of GS and GR is statistically significant when comparing the 4 settings

Median length of hospital stay: 9 (5-17, IM), 4 (1-10, A&E), zero (GP) and 18 (8-36, ICU) days (p<0.001)

Admission diagnosis: *kidney failure* (38.7%, IM), *cardiovascular diseases* (23.7% at A&E and 17.6% at GP) and *acute infections* (19.6%, ICU; p<0.001)

Most common GS: *Polypharmacy* (91.8% IM; 79.9% A&E; 53.6% GP; 98.2% ICU; p<0.001) and *Instability* (65.3% IM; 34.0% A&E; 49.6% GP; 71.4% ICU; p<0.001)

Most common GR: *Social* (86.7% IM; 86.0% A&E; 92.3% GP; ICU 84.8%; p=0.603) and *Good Living Conditions* (68.7% IM; 71.0% A&E; 67.2% GP; 56.9% ICU; p=0.326)

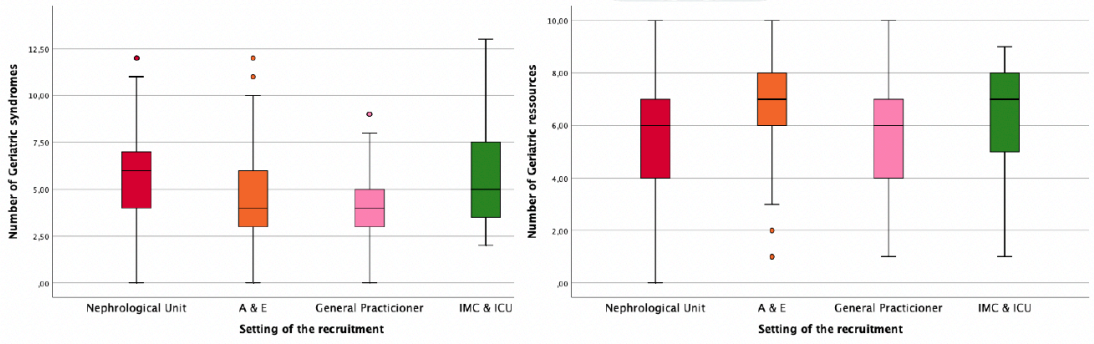


Figure 2&3: Both the number of GS (Figure 2, left) and the number of GR (Figure 3, right) were statistically significant (p<0.001). The highest number of GS were in patients admitted to IM with a median of 6 GS (4-7) (Figure 2, left), while GR were mostly present in patients admitted to the A&E and the ICU, with a median of 7 (6-8 and 5-8) (Figure 3, right).

5. Literature

1.**Meyer AM** et al., The prognostic significance of geriatric syndromes and resources. Aging Clin Exp Res. 2020 Jan; 32(1):115-124
2.**Ellis G** et al., Comprehensive geriatric assessment for older adults admitted to hospital: meta-analysis of randomized controlled trials. BMJ, 2011; 343
3.**Pilotto A.** , Development and validation of a multidimensional prognostic index for one-year mortality from comprehensive geriatric assessment in hospitalized older patients. Rejuvenation Res,2008;11:151-61
4.**Rubenstein LZ**, Effectiveness of geriatric evaluation unit. A randomized clinical trial.N Engl J Med, 1984;311:664-1670
5. **Volpato S**, Bazzano S, Fontana A, Ferrucci L, Pilotto A. Multidimensional Prognostic Index predicts mortality and length of stay during hospitalization in the older patients: a multicenter prospective study. J Gerontol A Biol Sci Med Sci .2015; 70:325-31

7.8 Supplement 6

Klinischer Fortschritt | Geriatrie

Thieme

Präventive Geriatrie: kognitiven Abbau verhindern

Autoren
Anna Maria Meyer[1*], Natalie Podolski[1*], Lena Pickert[1*], Maria Cristina Polidori[1, 2]

Institute
1 Klinische Altersforschung, Klinik II für Innere Medizin und Zentrum für Molekulare Medizin, Uniklinik Köln
2 CECAD, Universität zu Köln, Medizinische Fakultät und Uniklinik Köln

Bibliografie
DOI https://doi.org/10.1055/a-0955-9587
Dtsch Med Wochenschr 2020; 145: 146–150

ISSN 0012-0472

WAS IST NEU?

Prävention des kognitiven Abbaus Maßnahmen zur Früherkennung und zur Prävention des kognitiven Abbaus stehen im Vordergrund der Therapie. Im Gegensatz zur früheren Trennung zwischen neurodegenerativen und vaskulären Formen der Demenz wird aktuell die konsequente Therapie und Einstellung von kardiovaskulären Risikofaktoren angestrebt, um das Fortschreiten von möglicherweise allen Demenzformen zu verlangsamen. Die im Mai dieses Jahres von der Weltgesundheitsorganisation veröffentlichten Leitlinien geben Anhaltspunkte, wie dem Nachlassen der kognitiven Funktion mit zunehmendem Alter begegnet werden kann. Zu den Säulen der Prävention gehören eine ausgewogene Ernährung (für die Substitution einzelner, künstlicher Nährstoffe gibt es keine Evidenz), körperliche Aktivität (vor allem aerobes Training), ausreichender Schlaf, Konvivialität und soziale Interaktion (sensorische Störungen, gerade eine Beeinträchtigung des Hörens, dürfen nicht unterschätzt werden) sowie kognitive Aktivitäten und Übungen, die die allgemeinen, exekutiven und logischen Funktionen, die Denkgeschwindigkeit und das Arbeitsgedächtnis unterstützen.

Konsequenz für den klinischen Alltag Obwohl alle o. g. Bereiche des Lebensstils für die Prävention des kognitiven Abbaus wichtig sind, sind multidimensionale Interventionen nur dann für den Erhalt der Funktionen wirksam, wenn diese

- auf die Bedürfnisse jedes einzelnen Patienten zugeschnitten werden (die sogenannten personalized tailored interventions) und
- mit persönlichem Interesse, guter Lebensqualität und adäquatem Wohlbefinden verbunden sind.

Stand der Dinge

In einer kontinuierlich älter werdenden Gesellschaft erhalten altersassoziierte kognitive Erkrankungen zunehmende Aufmerksamkeit, auch dadurch, dass gerade das multifaktoriell bedingte demenzielle Syndrom mittlerweile eine sehr hohe Prävalenz erreicht hat [1]. Kognitive Störungen gehen mit wichtigen geriatrischen Syndromen wie Stürzen, Delir und mangelnder Adhärenz sowie mit Pflegebedürftigkeit einher. Allerdings wird die kognitive Beeinträchtigung, insbesondere bei Krankenhausaufenthalten anderer Ursache, nicht systematisch evaluiert. Trotz neuer diagnostischer Kriterien des National Institute of Aging und der Alzheimer-Association (NIA-AA) kommt die Mehrheit der kognitiven Störungen im hohen Alter vor und die schleichenden Symptome stellen sich über Jahrzehnte in einem Kontinuum zwischen intakter Hirnfunktion und Demenz dar.

Im klinischen Alltag wird zur umfassenden Erhebung der Ressourcen sowie funktionsbasierter Probleme älterer Patienten das Comprehensive Geriatric Assessment (CGA) genutzt. Durch das CGA lassen sich die physischen, psychischen, funktionellen und kognitiven Fähigkeiten der Patienten abbilden, wodurch gezielt ein individuelles Therapieschema entwickelt werden kann. Das CGA beinhaltet unter anderem Assessments zur Alltagskompetenz (z. B. Activities of Daily living), zur Ernährung (z. B. MNA-SF) und zur Kognition (MMST, SPMSQ), es werden aber auch die sozialen Lebensumstände des Patienten oder seine Medikation betrachtet. Ziel ist es, ein umfassendes Bild des Patienten zu erhalten [2].

Die spezielle Diagnostik kognitiver Funktionseinschränkungen wird aktuell zunehmend angepasst – die Fokussierung auf die klinische Symptomatik soll durch eine auf Biomarkern basierende Kategorisierung ergänzt werden. Hierdurch soll eine frühzeitige Diagnose von Demenzformen, wie z. B. die Alzheimer-Krankheit, ermöglicht werden, denn nur die Patienten, die an einem Morbus Alzheimer leiden, profitieren von einer Therapie mit Acetycholinesterasehemmstoffen oder Memantin [3]. Diese wirken allerdings symptomatisch, eine spezifische pharmakologische Behandlung bei den anderen Demenzformen gibt es nicht. Der monoklonale Antikörper Aducanumab verhindert die Akkumulation von Amyloid und reduziert bei gering betroffenen Alzheimer-Patienten das Risiko einer Krankheitsprogression. Der Hersteller hat in den USA eine Zulassung beantragt. Hingegen gibt es für eine medikamentöse

* Equal contributors.

Therapie zur Prävention von multifaktoriellen Demenzerkrankungen in der aktuellen S3-Leitlinie keine Evidenz. Lediglich eine Therapie von einzelnen Risikofaktoren, beispielsweise zur Reduktion eines erhöhten Blutdrucks durch Antihypertensiva als Risikoreduktion der vaskulären Demenz, steht aktuell zur Verfügung.

Da es keine heilende medikamentöse Therapie des demenziellen Syndroms oder der Altersdemenz gibt, steht hier die Prävention im Fokus. Zu den Risikofaktoren des demenziellen Syndroms gehören modifizierbare Lifestyle-Faktoren wie Rauchen, Alkoholkonsum, körperliche Inaktivität, Adipositas (siehe Zusatzinfo: Alzheimer's Association: 10 Ways to love your brain) sowie chronische Erkrankungen wie Diabetes, arterielle Hypertonie und Herz- und Niereninsuffizienz [4].

Enorm wichtig bleiben weiterhin die frühe Detektion und die Prävention von kognitiven Einbußen.

ALZHEIMER'S ASSOCIATION: 10 WAYS TO LOVE YOUR BRAIN

- Break a sweat! → regelmäßige körperliche Aktivität
- Hit the books! → lebenslanges Lernen
- Butt out! → Nichtrauchen
- Follow your heart! → Prävention kardiovaskulärer Risikofaktoren
- Heads up! → Prävention von Schädel-Hirn-Traumata
- Fuel up right! → ausgewogene Ernährung
- Catch some Zzz's! → Schlafhygiene
- Take care of your mental health! → Vermeidung von Stress und Depression
- Buddy up! → soziale Integration

Prävention des kognitiven Abbaus

Die im Mai 2019 von der WHO veröffentlichte Leitlinie zur Risikoreduktion des kognitiven Abbaus [5] gliedert die Empfehlung nach Evidenzqualität sowie in die Kategorien modifizierbare Lifestyle-Faktoren und chronische Erkrankungen (siehe Zusatzinfo: WHO-Leitlinien zur Verringerung des Risikos einer Demenzerkrankung).

Die S3-Leitlinie „Demenzen" [6], die WHO-Leitlinie und die Empfehlungen der Alzheimer-Association bestätigen: Die Prävention des kognitiven Abbaus basiert auf der Kontrolle von vaskulären Risikofaktoren und Erkrankungen sowie von 4 Hauptdomänen des Lebensstils:

- Ernährung,
- körperliche Aktivität,
- soziale Aktivität und
- kognitives Training.

WHO-LEITLINIEN ZUR VERRINGERUNG DES RISIKOS EINER DEMENZERKRANKUNG [5]

- Lifestylefaktoren:
  - körperliche Aktivität
  - Raucherentwöhnung
  - Ernährungsgewohnheiten
  - Alkoholentzug
  - kognitives Training
  - soziale Aktivität
- chronische Erkrankungen:
  - Adipositas
  - Bluthochdruck
  - Diabetes mellitus
  - Dyslipidämien
  - Depression
  - Schwerhörigkeit

Ernährung und Schlaf

Ein gesunder Lebensstil mit Vermeidung eines Nährstoffmangels und restriktiver Diäten im jungen Erwachsenenalter ist essenziell, um einem kognitiven Abbau vorzubeugen [4]. Neueste Studien weisen darauf hin, dass schon die frühkindliche Ernährung eine wesentliche Bedeutung für Wachstum und Funktion des Gehirns hat und somit die Weichen für eine spätere gute kognitive Funktion stellt [4].

Umfassende Reviews konnten immer wieder bestätigen, dass vitamin- und polyphenolreiche Diäten mit geringer Aufnahme an gesättigten Fettsäuren vor kognitivem Abbau schützen können, wie z. B. die häufig in der Literatur erwähnte mediterrane Diät [4]. Neuere Ergebnisse weisen allerdings auf eine regionale Komponente hin. In skandinavischen Ländern scheint die nordische Diät mit lokal vorhandenen Lebensmitteln besser geeignet zu sein, kognitiven Abbau zu verhindern. Grund hierfür könnte eine genetisch bedingte unterschiedliche Verstoffwechselung und Bioverfügbarkeit von Nährstoffen sein [4].

Die aktuelle Studienlage zeigt, dass auch pflanzenbasierte Diäten wie MIND (Mediterranean-DASH diet Intervention for Neurodegenerative Delay), DASH (Dietary Approach to Stop Hypertension) und entzündungshemmende Diäten insbesondere bei Personen mit einem erhöhten Risiko für Herz-Kreislauf-Erkrankungen kognitiv protektiv sein können [7]. Auch wenn bereits für zahlreiche Mikronährstoffe ein positiver Effekt auf die Kognition nachgewiesen werden konnte, gibt es aktuell keine Empfehlung zur Nährstoffsupplementation mit sogenannten Nutraceuticals (dt. Nutrazeutika, eine Zusammensetzung aus den englischen Begriffen „nutrition" – „Ernährung", und „pharmaceutical" – „pharmazeutisch") [5]. Die natürliche, vollwertige und regionale Ernährung scheint die für die Kognition protektivste Ernährungsform zu sein. Gesundheitskompetenz der Patienten im Hinblick auf Ernährung, Lebensmit-

tel und deren Zubereitung spielt eine wichtige Rolle in der Prävention von kognitiven Defiziten [4, 7, 8]. Erste Symptome einer Mangelernährung sollten möglichst früh erkannt und korrigiert werden, um einem Nährstoffmangel vorzubeugen [9]. Bei mangelernährten Personen sollte eine Verbesserung der Nahrungsaufnahme forciert werden, statt eine Nährstoffsupplementierung anzustreben. Auch Adipositas und kalorienreiche Diäten scheinen die Alterungsprozesse des Gehirns durch Inflammation schneller fortschreiten zu lassen [4, 7, 8].

Neben der Ernährung ist ein weiterer wesentlicher Faktor für gesundes kognitives Altern der Schlaf. Die WHO hat im Mai dieses Jahres für den neuen ICD-10 für Schlafstörungen die neue Diagnose der „Schlaf-Wach-Störungen" verabschiedet. Studien zeigen, dass Schlaf eine überragende Bedeutung für die Funktionsfähigkeit des Gehirns hat, denn Studien weisen darauf hin, dass Schlaf wesentlich daran beteiligt ist, das Nervensystem von toxischen Substanzen und Abfallprodukten zu reinigen, insbesondere auch von denen, die im Zusammenhang mit Demenzerkrankungen stehen [10]. Die häufigsten schlafbezogenen Störungen sind exogen durch schlechte Schlafhygiene oder einen Mangel an Schlafenszeit ausgelöst, was den Schlaf als präventiven kognitiven Faktor gut beeinflussen lässt. Die optimale Schlaflänge determiniert sich neuesten Erkenntnissen nach zwischen dem 20. und 30. Lebensjahr, liegt zwischen 4 und 10 Stunden und verändert sich im Laufe des Lebens – auch im Alter – nicht. Den Zusammenhang zwischen Schlaf und Kognition zeigt ebenfalls eine neuere Studie, die eine ausgeprägte jahreszeitenabhängige Variation in der kognitiven Leistungsfähigkeit aufzeigt – mit besserer Leistungsfähigkeit im Sommer und im Herbst im Vergleich zu Winter und Frühjahr. Grenzwerte der Diagnose neurokognitiver Störungen sollten hier überdacht werden [11]. Die Diagnostik und Behandlung von Schlaf-Wach-Störungen sollten daher ein wichtiges Ziel bei älteren Patienten sein, um eine qualitative Verbesserung von Schlaf gerade beim älteren Menschen zu erreichen, um dem kognitiven Abbau präventiv entgegenzutreten.

Sport

Studien konnten zeigen, dass Sport zu einer Senkung antiinflammatorischer Biomarker wie des C-reaktiven Proteins (CRP), des Tumornekrosefaktors alpha (TNF-α) und verschiedener Interleukine führt – Marker, die bekanntermaßen bei Personen mit Demenz in erhöhten Serumspiegeln vorliegen [8, 9, 12]. Gleichzeitig kann körperliche Aktivität die Entstehung von freien Sauerstoffradikalen und damit oxidativen Stress verringern [8, 9].

Neueste Studien der Mikrobiom-Forschung konnten zeigen, dass sportliche Aktivität eine modulierende Wirkung auf die mikrobielle Zusammensetzung und damit auch auf neurodegenerative Prozesse haben kann [13]. Die Ergebnisse weisen auch daraufhin, dass die gesteigerte zerebrale Durchblutung beim Sport den Abbau von hyperphosphorylierten Tau-Proteinen und β-Amyloidplaques fördern kann [14]. Tau-Proteine und Amyloidplaques spielen besonders bei der Alzheimer-Demenz eine wichtige Rolle.

Körperliche Aktivität hat auch direkt für den Patienten spürbare Auswirkungen wie Gewichtsreduktion, Blutdrucksenkung, erhöhte Blutdruckstabilität und bessere Leistungsfähigkeit, was bereits in zahlreichen Studien belegt werden konnte [4, 8, 9, 12]. Dabei kommt es nicht auf die Frequenz der körperlichen Aktivität an – wichtig scheint vielmehr, dass es sich um eine aerobe Aktivität handelt [4, 8, 9, 12]. Für nicht aerobe Sporteinheiten konnte kein positiver Effekt nachgewiesen werden [5].

Soziale Teilhabe

Studien zeigen, dass Personen mit einer längeren Teilhabe am Arbeits- und Sozialleben eine deutlich bessere kognitive Funktion gegenüber Personen mit einem weniger sozialaktiven Lebensstil aufweisen [2]. Hierbei könnten das gemeinschaftliche „Wir"-Gefühl und der soziale Rückhalt entscheidende Faktoren für die unterschiedliche Entwicklung der Kognition darstellen.

Eine wichtige Grundvoraussetzung für eine gesunde soziale Teilhabe ist die Hörfähigkeit der Patienten. Personen ohne Hörbeeinträchtigung zeigen eine bessere Aufrechterhaltung der kognitiven Fähigkeiten [15]. Erschwerte Kommunikation ist einer der wesentlichen Faktoren, der durch soziale Isolation zu kognitivem Funktionsverlust führen kann [2].

Kognitives Training

Neue Erkenntnisse deuten darauf hin, dass die Intelligenz durch kognitives Training gesteigert werden kann [16]. Vor allem in Bezug auf die kognitive Gesamtfunktion [17], die Denkgeschwindigkeit und das Arbeitsgedächtnis scheint kognitives Training einen steigernden Effekt zu haben. Der Fokus beim kognitiven Training sollte neben der Gedächtnisleistung auch auf den Exekutivfunktionen liegen, mit denen wir unsere Gefühle und Handlungen kontrollieren. Typische Übungen für die Kognition sind die, die Aufmerksamkeit, Konzentration, das Arbeitsgedächtnis, aber auch Fähigkeiten wie Problemlösung und Flexibilität unterstützen. Wichtig scheint es zu sein, dass sich die Patienten persönliche Ziele setzen, welche Alltagskompetenzen gesteigert werden sollen. Das kognitive Training sollte dann mit Fokus auf die persönlichen Ziele und mindestens über 2–3 Monate 2- bis 3-mal pro Woche durchgeführt werden [18]. Patienten, die vor Beginn des Trainings niedrige Werte in der neuropsychologischen Testung aufweisen, profitieren signifikant besser als Patienten mit höheren Baseline-Werten [19].

Die Übungen werden klassisch mit Stift und Papier (als sog. Pen&Pencil-Übung) durchgeführt, mittlerweile gibt es auch große Fortschritte im Bereich des „gamified training" [20], welches am PC durchgeführt wird und den Patienten neue Anreize bieten soll. Beispiel für ein kognitives Trainingsprogramm ist NEUROVitalis [21]. Auch in den aktuellen WHO-Leitlinien findet sich die Empfehlung zu kognitiver Aktivität – dennoch ist sie immer noch relativ schwach, weil die Evidenz für kognitives Training noch nicht ausreichend ist [5].

Klinische Relevanz

Eine ausgewogene Ernährung sollte auf den Patienten und seine Herkunft individuell abgestimmt sein. Nährstoffsupplementation kann eine natürliche und vollwertige Ernährung nicht ersetzen.
Schlafstörungen beim älteren Menschen sollten ernstgenommen, diagnostiziert und therapiert werden, da eine gute Schlafqualität und -quantität möglicherweise zur Prävention kognitiver Störungen beiträgt.
Körperliche Aktivität hat einen positiven Einfluss auf viele Aspekte der Pathogenese einer demenziellen Erkrankung. Patienten sollten zu jeglicher Art der aeroben Aktivität motiviert werden.
Beeinträchtigungen des Hörens und der Kommunikation sollten frühzeitig therapeutisch angegangen werden, um einen kognitiven Abbau zu verhindern.
Kognitive Aktivität und kognitives Training sollen dem alternden Menschen ohne kognitive Einbuße oder mit milden kognitiven Einschränkungen empfohlen werden.

Konsequenz für den klinischen Alltag

Die Studien der letzten Jahre konnten bestätigen, dass eine Monoprävention des kognitiven Abbaus nicht ausreicht. Die FINGER-Studie untersuchte den Effekt von Ernährung, physischem und kognitivem Training sowie Monitoring von vaskulären Risikofaktoren als teamintegrierte multidimensionale Intervention auf die kognitiven Leistungen und Alltagsfunktionen. Patienten in der Interventionsgruppe zeigten einen geringeren kognitiven Abbau [22]. Ältere Risikopatienten profitierten auch in Bezug auf ihre Multimorbidität [23]. Ebenfalls konnten neueste Ergebnisse der MAPT-Studie durch eine Langzeit-Omega-3-Supplementation zusammen mit Ernährungs- und Sportberatung, kognitivem Training und Therapie vaskulärer Risikofaktoren einen Rückgang von Gedächtnisbeschwerden vorweisen [24]. Die beste kognitive Prävention im Alter ist demnach das Ausschöpfen der Möglichkeiten aller 4 Säulen:

- Ernährung,
- Sport,
- soziale Teilhabe und
- kognitives Training.

Doch auch wenn eine Multidomänen-Prävention durchgeführt wird, können Studien oft nur einen begrenzten Effekt dieser Interventionen auf die Grundgesamtheit verzeichnen. Die Population der älteren Menschen ist bekanntlich sehr heterogen, was eine individuelle und personalisierte Prävention notwendig macht. Das Geriatrische Assessment (Comprehensive Geriatric Assessment, CGA) stellt ein optimales Instrument zur Bedarfsermittlung dar [2]. Darüber hinaus können durch ein CGA die verschiedenen Teilaspekte einer Gedächtnisstörung erfasst sowie der Verlauf und die Auswirkungen auf das alltägliche Leben (z. B. durch die Instrumental Activities of Daily Living – IADL) und geriatrische Syndrome und Ressourcen abgebildet werden [2].

Insgesamt gilt, dass sich die Prävention des kognitiven Funktionsverlusts an den Ressourcen, der Lebensqualität und vor allem am Wohlbefinden älterer Menschen orientieren muss.

Klinische Relevanz

Kognitive Prävention sollte als personalisierte Multidomänen-Intervention, basierend auf einem multifaktoriellen Konzept, entstehen. Es muss Spaß machen, kognitiv fit zu bleiben.

Fazit für die Praxis

Für eine effektive Prävention des kognitiven Abbaus mit zunehmendem Alter sollten alle Bereiche des Lebensstils (Ernährung, Bewegung, Erholung, soziale und kognitive Aktivitäten) und die damit assoziierte Kontrolle der vaskulären Risikofaktoren und Komorbiditäten moduliert werden. Dies sollte durch einen personalisierten, zielorientierten Ansatz erfolgen. Das multidimensionale Assessment (Comprehensive Geriatric Assessment, die Erfassung der körperlichen, psychosozialen und funktionellen Aspekte der Person) kann hierbei genutzt werden, um kognitive Einschränkungen frühzeitig zu erkennen und den Verlauf positiv zu beeinflussen.

Interessenkonflikt

Die Autoren geben an, dass kein Interessenkonflikt besteht.

Autorinnen/Autoren

Anna Maria Meyer
ist Assistenzärztin für Innere Medizin an der Klinik II für Innere Medizin an der Uniklinik Köln.
anna.meyer@uk-koeln.de

Natalie Podolski
ist Assistenzärztin für Innere Medizin an der Klinik II für Innere Medizin an der Uniklinik Köln.
natalie.podolski@uk-koeln.de

Lena Pickert
ist Doktorandin des Schwerpunkts Klinische Altersforschung an der Klinik II für Innere Medizin an der Uniklinik Köln.
lena.pickert@uk-koeln.de

Prof. Dr. Dr. Maria Cristina Polidori, FRCP
ist Fachärztin für Innere Medizin und Geriatrie, Oberärztin und Leiterin des Schwerpunkts Klinische Altersforschung an der Klinik II für Innere Medizin und Zentrum für Molekulare Medizin Köln der Uniklinik Köln und CECAD-Mitglied, Universität zu Köln, Medizinische Fakultät und Uniklinik Köln, Köln, Deutschland.
maria.polidori-nelles@uk-koeln.de

Korrespondenzadresse

Prof. Dr. Dr. Maria Cristina Polidori
Uniklinik Köln
Klinische Altersforschung, Klinik II für Innere Medizin
Kerpener Str. 62
50733 Köln
maria.polidori-nelles@uk-koeln.de

Literatur

[1] Winblad B, Amouyel P, Andrieu S. Defeating Alzheimer's disease and other dementias: a priority for European science and society. Lancet Neurol 2016; 15: 455–532. doi:10.1016/s1474-4422(16)00062-4

[2] Polidori MC. Comprehensive Geriatric Assessment in Patients with Cognitive Decline. In: Pilotto A, Martin F, eds.; Comprehensive Geriatric Assessment. Practical Issues in Geriatrics. Berlin: Springer; 2018

[3] Jack CR, Bennett DA, Blennow K et al. NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease. Alzheimers Dement 2018; 14: 535–562. doi:10.1016/j.jalz.2018.02.018

[4] Polidori MC. Lifestyle strategies in cognitive decline: Focus on nutrition. Special Issue of Nutrients 2019. 11(4)

[5] WHO. Risk reduction of cognitive decline and dementia. WHO guidelines. WHO Guidelines. Genf: WHO; 2019

[6] Deutsche Gesellschaft für Psychiatrie und Psychotherapie, Psychosomatik und Nervenheilkunde. S3-Leitlinie „Demenzen". Im Internet: https://www.awmf.org/uploads/tx_szleitlinien/038-013l_S3-Demenzen-2016-07.pdf Stand: 3.12.2019

[7] Chen X, Maguire B, Brodaty H et al. Dietary Patterns and Cognitive Health in Older Adults: A Systematic Review. J Alzheimers Dis 2019; 67: 583–619. doi:10.3233/JAD-180468

[8] Polidori MC. Dementia. In: Rattan S, ed.; Encyclopedia of Biomedical Gerontology. Cambridge, MA: Elsevier Academic Press; 2019

[9] Gerger P, Pai RK, Stuckenschneider T et al. Associations of Lipophilic Micronutrients with Physical and Cognitive Fitness in Persons with Mild Cognitive Impairment. Nutrients 2019; 11: E902. doi:10.3390/nu11040902

[10] Xie L, Kang H, Xu Q et al. Sleep drives metabolic clearance from adult brain. Science 2013; 342: 373–377

[11] Lim ASP, Gaiteri C, Yu L et al. Seasonal plasticity of cognition and related biological measures in adults with and without Alzheimer disease: Analysis of multiple cohorts. PLoS Med 2018; 15: e1002647

[12] Arvanitakis Z, Shah RC, Bennett DA. Diagnosis and Management of Dementia: Review. JAMA 2019; 322: 1589–1599. doi:10.1001/jama.2019.4782

[13] Schlegel P, Novotny M, Klimova B et al. „Muscle-Gut-Brain Axis": Can Physical Activity Help Patients with Alzheimer's Disease Due to Microbiome Modulation? J Alzheimers Dis 2019; 71: 861–878. doi:10.3233/jad-190460

[14] Trigiani LJ, Hamel E. An endothelial link between the benefits of physical exercise in dementia. J Cereb Blood Flow Metab 2017; 37: 2649–2664. doi:10.1177/0271678x17714655

[15] Völter C, Götze L, Bruene-Cohrs U et al. Hearing and cognition: neurocognitive test batteries in otorhinolaryngology. HNO 2019; Oct 18. doi:10.1007/s00106-019-00762-7

[16] Jaeggi SM, Buschkuehl M, Jonides J et al. Short- and long-term benefits of cognitive training. Proc Natl Acad Sci U S A 2011; 108: 10081–10086. doi:10.1073/pnas.1103228108

[17] Chiu HL, Chu H, Tsai JC et al. The effect of cognitive-based training for the healthy older people: A meta-analysis of randomized controlled trials. PLoS One 2017; 12: e0176742. doi:10.1371/journal.pone.0176742

[18] Kallio EL, Öhman H, Hietanen M et al. Effects of Cognitive Training on Cognition and Quality of Life of older Persons with dementia. J Am Geriatr Soc 2018; 66: 664–670. doi:10.111/jgs.15196

[19] Roheger M, Kessler J, Kalbe E. Structured Cognitive Training Yields Best Results in Healthy Older Adults, and Their ApoE4 State and Baseline Cognitive Level Predict Training Benefits. Cogn Behav Neurol 2019; 32: 76–86. doi:10.1097/WMN.0000000000000195

[20] Lumsden J, Edwards EA, Lawrence NS et al. Gamification of Cognitive Assessment and Cognitive Training: A Systematic Review of Applications and Efficacy. JMIR Serious Games 2016; 4: e11. doi:10.2196/games.5888

[21] Baller G, Kalbe E, Kaesberg S et al. NEUROvitalis. Neuropsychologisches Gruppentraining. Köln: Prolog; 2009

[22] Ngandu T, Lehtisalo J, Solomon A et al. A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial. Lancet 2015; 385: 2255–2263. doi:10.1016/s0140-6736(15)60461-5

[23] Marengoni A, Rizzuto D, Fratiglioni L et al. The Effect of a 2-Year Intervention Consisting of Diet, Physical Exercise, Cognitive Training, and Monitoring of Vascular Risk on Chronic Morbidity-the FINGER Randomized Controlled Trial. J Am Med Dir Assoc 2018; 19: 355–360 e351. doi:10.1016/j.jamda.2017.09.020

[24] Andrieu S, Cantet C, Bonnefoy M et al. Effect of long-term omega 3 polyunsaturated fatty acid supplementation with or without multidomain intervention on cognitive function in elderly adults with memory complaints (MAPT): a randomised, placebo-controlled trial. Lancet Neurol 2017; 16: 377–389. doi:10.1016/s1474-4422(17)30040-6

8. Attachment

8.1 Curriculum vitae

LEBENSLAUF LENA PICKERT

Geburtsdatum und -ort: 28.08.1995 in Fürth
Familienstand: ledig

Berufliche Laufbahn

01.01.2021- heute: Assistenzärztin der Medizinischen Klinik I, Klinik für Nephrologie, Transplantationsmedizin und Internistische Intensivmedizin des Krankenhauses Köln-Merheim, Kliniken der Stadt Köln

Schulische Ausbildung & Studium

27. November 2020: Approbation als Ärztin der Landesärztekammer Nordrhein

17. November 2020: Beendigung des Studienganges Humanmedizin mit der Absolvierung der mündlich-praktischen Prüfung (M3) mit der Note 1

November 2019 – Oktober 2020: Praktisches Jahr

1. Tertial: Neurologie (Uniklinik Köln)
2. Tertial: Chirurgie (Mayo University Hospital Castlebar, Irland und Uniklinik Köln)
3. Tertial: Innere Medizin (Uniklinik Köln)

Oktober 2019: Absolvierung der zweiten ärztlichen Basisprüfung (M2) mit der Note 2

April 2016 – Dezember 2020: Klinischer Studienabschnitt des Studiengangs Humanmedizin an der Universität zu Köln

März 2016: Abschluss des vorklinischen Studienabschnittes mit der Durchschnittsnote 2.0

April 2014 – März 2016: Vorklinischer Studienabschnitt des Studiengangs Humanmedizin an der Universität zu Köln

September 2005 – Juli 2013: Gymnasium Christian Ernestinum, Bayreuth
Abschluss Abitur, Durchschnittsnote 1.3

Arbeitserfahrung in Nebentätigkeiten

November 2019 – heute: Selbstständige Leiterin von Notfallschulungen (BLS und ALS) für Notfallschulungen Regional GmBH (Inh.: Benjamin Frings)

April 2016 – Oktober 2019: Studentische Hilfskraft im KISS – Kölner Interprofessionelles Skills Lab & Simulationszentrum

April 2016 – März 2019: Kompetenzfeldtutorin im Dekanat der Medizinischen Fakultät der Universität zu Köln

Famulaturen
Hausarztpraxis Dr. Gycha & Dr. Petterich in Bayreuth
Klinik II für Innere Medizin, Uniklinik Köln
Klinik für Frauenheilkunde und Geburtsmedizin, Krankenhaus Hietzing, Wien, Österreich
Klinik für Neurologie, Heilbronn
Klinik für Anästhesiologie und Intensivmedizin, Krankenhaus der Augustinerinnen, Köln
HNO-Facharztpraxis Dr. Pickert in Bayreuth

Forschung

Promotion unter akademischer Leitung von Prof. Dr. Dr. Maria Cristina Polidori Nelles am Schwerpunkt für Klinische Altersforschung, Klinik II für Innere Medizin des Universitätsklinikums Köln, Beginn Juni 2017
Forschungskoordination des Schwerpunkts für Klinische Altersforschung seit April 2019

Titel der Promotionsarbeit: Challenges and opportunities in the co-management of older inpatients undergoing high-performance medicine: Internal Medicine and Geriatrics in the Cologne model "Universitäre Altersmedizin"

Stipendien:
Reisestipendium der Paul-Martini-Stiftung zum Symposium „Arzneimitteltherapie bei Menschen im Alter" in Berlin, November 2019.
Reisestipendium der Deutschen Gesellschaft für Innere Medizin (DGIM) zur DGIM Konferenz in Wiesbaden, Mai 2019
Reisestipendium der Deutschen Gesellschaft für Geriatrie und Gerontologie (DGG) zur EuGMS Konferenz in Berlin, Oktober 2018
Reisestipendium der Deutschen Gesellschaft für Innere Medizin (DGIM) zur DGIM Konferenz in Mannheim, April 2018

Sprachkenntnisse

- Deutsch, Muttersprache
- Englisch, fließend in Wort und Schrift
- Latinum
- Graecum

8.2 List of publications

8.2.1 Publications (as first author)

Pickert L, Meyer AM, Becker I, Heeß A, Noetzel N, Brinkkötter P, Pilotto A, Benzing T, Polidori MC, Role of a multidimensional prognosis in-hospital monitoring for older patients with prolonged stay. Int J Clin Pract. 2021;00:e13989. https://doi.org/10.1111/ijcp.13989

Meyer AM, Podolski N, Pickert L, Polidori MC. Strategies to prevent age-related cognitive decline. Dtsch Med Wochenschr. 2020;145(3):146-5

8.2.2 Publications (as co-author)

Nolting NA, Hochleitner M, Pickert L, Meyer AM, Becker I, Benzing T, Kochanek M, Polidori MC. The CAM-ICU and the 4AT in older critically ill patients: Prevalence of delirium and implication for prognosis. 2021 (in submission process)

Müller FM, Meyer AM, Pickert L, Hees A, Becker I, Benzing T, Polidori MC. An interdisciplinary intervention is associated with overall improvement of older inpatients in a non-geriatric setting: A retrospective analysis of an observational, longitudinal study with one-year follow up. Geriatric Care. 2021 (accepted for publication 25.06.2021)

Rarek MP, Meyer AM, Pickert L, Pilotto A, Benzing T, Burst V, Polidori MC. The prognostic signature of health-related quality of life in older patients admitted to the emergency department: a 6-month follow-up study. Aging Clinical and Experimental Research. 2020.

Noetzel N, Meyer AM, Siri G, Pickert L, Heess A, Verleysdonk J, Benzing T, Pilotto A, Barbe AG, Polidori MC. The impact of oral health on prognosis of older multimorbid inpatients: the 6-month follow up MPI oral health study (MPIOH). Eur Geriatr Med. 2020.

8.2.3 Poster presentations (as first author)

Pickert et al.: Etablierung eines dreimaligen geriatrischen Assessments im Hinblick auf gezielte Förderung geriatrischer Patienten – Design und vorläufige Ergebnisse der Studie MPI-InGAH II (Multidimensional Prognostic Index – Influence of Geriatric Assessment on Hospitalisation); (DGIM conference in Mannheim, April 2018) (Supplement 1)

Pickert et al.: Veränderungen des Multidimensionalen Prognostischen Index (MPI) während der Hospitalisierung – Ergebnisse der Studie MPI-InGAH II (Multidimensional Prognostic Index – Influence of Geriatric Assessment on Hospitalisation); (DGG-Conference in Cologne, September 2018) (Supplement 2)

Pickert et al.: The role of prognosis for tailored multidimensional interventions in older multimorbid patients: The Multidimensional Prognostic Index (EuGMS conference in Berlin, October 2018) (Supplement 3)

Pickert et al.: Können standardmäßig erhobene Laborparameter ein Comprehensive Geriatric Assessment (CGA) ergänzen? Ein Vergleich der metabolischen Signatur von älteren multimorbiden Patienten (DGIM conference in Wiesbaden, May 2019) (Supplement 4)

Pickert et al.: Characteristics of geriatric syndromes and geriatric ressources of older, multimorbid patients in 4 different settings (EUGMS online conference October 2020) (Supplement 5)

Pickert, Schlotmann, Diesmer et al.: Der multidimensionale prognostische Index (MPI) für die prognostische Stratifizierung älterer, hospitalisierter Patienten mit COVID-19: Eine prospektive Beobachtungskohortenstudie (MPI_COVID-19) (DGG online conference September 2021)