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**Prävalenz und assoziierte Faktoren von Schmerz  
in der alternden Bevölkerung**

**Dissertation**

zur Erlangung des Doktorgrades Dr. rer. biol. hum.  
an der Medizinischen Fakultät der Universität Hamburg.

vorgelegt von:

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Hamburg 2022

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**Angenommen von der  
Medizinischen Fakultät der Universität Hamburg am:** 05.09.2022

**Veröffentlicht mit Genehmigung der  
Medizinischen Fakultät der Universität Hamburg.**

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**Datum der Disputation:** 05.09.2022

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## Liste der Abkürzungen

ADL	Activities of daily living
AgeCoDe	German Study on Ageing, Cognition and Dementia in Primary Care Patients (AgeCoDe)
AgeQualiDe	Needs, health service use, costs and health-related quality of life in a large sample of oldest-old primary care patients (85+)
BASE	Berlin Aging Study/Berliner Altersstudie
BMI	Body Mass Index
BPI	Brief Pain Inventory
CASMIN	Comparative analysis of social mobility in industrial nations
CHAPO	Challenges and potentials model of quality of life of the very old
CI	Confidence interval
ebd.	Eben dieses
ff.	Fortfolgende
F-Sozu	Fragebogen zur sozialen Unterstützung Kurzform 14
GCPS	Graded Chronic Pain Scale
GDS	Geriatric Depression Scale
IBM	International Business Machines
ICF	International Classification of Functioning, Disability and Health
ISAP	International Association for the Study of Pain
KNDD	Kompetenznetz Demenzen
LSDC	The Longitudinal Study of Danish Centenarians
M	Mean
MCI	Mild cognitive impairment
MMSE	Mini-Mental State Examination
MultiCare	Comorbidity and multimorbidity in primary health care
NCI	Nicht-kognitiv beeinträchtigt
NRW	Nordrhein-Westfalen
o.ä.	Oder ähnliches
OR	Odds ratio
PAVK	Periphere arterielle Verschlusskrankheit
PRS	Pain Rating Scale
SD	Standard deviation

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SE	Standard error
SHARE	Survey of Health, Ageing and Retirement in Europe
u.a.	Unter anderem
Vgl.	Vergleichend
WHO	World Health Organisation
z.B.	Zum Beispiel

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## Liste der Publikationen

### **1. Prevalence of pain and its associated factors among the oldest-olds in different care settings - results of the AgeQualiDe study**

Mallon T, Ernst A, Brettschneider C, König H, Luck T, Röhr S, Weyerer S, Werle J, Mösch E, Weeg D, Fuchs A, Pentzek M, Kleineidam L, Heser K, Riedel-Heller S, Maier W, Wiese B, Scherer M BMC FAM PRACT. 2018;19(1):85.

### **2. Lifestyle Aspects As A Predictor Of Pain Among Oldest-Old Primary Care Patients:A Longitudinal Cohort Study**

Mallon T, Eisele M, König H, Brettschneider C, Röhr S, Pabst A, Weyerer S, Werle J, Mösch E, Weeg D, Fuchs A, Pentzek M, Heser K, Wiese B, Kleineidam L, Wagner M, Riedel-Heller S, Maier W, Scherer M CLIN INTERV AGING . 2019;14(14):1881—1888.

### **3. The moderating effects of social support and depressive symptoms on pain among elderly multimorbid patients-data from the multicentre, prospective, observational cohort study MultiCare**

Mallon T, Schäfer I, Fuchs A, Gensichen J, Maier W, Riedel-Heller S, König H, Mergenthal K, Schön G, Wegscheider K, Weyerer S, Wiese B, van den Bussche H, Scherer M AGING MENT HEALTH. 2021;5; 1-7.

## 1. Synopsis

Schmerzen gehören zum Altern dazu – diese Annahme ist in der Bevölkerung laut Deutscher Schmerzgesellschaft e.V. sehr verbreitet (1). Jedoch ist bisher wenig darüber bekannt, wie häufig Schmerzen tatsächlich ab einem Alter von 80 Jahren vorkommen, welche Faktoren positiv und welche wiederum negativ mit dem Schmerzgeschehen in dieser Altersgruppe zusammenhängen. Dabei gilt die Gruppe der über 80-Jährigen als die am schnellsten wachsende Bevölkerungsgruppe in Deutschland. Hochrechnungen erwarten einen Anstieg von 4,2% im Jahre 2000 auf 13,4% im Jahr 2050 (2), wodurch auch mit einem erhöhten Behandlungsbedarf in der Altersgruppe zu rechnen ist. Zudem weisen aktuelle Prognosen zur Lebenserwartung der heute geborenen Personen auf eine weitere Steigerung der Lebenserwartung und somit auch auf eine Zunahme der Anzahl von Personen, die zur Gruppe der Hochaltrigen zählen (3).

Die vorliegenden Arbeit untersucht deshalb die Häufigkeit von Schmerzen und sowie mit Schmerzen assoziierten Faktoren für die Gruppe der Hochaltrigen und älteren multimorbidien Patient:innen in Deutschland. Grundlage für die Auswertung bilden die Daten zweier Kohortenstudien mit Hausarztpatient:innen aus Deutschland.

In der Diagnostik, Behandlung und Therapie chronischer Schmerzen hat sich das biopsychosoziale Modell durchgesetzt (4,5), welches neben biologischen Faktoren auch psychische und soziale Komponenten der Patient:innen miteinbezieht. Infolgedessen werden die besondere Lebenssituation der Hochaltrigen und multimorbidien Patient:innengruppe in auch diesem Kontext untersucht und Faktoren der individuellen Lebensweise wie z.B. Ernährung, Alkohol- und Tabakkonsum sowie die körperliche Aktivität mit berücksichtigt (6).

### 1.1. Hochaltrigkeit

Das hohe Alter ist häufig mit Einschränkungen in Bereichen der Gesundheit und Lebensführung konnotiert. Jedoch wendet sich die öffentliche Diskussion von der Stigmatisierung des ‚alten kranken‘ Menschen ab. Vielmehr wird angestrebt, den hochaltrigen Menschen in seiner Ganzheit und Komplexität zu erfassen und ihm so gerecht zu werden (7). Ein Ansatz ist dabei, den gesamten Lebenszyklus in den Ist-Zustand der Person mit einzubeziehen und eine Reduktion auf Verluste und Beeinträchtigungen zu vermeiden. Die Weltgesundheitsorganisation (WHO) betont in ihrem Weltbericht über *Altern und Gesundheit* den ressourcenorientierten Ansatz des Alterns und definiert „Gesundes Altern als [einen] Prozess der Entwicklung und Aufrechterhaltung der funktionalen Fähigkeit, die Wohlbefinden im Alter ermöglicht.“ (8). Der Definition liegt zum einen der Ansatz zugrunde, dass jedem Menschen körperliche und geistige (intrinsische) Kapazitäten zur Verfügung stehen, und der Mensch zum anderen in Wechselbeziehung mit seinem Lebensumfeld steht. Aus dieser

Interaktion ergeben sich funktionale Fähigkeiten, die bestimmen inwieweit eine Person die Ausgestaltung ihres/seines Lebens nach den eigenen Vorstellungen vollziehen kann. Dabei wird der Prozess des „Gesunden Alterns“ als dynamisch und steuerbar bis in den Lebensabschnitt der Hochaltrigkeit charakterisiert (vgl. ebd.).

### 1.1.1 Zur Definition der Hochaltrigkeit

Hochaltrigkeit, auch als das vierte Lebensalter bezeichnet, lässt sich in Form eines genauen zeitlichen Fixpunktes, wie beispielsweise der Übertritt in das Rentenalter als Schwelle zum dritten Lebensalter, schwer einordnen (9). Insbesondere die große Heterogenität der Population und die im Lebensverlauf unterschiedlich ausgeprägten sozialen, physischen, ökonomischen und kulturellen Unterschiede erschweren hier eine eindeutige Definitionsfindung (10,11). In der Literatur ist der Beginn der Hochaltrigkeit jedoch um das 75., spätestens das 85. Lebensjahr markiert (12). Für die Operationalisierung in Studien wird Hochaltrigkeit zwischen dem 80. und 85. Lebensjahr angesetzt. Aus demographischer Perspektive wird der Beginn der Hochaltrigkeit darüber definiert, dass 50 Prozent der Angehörigen eines Geburtsjahrgangs verstorben sind (13). Somit unterliegt die Bestimmung des Beginns der Hochaltrigkeit der aktuellen Entwicklung der Lebenserwartung.

Für die hier vorliegende Arbeit wird ein Alter von 80 Jahre und höher als Richtwert für den Beginn der Hochaltrigkeit angesetzt.

### 1.1.2 Aktuelle Studienlage

Das Thema der Hochaltrigkeit hat in den vergangenen Jahren zunehmend an Aufmerksamkeit erhalten, erscheint aber im Vergleich zu den vorhergehenden Lebensabschnitten in der Forschung immer noch unterrepräsentiert (14). Während eine Reihe von Studien zu 100-Jährigen und dem Schwerpunktthema Demenz existieren (z.B. Heidelberger Hundertjährigenstudie I und II, The Longitudinal Study of Danish Centenarians (LSDC) (15–17) wird die Gruppe der Hochaltrigen in der Forschung häufig nicht gesondert betrachtet bzw. als Gruppe der über 75-Jährigen zusammengefasst (vgl. SHARE-Study (18)) und ist erst seit Mitte der 1980er-Jahre international in den Fokus der Altersforschung genommen worden. Eine wichtige Weichenstellung für die Förderung der Altersforschung war der „Vierte Altenbericht zur Lage der älteren Generation in der Bundesrepublik Deutschland“ von 2002, der sich explizit mit den komplexen Lebensumständen hochaltriger- und demenziell erkrankter Menschen auseinandersetzte (19).

In der Forschungslandschaft kann für den deutschsprachigen Raum vor allem die Berliner Altersstudie (BASE) von Baltes et al. (2010) als wichtige Größe genannt werden (20). Die Kohortenstudie umfasste insgesamt 516 Personen im Alter von 70 bis 100 Jahren aus

Westberlin und stützt sich auf Daten aus einem Beobachtungszeitraum von 19 Jahren. Vor allem im späteren Verlauf der Studie wurde eine differenzierte Betrachtung und Analyse der Daten von Hochaltrigen (definiert als 85+) herangezogen.

Vielversprechend erscheint aus deutscher Sicht die seit 2019 als Langzeitstudie geführte Hochaltrigenstudie NRW 80+ (Quality of life and subjective well-being of the very old in North Rhine-Westphalia) der Universität Köln, die anhand einer repräsentativen Stichprobe der über 80-Jährigen in Nordrhein-Westfalen die Lebensqualität der Hochaltrigen mithilfe des integrativen CHAPO-Modells (challenges and potentials model of quality of life of the very old) untersuchen und neue Standards für die Inkludierung hochaltriger Menschen in die aktuelle Forschung erzielen möchte (21).

### 1.1.3 Bio-psycho-soziale Einflüsse im Lebensabschnitt der Hochaltrigkeit

Der Lebensabschnitt der Hochaltrigkeit ist in den meisten Fällen mit einer physischen, psychischen, sozialen und ökonomischen Veränderung der Lebensführung verbunden. Ausschlaggebend für die Beeinträchtigungen im hohen Alter und die Erlangung der Hochaltrigkeit sind vor allem die sozioökonomischen Verhältnisse und die Lebensweise vor dem vierten Lebensalter (22). Insbesondere Frauen sind im vierten Lebensalter häufig stärker von Altersarmut sowie physischen und psychischen Belastungen betroffen (10). Die Zunahme an Beeinträchtigungen kann dabei alle Lebensbereiche umfassen. Insbesondere die körperliche Gesundheit sowie die damit verbundene medizinische Versorgung als auch die soziale Komponente unterliegen durch den natürlichen Alterungsprozess und dem Verlust enger sozialer Kontakte großen Veränderungen in diesem Lebensabschnitt (23).

Auf physiologisch-biologischer Ebene machen sich körperliche Veränderungen und funktionelle Beeinträchtigungen durch altersbedingte Abbauprozesse bemerkbar. Insbesondere das Risiko für Multimorbidität und chronische Erkrankungen steigt in diesem Lebensabschnitt (24). Während das objektive Gesundheitsbefinden sinkt und die Beeinträchtigungen der Aktivitäten des täglichen Lebens (ADL) mit zunehmendem Alter steigen, scheint das subjektive Gesundheitsbefinden im hohen Alter jedoch relativ stabil zu sein (25). Auch erste Ergebnisse der NRW80+-Studie berichten, dass das subjektive Gesundheitsbefinden bei 60,1% der Befragten, über alle Altersgruppen hinweg, als positiv bewertet worden ist (26). Dennoch führen nachlassende Körperfunktionen und Einschränkungen der Mobilität häufig auch zur Inanspruchnahme von informeller oder formeller Pflege.

Auf psychologischer Ebene gibt es Hinweise darauf, dass sich insbesondere die Wahrnehmungsgeschwindigkeit als Aspekt der fluiden Intelligenz (Prozesse des Denkens) altersbedingt verringert, während auf der Ebene der kristallinen Intelligenz (Anwendung

erworbenen Wissens) nur geringe Verluste zu vermerken sind (27). Die soziale Beteiligung an Aktivitäten scheint den altersbedingten Verlust der Intelligenz jedoch abzufedern und die Wahrnehmungsgeschwindigkeit bis ins hohe Alter positiv zu beeinflussen (28). Studienergebnisse zeigen auch, dass die Wahrscheinlichkeit für die Entwicklung einer depressiven Symptomatik im Alter steigt (26). Ebenfalls steigt mit fortschreitendem Alter und Erreichen der Hochaltrigkeit die Wahrscheinlichkeit für kognitive Beeinträchtigungen und das Auftreten einer demenziellen Erkrankung, wobei die Prävalenz insbesondere für Frauen erhöht scheint (29–31). Als protektive Faktoren für kognitive Einschränkungen und Demenz im hohen Alter zeigten vor allem höhere Bildung, eine gute physische Verfassung, kein Schlaganfall in der medizinischen Biografie, das Ausbleiben einer depressiven Symptomatik sowie keine visuellen und auditiven Beeinträchtigungen einen signifikanten Einfluss (32). Auf sozialer Ebene ist der Altersprozess durch Veränderungen der eigenen sozialen Rolle, mit einer Verringerung des sozialen Netzwerks und einem Rückzug an sozialer Teilhabe verbunden (33). Zudem werden Kontaktabbrüche im hohen Alter häufiger im Zusammenhang mit weniger emotional-verbundenen Netzwerkpartner:innen vollzogen oder wenn sich Personen dem Tod nahe fühlen (34). Erste Ergebnisse der Hochaltrigenstudie NRW 80+ zeigten ebenfalls, dass in den höheren Altersgruppen eine Reduktion des sozialen Netzwerks von 6,2 Netzwerkpartner:innen bei den 80-84-Jährigen im Vergleich zu 4,9 Netzwerkpartner:innen bei den über 90-Jährigen auftrat (26). Die vielseitigen Veränderungen im Lebensabschnitt der Hochaltrigkeit verweisen mit zunehmendem Alter auf einen negativen Trend im Zusammenhang mit der Lebenszufriedenheit. Längsschnittlich betrachtet scheinen sich vor allem depressive Symptomatiken als auch der Verlust der Partnerin bei Männern negativ auf die Lebenszufriedenheit auszuwirken (35). Erste Ergebnisse der NRW80+-Studie verweisen zudem auf einen Alterseffekt, demnach sich eine Reduktion der Lebenszufriedenheit der über 90-Jährigen einstellt, während die Lebenszufriedenheit der unter 90-Jährigen relativ hoch bleibt. (26).

## 1.2 Herausforderung chronische Schmerzen im Alter

### 1.2.1 Definition Schmerz

Schmerzen werden nach der International Association for the Study of Pain (IASP) als ein unangenehmes Sinnes- und Gefühlserlebnis, das mit einer tatsächlichen oder drohenden Gewebeschädigung verknüpft ist oder diesem ähnelt, definiert (36). Darüber hinaus wurde die Definition um sechs Schlüsselbegriffe und die Etymologie, der Wortherkunft, erweitert. Darin wird hervorgehoben, dass:

- Schmerz immer eine individuelle Erfahrung ist, der biologische, psychologische und soziale Aspekte zugrunde liegen.
- Schmerzen und die Wahrnehmung von Schmerzen, die Nozizeption, unterschiedliche Phänomene sind.
- Schmerz nicht alleinig durch Aktivitäten der sensorischen Neuronen abgeleitet werden können.
- Schmerzkonzepte sich durch die individuelle Lebenserfahrung ausbilden.
- jede Schmerzäußerung einer Person auch als solche wahrgenommen werden sollte.
- obwohl Schmerz normalerweise eine adaptive Rolle übernimmt, es zu entgegengesetzten Auswirkungen in Bezug auf die soziale und psychologische Gesundheit kommen kann.
- die verbale Äußerung von Schmerzen nur als eine Form des Schmerzausdrucks gesehen werden kann. Ein Mangel an Ausdrucksmöglichkeit bedeutet nicht, dass Menschen oder andere Lebewesen keinen Schmerz empfinden können.<sup>1</sup>

### 1.2.2 Prävalenz und Auswirkung von Schmerzen im Alter

Die Prävalenz chronischer Schmerzen steigt mit zunehmendem Alter an (37). Angaben hierzu variieren jedoch stark abhängig von der Fragestellung und der angewandten Erhebungsmethodik. Für die Gruppe der 55-65-Jährigen liegt die Angabe zwischen 20-80%, bei den über 75-Jährigen variiert sie zwischen 25-80 Prozent. In der Gruppe der Hochaltrigen über 85-Jährigen sinkt sie jedoch leicht auf 25-60% (38,39). Gründe für den Prävalenzrückgang unter den Hochaltrigen wurden bisher nicht systematisch untersucht. Studienergebnisse berichten divergent über die Veränderung der Nozizeption im Alter sowie über altersbedingte biologische und psychosoziale Einflussfaktoren (40).

Die Entstehung chronischer Schmerzen geht im Verlauf des Alterungsprozesses insbesondere mit neurodegenerative Veränderungen, Veränderungen des Schlaf-Wach-Rhythmus, Inflammaging – ein chronisch, unterschwelliger Entzündungszustand aufgrund reduzierter Plastizität der Immunabwehr im Alter (41) -, dem Abbau des muskuloskeletalen Apparates sowie allgemeinen Veränderungen des Stoffwechsels einher (42,43). Dabei stellen altersbedingte Komorbiditäten wie degenerative muskuloskeletale Erkrankungen, Tumorerkrankungen, diabetische Polyneuropathie, periphere arterielle Verschlusskrankheit (PAVK), postherpetische Neuralgie, Trigeminusneuralgie, Arteritis temporalis und Polymyalgia rheumatica ein erhöhtes Risiko für Schmerzen im Alter dar (44,45).

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<sup>1</sup> Frei übersetzt nach <https://www.iasp-pain.org/PublicationsNews/NewsDetail.aspx?ItemNumber=10475>, letzter Zugriff 08.06.2021, 11:59 Uhr

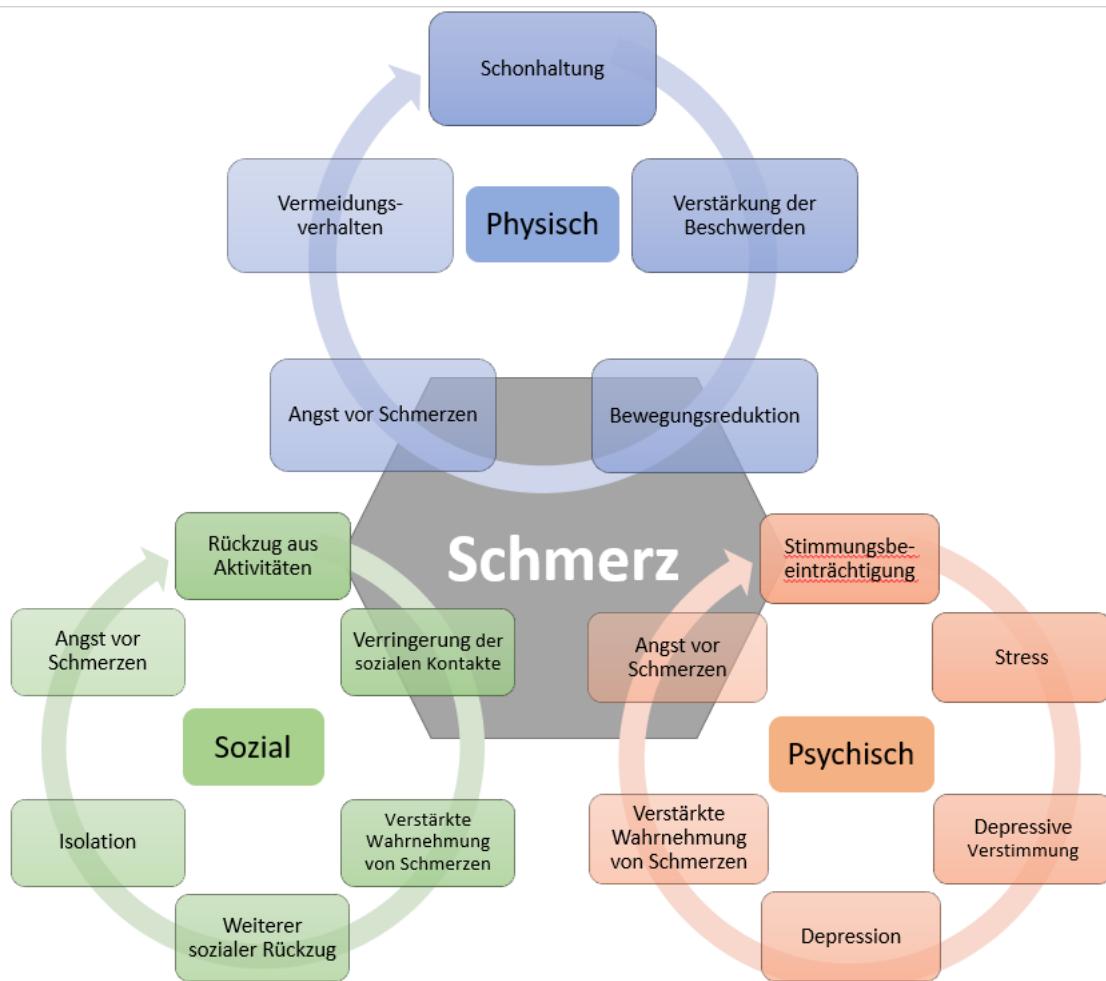
Neben den entstehenden körperlichen Beeinträchtigungen wirken sich chronische Schmerzen auch auf psychische und soziale Faktoren aus. Besonders häufig gehen chronische Schmerzen mit Depressivität und Angststörungen im Alter einher (44,46). Schmerzindizierte Einschränkungen im Alter wirken sich auch auf der sozialen Ebene aus. Es kann u.a. zu Verschiebung der sozialen Funktionen kommen (47). Zudem haben Schmerzen meist weitreichende Auswirkungen und können zu weiteren Einschränkungen im Alltag und Beeinträchtigungen der Lebensqualität führen (48). Besonders betroffen scheinen auch davon vor allem Frauen zu sein (49).

Aufgrund der komplexen Auswirkungen von Schmerzen folgt auch deren Behandlung einem ganzheitlichen Ansatz mit dem Ziel der Etablierung einer interdisziplinär-multimodalen Schmerztherapie. Das der Schmerzbehandlung zugrunde liegende biospsychosoziale Schmerzmodell (4,50) versucht dabei die Wechselwirkungen auf allen Ebenen anzusprechen und einzubinden.

### 1.3 Das biopsychosoziale Modell in Bezug auf Schmerzen

Den theoretischen Bezugsrahmen für die Verankerung der Thesis stellt das „Biopsychosoziale Modell von Gesundheit und Krankheit“ dar, welches George L. Engel 1977 aufstellte und sich seitdem insbesondere im Bereich der Schmerztherapie und Stressbewältigung etabliert hat (4). Engel's Modell verfolgt einen integrativen, medizinischen Ansatz, bei dem biologische, psychische und soziale Faktoren als eine miteinander agierende und in Austausch stehende Einheit betrachtet werden. Im Falle von Krankheit ist die Interaktion auf der biologischen, psychischen und sozialen Ebene gestört. Für eine erfolgreiche Behandlung müssen demnach alle Ebenen miteinbezogen werden (50).

In Bezug auf Schmerzen gilt es den „Schmerzkreislauf“ (siehe Grafik 1) zu unterbrechen. Auf physischer Ebene führen Schmerzen zu Vermeidungsverhalten und Bewegungsreduktion oder Schonhaltungen aus Angst vor Schmerzen, welche die Beschwerden verstärken und zur weiteren Bewegungsreduktion, zum Abbau von Muskelmasse, zu Überbelastung sowie zu Verspannungen und zu Versteifungen führen können. Auf psychischer Ebene kann die Angst vor Schmerzen u.a. zu Stress, Stimmungsbeeinträchtigungen und größeren psychischen Belastungen bis hin zur Depression führen, welche wiederum zur verstärkten Wahrnehmung von Schmerzen führen können. Auf sozialer Ebene kann aufgrund der körperlichen Einschränkungen und psychischen Belastungen ein Rückzug und Entkoppeln von sozialen Aktivitäten erfolgen, welche bis hin zur sozialen Isolation und Vereinsamung führen können (51).



Grafik 1: Schmerzkreislauf (Teufelskreislauf) auf der physischen, psychischen und sozialen Ebene (Grafik in Anlehnung an Nobis et al. Schmerz – eine Herausforderung, 2020, S. 5)

Hochaltrige Menschen sind aufgrund ihrer Lebenssituation und möglicher altersbedingter Einschränkungen besonders gefährdet in den Schmerzkreislauf zu geraten. Zum einen nimmt mit zunehmendem Alter die Anzahl der Erkrankungen zu und zum anderen ist die Wahrscheinlichkeit von Multimorbidität betroffen zu sein, erhöht (52,53). Altersbedingte Komorbiditäten gehen zudem häufig mit körperlichen Einschränkungen und Schmerzen einher, wodurch auch die Wahrscheinlichkeit an einer Depression zu erkranken erhöht wird (54). Zum anderen sinkt die Zahl der sozialen Kontakte im Alter und damit auch die Möglichkeit soziale Unterstützung und Hilfestellungen durch Andere zu erfahren. Des Weiteren kommt es im hohen Alter aufgrund von zunehmendem Pflegebedarf häufig zu Veränderungen der Wohnsituation. Für Deutschland liegt der Anteil der Pflegebedürftigen Personen der 70-74-Jährigen bei 8%, bei den 85 bis 89-Jährigen bei 44% und steigt für die Gruppe der 90+-Jährigen auf 76% (55). Laut Statistischem Bundesamt hatten 50 Prozent der im Pflegeheim vollstationär betreuten Personen bereits das 85. Lebensjahr erreicht oder waren älter (56).

Die altersbedingten Veränderungen und Aufgaben können für schmerzbetroffene Hochaltrige somit mit einer Reihe von zusätzlichen Schwierigkeiten verbunden sein und schnell in den Schmerzkreislauf führen. Eine gezielte und frühzeitige Unterstützung und Prävention auf allen drei Ebenen ist somit unabdingbar.

## 1.4 Fragestellung

Aufgrund der steigenden Lebenserwartung und der wachsenden Anzahl von hochaltrigen Menschen in der Bevölkerung sowie der thematischen Relevanz im Umgang mit Schmerzen im Alter sollen mit der Thesis das Vorkommen von Schmerzen (Prävalenz) als auch mit Schmerzen assoziierte Faktoren in der Gruppe der Hochaltrigen untersucht werden. Die übergeordneten Fragestellungen lauten: Wie ist die Prävalenz von Schmerzen in der hochaltrigen Bevölkerung? Welche Faktoren sind positiv als auch negativ mit dem Schmerzgeschehen im hohen Alter assoziiert? Welchen Einfluss hat die wahrgenommene soziale Unterstützung auf den Zusammenhang von depressiver Symptomatik und Schmerzen im Alter? Erwartet wird eine hohe Schmerzprävalenz, die mit steigendem Alter weiter zunimmt. Des Weiteren wird ausgehend von der Literaturrecherche ein signifikanter Einfluss der Faktoren Geschlecht, depressive Symptomatik, körperliche Aktivität und Body Mass Index (BMI) erwartet. Mit Blick auf das Stress-Puffer-Modell (57) wird vermutet, dass ein hohes Maß an wahrgenommener sozialer Unterstützung positiv auf das Schmerzgeschehen wirkt.

Die Fragenstellungen lauteten für jede Untersuchung explizit:

- 1) Prevalence of pain and its associated factors among the oldest-olds in different care settings – results of the AgeQualiDe study
  - a) Wie stellt sich das subjektive Schmerzempfinden im hohen Alter dar?
  - b) Wie wirkt sich das Schmerzempfinden auf die alltäglichen Aktivitäten aus?
  - c) Wie unterscheiden sich Patient:innen mit und ohne leichte kognitive Beeinträchtigungen in Bezug auf Schmerzen?
  - d) Wie verhält sich der Zusammenhang von Wohnform/Versorgungsform und Schmerz?
  
- 2) Lifestyle aspects as a predictor of pain among oldest-old primary care patients – A longitudinal cohort study
  - a) Anhand welcher Faktoren kann Schmerz im hohen Alter vorhergesagt werden?
  - b) Welche Faktoren der individuellen Lebensweise sind im Alter mit Bezug auf Schmerzen durch Patient:innen beeinflussbar?

3) The moderating effects of social support and depressive symptoms on pain among elderly multimorbid patients – data from the multicentre, prospective, observational cohort study MultiCare

- a) Welchen Einfluss hat die wahrgenommene soziale Unterstützung auf den Zusammenhang von depressiven Symptomen und die Schmerzintensität sowie die Beeinträchtigungen durch Schmerzen im Alltag bei multimorbidem Patient:innen?

## 1.5 Methodik

### 1.5.1 Studiendesign und Stichproben

#### *Kurze Kohortenbeschreibung*

Für die hier präsentierten Analysen aus Untersuchung 1 und 2 konnten die Daten von 738 Proband:innen der AgeCoDe/AgeQualiDe-Kohorte zum Zeitpunkt der AgeQualiDe-Baseline-Befragung genutzt werden. Die Kohorte zeichnet sich durch ihr hohes Alter aus. Zum Zeitpunkt der AgeQualiDe-Baseline-Erhebung betraf das Durchschnittsalter der Teilnehmenden 88,8 Jahre. Unter den Teilnehmenden waren 67% Frauen und über die Hälfte der Teilnehmenden (55,3%) verfügte über eine geringe Bildung (Volksschulabschluss o.ä.). Zudem lebten über 70% der Teilnehmenden noch ohne professionelle pflegerische Unterstützung in der Häuslichkeit. Bei der AgeCoDe/AgeQualiDe-Kohorte handelt es sich um eine gesunde Kohorte hochaltriger deutscher Hausarztpatient:innen.

Für die Fragestellung der Untersuchung 3 wurden die Daten der Baseline-Erhebung und Follow-Up 3-Erhebung der MultiCare-Kohorte genutzt. Zum Zeitpunkt des Follow-Up 3 konnten Daten von 1865 Patient:innen der Studie in die Analysen einbezogen werden. Das Durchschnittsalter der Proband:innen lag zu diesem Zeitpunkt bei 77,6 Jahren. Rund 60% der Teilnehmenden waren weiblich und verfügte über einen geringen Bildungsstatus, 52% waren verpartner und 59% lebten mit einer weiteren Person in einem Haushalt. Bei der MultiCare-Kohorte handelt es sich um eine etwas jüngere, jedoch deutlich gesundheitlich belastetere Kohorte alter Menschen aus Deutschland.

Beiden Studien sind prospektive, multizentrische Kohortenstudien. Eine ausführliche Beschreibung der Studienmethodik (Rekrutierung, Ein- und Ausschlusskriterien) befindet sich auf Seite 32 und 53 dieser Arbeit.

**Tabelle 1: Vergleichende Darstellung der deskriptiven Daten der Baseline-Erhebungen der Studien AgeQualiDe und MultiCare**

	<b>AgeQualiDe (N=738)</b>	<b>MultiCare (N=3189)</b>
Geschlecht: N (%)		
Männlich	239 (32,5)	1298 (40,7)
Weiblich	497 (67,5)	1891 (59,3)
Alter in Jahren: M (SD)	88,8 (3,0)	74,4 (5,19)
Bildung: N (%)		
Niedrig	408 (55,3)	1986 (62,3)
Mittel	226 (30,6)	856 (26,8)
Hoch	104 (14,1)	347 (10,9)
Familienstand: N (%)		
Ohne Partner	463 (63,2)	1791 (43,8)
Mit Partner	271 (36,8)	1397 (56,2)
Haushalt: N (%)		
Alleinlebend	417 (54,3)	1189 (37,3)
Nicht alleinlebend	237 (30,8)	2000 (62,7)
Depressionsscore (GDS): M (SD)	1,99 (2,05)	2,57 (2,61)
Heutiger Schmerzwert: M (SD)	26,15 (26,7)	-
Schmerzintensität (GCPS): M (SD)	-	34,55 (25,55)
Schmerzbeeinträchtigung (GCPS): M (SD)	-	25,96 (29,22)

Abkürzungen: M: Mean; SD: Standard deviation; GDS: Geriatric Depression Score; GCPS: Graded Chronic Pain Scale

### 1.5.2 Endpunkte

#### *Endpunkte von Schmerzen*

Zur Beantwortung der Fragestellungen wurde jeweils eine Form der Schmerzerhebung als Endpunkt gewählt. Für die Untersuchung 1 und 2 wurde auf zwei Fragen aus der deutschen Version des Brief Pain Inventory (BPI) zurückgegriffen (58), die während des strukturierten Interviews abgefragt worden sind. Proband:innen mussten zum einen die Stärke der heutigen Schmerzen auf einer numerischen Skala (PRS – pain rating scale) von 0 bis 100 angeben und im zweiten Schritt die Beeinträchtigungen im Alltag durch Schmerzen in den letzten 24 Stunden auf einer Likert Skala (überhaupt nicht, ein wenig, mittelmäßig, ziemlich, äußerst) nennen.

Die Angaben der Proband:innen wurden in vier Schmerzgruppen eingeteilt: „No pain“ für einen Schmerz-Wert von „0“, „milde Schmerzen“ für einen Schmerz-Wert zwischen 1-30, „moderate Schmerzen“ für einen Wert zwischen 31-60 und „starke Schmerzen“ für Werte von 61 bis 100. Zusätzlich wurde in Untersuchung 1 die Schmerzmedikation der letzten drei Monate erhoben. Alle Medikamente aus dem Anatomisch-therapeutisch-chemischem Klassifikationssystem mit dem Code N02 wurden in die Analysen mit aufgenommen.

## 1. Synopsis

In Untersuchung 3 wurde die Schmerzintensität sowie die schmerzbezogene Beeinträchtigung im Alltag anhand der Graded Chronic Pain Scale (GCPS) erhoben (59). Der Wert zur Schmerzintensität wurde anhand der Angaben zur durchschnittlichen Schmerzstärke der letzten vier Wochen, der aktuellen Schmerzen und der größten Schmerzstärke in den letzten vier Wochen (jeweils mit einer Skala von 0 (keine Schmerzen) bis 10 (schlimmste Schmerzen)) gebildet. Die schmerzbezogenen Beeinträchtigungen im Alltag beinhalteten Familienaktivitäten, Freizeit und Arbeitsfähigkeit. Die Beeinträchtigung wurde ebenfalls auf einer Skala von 0 (keine Beeinträchtigung) bis 10 (komplette Beeinträchtigung) erfasst. Über alle Angaben wurde ein Wert gebildet.

Aufgrund der unterschiedlichen Fragestellungen gab es hinsichtlich der weiteren Parameter Unterschiede in den Analysen. Eine detaillierte Übersicht der relevanten Parameter je Untersuchung ist in Tabelle 2 zu finden.

**Tabelle 2: Übersicht der Parameter gelistet nach Untersuchung**

Nr.	Variable	Prevalence of Pain	Lifestyle Aspects	Social Support
1	Alter	x	x	x
2	Geschlecht	x	x	x
3	Familienstand	-	x	x
4	Bildungsniveau	x	x	x
5	Body Mass Index	x	x	x
6	Wohnform			
	6a Art der Unterbringung	x	-	x
	6b Partner	-	-	x
7	Depressive Symptome (GDS)	x	x	x
8	Barthel-Index	x	-	-
9	Mini Mental Status	x	-	-
10	Rauchverhalten	-	x	-
11	Alkoholkonsum	-	x	-
12	Physikalische Aktivität	-	x	-
13	Schmerzassoziierte Komorbiditäten	-	x	-
14	Wahrgenommene soziale Unterstützung (F-SoZu)	-	-	x
15	Krankheitsschwere	-	-	x
16	Heutige Schmerzstärke	x	x	-
17	Schmerzintensität	-	-	x
18	Beeinträchtigung im Alltag durch Schmerzen	x	x	x
19	Schmerzmedikation	x	-	-

Abkürzungen:

GDS: Geriatric Depression Scale; F-SoZu: Fragebogen zur sozialen Unterstützung K14

### *Parameter aller Untersuchungen*

In allen Untersuchungen wurden neben Alter und Geschlecht folgende Parameter erfasst und in die statistischen Analysen mit einbezogen: Bildungsniveau anhand des CASMIN-Kriterium (60) in niedrig, mittel und hoch, die depressive Symptomatik mithilfe der Kurzform der Geriatrischen Depressionsskala (GDS) (61), anhand derer für jede Person ein individueller Wert von „0“ (keine Depression) bis „15“ (schwerwiegende Depression) berechnet wurde. Eine depressive Symptomatik wurde für Werte ab  $\geq 6$  angenommen und der BMI.

Familienstand und die Wohnform wurden jeweils in zwei der drei Untersuchungen betrachtet. Die Wohnform wurde für Untersuchung 1 und 2 unterteilt in: Zuhause lebend ohne Pflege, Zuhause lebend mit Pflege, im Pflegeheim lebend und im betreuten Wohnen lebend. Für Untersuchung 3 wurden Teilnehmende als alleinlebend eingruppiert, sofern sie allein, im Betreuten Wohnen oder Pflegeheim lebten. Die zweite Kategorie bildeten alle Teilnehmenden, die mit einer weiteren Person (Partner:in oder zusammen mit einer sonstigen Person) in einem Haushalt zusammenlebten.

### *Weitere Parameter*

In Untersuchung 1 wurde zusätzlich eine Subanalyse für Proband:innen mit und ohne kognitiver Beeinträchtigung durchgeführt. Dazu wurde die Mini-Mental State Examination (MMSE) angewandt. Bei Werten unter 25 wurde von einer leichten kognitiven Beeinträchtigung (mild cognitive impairment, MCI) ausgegangen. Außerdem standen die Beeinträchtigungen im Alltag (Barthel-Index (62)) im Vordergrund der ersten Untersuchung. In Untersuchung 2 wurden Faktoren der individuellen Lebensweise und ihre Assoziation zum Schmerzgeschehen betrachtet. Folgende Parameter wurden dafür herangezogen: Rauchverhalten (aktiver Raucher, ehemaliger Raucher und Nichtraucher), Alkoholkonsum (Anzahl der konsumierten alkoholischen Getränke innerhalb einer Woche) und körperliche Aktivität (täglich, mehrmals die Woche, einmal pro Woche, weniger als ein Mal pro Woche, nie innerhalb der letzten vier Wochen). Des Weiteren wurden schmerzrelevante Komorbiditäten (chronische Rückenschmerzen, koronare Herzkrankheit, Arthrose, Gicht, PAVK) untersucht.

In Untersuchung 3 stand der Einfluss der wahrgenommenen sozialen Unterstützung (Fragebogen zur sozialen Unterstützung (F-SozU) K14 (63)) im Fokus. Untersucht wurden die Dimensionen: emotionale Unterstützung (z.B. Emotionen zeigen können, Zuwendung in schwierigen Situationen), instrumentelle Unterstützung (z.B. Hilfe bei praktischen Problemen im Haushalt) und soziale Integration (z.B. Zugehörigkeit zu einer Gruppe). Des Weiteren wurde die Schwere der Erkrankungen mittels der konstruierten Variable „Krankheitslast“

abgebildet (64). Die Einteilung erfolgte mit einer fünfstufigen Likert-Skala (unbedeutend, leicht, mittelschwer, schwer, sehr schwer).

### 1.5.3 Statistische Auswertungen

Für Untersuchung 1 wurden die Daten von allen Proband:innen mit einem Mini Mental Score von  $\geq 19$  und vorhandener PRS in die Analysen aus der AgeQualiDe-Baseline-Erhebung aufgenommen. Für die abhängigen Variablen wurden vier ordinal logistische Regressionsmodelle gerechnet, die für die Variablen Geschlecht, Alter, Bildungsniveau, Wohnform, Schmerzmedikation, BMI, Barthel Index und depressive Symptome angewandt wurden. Model 2 und 3 beinhalten Subanalysen für die Prävalenz von Schmerz in Abhängigkeit der kognitiven Beeinträchtigung. Model 4 beinhaltet die Analyse zur Beeinträchtigung im Alltag durch Schmerzen.

Für Untersuchung 2 standen die Daten der dritten Follow-Up-Erhebung von AgeCode aus 2008/2009 und der AgeQualiDe-Baseline-Erhebung von 2014 zur Verfügung. Model 1 wurde auf Grundlage der Angaben der PRS berechnet. Model 2 basiert auf den Angaben der Skala zur Beeinträchtigung durch Schmerzen im Alltag. In Model 1 wurde eine logistische Regression angewandt, in Modell 2 aufgrund der Kategorien eine ordinal logistische Regression. Für beide Modelle wurde nach Alter, Geschlecht, Bildungsniveau und Familienstatus adjustiert. Zusätzlich wurde für die Faktoren körperliche Aktivitäten, Rauchverhalten, Alkoholkonsum, BMI, depressive Symptome und die vier schmerzassoziierten Komorbiditäten chronischer Rückenschmerz, Gicht, Osteoarrose und periphere arterielle Verschlusskrankheit adjustiert.

Zwei lineare Mehrebenenmodelle für gemischte Effekte wurden für die Fragestellung aus Untersuchung 3 berechnet. Um den Einfluss von wahrgenommener sozialer Unterstützung zu betrachten, wurde der Interaktionsterm aus wahrgenommener sozialer Unterstützung und dem Depressionsscore (GDS) in die Analysen eingeschlossen. Die Schmerzintensität wurde als primärer Endpunkt in Model 1 verwendet. Model 2 nutzte die schmerzbezogene Beeinträchtigung im Alltag als primären Endpunkt. In beiden Modellen wurde für Alter, Geschlecht, Bildungsniveau, BMI, Familienstand, Haushaltsform und Schwere der Krankheitslast kontrolliert.

Für Untersuchung 1 und 2 wurde die SAS 9.3 Software für die logistischen Regressionen verwendet und IBM SPSS Statistics 23 für die übrigen statistischen Analysen. Für Untersuchung 3 erfolgten die Analysen mit IBM SPSS Statistics 26. Das statistische Signifikanzniveau wurde jeweils auf 0,05 gesetzt.

## 1.6 Zusammenfassung der Ergebnisse

Im Folgenden werden die Ergebnisse nach Schwerpunkt und jeweils für alle drei Untersuchungen zusammenfassend dargestellt.

### *Prävalenz von Schmerzen*

In Untersuchung 1 wurde der Frage nach der Prävalenz von Schmerz in der hochaltrigen Bevölkerung nachgegangen. Hierbei zeigte sich, dass bei 63% der hochaltrigen befragten Personen milde bis starke Schmerzen vorlagen. Mit Fokus auf die Wohnsituation fand sich die höchste Schmerzprävalenz von 75,2% bei Proband:innen, die in der Häuslichkeit mit pflegerischer Unterstützung lebten.

Die Schmerzintensität unter den multimorbidien alten Personen zur Baseline-Erhebung im Mittel bei 34,55 von 100 Punkten (26,32 zum Follow-UP) und die Beeinträchtigung durch Schmerzen im Alltag bei 25,96 von 100 Punkten (26,30 zum Follow-Up).

### *Geschlecht und Alter*

In allen drei Untersuchungen zeigte die Variable Geschlecht einen signifikanten Einfluss. Dabei fanden sich in Untersuchung 1 und 3 jeweils für Männer signifikant weniger Schmerzen ( $OR = 0,61$ ; 95%-CI [0,45–0,84]) bzw. signifikant geringere Schmerzintensitätswerte  $-11,07$  ( $SE = 0,076$ ; 95%-CI [-12,56; -9,58]) im Vergleich zu Frauen. Ein ähnliches Ergebnis fand sich für die Beeinträchtigungen im Alltag durch Schmerzen (Untersuchung 1:  $OR = 0,59$ ; 95%-CI [80,43–0,80]; Untersuchung 3:  $8,94$  ( $SE = 0,84$ ; 95%-CI [-10,60; -7,29])). Schließlich zeigte Untersuchung 2, dass Frauen im Vergleich zu Männern im Durchschnitt einen um 6 Punkte erhöhten Schmerzwert auf der PRS aufweisen. Dieses Ergebnis war ebenfalls signifikant ( $coef. 6,00$ ;  $P>t = 0,044$ ).

Die Unterteilung der Stichprobe in zwei Altersgruppen (Untersuchung 1) brachte ein signifikantes Ergebnis für die älteren Personen. So zeigte die Altersgruppen der 90- bis 94-Jährigen signifikant geringere Werte auf der PRS ( $OR = 0,65$ ; 95%-CI [0,48–0,88]) im Vergleich zu den unter 90-Jährigen. Ebenfalls fand sich in der Untersuchung der multimorbidien alten Personen (Untersuchung 3) ein signifikantes Ergebnis für das Alter. Die Verstärkung der schmerzbezogenen Beeinträchtigungen im Alltag stieg mit zunehmendem Alter an:  $0,21$  ( $SE = 0,08$ ; 95%-CI [0,06;0,36]).

### *Negativ assoziierte Schmerzfaktoren*

Untersuchung 1 zeigte, dass die Einnahme von Schmerzmitteln ( $OR = 2,17$ ; 95%-CI [1,48–3,16]), eine depressive Symptomatik ( $OR = 1,15$ ; 95%-CI [1,08–1,22]) und Personen, die in der Häuslichkeit Pflege erhalten ( $OR = 1,60$ ; 95%-CI [1,01–2,53]) negativ mit Schmerzen

assoziiert sind. Diese Faktoren führten neben dem BMI für Personen mit Übergewicht auch zu signifikant stärkeren Beeinträchtigungen durch Schmerzen im Alltag (statistische Angaben siehe Seite 33ff.).

Als weitere negative Assoziationen zeigte Untersuchung 2 signifikant erhöhte Werte der PRS für den BMI (coef. 0,57; P>t = 0,015) sowie die Komorbiditäten PAVK (coef. 13,51; P>t = 0,00) und chronischen Rückenschmerzen (coef. 6,64; P>t = 0,003). Bei vorhandenen chronischen Rückenschmerzen war der Schmerzwert somit um 6,6 Punkte auf der PRS erhöht und bei PAVK um 13,5 Punkte. Zu Beeinträchtigungen im Alltag aufgrund von Schmerzen kam es bei Personen, die an chronischen Rückenschmerzen (OR = 2,03; 95%-CI [1,48 – 2,79]), Osteoarthrose (OR = 1,49; 95%-CI [1,09 – 2,04]) oder depressiven Symptomen (OR = 1,10; 95%-CI [1,02 – 1,08]) litten.

Unter den multimorbidien alten Personen (Untersuchung 3) fanden sich signifikant erhöhte Schmerzintensitätswerte für den BMI 0,52 (SE = 0,07; 95%-CI [0,38;0,66]) und die Krankheitslast 0,42 (SE = 0,04; 95%-CI [0,34;0,51]). Einen signifikanten Einfluss auf die Verstärkung der schmerzbezogenen Beeinträchtigungen im Alltag fand sich für die Parameter: Depression 2,22 (SE = 0,71; 95%-CI [0,84;3,61]), BMI 0,70 (SE = 0,08; 95%-CI [0,54;0,86]) und Krankheitslast 0,48 (SE = 0,88; 95%-CI [0,39;0,58]).

### *Positiv assoziierte Schmerzfaktoren*

Als positiv assoziierter Schmerzfaktor ist die Unterbringung in einem Pflegeheim (OR = 0,51; 95%-CI 0,28–0,93) zu nennen, die zu signifikant geringeren Beeinträchtigungen durch Schmerzen im Alltag führte. Des Weiteren zeigten ehemalige Raucher:innen einen signifikant, um fünf Punkte geringeren Schmerzwert auf der PRS im Vergleich zu Nichtraucher:innen -5,23 (95%-CI [-9,90; -6,63]; p = 0,03). Ebenfalls zeigte sich ein signifikantes Ergebnis für die Bildung -5,05 (95%-CI [-9,48; -6,62]; p = 0,03). So hatten Personen mit mittlerer Bildung einen signifikant geringeren Schmerzwert als Personen mit niedrigerer Bildung. Einen ähnlichen positiven Einfluss der Variable Bildung fand sich auch für die multimorbidien älteren Personen (Untersuchung 3). So fanden sich signifikant geringere Schmerzintensitätswerte für Personen mit mittlerer -2,16 (SE = 0,82; 95%-CI [-3,77; -0,55]) und höherer Bildung -3,50 (SE = 1,16; 95%-CI [-5,77; -1,23]) im Vergleich zu Personen mit geringer Bildung. Keine signifikanten Assoziationen zeigten die Aspekte körperliche Aktivitäten und der Alkoholkonsum.

### *Einfluss der wahrgenommenen sozialen Unterstützung*

Die Untersuchung der moderierenden Rolle der wahrgenommenen sozialen Unterstützung zeigte eine signifikant positive Interaktion für die Schmerzintensität 0,41 (SE = 0,17; 95%-CI [0,08;0,74]). Somit verstärkt sich die Schmerzintensität bei Zunahme der wahrgenommenen

sozialen Unterstützung in Verbindung mit der depressiven Symptomatik. Für den zweiten Parameter Beeinträchtigung durch Schmerzen im Alltag konnte kein signifikanter Einfluss der wahrgenommenen sozialen Unterstützung gefunden werden.

### *Kognitive Beeinträchtigung*

Die Subgruppenanalyse (Untersuchung 1) für Proband:innen mit und ohne kognitive Beeinträchtigung zeigte einen signifikanten Unterschied ( $\chi^2[3] = 4,45; p = ,035$ ). Analog zur gesamten Stichprobe gaben Männer beider Gruppen weniger Schmerzen an (Nicht-kognitiv beeinträchtigt (NCI): OR = 0,61; 95%-CI [0,44–0,85] und MCI: OR = 0,21; 95%-CI [0,05–0,93]). Für beide Gruppen gab es des Weiteren signifikant erhöhte PRS-Werte, sofern eine depressive Symptomatik vorlag (NCI: OR = 1,14; 95%-CI [1,07–1,22]; MCI: OR = 1,42; 95%-CI [1,01–1,99]). Zusätzlich zeigten MCI-Proband:innen, die im Pflegeheim versorgt worden, signifikant geringere PRS-Werte (OR = 0,08; 95%-CI [0,01–0,48]). Darüber hinaus decken sich die Ergebnisse der Nicht-MCI-Gruppe mit den Resultaten für die Analyse der gesamten Stichprobe (detaillierte statistische Angaben siehe Seite 33ff.).

## 1.7 Diskussion

Die vorliegende Arbeit untersuchte die Prävalenz von Schmerz und die Beeinträchtigung durch Schmerzen im Alltag in einer hochaltrigen sowie multimorbid Patient:innengruppe. Zusätzlich wurden die Kohorten auf mit Schmerzen assoziierte Faktoren untersucht.

Die Ergebnisse zeigen, dass die Prävalenz von Schmerzen bei 63% der hochaltrigen Personen auftrat und ältere multimorbide Patient:innen von einer erhöhten Schmerzintensität und Beeinträchtigungen durch Schmerzen im Alltag betroffen waren. Die Ausprägung der Schmerzintensität variierte dabei jedoch deutlich und ist bei multimorbid Patient:innen u.a. von der Krankheitslast abhängig. Ab der Altersgrenze von 90 Jahren und älter traten Schmerzen bei gesunden Personen seltener auf. Beeinträchtigungen durch Schmerzen im Alltag betrafen ebenfalls mehr als zwei Drittel der untersuchten Personen und signifikant häufiger Frauen bzw. seltener Männer. Als mit Schmerzen assoziierte Faktoren zeigten folgende Parameter einen signifikanten Zusammenhang: Geschlecht, Alter, Bildungsniveau, Art der Wohn- bzw. Versorgungsform, BMI, Rauchverhalten, Krankheitslast sowie die Erkrankungen chronische Rückenschmerzen, PAVK, Osteoarrose und eine depressive Symptomatik. Des Weiteren zeigte sich eine positive Interaktion des Moderators wahrgenommene soziale Unterstützung für den Zusammenhang von depressiven Symptomen und Schmerzintensität bei multimorbid Patient:innen.

### 1.7.1 Zentrale Stärken und Schwächen

Hervorzuheben sind vor allem die beiden zur Auswertung herangezogenen Studien AgeCoDe/AgeQualiDe als auch MultiCare an sich. Die AgeCode/AgeQualiDe-Studie liefert Daten von hochaltrigen Patient:innen. Mit der MultiCare-Studie stehen Daten von multimorbid alten Patient:innen zur Verfügung: Beide Studien verfügen über eine große Anzahl an Hausarztpatient:innen aus Deutschland. Zudem fanden in beiden Studien umfassende, standardisierte Erhebungen mit qualifizierten Interviewer:innen in der Häuslichkeit der Proband:innen statt. Beide Studienschwerpunkte, Hochaltrigkeit und Multimorbidität sind zudem in der Studienlandschaft nach wie vor unterrepräsentiert und bedürfen aufgrund der demografischen Entwicklung mehr Aufmerksamkeit.

Beide Studien fanden in einem ähnlichen Zeitrahmen statt, hatten sehr ähnliche Ein- und Ausschlusskriterien und wurden zum Großteil in den gleichen Städten rekrutiert. Dennoch sind die schmerzbezogenen Erhebungsinstrumente nicht direkt vergleichbar. Des Weiteren wurde in AgeCoDe/AgeQualiDe nicht explizit zwischen akutem und chronischem Schmerz unterschieden, sondern nach den Schmerzen der letzten 24 Stunden (BPI) gefragt. Demgegenüber kam bei MultiCare ein Fragebogen zu chronischen Schmerzen (GCPS) zum Einsatz. Ebenfalls ist zu erwähnen, dass der Schmerzaspekt in beiden Studien nur eine sekundäre Rolle einnahm und somit nicht für alle relevanten Faktoren kontrolliert werden konnte.

In beiden Studien ist aufgrund der Anzahl der Studienabrecher:innen von Fehlern durch die Schrumpfung der Kohorten (attrition bias) auszugehen. Ebenfalls können Erinnerungsfehler (recall bias) oder Antwortverzerrungen (response bias) in den standardisierten Interviews sowie Interviewer:inneneffekte nicht ausgeschlossen werden.

### 1.7.2 Einordnung in den Forschungsstand

#### *Biologische Aspekte*

Anhand der Untersuchung wurde deutlich, dass vor allem Frauen auch in der Hochaltrigkeit und von Multimorbidität betroffene Frauen häufiger an Schmerzen und Beeinträchtigungen durch Schmerzen im Alltag leiden bzw. Männer von geringeren Schmerzen und Beeinträchtigungen berichten. Dieser Geschlechtsunterschied ist bereits für jüngere Altersklassen vielfach untersucht und bestätigt worden, wobei sich hier die Grundannahme eines übergreifenden Geschlechterunterschiedes in der menschlichen Biologie hinsichtlich der Schmerzwahrnehmung zu verfestigen scheint (65–67).

Die Ergebnisse zeigen jedoch, dass es zumindest unter den gesunden Hochaltrigen zu keiner weiteren Intensivierung der Schmerzen, sondern tendenziell zur Verringerung der Schmerzen mit zunehmendem Alter kommen kann. Zyczkowska et al. (2007) konnten ebenfalls zeigen,

dass Schmerzen in jeder der fünf Jahre umfassenden Alterskategorie geringer werden und die Anzahl der Personen ohne Schmerzen mit steigendem Alter zunimmt (68). In den Untersuchungen zu Multimorbidität unter hochaltrigen Personen zeigte sich ebenfalls, dass die Gruppe der über 100-Jährigen weniger Erkrankungen aufwies als Personen, die zwischen 80-89 Jahren oder 90-99 Jahren starben (69). Dieses Ergebnis lässt vermuten, dass Personen, die den Lebensabschnitt der Hochaltrigkeit erreichen, über eine gewisse Robustheit verfügen, welche sich vermutlich positiv auf das Schmerzgeschehen auswirkt. Hinweise darauf liefert u.a. die Berliner Altersstudie (20).

### *Psychische Aspekte*

Schmerzen und Depressivität scheinen auch im hohen Alter eng miteinander korreliert, was nochmals die Tragweite und den Einfluss beider Faktoren unterstreicht. Die weitreichenden Auswirkungen auf die Lebensführung und die Lebensqualität führen auch in der Hochaltrigkeit zu vielfältigen Einschränkungen (70). Des Weiteren schätzen von Schmerzen und Depression betroffene Hochaltrige ihre Gesundheit schlechter ein (71). Da sich Schmerzen und Depression gegenseitig bedingen (72–74), ist idealerweise ein frühzeitiges und wiederkehrendes Screening zu implementieren, insbesondere bei Patient:innen mit den hier signifikant assoziierten Komorbiditäten (chronische Rückenschmerzen, PAVK, Osteoarrose und depressive Symptomatik). Erste Ansätze finden sich hierfür in der Nationalen VersorgungsLeitlinie Nicht-spezifischer Kreuzschmerz (75). Da es sich bei den Komorbiditäten um häufig auftretende Erkrankungen im fortschreitenden Alter handelt, besteht die Möglichkeit frühzeitig präventive Ansätze und gezielt Wissen zu den Erkrankungen z.B. im Rahmen der hausärztlichen Routineuntersuchungen zu vermitteln und so eventuelle Langzeitfolgen vorzubeugen.

### *Soziale Aspekte*

Neben der wahrgenommenen sozialen Unterstützung wurden unter den sozialen Aspekten auch die Ergebnisse zum BMI, Rauchverhalten, Bildung sowie zur Wohn- und Versorgungsform zusammengefasst, da diese Faktoren zwar keine rein sozialen Aspekte sind, aber eine gewisse Schnittmenge in den Bereich ausweisen. Für genannten Faktoren fanden sich signifikante Assoziationen mit der Prävalenz und den Beeinträchtigungen durch Schmerzen im Alltag, was sich mit Ergebnissen von Studien zu jüngeren Altersgruppen deckt (76–78). Die Faktoren der individuellen Lebensweise (z.B. Rauchverhalten, Ernährung, körperliche Aktivität) können als bedingt modifizierbar eingestuft werden, da Patient:innen eigenständig durch ihre Lebensweise und Entscheidungen darauf Einfluss nehmen können (79).

## 1. Synopsis

Insbesondere der BMI ist durch gesunde Ernährung und Bewegung beeinflussbar. Schwierigkeiten bestehen jedoch in der dauerhaften Umsetzung und der altersbedingten Einschränkungen, wie z.B. der Mobilität und Zunahme von Gebrechlichkeit. Studien zur körperlichen Aktivität in der alternden Bevölkerung verwiesen dabei auf die Tendenz zur geringeren körperlichen Aktivität mit zunehmendem Alter. So liegt die sportliche Inaktivität der 70 bis 74-Jährigen noch bei 34%, steigt sich jedoch bei den 80 bis 85-Jährigen auf 60% (80), womit u.a. auch das nicht-signifikante Ergebnis für die Anzahl der körperlichen Aktivitäten unter den hochaltrigen Personen erklärt werden kann (Untersuchung 2). Dennoch können gezielte Kraftübungen auch in der Hochaltrigkeit zur Verbesserung der funktionalen Fähigkeiten und Muskelkraft beitragen (81). Der Lebensabschnitt der Hochaltrigkeit als auch die Auswirkungen von Multimorbidität erfordern somit eine Anpassung der Bewegungs- und Trainingskonzepte für die Zielgruppe. Dekker et al. (2019) weisen darauf hin, dass bestehende Empfehlungen zu Bewegung wie z.B. der World Health Organisation (WHO) bisher eher allgemein oder auf spezifische Erkrankungen formuliert sind und die Schwierigkeiten der multimorbidien Klientel nicht ausreichend abbilden (82). Sie postulieren deshalb ein auf die Gesundheitsumstände abgestimmtes Konzept für Menschen mit Multimorbidität, welches ein Gesundheitsassessment, die Anpassung von Übungen an die Erkrankung, Verhaltensänderungen und ärztliche Begutachtung miteinbezieht (vgl. ebd.).

Des Weiteren deuten die Ergebnisse dieser Arbeit an, dass eine erfolgreiche Rauchentwöhnung zu geringeren Schmerzen im hohen Alter führen kann. Rauchen stellt im Zusammenhang mit chronischen Schmerzen ein erhöhtes Risiko für eine erhöhte Symptomlast dar (83). So weisen Raucher:innen signifikant erhöhte Beeinträchtigungen durch Schmerzen, erhöhte Schmerzintensitäten, körperliche Beeinträchtigungen, Schlafprobleme und emotionale Beeinträchtigungen im Vergleich zu Nichtraucher:innen auf (84).

Als weitere Komponente wurde der Einfluss der wahrgenommenen sozialen Unterstützung bei multimorbidien Patient:innen untersucht. Entgegen des Stress-Puffer- Modells führte die wahrgenommene soziale Unterstützung jedoch zur Verstärkung der Schmerzen. Sekundärer Krankheitsgewinn könnte für die multimorbidien Patient:innen als mögliche Erklärung herangezogen werden. So verweisen Studien auf eine Verstärkung des Schmerzverhaltens, sofern die Umwelt sich dem Leiden der betroffenen Person zuwendet (85). Inwiefern die soziale Nähe und die Möglichkeit zum Austausch die Schmerzthematik zusätzlich verstärkt oder das Teilergebnis zur komplexen Situation multimorbider Patient:innen beiträgt, bleibt für zukünftige Arbeiten zu untersuchen.

Auch die Wohnform und Art der Versorgung scheint sich auf die Schmerzintensität und -versorgung auszuwirken (69). Die Ergebnisse deuten darauf hin, dass es für hochaltrige Personen eine Diskrepanz zwischen Zuhause mit ambulanten Pflegedienst - und im

Pflegeheim versorgten Personen in Bezug auf Schmerzen gibt. Ambulant versorgte Personen wiesen dabei die höchsten Schmerzwerte auf. Das komplexe Zusammenspiel von vertrauten Mitmenschen und Umgebung sowie Zeit- und Personalmangel seitens der Pflegekräfte können nur einen Bruchteil dieses Ergebnisses erklären.

### 1.7.3 Ausblick

Die hier vorliegenden Ergebnisse zeigen, dass sich auch in der Hochaltrigkeit Faktoren finden lassen, die positiv als auch negativ mit Schmerzen assoziiert sind. Die drei Bereiche – die biologische, psychologische und soziale Lebenswelt sind dabei weiterhin eng miteinander verwoben. Auf der biologischen Ebene treten der Einfluss des Geschlechts und das Alter an sich hervor. Überschneidung gibt es in der biologischen zur psychologischen Ebene, insbesondere bei vorliegender depressiver Symptomatik und bei mit Schmerzen assoziierten Erkrankungen. Der BMI, das Bildungsniveau, das Rauchverhalten, die Wohn- und Versorgungsform sowie die wahrgenommene soziale Unterstützung zeigten signifikante Assoziationen mit Schmerzen.

Zukünftige Studien könnten den Einfluss der Wohn- und Versorgungsform vertiefend beleuchten, denn 80 Prozent der pflegebedürftigen Menschen (3,3 Millionen Menschen, Stand 2019) wurden in Deutschland in der Häuslichkeit gepflegt (86). Da insbesondere bei der Versorgung in der Häuslichkeit die höchsten Schmerzprävalenzwerte auftraten, wäre eine weiterführende Untersuchung zum Schmerzmanagement im ambulanten Pflegekontext ein nächster Schritt. Ebenfalls bleibt zu bedenken, dass der Fokus in der Hochaltrigkeit als auch bei multimorbidem alten Personen eher auf der Steigerung und Aufrechterhaltung der Funktionalität liegt und Schmerzfreiheit nicht als primäres Ziel gilt (37). Es bedarf zudem weiterer Konzepte, die die Faktoren individueller Lebensweisen (z.B. Ernährung, Bewegung) ansprechen und auf die besonderen Lebensumstände in der Hochaltrigkeit bzw. auf den multimorbidem Menschen abgestimmt sind. Ein erster Ansatz ist dabei u.a. das Projekt „Bewegende Alteneinrichtungen und Pflegedienste 2.0“ aus Nordrhein-Westfalen, welches über Kooperationen zwischen Pflegeeinrichtungen und Sportvereinen Bewegungsangebote in den Pflegeeinrichtungen umsetzt.

Mit den Ergebnissen leistet die hier vorliegende Arbeit einen Beitrag zum besseren Verständnis des Themas Hochaltrigkeit und Schmerzgeschehen und erweitert den aktuellen Erkenntnisstand um einen kleinen Puzzlestein. Die hier dargestellten und untersuchten Faktoren sind jedoch nur ein Teil des komplexen Zusammenspiels von Schmerzen und den Faktoren individueller Lebensweise, genetischer Prädispositionen sowie äußerer Lebensumstände. Die Schwierigkeit in der Ergründung und Verhinderung bzw. Verringerung

## 1. Synopsis

des Schmerzgeschehens im Alter bleibt eine herausfordernde Aufgabe für die medizinischen Versorger:innen und zukünftige Studienvorhaben.

## 2. Prevalence of pain and its associated factors among the oldest-olds in different care settings – results of the AgeQualiDe study

### Abstract

Tina Mallon, Annette Ernst, Christian Brettschneider, Hans-Helmut König, Tobias Luck, Susanne Röhr, Siegfried Weyerer, Jochen Werle, Edelgard Mösch, Dagmar Weeg, Angela Fuchs, Michael Pentzek, Luca Kleineidam, Kathrin Heser, Steffi Riedel-Heller, Wolfgang Maier, Birgitt Wiese, Martin Scherer for the AgeCoDe & AgeQualiDe study group

**Background:** The prevalence of pain is very common in the oldest age group. Managing pain successfully is a key topic in primary care, especially within the ageing population. Different care settings might have an impact on the prevalence of pain and everyday life.

**Methods:** Participants from the German longitudinal cohort study on Needs, Health Service Use, Costs and Healthrelated Quality of Life in a large Sample of Oldest-old Primary Care Patients (85+) (AgeQualiDe) were asked to rate their severity of pain as well as the impairment with daily activities. Besides gender, age, education, BMI and use of analgesics we focused on the current housing situation and on cognitive state. Associations of the dependent measures were tested using four ordinal logistic regression models. Model 1 and 4 consisted of the overall sample, model 2 and 3 were divided according to no cognitive impairment (NCI) and mild cognitive impairment (MCI).

**Results:** Results show a decline in pain at very old age but nonetheless a high prevalence among the 85+ year olds. Sixty-three per cent of the participants report mild to severe pain and 69% of the participants mild to extreme impairment due to pain with daily activities. Use of analgesics, depression and living at home with care support are significantly associated with higher and male gender with lower pain ratings.

**Conclusions:** Sufficient pain management among the oldest age group is inevitable. Outpatient care settings are at risk of overlooking pain. Therefore, focus should be set on pain management in these settings.

**Keywords:** Prevalence of pain, Impairment in daily activities, Care setting, Primary care

Erschienen in: BMC Family Practice, 2018, 19:85.

RESEARCH ARTICLE

Open Access



# Prevalence of pain and its associated factors among the oldest-olds in different care settings – results of the AgeQualiDe study

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## Abstract

**Background:** The prevalence of pain is very common in the oldest age group. Managing pain successfully is a key topic in primary care, especially within the ageing population. Different care settings might have an impact on the prevalence of pain and everyday life.

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## Background

Due to physical or mental illness or disability 42% of women and 29.6% of men aged 85–89 years receive care in Germany (care is termed according to the German law SGB XI). This number increases again for the 90+ year-olds (67.9% women, 51.8% men) [1]. These numbers show that with the aging population more attention has to be paid

to prevalence and management of pain which goes beyond the treatment with analgesics only and includes alternative options such as relaxation techniques or biofeedback in the oldest age group (85+ years). The presence of daily pain leads to a decline on activities of daily living, especially for cognitive impaired individuals [2–5]. Lower levels of education, female gender and a high Body Mass Index (BMI) seem to entail acute and/or chronic pain [2, 6–8]. Individuals reporting more severe pain were found to score significantly lower in memory tests,

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## 2. Prevalence of pain and its associated factors among the oldest-olds in different care settings – results of the AgeQualiDe study

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for executive function and showed an impaired attentional capacity [2] which has an impact on quality of life and one's independence. Along with other special needs developed with growing age such as geriatric syndromes, frailty, comorbidities, falls and functional decline [9–12] the use of a care service or moving to a care facility is an inevitable consequence in many cases.

The German health care system supplies care at home either with the help of a relative or through a mobile care service. Otherwise moving to a care home or to a facility with "assisted living" (Betreutes Wohnen) which aims at maintaining one's independence by providing helpful services e.g., barrier-free apartment, emergency call, meals and a quick access to care support are other options if care is needed [1].

Acute pain is experienced regularly by up to 49–83% of elderly individuals above the age of 60 living in care homes and 40% of elderly individuals living in the community [13, 14]. Each care setting has its own challenges in dealing with pain and pain management such as shortness of time, lack of staff or lack of knowledge [15] but the effects on pain and the apparent housing situation have not been studied in depth yet. However, studies revealed that patients above the age of 85 were found to be less likely to receive adequate analgesic treatment or even none at all [16] and inadequate pain assessment [6, 17, 18]. Very few studies include the group of over 85-year-olds in their research. Therefore, we aimed at uncovering underlying differences in pain prevalence and management and hence our research questions focused on the prevalence of pain in the oldest age group with emphasis on the housing situation, on associated factors with pain and the impact of pain on activities of daily living.

## Methods

### *Study design and sampling*

The data were derived from the German longitudinal cohort study on Needs, Health Service Use, Costs and Health-related Quality of Life in a large Sample of Oldest-old Primary Care Patients (85+) (AgeQualiDe) which is considered a follow-on study (follow-up 7 to 9) on Ageing, Cognition and Dementia in Primary Care Patients (AgeCoDe) (75+). In our analysis, we provide cross-sectional results from the baseline of AgeQualiDe that is the 7th follow-up of AgeCoDe. For the initial study 3327 patients had been recruited from over 138 general practitioners (GP) in six German cities (Bonn, Düsseldorf, Hamburg, Leipzig, Mannheim, Munich) in 2003. All GP patients who participated in the

study provided written informed consent prior to their participation. Both studies – AgeCoDe and AgeQualiDe – have been approved by the ethics committees of all participating study centres and comply with the ethical standards of the Declaration of Helsinki. Criteria for inclusion in the original study in 2003 were aged 75 and over, the absence of dementia and a minimum of one contact with the GP per year. Patients had been excluded if one of the following aspects applied: GP consultations only by home visits, lack of the German language, a severe illness with an anticipated fatal outcome within three months, blindness, deafness, inability of consent, residence in a nursing home and not being a patient of the participating GP. The study design of AgeCoDe has been described in detail elsewhere [19]. Within the AgeCoDe study six follow-up waves have been carried out in 1.5-year intervals. With the beginning of follow-up wave 7/ AgeQualiDe baseline 868 individuals are still remaining in the sample. The missing individuals had died before this study wave, refused participation, dropped-out or were otherwise unable to participate. From the baseline sample 757 individuals scored 19 or above in the Mini-Mental-Examination and from them 738 completed the PRS. Mean age of the participants was 88.8 years (SD 2995).

## Measures

### *Pain*

The pain assessments were part of a structured clinical interview by trained physicians and psychologists during visits to the participants' homes. Participants were presented with two questions based on the validated version of the German Brief Pain Inventory [20]. First participants had to rate today's severity of pain on a one-dimensional numeric pain rating scale (PRS) ranging from 0 to 100 (no pain to worst pain imaginable). Participants were then grouped and assigned to four categories: "no pain" for participants scoring 0 in the PRS, "mild pain" when scoring between 1 and 30, "moderate pain" when scoring 31–60 and "severe pain" when scoring 61 and above in the PRS. Secondly, participants were asked to rate the impairment with daily activities caused by pain in the last 24 h on a five-point Likert-scale, ranging from 1 (no impairment) to 5 (extreme impairment). Furthermore, the use of analgesics was assessed by recording the name and number of all prescribed and over-the-counter drugs the participant used in the last 3 months. All drugs belonging to the

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Anatomical Therapeutic Chemical–Code subgroup N02 were included in the analgesic use evaluation in our analysis.

### Demography and housing

Items on sex, age, Body Mass Index (BMI), level of education and the current housing situation were assessed. Participants were grouped into two age brackets: up until 89 years old and 90+ years old. For BMI participants were grouped into underweight = < 18.5, normal weight = 18.5–24.9, overweight = 25–29.9 and obesity = BMI of 30 or higher. The level of participant's education has been categorized into primary, secondary and tertiary according to the CASMIN criteria [21]. The housing situation was assessed during the interview by the question "Do you live alone or together with another person in a common-household?" Participants were grouped into "living at home without care support", "living at home with care support", "living in a care-home" and "assisted living".

### Cognitive function and clinical variables

Cognitive function was assessed using the Mini-Mental State Examination (MMSE) [22] to detect cognitive impairment. MMSE score below 25 was used as cut-off point for mild cognitive impairment (MCI). Depressive symptoms were measured using the Geriatric Depression Scale [23] consisting of 15 items. A score ranging from 0 to 15 was calculated for each individual (for more details, Weyerer et al. 2008 [19]). Furthermore, the impairments of activities of daily living (IADL) e.g., eating, walking stairs, wash/shower were assessed using the Barthel-Index [24]. A score ranging from 100 (independent from care support) to 0 (dependent on care support) was calculated for each participant.

### Statistical analysis

Analyses were carried out for participants who scored 19 and above in the Mini-Mental State Examination (MMSE) ( $n = 757$ ) and from whom we assessed the PRS ( $n = 738$ ).

Demographic and clinical characteristics were assessed. Our dependent variables prevalence of pain and impairment with daily living were divided into the groups mentioned above. Associations were tested using Pearson's  $\chi^2$  test for categorical variables, one-way ANOVA for continuous variables and Kruskal-Wallis-test for variables that violated assumptions of normality.

Associations of the dependent measures "prevalence of pain" and "impairment with activities of daily living" were then tested with ordinal logistic regression models adjusting for sex, age, education, housing situation, analgesics, BMI, IADL and Depression. Three models were created for prevalence of pain (1–3) and one model for impairment in daily living (4). All models include all factors and categories apart from MMSE. In model 1 MMSE is included for the overall sample. In model 2 we included participants with MMSE above 25 (non-cognitively impaired group – NCI) and in model 3 for participants with MMSE up to 25 (mild cognitively impaired group – MCI). Model 4 has been calculated for the overall sample for impairment in daily living. It was also repeated for the two MMSE groups but no significant differences appeared. Additionally, interaction effects have been calculated for age and living in a care home but showed no statistical significance. Data for MMSE and interaction effects is given upon request. SAS 9.3 software was used for logistic regression analysis and SPSS Statistics 23 for the remaining statistical analysis. Statistical significance level was set to alpha 0.05.

## Results

### Demography and prevalence of pain

General and demographic characteristics of our sample are displayed in Table 1. Results are shown for the total sample and stratified by the four categories of pain. Female gender was predominant in the sample (67.5%). Sixty-three per cent of the participants reported mild to severe pain of which 57.5% are male and 65.7% female. Thirty-seven per cent of the participants reported no pain (M: 26.15, SD: 26.68). Assessing the housing situation participants using assisted living show the lowest prevalence of pain (54.2%) followed by care home residents (60%) and participants living at home without care support (61.7%). The highest prevalence of pain was reported by participants living at home with care support (75.2%). Furthermore, the latter group reported the highest average pain scores. In this group 39% of the sample reported moderate and 19% severe pain. In contrast, participants living at home without care support and afflicted with pain scored highest in the mild pain category (29.4%).

Of those participants experiencing pain 67.8% did not take any analgesics at the time. Focusing on

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**Table 1 Sample of Descriptives and Demography**

	All N (%)	No Pain N (%)	Mild Pain N (%)	Moderate Pain N(%)	Severe Pain N(%)	Pearson $\chi^2$
Participants (N)	738	273 (37.0)	195 (26.4)	191 (25.9)	79 (10.7)	
Gender						$\chi^2 [3] = 19.47 \text{ p} = <.001$
Male	240 (32.5)	102 (37.4)	77 (39.5)	42 (22.0)	19 (24.1)	
Female	498 (67.5)	171 (62.6)	118 (60.5)	149 (78.0)	60 (75.9)	
Age (y), M (SD)	88.8 (3.0)					$\chi^2 [3] = 9.18 \text{ p} = .027$
$\leq 89$	476 (64.5)	163 (59.7)	134 (68.7)	119 (62.3)	60 (75.9)	
$\geq 90$	262 (35.5)	110 (40.3)	61 (31.3)	72 (37.7)	19 (24.1)	
Education						$\chi^2 [6] = 27.17 \text{ p} = <.001$
Primary	408 (55.3)	151 (55.3)	90 (46.2)	117 (61.3)	50 (63.3)	
Secondary	226 (30.6)	91 (3.3)	59 (30.2)	59 (30.9)	17 (21.5)	
Tertiary	104 (14.1)	31 (11.4)	46 (23.6)	15 (7.8)	12 (15.2)	
Housing						$\chi^2 [9] = 1.89 \text{ p} = <.001$
At home <sup>a</sup>	520 (70.5)	199 (72.9)	153 (78.5)	118 (61.8)	50 (63.3)	
At home <sup>b</sup>	105 (14.2)	26 (9.5)	18 (9.2)	41 (21.5)	20 (25.3)	
Assisted living	65 (8.8)	22 (8.1)	11 (5.6)	10 (5.2)	5 (6.3)	
Care home	48 (6.5)	26 (9.5)	13 (6.7)	22 (11.5)	4 (5.1)	
Analgesics*						$\chi^2 [3] = 5.01 \text{ p} = <.001$
Yes	181 (24.5)	33 (12.1)	42 (21.5)	73 (38.2)	33 (41.8)	
No	546 (74.0)	234 (89.0)	151 (77.4)	115 (60.2)	46 (58.2)	
BMI, M (SD)*	25.2 (3.8)					$\chi^2 [9] = 8.96 \text{ p} = .441$
Normal weight	340 (49.1)	129 (47.3)	95 (48.7)	83 (43.5)	33 (41.7)	
Underweight	17 (2.5)	9 (3.3)	3 (1.5)	2 (1.0)	3 (3.8)	
Overweight	265 (38.3)	88 (32.2)	69 (35.4)	79 (41.4)	29 (36.7)	
Obese	70 (10.1)	23 (8.4)	18 (9.2)	18 (9.4)	11 (13.9)	
MMSE						$\chi^2 [3] = 8.30 \text{ p} = .040$
$< 25$	79 (10.7)	38 (13.9)	16 (8.2)	22 (11.5)	3 (3.8)	
$\geq 25$	659 (89.3)	235 (86.1)	179 (91.8)	169 (88.5)	76 (96.2)	
Impairment in daily activities*						$\chi^2 [15] = 521.90 \text{ p} = <.001$
None	229 (31.0)	181 (66.3)	42 (21.5)	6 (3.1)	0 (0.0)	
Mild	215 (29.1)	65 (23.8)	91 (46.6)	47 (24.6)	12 (15.2)	
Medium	158 (21.4)	24 (8.8)	50 (25.6)	73 (38.2)	11 (13.9)	
Moderate	113 (15.3)	3 (1.1)	10 (5.1)	62 (32.5)	38 (48.1)	
Extreme	21 (2.8)	0 (0.0)	1 (0.5)	3 (1.6)	17 (21.5)	

Notes:

M mean

SD standard deviation

Data are presented as number (%)

Alpha was set to 0.05

\*Due to missing values not all sums add up to 100%.

<sup>a</sup>Participants without care support.

<sup>b</sup>Participants with care support

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Table 2 Associations of prevalence of pain for all participants, for participants with MMSE > 25, for participants ≤25 and impairment in daily living for all participants

Variable	Model 1			Model 2			Model 3			Model 4		
	OR	95% CI	p	OR	95% CI	P	OR	95% CI	P	OR	95% CI	p
Gender												
Female	-	-	-	-	-	-	-	-	-	-	-	-
Male	0.61	0.45–0.84	<.01	0.61	0.44–0.84	<.01	0.21	0.05–0.93	0.04	0.59	0.43–0.81	<.01
Age												
< = 89	-	-	-	-	-	-	-	-	-	-	-	-
≥ 90	0.65	0.48–0.88	<.01	0.61	0.44–0.84	<.01	2.17	0.50–9.36	0.30	0.88	0.65–1.19	0.41
Education												
Primary	-	-	-	-	-	-	-	-	-	-	-	-
Secondary	0.75	0.54–1.02	0.07	0.73	0.52–1.01	0.06	4.83	0.71–32.94	0.11	0.76	0.56–1.05	0.09
Tertiary	1.12	0.73–1.71	0.60	1.18	0.76–1.83	0.47	1.31	0.17–10.40	0.79	0.97	0.63–1.48	0.88
Housing												
Living at home <sup>a</sup>	-	-	-	-	-	-	-	-	-	-	-	-
Living at home <sup>b</sup>	1.60	1.01–2.53	0.04	1.70	1.04–2.78	0.04	1.44	0.30–6.90	0.65	1.72	1.08–2.74	0.02
Assisted living	0.71	0.38–1.31	0.27	0.90	0.47–1.71	0.75	<.01	<.001	0.96	0.61	0.33–1.13	0.12
Care home	0.68	0.37–1.24	0.21	0.78	0.39–1.57	0.48	0.08	0.01–0.48	<.01	0.51	0.28–0.93	0.03
Use of Analgesics <sup>c</sup>	2.17	1.48–3.16	<.01	2.13	1.42–3.18	<.01	2.62	0.49–13.98	2.62	2.75	1.88–4.03	<.01
BMI												
Adiposity	1.14	0.71–1.84	0.60	1.17	0.71–1.92	0.53	0.24	0.02–2.81	0.25	1.48	0.92–2.39	0.11
Overweight	1.21	0.89–1.65	0.22	1.19	0.86–1.63	0.30	3.14	0.71–13.99	0.13	1.37	1.01–1.86	0.05
Normal weight	-	-	-	-	-	-	-	-	-	-	-	-
Underweight	0.74	0.29–1.91	0.53	0.55	0.20–1.53	0.25	2.88	0.07–114.06	0.57	1.36	0.05–3.48	0.52
Barthel Index <sup>d</sup>	0.99	0.98–1.01	0.19	0.99	0.98–1.01	0.30	1.01	0.96–1.07	0.64	0.99	0.98–1.01	0.27
Depressive symptoms <sup>e</sup>	1.15	1.08–1.22	<.01	1.14	1.07–1.22	<.01	1.42	1.01–1.99	0.04	1.14	1.07–1.21	<.01
MMSE <sup>f</sup>	0.60	0.35–1.03	0.06	-	-	-	-	-	-	0.69	0.41–1.17	0.17

Notes: OR Odds Ratio, Alpha was set to 0.05

<sup>a</sup> Participants without care support

<sup>b</sup> Participants with care support

<sup>c</sup> use of analgesics: dichotomized

<sup>d</sup>Barthel Index: score 0–100

<sup>e</sup>GDS score 0–15

<sup>f</sup>MMSE: score 0–30, cut-off ≤25 for mild cognitive impairment, > 25 no cognitive impairment

the cognitive status 51.9% of participants with MCI and 64.3% of participants with NCI reported pain. This difference reached statistical significance ( $\chi^2 [3] = 4.45$ ,  $p = .035$ ). In total 229 (31%) participants reported no impairment and 509 (69%) participants mild to extreme impairment due to pain with daily activities. The bivariate analyses were carried out for the measures age, sex, cognitive impairment (MMSE), analgesics, housing situation, Barthel-

Index, BMI and education (see Table 1). Significant differences were appeared between the two age groups ( $\chi^2 [3] = 9.18$ ,  $p = .027$ ), for men and women ( $\chi^2 [3] = 19.47$ ,  $p = <.001$ ), for the education groups ( $\chi^2 [6] = 27.17$ ,  $p = <.001$ ), between use and no use of analgesics ( $\chi^2 [3] = 55.01$ ,  $p = <.001$ ) and for the four different housing situations ( $\chi^2 [9] = 31.89$ ,  $p = <.001$ ). No significant result was found for the BMI groups nor for Barthel-Index scores. These variables

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were then put into the multivariate analysis (model 1 – model 4). Results are presented in Table 2.

### **Model 1 – Overall pain ratings**

In model 1 we tested the association of demographic and clinical characteristics on the overall sample. Male sex was statistically significantly associated with lower PRS (OR 0.61, 95% CI 0.45–0.84) while contrary associations were found for age. Individuals between 90 to 94 years of age scored significantly lower in the PRS (OR 0.65, 95% CI 0.48–0.88) than the younger age bracket. Considering the housing situation higher PRS was significantly associated with participants living at home with care support. There is a 1.6 higher possibility of experiencing pain for this group than living at home without care support (OR 1.60, 95% CI 1.01–2.53). There was also a significant association for analgesics. Participants receiving analgesics experience twice as much pain (OR 2.17, 95% CI 1.48–3.16). Furthermore, higher PRS was significantly associated with depression (OR 1.15, 95% CI 1.08–1.22).

No significant evidence showed for differences in education, BMI or Barthel-Index.

### **Model 2 and 3 - MMSE status**

In model two and three we divided the sample in NCI and MCI participants and found significant associations for both groups: Again, male sex was significantly associated with lower pain ratings for both groups (NCI: OR 0.61, 95% CI 0.44–0.85 and MCI: OR 0.21, 95% CI 0.05–0.93). Significant associations for age appeared according to model 1 for NCI aged 90 to 94 years old. The older age group scored significantly lower in the PRS (OR 0.61, 95% CI 0.44–0.84). No association with age was found for the group the MCI-participants. Concerning the housing situation living at home with care support was significantly associated with higher ratings on the PRS for NCI (OR 1.70, 95% CI 1.04–2.78) and significantly associated with lower ratings on the PRS for MCI-participants living in a care-home (OR 0.08, 95% CI 0.01–0.48). Also, for both groups higher PRS was significantly associated with depression (NCI: OR 1.14, 95% CI 1.07–1.22 and MCI: OR 1.42, 95% CI 1.01–1.99). Significant associations for analgesics were found for NCI. Those taking analgesics reported twice as much pain (OR 2.12, 95% CI 1.42–3.18). No significant figures appeared for education, BMI or Barthel-Index.

### **Model 4 - impairment in daily activities**

In model 4 we analysed the impairment in daily activities for the overall sample. Again, we found a significant association for lower impairment in daily activities with male sex (OR 0.59, 95% CI 0.43–0.80), analgesics (OR 2.75, 95% CI 1.88–4.03) and depression (OR 1.14, 95% CI 1.07–1.21). The housing situation showed significant less impairment in daily activities for participants living in a care home (OR 0.51, 95% CI 0.28–0.93) and more impairment for participants living at home with care support (OR 1.72, 95% CI 1.08–2.74). For BMI stronger impairment in daily activities was significantly associated with overweight participants (OR 1.37, 95% CI 1.01–1.86). Education and Barthel-Index did not reach statistical significance.

## **Discussion**

This was one of a few existing studies focusing on the prevalence of pain and associated factors such as age, gender, use of analgesics, cognitive state, medication and depression among the population of 85+ year olds.

### **Age**

The study demonstrated a high prevalence of pain (63%) among the age group of 85+ and strong experience impairments with everyday life due to pain (69%). Additionally, our findings suggest that older adults report less pain. These findings are supported by Zyczkowska (2007) [25] who reported decreasing pain scores with growing age for both men and women. The researchers name a changing, more accepting attitude towards pain with increasing age, a “survival bias” meaning only the healthiest managed to reach very old age as possible grounds for these results. In depth research could provide more distinct answers into what leads to these changes in old age and may help overcome fears of ageing.

### **Gender**

Regardless of the cognitive state, men seem to experience less pain and impairment in everyday life due to pain. According to these findings, female gender could increase the risk of experiencing pain. Similar finding have been reported in literature across all age groups [6, 25, 26]. Reasons can be differences in individual pain perception, personal coping strategies or social settings [27, 28]. Gaining a better understanding of the different kinds of pain may also play an important role and may allow

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deeper insight of coping strategies and physiological factors in men and women [29, 30].

### Housing situation

Regarding the housing situation, our data show differences for the housing arrangements chosen in late life. In our sample, 47.8% of women and 34.5% of men aged 90+ years are living in care homes where activities of daily living are reduced and support through care staff is given in many areas [1] which may reduce possible pain hazards. Furthermore, it can be speculated that the availability and home visits of general practitioners are at a higher frequency than in any other housing setting which could have positive effects on pain management. It may also explain why on the other hand participants living at home receiving care experience significantly more pain and more impairment in activities of daily living. Health care services providing care in the community are generally under immense time pressure and restriction of duties applied by the indication of care level or previous health care assessments e.g., supplying medication, changing bandaging, wash the person. It is also unclear whether pain assessment is part of health care services in the community by default nor if caring relatives focus on the issue. Hence the differences in pain prevalence point to a gap in pain management in outpatient care settings.

### Analgesics and cognitive state

Besides reducing pain hazards the use of analgesics plays an important role in pain management. Our results show individuals taking analgesics experience more pain and more impairment in everyday life. This connection may be even stronger due to strong side effects caused by analgesics which further reduce quality of life. Regarding the use of analgesics we found that a large group of participants with pain do not receive analgesics at all which could be explained by missing access to direct medical care, embellishment of pain, refusal to take analgesics, acceptance of pain as one part of growing older or changes in cognitive state. Bauer et al. [31] divided their sample similarly into cognitive unimpaired (CUS) and cognitively impaired participants (CI) with the subgroups of verbal ability (CI-V) and inability (CI-NV) to communicate pain. Though cut-off scores for cognitive impairment varied, the findings point into a similar direction. CUS participants were more likely to receive analgesics while CI participant's risk of not receiving analgesics despite pain indication was significantly increased by up to 2.6 (CI-V) and 3.4 (CI-NV) times. In our sample NCI patients reported twice as much pain despite receiving analgesics. One would have

assumed that individuals who are verbally able to express their pain and receive the accurate medication should no longer suffer from pain. This instance may have occurred due to chronic or worsened pain conditions, wrong usage of medication or inadequate medication. In order to minimize the number of adverse side effects patients may also choose to take a lower dosage in order to manage both their level of pain and the adverse side effects. However, giving patients the possibility to address their pain on a regular basis might help to uncover such conflicting circumstances. Maxwell et al. [32] focused on prevalence of pain among nursing home residents and reported one-fifth of the residents with daily pain did not receive analgesics. Also, residents aged 75+ years with cognitive impairment or the requirement of an interpreter were significantly less likely to receive an opioid alone or in combination with a non-opioid. This highlights the important fact that changes in cognitive state may hinder the detection of pain and alternative ways to assess the level of pain are needed for patients with cognitive impairment.

In relation to the cognitive state of the participants our results are partly contrary compared to existing literature. Bauer et al. [31] reported higher pain prevalence and less pain related medication for MCI. A pilot study by Monroe et al. [33] indicated greater pain intensity while our data showed significantly lower prevalence of pain for care home settings for MCI participants.

### Depression

As for depression our results demonstrated consistent associations with pain and depression as found by a number of previous studies with younger participants [8, 34, 35]. Throughout the data pain and impairments due to pain and depression were highly correlated for very old people. As de Wall [35] showed perceived control plays a crucial role as mediator between pain and the presence of depressive disorders. With growing age perceived control will very likely decline and support will be needed in physical, psychological, medical and social areas of life. Therefore, the group of the very old could be considered to be under greater risk of depression and preventive measure should be put in place.

### Strength and limitations

The strength of our study lies in the large number of participants aged 85+ who gave extensive insight in their medical, social and psychological aspects of life. The large sample size allowed us to look closer at the connection between cognitive state and the

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housing arrangement which is becoming more important due to the growing number of individuals using care services.

However, we cannot exclude bias. We focused on pain at the point of time while the interview was performed but did not distinguish between chronic and acute pain in our assessments. The pain assessment was carried out using a simple question. It can be speculated whether the test was suitable for this MCI participants though all participants were verbally able to respond. Also, we assessed the medication taken regularly and on demand but analgesics taken in the morning or analgesics not used despite being prescribed could have changed the evaluation. A question whether the medication has been taken in the morning was not included in the assessment. We also did not look at specific pain sites because the interview was already quite extensive.

In order to group the participants into the forms of housing we used the level of care giving through a medical assessment carried out by authorities as an indication which excluded participants receiving support through family members only.

### Implications for clinicians and research

The results of the study show that pain scores decrease with age yet the reasons for the results have not been uncovered and can only be speculated upon. In order to explain the differences regarding the housing situation further investigation on the assessment of pain in ambulatory care settings is needed. The integration of routine pain assessments in both ambulatory and care home settings could help to overcome the differences in care settings and lower the number of patients suffering from pain despite taking analgesics. It remains unclear to what extend pain assessments are carried out in the ambulatory care setting in Germany. A general evaluation on this topic may help to identify key aspects in this area. In order to support caring relatives a form of special training or an advisory board may help to sensitize on the topic. For patients with MCI pain assessments should be adapted in order to ensure an accurate treatment and successful aging.

### Conclusions

In conclusion, our results give new insight into prevalence of pain and impairment of activities of daily living for the oldest age groups of our society. Even though pain ratings decrease with age pain is still highly prevalent and successful management of pain is indispensable. Especially women and individuals with comorbidities such as depression are more likely to experience pain in very old age.

The appropriate utilization of analgesics remains a problematic issue for individuals affected by pain. Also, the form of housing arrangement chosen in late life seems to be associated with the prevalence of pain. Individuals receiving outpatient care experience significantly more pain. These differences point to a gap in pain management especially in outpatient care settings. This could be due to a lack of interaction between care staff and general practitioners or missing standards on pain evaluation. Considering the growing number of individuals aged 85+ the group of the oldest-old shows an increasing demand of care support including management and treatment of pain.

### Abbreviations

AgeCode: German Study on Ageing, Cognition and Dementia in Primary Care Patients; AgeQualiDe: Study on needs, health service use, costs and healthrelated quality of life in a large sample of oldest-old primary care patients; BMI: Body Mass Index; CI: Confidence interval; MCI: Mild Cognitive Impairment; NCI: No Cognitive Impairment; OR: Odds ration; PRS: Pain Rating Scale

### Acknowledgements

We want to thank both all participating patients and their general practitioners for their good collaboration.

Members of the AgeCoDe Study Group: Wolfgang Maier (Principal Investigator), Martin Scherer (Principal Investigator), Hendrik van den Bussche (Principal Investigators: 2002–2011), Heinz-Harald Abholz, Christian Brettschneider, Cadja Bachmann, Horst Bickel, Wolfgang Blank, Sandra Eifflaender-Gorfer, Marion Eisele, Annette Ernst, Angela Fuchs, André Hajek, Kathrin Heser, Frank Jessen, Hanna Kaduszkiewicz, Teresa Kaufeler, Mirjam Köhler, Hans-Helmut König, Alexander Koppara, Diana Lubisch, Tobias Luck, Dagmar Lümann, Melanie Lappa, Tina Mallon, Manfred Mayer, Edelgard Mösch, Michael Pentzek, Jana Prokein, Steffi G. Riedel-Heller, Susanne Röhr, Anna Schumacher, Janine Stein, Susanne Steinmann, Franziska Tebarth, Carolin van der Leeden, Michael Wagner, Klaus Weckbecker, Dagmar Weeg, Jochen Werle, Siegfried Weyerer, Birgitt Wiese, Steffen Wolfsgruber, Thomas Zimmermann.

### Funding

This publication is part of the German Research Network on Dementia (KND), the German Research Network on Degenerative Dementia (KNDD; German Study on Ageing, Cognition and Dementia in Primary Care Patients; AgeCoDe), and the Health Service Research Initiative (Study on Needs, health service use, costs and health-related quality of life in a large sample of oldest-old primary care patients (85+; AgeQualiDe)) and was funded by the German Federal Ministry of Education and Research (grants KND: 01GI0102, 01GI0420, 01GI0422, 01GI0423, 01GI0429, 01GI0431, 01GI0433, 01GI0434; grants KNDD: 01GI0710, 01GI0711, 01GI0712, 01GI0713, 01GI0714, 01GI0715, 01GI0716; grants Health Service Research Initiative: 01GY1322A, 01GY1322B, 01GY1322C, 01GY1322D, 01GY1322E, 01GY1322F, 01GY1322G). Dr. Francisca S. Then has been supported in working on the manuscript by LIFE – Leipzig Research Center for Civilization Diseases, Universität Leipzig. Her collaboration within LIFE was funded by means of the European Social Fund and the Free State of Saxony. We acknowledge support from the German Research Foundation (DFG) and Universität Leipzig within the program of Open Access Publishing. The funders were not involved in the design of the study, in collection, analysis, and interpretation of data, or in writing the manuscript.

### Availability of data and materials

Due to ethical restrictions involving patients' data, underlying data are only available on reasonable request. Interested parties may contact the Working Group Medical Statistics and IT-Infrastructure, Institute

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### Authors' contributions

Analysed and interpreted the data and drafted the manuscript: TM, BW. Supported in analysis and interpretation of the data and drafting of the manuscript: TL, DL, BW. Acquired the data: TL, CVDL, KH, AF, SM, TM, DW, CB, JW. Conceived and designed the study: BW, HB, HHK, SW, MW, MS, WM, SGRH. Revised the manuscript critically for important intellectual content: AE, CB, HHK, TL, SR, SW, JW, EM, DW, AF, MP, LK, KH, SRH, WM, BW, MS. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate Data were derived from the AgeQualiDe study. All GP patients who participated in the study provided written informed consent prior to their participation. The study been approved by the ethics committees of all participating study centers and comply with the ethical standards of the Declaration of Helsinki.

Ethics Commission of the Medical Association Hamburg (reference number: MC-390/13)

Ethics Committee of the Medical Faculty of the Rheinische Friedrich-Wilhelms-University of Bonn (reference number: 369/13)

Medical Ethics Commission II of the Medical Faculty Mannheim/Heidelberg University (reference number: 2013-662 N-MA)

Ethics Committee of the Faculty of Medicine of the University of Leipzig (reference number: 309/2007; 333–13-18,112,013)

Ethical Committee of the Medical Faculty of the Heinrich-Heine-University Düsseldorf (reference number: 2999)

Ethics Committee of the Faculty of Medicine of the Technical University of Munich (reference number: 713/02 E)

### Competing interests

The authors declare that they have no competing interests.

### Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

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Received: 7 July 2017 Accepted: 21 May 2018

Published online: 09 June 2018

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### 3. Lifestyle aspects as a predictor of pain among oldest-old primary care patients - a longitudinal cohort study

#### Abstract

Tina Mallon, Marion Eisele, Hans-Helmut König, Christian Brettschneider, Susanne Röhr, Alexander Pabst, Siegfried Weyerer, Jochen Werle, Edelgard Mösch, Dagmar Weeg, Angela Fuchs, Michael Pentzek, Kathrin Heser, Birgitt Wiese, Luca Kleineidam, Michael Wagner, Steffi Riedel-Heller, Wolfgang Maier, Martin Scherer

**Background:** Dealing with the high prevalence of pain among the oldest-old (+75) is becoming a major health issue. Therefore, the aim of the study was to uncover health-related lifestyle behaviors (HLB) and age-related comorbidities which may predict, influence and prevent pain in old age.

**Methods:** In this longitudinal cohort study, data were obtained initially from 3.327 individuals aged 75+ from over 138 general practitioners (GP) during structured clinical interviews in 2003. Nine follow-ups (FU) were assessed until 2017. Available data from 736 individuals scoring in FU3 and FU7 were included in this analysis. Data were assembled in an ambulatory setting at participant's homes. Associations were tested using a linear regression model (model 1) and ordered logistic regression model (model 2).

**Results:** Statistical analyses revealed increased likelihood to experience pain for participants with comorbidities such as peripheral arterial disease (PAD) (coef. 13.51,  $P > t = 0.00$ ) or chronic back pain (CBP) (coef. 6.64,  $P > t = 0.003$ ) or higher body mass index (BMI) (coef. 0.57,  $P > t = 0.015$ ) and, female gender (coef. 6.00, SE 3.0,  $t = 2.02$ ,  $P > t = 0.044$ ). Participants with medium education and former smokers showed significantly lower pain rating (coef. -5.05,  $P > t = 0.026$ ; coef. -5.27,  $P > t = 0.026$ ). Suffering from chronic back pain ( $OR = 2.03$ ), osteoarthritis ( $OR = 1.49$ ) or depressive symptoms ( $OR = 1.10$ ) raised the odds to experience impairments in daily living due to pain. Physical activity showed no significant results.

**Conclusions:** Chronic conditions such as PAD, or CBP, female gender and higher BMI may increase the risk of experiencing more pain while successful smoking cessation can lower pain ratings at old age. Early and consistent support through GPs should be given to older patients in order to prevent pain at old age.

**Keywords:** oldest-old, health-related aspects, pain prevention, longitudinal cohort study, chronic conditions

# Lifestyle Aspects As A Predictor Of Pain Among Oldest-Old Primary Care Patients – A Longitudinal Cohort Study

This article was published in the following Dove Press journal:  
*Clinical Interventions in Aging*

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**Purpose:** Dealing with the high prevalence of pain among the oldest-old (+75) is becoming a major health issue. Therefore, the aim of the study was to uncover health-related lifestyle behaviors (HLB) and age-related comorbidities which may predict, influence and prevent pain in old age.

**Patients and methods:** In this longitudinal cohort study, data were obtained initially from 3,327 individuals aged 75+ from over 138 general practitioners (GP) during structured clinical interviews in 2003. Nine follow-ups (FU) were assessed until 2017. Available data from 736 individuals scoring in FU3 and FU7 were included in this analysis. Data were assembled in an ambulatory setting at participant's homes. Associations were tested using a linear regression model (model 1) and ordered logistic regression model (model 2).

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**Conclusion:** Chronic conditions such as PAD, or CBP, female gender and higher BMI may increase the risk of experiencing more pain while successful smoking cessation can lower pain ratings at old age. Early and consistent support through GPs should be given to older patients in order to prevent pain at old age.

**Keywords:** oldest-old, health-related aspects, pain prevention, longitudinal cohort study, chronic conditions

## Plain Language Summary

Many people nowadays reach the age of 75 years and above. With old age, people often suffer from pain. To help understand how pain at old age can be prevented and what kind of a lifestyle might influence the amount of pain one experiences later in life, we used data from a large group of people aged 75+ from Germany to help us understand the situation a little better.

In total, 3,327 people took part in this study which ran from 2003 until 2017. Data from 736 people were used to help answer our questions. After analysis of the data, we found that alongside being female and/or overweight, people with a chronic illness such as peripheral arterial disease or chronic back pain have a higher chance of feeling pain at old age. Also, people suffering from chronic back pain, osteoarthritis and problems with depression could have more difficulties carrying out their daily activities because of pain. People who stopped smoking or went to high school have a lower chance of feeling pain at old.

Clinical Interventions in Aging 2019:14 1881–1888

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### 3. Lifestyle aspects as a predictor of pain among oldest-old primary care patients - a longitudinal cohort study

#### Introduction

Research on healthy lifestyle behavior (HLB) found evidence for associations between HLB and the risk of morbidity, mortality and the prognosis, and prevention of chronic diseases.<sup>1-3</sup> HLB generally includes the following aspects: physical activity, healthy body weight, non-smoking, healthy diet and low level of alcohol consumption which can be considered as modifiable lifestyle factors.

Pain has been identified as a growing threat to healthy aging and is highly prevalent among the population. Numbers on the prevalence of pain among older populations (75+) range between 25% and 80% which make pain management and prevention of pain necessary.<sup>4</sup> Following our previous cross-sectional analyses on the prevalence of pain at old age, we recognized the importance of modifiable lifestyle factors which may play an important role in conjunction with preventing pain in the group of the old-old.<sup>5</sup> In our study, 63% of oldest-old participants reported mild to severe pain as well as high impairments in activities of daily living (IADL) due to pain. At higher age multimorbidity becomes more likely. Of the comorbidities common in high age, chronic low-back problems, chronic gout and depression have been identified as diseases that are related to chronic pain amongst multi-morbid patients.<sup>6</sup> Regarding the aging population, aspects on HLB have not been investigated in terms of their association with pain, IADL and age-related comorbidities.

It was, therefore, our aim in this study to uncover factors that may predict, influence and prevent pain in old age. Using a longitudinal approach, we paid special attention to modifiable lifestyle factors such as physical activity, smoking, BMI, intake of alcohol as well as age-related comorbidities. We hypothesize that the HLB aspects have an influence on predicting and preventing pain at a very old age.

#### Method

The large cohort of primary care patients aged 75+ from the German longitudinal cohort study on Ageing, Cognition and Dementia in Primary Care Patients (AgeCoDe) and its follow-up study on Needs, Health Service Use, Costs and Health-related Quality of Life (85+) which was based on the same cohort of patients (AgeQualiDe) provided the data for our analysis.

In 2003, 3,327 patients and 138 general practitioners (GP) in six German cities (Bonn, Düsseldorf, Hamburg, Leipzig, Mannheim, Munich) were recruited for the AgeCoDe cohort. Written

informed consent was obtained from all participants prior to their participation. The study design of AgeCoDe has been described in detail elsewhere.<sup>7</sup> In brief, AgeCoDe covered six follow-up assessments (FU) after baseline assessment with 18-month intervals in between each FU. AgeQualiDe covered three additional FU in 10-month intervals from 2014 onwards. The number of participants had decreased to 868 due to deaths or withdrawing of consent.

The AgeCoDe study inclusion criteria were the following: participants aged 75 and above, the absence of dementia, and a minimum of one contact with the GP per year. Participants were excluded if one of the following aspects applied to them: GP consultations only by home visits, lack of the German language, a severe illness with an anticipated fatal outcome within 3 months, suffering from dementia, blindness, deafness, inability to provide informed consent, residing in a nursing home and not being a patient of the participating GP.

Both studies have been approved by the ethics committees of all participating study centers and comply with the ethical standards of the Declaration of Helsinki.

In our longitudinal analysis, we use AgeCoDe/AgeQualiDe data from 2008/2009 (AgeCoDe FU 3) to predict pain in 2014 (AgeCoDe FU 7/AgeQualiDe Baseline). Additionally, for each FU, GPs filled out questionnaires regarding the medical condition of each participant. For our analysis, we used data from 736 participants of the AgeQualiDe baseline assessment. Participants with scores of 19 and above in the Mini-Mental Examination and a valid PRS were included.

#### Measures

**Pain:** At FU 7 each participant rated the severity of pain for the present-day during each structured clinical interview with a trained psychologist or physician. The rating was based on the validated version of the German Brief Pain Inventory using a one-dimensional numeric pain rating scale (PRS) ranging from 0 to 100 (no pain to worst pain imaginable). Additionally, participants rated IADL caused by pain within the last 24 hours using a 5-point Likert scale, ranging from 1 (no impairment) to 5 (extreme impairment).<sup>8</sup>

We chose physical activity, smoking habits, BMI, consumption of alcohol, and the comorbidities depressive symptoms, CBP, and gout as our main predictor variable based on literature research,<sup>6,9,10</sup> and additionally included comorbidities such as osteoarthritis, CHD and PAD based on clinical reasoning and expertise from medical staff. The

### 3. Lifestyle aspects as a predictor of pain among oldest-old primary care patients - a longitudinal cohort study

potential confounding variables included sociodemographic variables of gender, age, family status, body mass index (BMI) and education. Education levels of participants have been categorized into low, medium and high according to the CASMIN criteria.<sup>11</sup>

Physical activity was assessed based on previous research on leisure activities and risk of dementia in the elderly.<sup>12</sup> We extended the list of activities with activities our study participants named regularly and included the following: riding a bike, hiking or going for longer walks, swimming, exercising or gymnastics, work in house and garden, caring for grand-children or other relatives, other activities such as dancing, bowling, golf, or jogging. Physical activities were measured on a five-point Likert scale (every day, a few times a week, once a week, less than once a week, never within the last 4 weeks). Any activity exercised only once a week or less was rated as 0, any activity exercised at least a few times a week was rated as 1. For each participant, a sum was calculated and used for analysis.

The Geriatric Depression Scale was used to measure depressive symptoms, consisting of 15 items. A score ranging from 0 to 15 was calculated for each individual.<sup>13</sup> Smoking status was classified into never smoker, former or active smoker at baseline visit and was used as a proxy for FU3. Consumption of alcohol was assessed by the number of alcoholic drinks taken within a week and grouped into "none", "1–2, 3–4 or 5–6 days a week" and "daily".

#### Statistical Analysis

For our analysis, we used data from the FU3 assessment of AgeCoDe and the baseline assessment from AgeQualiDe. Analysis was carried out for all individuals with available data for both time points and with ratings on the PRS ( $n = 736$ ). A linear regression model (model 1) and an ordered logistic regression model (model 2) was calculated in order to identify the impact of our variables on the prevalence of pain at follow-up seven. Model one is based on the original pain scale and model two on IADL due to pain.

Both models were adjusted for age, sex, education, and family status, physical activity, smoking status, alcohol intake, and BMI, and comorbidities such as depressive symptoms, osteoarthritis, CBP, gout, CHD, and PAD.

Logistic regression analyses were carried out using SAS 9.3 software. Additional analyses have been conducted with SPSS Statistics. The level of statistical significance was set to alpha 0.05.

#### Results

Table 1 provides the descriptives of the analytic sample. The mean age of our sample was 83 years at follow-up three and 89 years at follow-up seven. The average pain rating at follow-up seven was 26.2 on the PRS. Average IADL due to pain was stated by 2.31.

Table 2 provides statistical results for both measures PRS (model one) and IADL due to pain (model two). Statistical analysis for model one revealed the following factors as risk factors for a higher PRS: female gender, PAD, CBP, and higher BMI. On average female gender was associated with 6-point higher ratings on the PRS compared to the PRS of men. Ratings on the PRS when affected by CBP are 6.6 points higher and those suffering from PAD 13.5 points higher compared to individuals without these comorbidities. A weak but significant result was also shown for higher BMI. On the contrary, medium education compared to lower education and former smokers compared to never smokers showed significantly lower pain rating by five points on the PRS.

In model two, three health-related risk factors could be identified for IADL due to pain: CBP ( $p = 0.000$ ; OR = 2.03), osteoarthritis ( $p = 0.01$ ; OR = 1.49) and depressive symptoms ( $p = 0.02$ ; OR = 1.10) (see Table 2).

No significant results were found for our main predictor variables such as number of physical activities or consumption of alcohol. Suffering from gout or CHD was also not associated with pain.

**Table 1 Descriptives Of The Sample At FU3 (Mean Age 83 Years)**

Variable	N	(%)	Mean (SD)
Participants	736	(100)	
Gender			–
Male	239	(32.5)	
Female	497	(67.5)	
Education			–
Low	407	(55.3)	
Medium	225	(30.6)	
High	104	(14.1)	
Marital status			–
Single	50	(6.8)	
Married	271	(36.8)	
Divorced	37	(5.0)	
Widowed	376	(51.2)	
Body mass index	–	–	26.12 (4.46)

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Smoker			-
Never	411	(55.8)	
Ex-Smoker	288	(39.1)	
Smoker	37	(5.0)	
Alcohol intake			-
None	321	(43.7)	
<1 drink a day	223	(30.4)	
1–2 drinks a day	101	(13.8)	
≥2 drinks a day	89	(12.1)	
Physical activities			-
None per week	30	(4.1)	
1 per week	195	(26.7)	
2 per week	273	(37.4)	
3 per week	179	(24.5)	
4+ per week	53	(7.3)	
Depressive symptoms	-	-	1.99 (2.05)
Comorbidities			-
Coronary artery disease	203	(29.8)	
Peripheral arterial disease	54	(7.9)	
Chronic back pain	291	(42.8)	
Osteoarthritis	374	(54.9)	
Gout	125	(18.3)	

Note: Data are presented as number (%).

## Discussion

### Summary

The longitudinal study investigated the relationship of HLB and age-related comorbidities on pain at a very old age. The results point to an association for PAD, and CBP with higher pain ratings at an older age. Furthermore, female gender is associated with higher pain ratings as well as higher BMI scores. Additionally, comorbidities such as CBP, osteoarthritis, and depressive symptoms show associations with higher IADL due to pain. Regarding the modifiable lifestyle factors, successful smoking cessation and lower BMI were significantly associated with lower pain ratings. Identifying and working on modifiable lifestyle factors with the patients towards a better HLB could help to prevent pain at old age.

### Strength And Limitations

The strengths lie in the longitudinal design of the study as well as a large number of participants aged 85+ giving extensive insight into their medical, social and psychological aspects of life. The large sample size allowed us to investigate lifestyle aspects in relation to pain at a high age which very few studies have done so far. Also, our study sample can be

considered representative for general practice patients who are living by themselves and are able to consult their GP in their office.

Yet, we cannot exclude selection bias for only healthy participants who were still able to visit their GP at the practice were included. Bias due to attrition cannot be excluded because some participants have been excluded mainly due to death or refusal. Also, no further analyses have been carried out to compare PRS and IADL due to pain for included and excluded participants for FU3. Furthermore, we did not assign the participants to a stage of chronic illnesses at the point of time. Therefore, chronic conditions could have reached a higher stage and impacted to a larger extent. Regarding physical activity, we focused on self-reported physical activity measures, which are affected by recall bias. Also, survival bias might have affected the generalizability of the results towards the healthier population.

### Comparison With Existing Literature

Participants suffering from PAD or CBP show strong associations with higher pain and higher IADL due to pain than individuals without these conditions. This could be due to the progression of the illness itself but also avoidance of movement in fear of pain. Yet, while exercising is one of the main effective non-pharmacologic therapy approaches for CBP patients in order to reduce pain research indicates a drop in physical activity levels with growing age which might be one of the reasons why in our analysis, the number of physical activities did not show any significant influence on pain.<sup>9,14–16</sup> Nevertheless, physical activity remains crucial modifiable health factor to maintain the status quo, and has been shown to reduce levels of depression and pain, increase the quality of life, self-esteem, and retain independence.<sup>17–19</sup> Our results also show a lower risk of experiencing more pain for former smokers compared to never smokers. Research indicates a pain-related smoking behavior. Higher rates of cigarette smoking and shorter latencies between smoking cigarettes have been reported among individuals with chronic pain.<sup>20,21</sup> Smoking cigarettes may serve as a coping strategy in order to reduce pain, yet greater pain sensitivity, a larger number of pain locations and pain interference have been seen among smokers suffering from pain.<sup>22,23</sup>

### 3. Lifestyle aspects as a predictor of pain among oldest-old primary care patients - a longitudinal cohort study

**Table 2** Results Of The Linear Regression Model For Pain Rating Scale (PRS, Scores 0–100) In Model 1 And For The Ordinal Logistic Regression For Impairment Of Daily Living Due To Pain (IDLP, Scores 1–5) In Model 2 At FU7 (Mean Age 88.8 Years)

Variable	PRS	Model 1			IDLP	Model 2		
		Mean (SD)	Coeff.	95% CI		OR	95% CI	p
Participants	26.16 (26.69)	-	-	-	2.31 (1.20)	-	-	-
Gender								
Male	20.17	-	-	-	2.05	-	-	-
Female	29.04	6.00	0.16 to 11.83	0.04	2.44	1.30	0.84 to 2.01	0.23
Education								
Low	28.47	-	-	-	2.39	-	-	-
Medium	23.03	-5.05	-9.48 to -0.62	0.03	2.24	0.90	0.65 to 1.24	0.50
High	23.89	1.95	-4.08 to 7.99	0.53	2.17	1.10	0.72 to 1.71	0.65
Age	-	-0.64	-1.32 to 0.04	0.07	-	0.96	0.92 to 1.01	0.13
Marital status								
Single	34.50	-	-	-	2.62	-	-	-
Married	21.35	-4.31	-13.14 to 4.52	0.34	2.08	0.77	0.40 to 1.46	0.42
Divorced	31.19	5.43	-6.11 to 16.97	0.36	2.28	0.84	0.67 to 1.91	0.67
Widowed	26.82	-2.03	-10.15 to 6.09	0.62	2.37	0.99	0.55 to 1.79	0.97
Body mass index	-	0.57	0.11 to 1.03	0.02	-	1.03	1.00 to 1.07	0.06
Smoker								
Never	28.94	-	-	-	2.42	-	-	-
Ex-Smoker	22.11	-5.23	-9.90 to -0.63	0.03	2.18	0.90	0.64 to 1.26	0.54
Smoker	26.76	-7.58	-17.18 to 2.03	0.12	2.16	0.66	0.34 to 1.28	0.22
Alcohol intake								
None	27.96	-	-	-	2.48	-	-	-
<1 drink a day	26.03	1.62	-3.12 to 6.39	0.50	2.25	0.90	0.64 to 1.27	0.56
1–2 drinks a day	24.60	2.27	-3.92 to 8.47	0.47	2.21	0.90	0.57 to 1.42	0.65
≥2 drinks a day	23.30	2.76	-4.51 to 10.04	0.46	2.09	0.83	0.49 to 1.41	0.50
Physical activities								
None per week	23.93 (24.66)	-	-	-	2.10 (1.06)	-	-	-
1 per week	29.04 (28.98)	4.98	-5.18 to 15.13	0.34	2.55 (1.33)	1.94	0.92 to 4.01	0.08
2 per week	24.94 (25.61)	1.24	-8.83 to 11.31	0.81	2.25 (1.17)	1.43	0.68 to 3.00	0.34
3 per week	25.98 (26.59)	4.60	-5.82 to 15.02	0.39	2.27 (1.13)	1.68	0.79 to 3.58	0.18
4+ per week	23.30 (24.26)	5.07	-6.99 to 17.12	0.41	2.08 (1.05)	1.41	0.59 to 3.37	0.45
Depressive symptoms	-	0.72	-0.30 to 1.74	0.17	-	1.10	1.02 to 1.18	0.02
Comorbidities								
Coronary artery disease (no)	24.08	-	-	-	2.21	-	-	-
Coronary artery disease (yes)	26.51	2.25	-2.18 to 6.68	0.32	2.39	1.02	0.74 to 1.40	0.92
Peripheral arterial disease (no)	24.16	-	-	-	2.26	-	-	-
Peripheral arterial disease (yes)	31.94	13.51	5.95 to 21.06	0.00	2.39	1.24	0.70 to 2.20	0.46
Chronic back pain (no)	18.51	-	-	-	1.94	-	-	-
Chronic back pain (yes)	32.30	6.64	2.32 to 10.97	0.00	2.66	2.03	1.48 to 2.79	0.00
Osteoarthritis (no)	19.40	-	-	-	1.99	-	-	-
Osteoarthritis (yes)	27.92	4.17	-0.17 to 8.52	0.06	2.42	1.49	1.09 to 2.04	0.01
Gout (no)	24.30	-	-	-	2.24	-	-	-
Gout (yes)	27.40	0.35	-4.78 to 5.50	0.89	2.42	1.06	0.72 to 1.54	0.78

Notes: Alpha was set to 0.05; bold values indicate significance.

Furthermore, daily smokers reported more chronic pain than never smokers or former smokers.<sup>24</sup> Addressing the modifiable health factor “smoking”

and breaking the hypothesized “positive feedback loop” at an early age – more pain leading to higher cigarette intake – may, therefore, play a crucial role.

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According to our findings, former smokers are still at risk of pain at old age but may experience less when smoking cessation is successful.

In accordance with existing literature, female gender and higher BMI are associated with higher pain ratings. Research found evidence for increased pain sensitivity in women and obese individuals, as well as greater pain-related distress and differences in responsivity to pharmacological and non-pharmacological pain interventions among women.<sup>25-27</sup> While gender differences may be caused by biopsychosocial mechanisms, the BMI presents an important modifiable health factor.<sup>28</sup> There is great evidence that obese patients profit from weight reduction with lower pain rating and less pain-related functional impairment.<sup>29</sup>

Concepts of healthy living suggest little consumption of alcohol as one of the main healthy lifestyle factors.<sup>2,3</sup> However, in our study, the consumption of alcohol as well as the comorbidities gout or CHD do not show significant results. We interpret our findings that a different focus may be needed for pain at old age due to the increase in comorbidities and physical restraints yet, promoting HLB throughout any age group can impact positively on patients.

#### Implications For Research And Practice

We could identify successful smoking cessation and reducing obesity as a potentially positive HLB in terms of reducing and preventing pain at old age. Current smokers should be motivated and supported in successful smoking cessation in earlier stages of life. Similarly, support should be given to overweight patients in order to reduce weight to lower the BMI. Empowering the patients to actively change for a healthier lifestyle should be in the center of attention besides promoting preventive programs. Yet, while other research showed evidence that physical activity can impact on pain at a younger age,<sup>5</sup> we could not show associations for our large study population. Given the high age of our participants maintaining the current health status could be more realistic than improving it.

As we did not investigate to what extent GPs address HLB which can be influenced by the patients themselves such as BMI, physical activity, or smoking further research should focus on GPs attitude towards these aspects in relation to the age of the patients. Identifying and developing approaches with a focus on empowering patients on HLB which also connect to the special needs of the aging population

could add a positive prospect on dealing with pain at old age.

#### Ethics Approval And Consent To Participate

Data were derived from the AgeCoDe (study part one: Baseline until FU2, and two: FU3 until FU6) and AgeQualiDe (study part three: FU7 until FU9) study. All GP patients who participated in the study provided written informed consent prior to their participation. The study has been approved by the local ethics committees of all participating study centers and comply with the ethical standards of the Declaration of Helsinki.

Ethics Commission of the Medical Association Hamburg (reference number: OB/08/02, 2817/2007, and MC-390/13)

- Ethics Committee of the Medical Faculty of the Rheinische Friedrich-Wilhelms-University of Bonn (reference number: 050/02, 258/07, and 369/13)
- Medical Ethics Commission II of the Medical Faculty Mannheim/Heidelberg University (reference number: 2026.4/2002, 2007-253E-MA, and 2013-662N-MA)
- Ethics Committee of the Faculty of Medicine of the University of Leipzig (reference number: 143/2002, 309/2007, and 333-13-18112013)
- Ethical Committee of the Medical Faculty of the Heinrich-Heine-University Düsseldorf (reference number: 2079/2002, 2999/2008, and 2999)
- Ethics Committee of the Faculty of Medicine of the Technical University of Munich (reference number: 713/02, and 713/02 E)

#### Data Sharing

Due to ethical restrictions involving patients' data, underlying data are only available on reasonable request. Interested parties may contact the Working Group Medical Statistics and IT-Infrastructure, Institute for General Practice, Hannover Medical School, Hannover, Germany (Birgitt Wiese; wiese.birgitt@mh-hannover.de).

#### Acknowledgement

We want to thank both all participating patients and their general practitioners for their good collaboration.

#### Author Contributions

Members of the AgeCoDe/AgeQualiDe research study group have been involved in the following matters: Analysing and interpreting data and drafting the manuscript: TM, BW, ME. Substantial contribution to the analysis and interpretation of the data and

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drafting of the manuscript: TM, ME, BW. Substantial acquisition of data: KH, AF, TM, JW, SW, DW, CB, SR, AP, EM, MP, LK, MW. Substantial contribution to the conception and design of the study: BW, HB, HHK, SW, MW, MS, WM, SGRH. Revised the manuscript critically for important intellectual content: all authors. All authors (TM, ME, HHK, CB, SR, AP, SW, JW, EM, DW, AF, MP, KH, BW, LK, MW, SGRH, WM, MS) read and approved the final version of the manuscript and accept direct responsibility for the manuscript. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

#### Funding

This publication is part of the German Research Network on Dementia (KND), the German Research Network on Degenerative Dementia (KNDD; German Study on Ageing, Cognition and Dementia in Primary Care Patients; AgeCoDe), and the Health Service Research Initiative (Study on Needs, health service use, costs and health-related quality of life in a large sample of oldest-old primary care patients (85+; AgeQualiDe)) and was funded by the German Federal Ministry of Education and Research (grants KND: 01GI0102, 01GI0420, 01GI0422, 01GI0423, 01GI0429, 01GI0431, 01GI0433, 01GI0434; grants KNDD: 01GI0710, 01GI0711, 01GI0712, 01GI0713, 01GI0714, 01GI0715, 01GI0716; grants Health Service Research Initiative: 01GY1322A, 01GY1322B, 01GY1322C, 01GY1322D, 01GY1322E, 01GY1322F, 01GY1322G). Dr. Francisca S. has been supported in working on the manuscript by LIFE – Leipzig Research Centre for Civilization Diseases, Universität Leipzig. Her collaboration within LIFE was funded by means of the European Social Fund and the Free State of Saxony. We acknowledge the support from the German Research Foundation (DFG) and Universität Leipzig within the program of Open Access Publishing. The funders were not involved in the design of the study, in collection, analysis, and interpretation of data, or in writing the manuscript.

#### Disclosure

Dr Marion Eisele reports grants from the German Federal Ministry of Education and Research, during the conduct of the study. Prof. Dr. Hans-Helmut König reports grants from the German Federal Ministry of Education and Research (BMBF), during the conduct of the study. The authors declare no other conflicts of financial interests or other interests in relation to the present study.

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## 4. The moderating effects of social support and depressive symptoms on pain among elderly multimorbid patients - data from the multicentre, prospective, observational cohort study MultiCare

### Abstract

Tina Mallon, Ingmar Schäfer, Angela Fuchs, Jochen Gensichen, Wolfgang Maier, Steffi Riedel-Heller, Hans-Helmut König, Karola Mergenthal, Gerhard Schön, Karl Wegscheider, Siegfried Weyerer, Birgitt Wiese, Hendrik van den Bussche and Martin Scherer

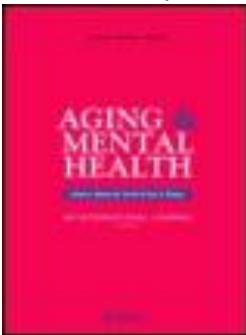
**Background:** Depressive symptoms and chronic pain are common among patients with multimorbidity creating a complex medical condition for both the patient and the general practitioner. Perceived social support may function as a protective measure. To examine the impact of perceived social support as a potential moderator between depressive symptoms and pain intensity and pain disability in daily activities in multimorbid patients aged 75+.

**Methods:** Data from 3,189 patients of the German longitudinal cohort study MultiCare were obtained at baseline and follow-ups during 5 years. Multilevel linear mixed-effects analyses were conducted for pain intensity (model 1) and pain disability in daily activities (model 2). The interaction term social support by depression score was included to test for moderation.

**Results** □ The interaction between social support and depressive symptoms was significantly associated with the pain intensity score 0.41 (SE=.17; 95-CI[.08;.74]) but not with the pain disability score 0.35 (SE=.19; 95-CI[-.01;.72]). Additionally, men and individuals with medium or higher educational level showed reduced pain intensity and disability scores. Pain disability scores increased with age and depressive symptoms. Increased pain scores were also found for body mass index and burden of multimorbidity.

**Conclusions:** Perceived social support amplified the association of depressive symptoms on pain intensity and did not show a protective function. The high scores of perceived social support among the participants may point to the practice of secondary gain due to the patients immense health burden.

**Key Words:** Pain; depression; multimorbidity; social support; burden



# The moderating effects of social support and depressive symptoms on pain among elderly multimorbid patients—data from the multicentre, prospective, observational cohort study MultiCare

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**To cite this article:** Tina Mallon, Ingmar Schäfer, Angela Fuchs, Jochen Gensichen, Wolfgang Maier, Steffi Riedel-Heller, Hans-Helmut König, Karola Mergenthal, Gerhard Schön, Karl Wegscheider, Siegfried Weyerer, Birgitt Wiese, Hendrik van den Bussche & Martin Scherer (2021): The moderating effects of social support and depressive symptoms on pain among elderly multimorbid patients—data from the multicentre, prospective, observational cohort study MultiCare, Aging & Mental Health, DOI: [10.1080/13607863.2021.1916882](https://doi.org/10.1080/13607863.2021.1916882)

**To link to this article:** <https://doi.org/10.1080/13607863.2021.1916882>



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## The moderating effects of social support and depressive symptoms on pain among elderly multimorbid patients—data from the multicentre, prospective, observational cohort study MultiCare

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### ABSTRACT

**Objectives:** Depressive symptoms and chronic pain are common among patients with multimorbidity creating a complex medical condition for both the patient and the general practitioner. Perceived social support may function as a protective measure. To examine the impact of perceived social support as a potential moderator between depressive symptoms and pain intensity and pain disability in daily activities in multimorbid patients aged 75+.

**Method:** Data from 3,189 patients of the German longitudinal cohort study MultiCare were obtained at baseline and follow-ups during 5 years. Multilevel linear mixed-effects analyses were conducted for pain intensity (model 1) and pain disability in daily activities (model 2). The interaction term social support by depression score was included to test for moderation.

**Results:** The interaction between social support and depressive symptoms was significantly associated with the pain intensity score 0.41 (SE=.17; 95-CI[.08;.74]) but not with the pain disability score 0.35 (SE=.19; 95-CI[-.01;.72]). Additionally, men and individuals with medium or higher educational level showed reduced pain intensity and disability scores. Pain disability scores increased with age and depressive symptoms. Increased pain scores were also found for body mass index and burden of multimorbidity.

**Conclusion:** Perceived social support amplified the association of depressive symptoms on pain intensity and did not show a protective function. The high scores of perceived social support among the participants may point to the practice of secondary gain due to the patients' immense health burden.

### ARTICLE HISTORY

Received 11 February 2021

Accepted 6 April 2021

### KEYWORDS

Pain; depression; multimorbidity; social support; burden

### Introduction

The co-occurrence of pain and depressive symptoms is common among patients with multimorbidity (Chou, 2007; Wicke et al., 2014), defined as the coexistence of two or more chronic conditions in the same individual (Schäfer et al., 2009). The coexistence of physical and mental health problems adds additional complexity to the medical treatment and condition of multimorbid patients particularly for women, and socioeconomically deprived individuals (Barnett et al., 2012; Cassell et al., 2018; Schäfer et al., 2010; Scherer et al., 2016). As the likelihood for multimorbidity increases with age (Tsiachristas, van Ginneken, & Rijken, 2018; Wang et al., 2019), the most common form for multimorbidity was found to be a mixed physical and mental form in 40% of

patients above the age of 55 with depression and pain among the five most prevalent conditions (McLean et al., 2014). Additionally, both pain and depression show strong associations with reduced social participation (Wilkie et al., 2016) and increased risk of social isolation (Hämmig, 2019).

Social support may serve as a preventive factor as studies have been indicating a reduced mortality in patients with higher social support (Mazzella et al., 2010; Olaya et al., 2017). Following the stress-buffering hypothesis of social support (S. Cohen & Wills, 1985), there is a growing body of evidence for decreasing pain experiences due to reduced stressors (Che, Cash, Ng, Fitzgerald, & Fitzgibbon, 2018) such as physical suffering, functional impairment, and depressive

#### 4. The moderating effects of social support and depressive symptoms on pain among elderly multimorbid patients - data from the multicentre, prospective, observational cohort study MultiCare

symptoms which positively influence health-related quality of life (Hatfield, Hirsch, & Lyness, 2013; Wicke et al., 2014). Furthermore, perceived social support, understood as the perception of available supportive resources, has been reported to help in coping with multiple chronic conditions and in self-management of the complex condition (Coventry, Fisher, Kenning, Bee, & Bower, 2014). Hence, perceived social support may also attenuate the effect of depression on pain in multimorbid patients at old age.

The relationship between pain and depression is believed to be bidirectional with equal adverse influence on one another (Chou, 2007; Kroenke et al., 2011). While 50% of patients with pain develop a depression, 30 to 60% of patients with depression also experience pain (Goesling, Clauw, & Hassett, 2013). Research studies have investigated the effect of social support and pain on depression (Brandstetter et al., 2017), while the function of social support between depressive symptoms and pain experiences has been understudied, especially among multimorbid patients (Hanssen, Naarding, Collard, Comijs, & Oude Voshaar, 2014). However, with strong social support from family and spouses patients suffering from arthritis or breast cancer showed a decrease in depressive and pain symptoms (Hughes et al., 2014; Hung et al., 2017).

As the number of patients suffering from multimorbidity is rising rapidly and age-related chronic health conditions such as chronic pain or depression are becoming a major health care concern (Marengoni et al., 2011) perceived social support may be a beneficial and protective factor for this particular group of patients. Therefore, the aim of our study was to investigate the moderating effects of perceived social support on the association between depressive symptoms and pain intensity as well as pain disability in daily activities (e.g., family and social activities, recreation time, ability to work) among patients with multimorbidity. We follow the hypothesis that perceived social support will attenuate the association between depressive symptoms and pain intensity as well as pain disability in daily activities, hence lower the pain ratings in patients with multimorbidity.

#### Materials and methods

MultiCare was designed as a multicentre, prospective, observational cohort study (Trial registration ISRCTN89818205) which has been described in detail elsewhere (Schäfer et al., 2009, Schäfer et al., 2012, Schäfer et al., 2019). In short, multimorbid patients have been recruited from 158 general practitioner practices in eight German cities (Bonn, Düsseldorf,

Frankfurt am Main, Hamburg, Jena, Leipzig, Mannheim and Munich). Patients were included if they met the following criteria: between 65 and 85 years of age, a minimum of one consultation with the general practitioner (GP) in the past three months. A list with all patients who met the inclusion criteria was created in each GP practice and 50 patients were randomly selected and contacted for written informed consent. We defined multimorbidity as the coexistence of at least three chronic conditions out of a list of 29 diseases. Exclusion criteria were: inability to participate in an interview for reasons of blindness or deafness, the participating GP was not their regular GP, lack of German language skills, residence in a nursing home, severe illness with a likely fatal outcome within the next three months according to the GP, missing capacity to consent due to dementia and involvement in other research studies at the time of recruitment.

In total, 24,862 patients were randomly selected. 17,690 patients were excluded from which 13,935 patients did not meet our definition of multimorbidity or suffered from dementia, and further 3,755 patients were excluded due to the other exclusion criteria. However, 7,172 patients met our inclusion criteria and were contacted and informed. Finally, 3,317 patients signed the informed consent and participated in our study. Additionally, 128 patients were excluded retrospectively due to passing away before undertaking the baseline interview or meeting one of the exclusion criteria without the GP's knowledge. In the end, 3,189 patients were included in the study.

Participants were interviewed four times in intervals of fifteen months between July 2008 and December 2013. Interviews were carried out by trained psychologists or medical staff and took place at the participant's home. Additionally, all participating GPs filled out a questionnaire at each time of data collection.

Between baseline and follow-up three 1,119 participants were lost due to death, worsened health conditions, or inability to contact. The sample size had been further reduced due to our variable burden of morbidity which could only be obtained through GP interviews. GP data is complete for baseline but missing for a total of 421 participants at follow-up three resulting in a final sample size of 1865 participants at follow-up three.

The MultiCare Cohort Study was approved by the local ethics committee in February 2008 and amended in November 2008.

#### Pain intensity and pain-related disability in daily activities

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To measure pain intensity and pain-related disability in daily activities sub-scores of the Graded Chronic Pain Scale (GCPS) were used according to the manual guidelines (Klasen, Hallner, Schaub, Willburger, & Hasenbring, 2004) which were collected during the patient interviews. Pain intensity was rated on three reference points: on average, at the current time and worst pain. Each item was rated from 0 (no pain) to 10 (worst imaginable pain). The pain intensity score was calculated with arithmetic mean of the items 1 to 3, multiplied by 10 resulting in a score ranging from 0 (no pain intensity) to 100 (worst pain intensity). Pain-related disability in daily activities (e.g., family and social activities, recreation time, ability to work) was measured as persisting impairment over the last three months, and in regard to the current medication. Each item was measured on a scale from 0 (no impairment) to 10 (complete impairment). The pain disability score was calculated with arithmetic mean for the items 6 to 8, multiplied by 10 resulting in a score ranging from 0 (no pain disability) to 100 (worst pain disability). Both scores were calculated if all three items were available.

##### **Depressive symptoms (GDS)**

Depressive symptoms were measured with the short version of the Geriatric Depression Scale (Yesavage, 1988), consisting of 15 items. A score was calculated for each individual ranging from 0 (no depression) to 15 (severe depression). Cut-off for depressive symptomatology was a score of 6 points and above.

##### **General perceived social support (F-SozU-Score)**

General perceived social support was measured using the German scale "Fragebogen zur sozialen Unterstützung (F-SozU) K14" (Fydrich, Sommer, Tydecks, & Brähler, 2009). The questionnaire focuses on perceived social support by the social environment excluding support from health care services. The F-SozU K14 scale consists of three dimensions: emotional support (e.g., ability to show emotion, receiving comfort in difficult situations), instrumental support (e.g., help with practical problems around the house) and social integration (belongingness). Social support is rated on a five-point Likert scale ranging from 1 (does not apply) to 5 (exactly applicable). Higher ratings state higher social support.

##### **Burden of multimorbidity**

In order to portray the impact of multimorbidity in our data we calculated the variable "burden of multimorbidity" by adding a severity rating for each of the participant's disease provided by the GP out of 46 listed diseases. Severity was rated on a five-point

Likert scale with 0 indicating marginal burden and 4 indicating very severe burden.

Furthermore, the following socio-demographic measures were included in our analyses: age, sex, level of education (low, medium, high) according to the CASMIN criteria (Brauns & Steinmann, 1999), body mass index (BMI), marital status, and form of household. For our analyses we grouped marital status into with partner (married) and without partner (single, separated, divorced or widowed). The form of household was grouped into living alone (single household, assisted living, care home) and living with someone (household with a partner, relative or other).

##### **Statistical analysis**

Data from baseline and follow-up 3 were used for our multilevel linear mixed-effects analyses allowing for fixed effects on covariates and random effects at study centre level as well as GP practice within study centre level. To test the moderating impact of perceived social support, the interaction term for F-SozU-Score and GDS-score was included. Analyses were carried out for the two main outcome parameters pain intensity score (model 1) and the pain disability score (model 2). In both analyses, we controlled for age, sex, level of education, marital status, form of household, BMI and burden of multimorbidity.

Additionally, least square means were calculated for 'point of time' and sex. Analyses were carried out using IBM SPSS version 26 (IBM, Armonk, New York, USA). P-values lower than alpha = 0.05 are considered statistically significant.

## **Results**

### **Population characteristics**

The majority of our population was female (60%) and mean age at baseline was 74.4 years ( $\pm 5.19$ ). More than 62% had a lower educational background, over half of our population was still in a relationship with a partner and shared the house- hold with their partner, relative or others. Mean BMI was 28.2 ( $\pm 4.84$ ) indicating overweight according to the WHO classification (Weir & Jan, 2020). Mean GDS was 2.6 ( $\pm 2.61$ ) indicating average scores below the threshold for mild depression. General perceived social support was high with a mean of 4.1 ( $\pm .69$ ). Our calculated variable burden of multimorbidity reached a mean of 11.2. This could result from e.g., a low number of highly severe diseases or a high number of marginally severe diseases. Pain intensity scores were higher than pain disability scores at both time points.

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A detailed description of the descriptive data can be found in Table 1.

**Table 1.** Descriptive data of the study sample.

	Baseline (N = 3189)	Follow-Up 3 (N = 2054)
<b>Descriptive data</b>		
Gender: n (%)		
Male	1298 (40.7)	853 (40.4)
Female	1891 (59.3)	1261 (59.6)
Age: Mean (SD)	74.40 (5.19)	77.56 (4.94)
Education: n (%)		
Low	1986 (62.3)	1226 (59.3)
Medium	856 (26.8)	570 (27.6)
High	347 (10.9)	270 (13.1)
Marital Status: n (%)		
Without partner	1791 (43.8)	949 (47.3)
With partner	1397 (56.2)	1087 (52.7)
Household: n (%)		
Living alone	1189 (37.3)	841 (40.7)
Living with someone	2000 (62.7)	1225 (59.3)
BMI: Mean (SD)	28.22 (4.84)	28.28 (4.90)
GDS: Mean (SD)	2.57 (2.61)	2.51 (2.69)
Social support: Mean (SD)	4.10 (.69)	3.69 (.60)
Burden of multimorbidity: Mean (SD)	11.19 (5.11)	28.92 (12.03)
Pain intensity: Mean (SD)	34.55 (25.55)	33.13(26.32)
Pain Disability: Mean (SD)	25.96 (29.22)	26.30 (29.47)

SD, Standard deviation; BMI, Body Mass index; GDS, Geriatric

Depression Scale.

#### Moderating role of general perceived social support

In our analyses on the leading question of the moderating role of perceived social support we found a significant positive inter-action in model one on the pain intensity score 0.41 (SE = 0.17; 95-CI[0.08;0.74]). As a consequence, other main effects found in our analyses cannot be interpreted solely. The significant positive interaction term indicates that perceived social support influences the relationship of depressive symptoms and pain intensity contrarily to our hypothesis, resulting in higher pain intensity scores. Hence, increased perceived social support increases the impact of depressive symptoms on pain intensity. Figure 1 shows an illustration of the interaction effect. Three values of the moderator were used to plot the predicted values: the mean, as well as the value one standard deviation above, and below the mean (J. Cohen & Cohen, 2003). In model two, the interaction effect was not significant for the pain disability score 0.35 (SE = 0.19; 95-CI[-0.01;0.72]).

**Table 2.** Analyses for pain intensity scores - results from linear mixed-effects analyses adjusted for random effects at study centre and GP practice within study centre level.

Pain intensity	estimation of fixed parameters				
	Estimate	SE	p-value	95%CI	
Gender					
Male	-11.07	0.76	.000	-12.56	-9.58
Female	-	-	-	-	-
Age	-0.08	0.07	0.27	-0.21	0.06
Education					
Low	-	-	-	-	-
Medium	-2.16	0.82	0.01	-3.77	-0.55
High	-3.50	1.16	0.00	-5.77	-1.23
Partner					
Without partner	-0.69	1.21	0.57	-3.07	1.69
With partner	-	-	-	-	-
Household					
Living alone	-1.99	1.23	0.11	-4.41	0.43
Living with someone	-	-	-	-	-
BMI	0.52	0.07	0.00	0.38	0.66
GDS	0.76	0.63	0.23	-0.49	2.00
Social support	-2.88	1.15	0.01	-5.13	-0.63
Burden	0.42	0.04	0.00	0.34	0.51
GDS * Social support	0.41	0.17	0.01	0.08	0.74
Time	8.33	1.08	.000	6.21	10.44

CI, confidence interval;

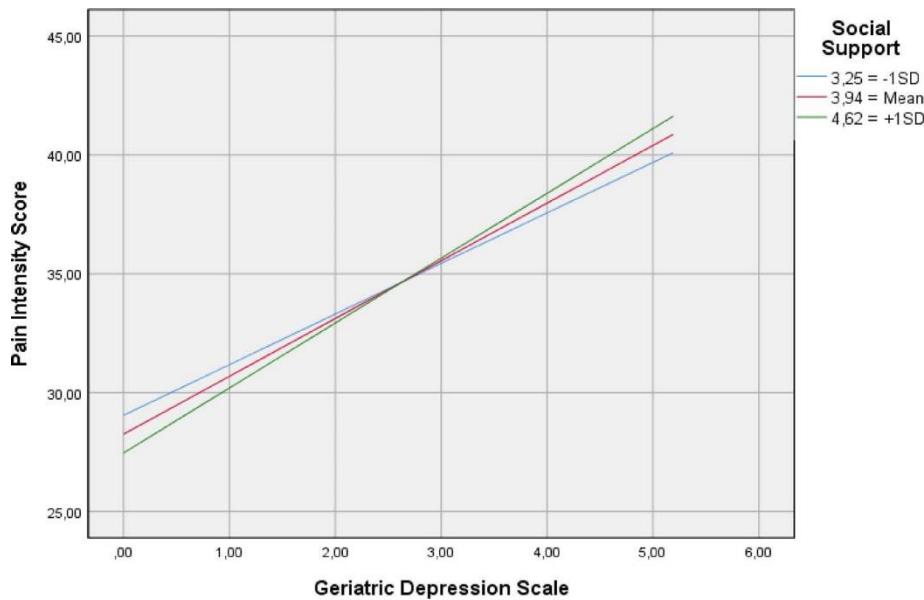
Se, standard error; BMI, Body Mass Index; GDS, Geriatric

Depression Scale. Alpha set to 0.05.

**Table 3.** Analyses for pain disability scores - results from linear mixed-effects analyses adjusted for random effects at study centre and GP practice within study centre level.

Pain Disability	estimation of fixed parameters				
	Estimate	SE	p-value	95% CI	
Gender					
Male	-8.94	0.84	.00	-10.60	-7.29
Female	-	-	-	-	-
Age	0.21	0.08	0.01	0.06	0.36
Education					
Low	-	-	-	-	-
Medium	-0.83	0.91	0.36	-2.61	0.96
High	-3.23	1.29	0.01	-5.75	-0.71
Partner					
No	1.08	1.34	0.42	-1.56	3.72
Yes	-	-	-	-	-
Household					
Living alone	-2.27	1.37	0.10	-4.95	0.42
Living with s.o.	-	-	-	-	-
BMI	0.70	0.08	0.00	0.54	0.86
GDS	2.22	0.71	0.00	0.84	3.61
Social support	-0.46	0.88	0.61	-2.10	1.28
Burden	0.48	0.05	0.00	0.39	0.58
GDS * Social support	0.35	0.19	0.06	-0.01	0.72
Time	8.62	1.20	0.00	6.27	10.97

BMI, Body Mass Index; GDS, Geriatric Depression Scale; s.o. someone; Alpha set to 0.05.



*Figure 1 Illustration of the interaction between social support and depressive symptoms on the pain intensity score.*  
SD, standard deviation

### Pain intensity

We found significantly reduced pain intensity scores for men by 11 points on the pain intensity score  $-11.07$  ( $SE=0.076$ ; 95-CI[-12.56; -9.58]), showing marginal means for men at 25.7 and 36.7 for women as well as for individuals with medium  $-2.16$  ( $SE=.82$ ; 95-CI[-3.77; -0.55]) or higher educational level  $-3.50$  ( $SE = 1.16$ ; 95-CI[-5.77; -1.23]). Furthermore, BMI 0.52 ( $SE = 0.07$ ; 95-CI[0.38;0.66]) and burden of multimorbidity 0.42 ( $SE = 0.04$ ; 95-CI[0.34;0.51]) were significantly associated with increased pain intensity scores. Age and living with or without a partner showed no significant results. We also found a significant result for the time of assessing pain intensity, indicating higher pain intensity at baseline assessment 8.33 ( $SE = 1.08$ ; 95-CI[6.21;10.44]). In model 1,  $-2 \log \text{likelihood}$  was 43062.62.

### Pain disability score

We found a significant difference for less pain disability in daily activities in men by 8.94 points and participants with higher education by 3.23 point. Similar to the pain intensity scale, BMI .70 ( $SE=.08$ ; 95-CI[.54;.86]), burden of multimorbidity .48 ( $SE=.88$ ; 95-CI[.39;.58]) and time of assessment 8.62 ( $SE = 1.20$ ; 95-CI[6.27;10.97]) were associated with significant increase in pain disability. Additionally, GDS 2.22 ( $SE=.71$ ; 95-CI[.84;3.61]) and age .21 ( $SE=.08$ ; 95-

CI[.06;.36]) showed significantly increased pain disability scores. In model 2,  $-2 \log \text{likelihood}$  was 43821.57.

Tables 2 and 3 provide statistical results for the pain intensity and pain-related disability scores.

### Discussion

#### Main results

In these longitudinal analyses of the MultiCare Cohort Study we investigated the moderating effects of perceived social support on the association between depressive symptoms and pain intensity as well as pain disability in daily activities among multimorbid patients. A positive moderating effect was found on the pain intensity score indicating that increased perceived social support amplified the association of depressive symptoms on pain intensity. No significant moderating effect on the pain disability score was found.

Additionally, to our main results, analyses on descriptive parameters showed reduced pain intensity and disability scores for men and individuals with medium or higher educational achievements. In model 2 increased pain disability scores were found for age and GDS which is in line with previous research (Mallon et al., 2018). Furthermore, increased pain scores were found for BMI, burden of multimorbidity and time of assessment, respectively.

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##### Comparison with literature

Our results underline the negative impact of depression on pain in older adults as has been shown in other studies (Dorner et al., 2018; Lee, Kahana, & Kahana, 2016). The stress-buffering effect of perceived social support could not be shown in our analyses. In fact, the converse result emerged. While perceived social support and social networks have been shown to work as a protective shield in terms of pain intensity and interference (Musich, Wang, Slindée, Kraemer, & Yeh, 2019), our data suggests the inverse effect of the buffering effect of social support on the relationship of depressive symptoms on pain in multimorbid patients. This could be due to the distinct characteristic of the multimorbidity cohort. Despite the high age in the cohort, the larger amounts of participants were still married and shared a household with another person which makes support accessible as suffering from multimorbidity has been shown to increase social care needs (McGilton et al., 2018; Rijken & van der Heide, 2019). It may also point towards a specific form of pain behaviour adapted by this group of patients. Some forms of pain behaviour have shown to vary depending on the pain response from the spouse and a greater number of pain behaviours have been reported with higher levels of enacted support (Paulsen & Altmaier, 1995). Also, the kind of social support perceived may cause distinct pain behaviours (Linton & Shaw, 2011). While solely instrumental support has been shown to negatively impact pain behaviours, emotional support and support in coping with pain showed reduced pain behaviours (Basler et al., 2006).

Furthermore, it may place emphasis on the medical condition caused by multimorbidity and its related burden itself, increasing general pain intensity but also placing additional focus on the subject. On the other hand, it creates an awareness of the poor health condition which may increase support in daily activities thus reducing the pain disability score. This may explain our findings on the pain disability score which are similar to studies on functional impairment showing reduced impairment with increasing social support (Hajek et al., 2017). Social support showed a protective function on survival for individuals with one or two physical illnesses (Olaya et al., 2017). Nevertheless, the effect vanished for individuals with more than two illnesses. Hence, social support may function differently among patients with multimorbidity. By these means, multimorbid patients may apply secondary gain as a form of psychological motivation meaning the presence of several chronic conditions may lead the patients to

enlist more support from family, friends, or medical care providers.

Special emphasis should also be put on the increase of the multimorbidity burden over time. It indicates the immense strains and multiple challenges multimorbid patients are faced with at high age (van der Aa, van den Broeke, Stronks, & Plochg, 2017). As pain can be regarded as a widespread and disease comprehensive symptom, accessing one's supportive social network may become even more important with increasing age (Kuluski et al., 2019).

##### Implications for practice

Our results contribute to the knowledge of the co-occurrence of depression and chronic pain and adds new knowledge for the growing number of patients with multimorbidity. Our results are new in the way that they point to an apparently negative aspect of perceived social support.

Patients suffering from multimorbidity are twice more likely to develop a depressive disorder (Read, Sharpe, Modini, & Dear, 2017) thus are likely to experience pain. As the number of pain sites and comorbidities increases with age psychological and social well-being may gain greater importance in order to sustain status quo of quality of life at old age. A holistic approach which specifically incorporates patient-centred care seems necessary and may improve the physical, mental and social well-being of multimorbid patients.

Future research should investigate into patient-centred care approaches and use the existing knowledge on patterns in multimorbidity and pain (Scherer et al., 2016). The complex correlation of multimorbidity aspects calls for a specific disease management program which incorporates depression and pain screenings as well as social network evaluation among other multimorbidity related parameters. In more depth, the kind of social support provided, whether emotional, instrumental, or informal by spouses or family and relatives may play a crucial role in terms of the patient's pain behaviour and should be investigated further in order to provide family members with helping guidelines.

##### Strengths and limitations

The strengths of our analyses lie in the large cohort sample which can be considered representative for elderly, urban, multimorbid primary care patients in Germany. Our analyses are new to the sample of patients with multimorbidity. While most research focuses on the pain-depression-interaction, we investigated the depression-pain-relationship with special focus on perceived social support. However,

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generalisability of our data is restricted due to the missing recruitment of GPs in rural areas, and exclusion of patients with dementia or patients in nursing homes.

The applied questionnaire for perceived social support was obtained by self-report and did not include information on the social network size of the participant nor distinguish between emotional, instrumental or informational support which may cause a discrepancy between actual received and personally perceived support. Also, perceived social support was high at both time points which may account for some of the results.

The sample inclusion criteria were set for at least three or more morbidities. However, not all kinds of diseases are related to pain or disability. This might be the reason why we could not find a significant effect of social support on pain disability.

Additionally, as we collected data during a 5-year period, results may also be influenced by survivor bias as 41.5% of the participants had dropped out of the study at the end of follow-up three. Also, due to the missing sample size calculation for MultiCare significant predictors of our outcomes might have been missed due to limited statistical power.

#### Conclusions

We investigated the moderating effects of perceived social support on the association between depressive symptoms and pain intensity as well as pain disability in daily activities among patients with multimorbidity. Our results suggest that social support amplifies the association between depressive symptoms and pain intensity which may point to a different function of social support among patients with multimorbidity. Hence, we could not support the stress-buffering hypothesis of social support with our data. As mixed physical and mental forms of multimorbidity are increasing further in-depth investigation is needed.

#### Acknowledgements

We are grateful to the general practitioners in Bonn, Dusseldorf, Frankfurt/Main, Hamburg, Jena, Leipzig, Mannheim and Munich who supplied the clinical information on their patients, namely Theodor Alfen, Martina Amm, Katrin Ascher, Philipp Ascher, Heinz-Michael Assmann, Hubertus Axthelm, Leonhard Badmann, Horst Bauer, Veit-Harold Bauer, Sylvia Baumback, Brigitte Behrend-Berlin, Rainer Bents, Werner Besier, Liv Betge, Arno Bewig, Hannes Blankenfeld, Harald Bohnau, Claudia Böhnke, Ulrike Börgerding, Gundula Bormann, Martin Braun, Inge Bürfent, Klaus Busch, Jürgen Claus, Peter Dick, Heide Dickenbrok, Wolfgang Dörr, Nadejda Dörrler-Naidenoff, Ralf Dumjahn, Norbert Eckhardt, Richard Ellersdorfer, Doris Fischer-Radizi, Martin Fleckenstein, Anna Frangoulis, Daniela

Freise, Denise Fricke, Nicola Fritz, Sabine Füllgraf-Horst, Angelika Gabriel-Müller, Rainer Gareis, Benno Gelshorn, Maria Göbel-Schlatholt, Manuela Godorr, Jutta Goertz, Cornelia Gold, Stefanie Grabs, Hartmut Grella, Peter Gütte, Elisabeth Gummersbach, Heinz Gürster, Eva Hager, Wolfgang-Christoph Hager, Henning Harder, Matthias Harms, Dagmar Harnisch, Marie-Luise von der Heide, Katharina Hein, Ludger Helm, Silvia Helm, Udo Hilsmann, Claus W. Hinrichs, Bernhard Hoff, Karl-Friedrich Holtz, Wolf-Dietrich Honig, Christian Hottas, Helmut Ilstadt, Detmar Jobst, Gunter Kässner, Volker Kielstein, Gabriele Kirsch, Thomas Kochems, Martina Koch-Preißer, Andreas Koeppel, Almut Körner, Gabriele Krause, Jens Krautheim, Nicolas Kreff, Daniela Kreuzer, Franz Kreuzer, Judith Künstler, Christiane Kunz, Doris Kurzeja-Hüschen, Felizitas Leitner, Holger Liebermann, Ina Lipp, Thomas Lipp, Bernd Löbbert, Guido Marx, Stefan Maydl, Manfred Mayer, Stefan-Wolfgang Meier, Jürgen Meissner, Anne Meister, Ruth Möhrke, Christian Mörchen, Andrea Moritz, Ute Mühlmann, Gabi Müller, Sabine Müller, Karl-Christian Münter, Helga Nowak, Erwin Ottahal, Christina Panzer, Thomas Paschke, Helmut Perleberg, Eberhard Prechtel, Hubertus Protz, Sandra Quantz, Eva-Maria Rappen-Cremer, Thomas Reckers, Elke Reichert, Birgitt Richter-Polynice, Franz Roegele, Heinz-Peter Romberg, Anette Rommel, Michael Rothe, Uwe Rumbach, Michael Schilp, Franz Schlensog, Ina Schmalbruch, Angela Schmid, Holger Schmidt, Lothar Schmittdiel, Matthias Schneider, Ulrich Schott, Gerhard Schulze, Heribert Schützendorf, Harald Siegmund, Gerd Specht, Karsten Sperling, Meingard Staude, Hans-Günter Stieglitz, Martin Strickfaden, Hans-Christian Taut, Johann Thaller, Uwe Thürmer, Ljudmila Titova, Michael Traub, Martin Tschoke, Maya Tügel, Christian Uhle, Kristina Vogel, Florian Vorderwülbecke, Hella Voß, Christoph Weber, Klaus Weckbecker, Sebastian Weichert, Sabine Weidnitzer, Brigitte Weingärtner, Karl-Michael Werner, Hartmut Wetzel, Edgar Widmann, Alexander Winkler, Otto-Peter Witt, Martin Wolfrum, Rudolf Wolter, Armin Wunder, and Steffi Wünsch. We also thank Corinna Contenius, Cornelia Eichhorn, Sarah Floehr, Vera Kleppel, Heidi Kubieziel, Rebekka Maier, Natascha Malukow, Karola Mergenthal, Christine Müller, Sandra Müller, Michaela Schwarzbach, Wibke Selbig, Astrid Steen, Miriam Steigerwald, and Meike Thiele for data collection as well as Ulrike Barth, Elena Hoffmann, Friederike Isensee, Leyla Kalaz, Heidi Kubieziel, Helga Mayer, Karine Mnatsakanyan, Michael Paulitsch, Merima Ramic, Sandra Rauck, Nico Schneider, Jakob Schroeder, Susann Schumann, and Daniel Steigerwald for data entry

#### Disclosure statement

No potential conflict of interest was reported by the author(s).

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## 6. Zusammenfassung

Die Gruppe der Hochaltrigen (80 Jahre und älter) wird aufgrund der demografischen Verschiebung in den nächsten Jahren deutlich anwachsen. Jedoch ist der Lebensabschnitt der Hochaltrigkeit vor allem in Bezug auf das Schmerzgeschehen noch nicht ausreichend untersucht. Da Schmerzen weitreichende und umfassende Auswirkungen auf die Lebenswelt der betroffenen Personen haben, beschäftigt sich die vorliegende Arbeit mit der Prävalenz von Schmerzen und mit Schmerzen assoziierten Faktoren für die Gruppe der Hochaltrigen und älteren multimorbid Patient:innen (75 Jahre und älter) in Deutschland. Grundlage für die Auswertung bilden die Daten zweier Langzeitstudien mit Hausarztpatient:innen aus Deutschland.

Die erste Untersuchung zeigte, dass die Prävalenz mit einem Wert von 63% unter den hochaltrigen Patient:innen als relativ hoch angesehen werden kann. Dabei wiesen insbesondere Männer geringere - und Personen mit depressiver Symptomatik höhere Schmerzen im hohen Alter auf. Des Weiteren verweisen die Ergebnisse auf einen Zusammenhang der Wohn- und Versorgungsform mit Schmerzen. Vor allem Personen, die ambulante Pflege in der eigenen Häuslichkeit erhielten, wiesen signifikant erhöhte Schmerzwerte auf.

In der zweiten Untersuchung wurden Faktoren der individuellen Lebensweise und schmerzrelevante Komorbiditäten im Zusammenhang mit Schmerzen in der Hochaltrigkeit untersucht. Dabei war die erfolgreiche Rauchentwöhnung signifikant positiv mit Schmerzen im Alter assoziiert und führte zu geringeren Schmerzwerten auf der PRS. Dem gegenüber waren chronische Rückenschmerzen, die periphere arterielle Verschlusskrankheit und ein hoher Body Mass Index negativ mit Schmerzen im Alter assoziiert. Ebenfalls waren Frauen signifikant mehr von Schmerzen im hohen Alter betroffen als Männer. Signifikant erhöhte Beeinträchtigungen durch Schmerzen im Alltag zeigten vor allem Personen mit Arthrose und depressiver Symptomatik.

Die dritte Untersuchung betrachtete den Einfluss der wahrgenommenen sozialen Unterstützung auf den Zusammenhang von depressiver Symptomatik und der Schmerzintensität bzw. der Beeinträchtigungen durch Schmerzen im Alltag bei multimorbid Patient:innen. Entgegen unserer Erwartungen zeigte sich, dass eine Zunahme an wahrgenommener sozialer Unterstützung mit einer Zunahme des Zusammenhangs von depressiver Symptomatik und Schmerzintensität einhergeht und das Schmerzgeschehen verstärkt wurde.

Der Umgang mit - und die Behandlung von Schmerzen im hohen Alter bleibt damit eine Herausforderung für die betroffenen Personen als auch ihre Versorger:innen.

## 7. Summary

The oldest-old (people aged 80 years and above) are a rapidly growing group due to the demographic changes among the general population. However, this late stage of life has been understudied particularly in the field of pain research. The experience of pain has a substantial impact on the life and daily living of the individual. Therefore, this thesis focusses on the prevalence of pain and the relationship of pain-related aspects among the oldest-old and older multimorbid patients (age 75 and above) in Germany. Two longitudinal cohort studies from German primary care patients provided the data for the analyses.

The first study revealed the prevalence of pain was ranking rather high among the oldest-old with 63%. Men reported significantly less pain, while people with depressive symptoms scored significantly higher on the PRS. Also, results showed an influence of one's housing and care situation in regard to pain. Primarily, oldest-old receiving medical care at home showed the highest pain ratings.

The second study paid special attention to health-related lifestyle behaviour and pain-related comorbidities at old age. A significant positive impact on pain ratings was found for successful smoking cessation. However, negative associations were found for patients suffering from chronic back pain, peripheral arterial disease and high body mass index which resulted in significantly higher pain rating scores. Also, women experienced significantly more pain than men. Significantly more impairment in daily activities due to pain was found for patients with osteoarthritis and depressive symptoms.

The third study investigated the impact of perceived social support on the relationship between depressive symptoms and pain intensity as well as pain disability in daily activities among old multimorbid patients. Despite the expectation, an increase in perceived social support led to an increase on the relationship of depressive symptoms and pain intensity, hence increased the pain experience.

Treating and handling pain at old age remains a challenge for patients affected by pain as well as their medical advisers and care supporters.

## 8. Erklärung des Eigenanteils an den Publikationen

Für die AgeCoDe/AgeQualiDe- Untersuchungen eins und zwei habe ich über fünf Jahre (2011-2016) die Follow-Up-Interviews mit den teilnehmenden Proband:innen für die Zeiträume Follow-Up 6 bis Follow-Up 9 geführt, die Daten für den Hamburger Standort eingepflegt und verwaltet sowie die Erstautorenschaft übernommen.

Für das Anfertigen der Manuskripte recherchierte ich relevante Literatur und besprach das Vorgehen mit Prof. Dr. med. Martin Scherer. Ich führte die statistischen Auswertungen durch, wobei ich von Birgit Wiese und Dr. Marion Eisele unterstützt worden bin. Der Erstentwurf der Manuskripte wurde von mir verfasst. Diesen reichte ich an die Co-Autor:innen zur Ergänzung sowie für weitere Anregungen weiter. Die Einarbeitung der Kommentare der Co-Autor:innen sowie die Einreichung der Manuskripte bei den vorgesehenen Journals erfolgte durch mich. Ebenso übernahm ich die Überarbeitung der Manuskripte während der Reviewprozesse und erhielt durch Dr. Marion Eisele Unterstützung.

Für die MultiCare-Untersuchung konnte ich auf den bestehenden Datensatz zurückgreifen. Mit Prof. Dr. med. Martin Scherer und Dr. Ingmar Schäfer stimmte ich die inhaltliche Ausrichtung des Manuskripts ab und entwarf einen Analyseplan. Die statistischen Auswertungen wurden gemeinsam mit Dr. Ingmar Schäfer und Eric Bibiza-Freiwald aus der biometrischen Abteilung vorgenommen. Den ersten Entwurf des Manuskripts verfasste ich und stellte ihn den Co-Autor:innen zur Verfügung. Die rückgemeldeten Kommentare von den beteiligten Co-Autor:innen arbeitete ich ein. Die Einreichung des fertigen Manuskripts sowie die Überarbeitung des Manuskripts im Reviewprozess führte ich durch und erhielt im Reviewprozess Unterstützung von Dr. Ingmar Schäfer.

## 9. Danksagung

Mein Dank gilt Prof. Dr. Martin Scherer für die Begleitung meiner Promotion über die vergangenen Jahre. Des Weiteren danke ich meinen Co-Autor:innen für die gute Zusammenarbeit, die Anmerkungen und hilfreichen Gedanken ebenso wie den Mitgliedern meines Thesis-Komitees Prof. Dr. Olaf von dem Knesebeck und Prof. Dr. Bernd Löwe für den konstruktiven Austausch und ihre Zeit.

Ganz herzlich möchte ich mich auch bei Dr. Marion Eisele für die begleitenden Gespräche, Motivation und Unterstützung während meiner Promotionszeit, aber auch über die gesamte Zeit am Institut hinaus bedanken. Dr. Ingmar Schäfer, Birgitt Wiese und Eric Bibiza-Freiwald gilt ebenfalls ein Dank für die gute Beratung zu statistischen Fragen.

Bedanken möchte ich mich auch bei meinen Kolleg:innen des Instituts für die hilfreichen Gespräche, ihr geteiltes Wissen als auch die Beratung und internen Veranstaltungen von Dr. Thomas Zimmermann und Dr. Nadine Pohontsch.

Ganz besonders danken möchte ich meinem Mann, Wayne, meiner kleinen Tochter Anouk sowie meiner Familie und meinen Freund:innen, die mich über die Jahre bestärkt haben, die Promotion voranzubringen und immer unterstützend an meiner Seite geblieben sind.

## **10. Lebenslauf**

Der Lebenslauf ist aus datenschutzrechtlichen Gründen nicht enthalten.

## 11. Eidesstattliche Erklärung

Ich versichere ausdrücklich, dass ich die Arbeit selbständig und ohne fremde Hilfe verfasst, andere als die von mir angegebenen Quellen und Hilfsmittel nicht benutzt und die aus den benutzten Werken wörtlich oder inhaltlich entnommenen Stellen einzeln nach Ausgabe (Auflage und Jahr des Erscheinens), Band und Seite des benutzten Werkes kenntlich gemacht habe.

Ferner versichere ich, dass ich die Dissertation bisher nicht einem Fachvertreter an einer anderen Hochschule zur Überprüfung vorgelegt oder mich anderweitig um Zulassung zur Promotion beworben habe.

Ich erkläre mich einverstanden, dass meine Dissertation vom Dekanat der Medizinischen Fakultät mit einer gängigen Software zur Erkennung von Plagiaten überprüft werden kann.

Unterschrift .....